Supporting Information for

Spatially-Decomposed Free Energy of Solvation Based on the Endpoint Density-Functional Method

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Numerical values of $\Delta\mu(i)/v(i)$, $u(i)/v(i)$, $\Delta\mu(i)$, and $u(i)$ are provided with $\rho_0 v(i)$, where ρ_0 is the number density of pure water. $\rho_0 v(i)$ is equal to the average number of water molecules contained in the volume $v(i)$ at the pure-solvent state. Each value of $\Delta\mu(i)/v(i)$ and $u(i)/v(i)$ is listed in the unit of 10^{-3} kcal/mol/Å^3 and is rounded to a multiple of 10^{-5} kcal/mol/Å^3. The corresponding error is expressed at 95% confidence interval (twice the standard error), and is not shown when it is smaller than 10^{-5} kcal/mol/Å^3. The value is expressed in kcal/mol to two decimal places for $\Delta\mu(i)$ and $u(i)$; the error is given at 95% confidence interval and is not written when it is smaller than 0.01 kcal/mol.

The row of "sub-total" provides the sum of the contributions over the excluded-volume to the outer regions for each site; the "far-separated" contribution is not incorporated there. $\rho_0 v(i)$ is not shown in the rows of "far-separated", "total (with spatial decomposition)", "total (without spatial decomposition)", and "total (exact)" since it grows with the system size in an unbounded region. The entries for $\Delta\mu(i)/v(i)$ and $u(i)/v(i)$ are left blank for the "far-separated" region since this region is unbounded. The long-range correction of the Lennard-Jones interaction is incorporated into $\Delta\mu(i)$ and $u(i)$ in the "far-separated" region.

The sums of $\Delta\mu(i)$ and $u(i)$ over all the regions are shown in the row of "total (with spatial decomposition)". In that row, there are no entries for $\Delta\mu(i)/v(i)$ and $u(i)/v(i)$ since they are for the densities of the solvation free energy and solute-solvent interaction energy in spatially decomposed regions, respectively. The row of "total (without spatial decomposition)" lists the values of the (total) solvation free energy and solute-solvent energy computed without introducing the spatial decomposition. The total free energy of solvation with and without spatial decomposition correspond to eqs 25 and 11 of the main text, respectively. In the method of energy representation, the free energy is approximately evaluated and solute-solvent energy is exact. The total value of the latter is thus the same between the rows of "total (with spatial decomposition)" and "total (without spatial decomposition)", while the former can be different between the two rows even when expressed in total. The difference is actually a measure of the performance of the approximate functional adopted in the energy-representation method, and is within 0.1 kcal/mol for the small solutes. Alanine dipeptide exhibits larger differences of 0.4–0.6 kcal/mol, while the relative free energies among the four conformations agree within 0.2 kcal/mol.

Equation 11 of the main text provides the solvation free energy in the (one-dimensional) energy-representation method, and is spatially decomposed with eqs 25 and 26. Although these equations are exact, the present work adopted the approximation for the integration over the coupling parameter as described in Appendix A and in previous works.[1–3] To assess the performance of the approximate scheme, the (total) solvation free energy was also computed with the method of Bennett acceptance ratio.[4,5] This is an exact method for computing the free energy, and is conducted by introducing a set of intermediate states connecting the initial state without the solute and the final state with the solute at full coupling. The coupling parameters of λ_{LJ} and λ_{elec} are employed to describe the process of solute insertion and control the Lennard-Jones (LJ) and electrostatic terms of solute-solvent potential, respectively ($0 \leq \lambda_{\mathrm{LJ}} \leq 1, 0 \leq \lambda_{\mathrm{elec}} \leq 1$). In the present calculations, the soft-core potential was adopted for the site-site interaction in the form of

$$\lambda_{\mathrm{elec}} \frac{q_u q_v}{r} + 4\epsilon\lambda_{\mathrm{LJ}} \left(\frac{\sigma^{12}}{[\alpha\sigma^6(1-\lambda_{\mathrm{LJ}}) + r^6]^2} - \frac{\sigma^6}{\alpha\sigma^6(1-\lambda_{\mathrm{LJ}}) + r^6} \right)$$

where ϵ and σ are the LJ energy and length parameters, respectively, q_u and q_v are the charges on the solute and solvent sites, respectively, and r is the radial distance between a pair of interaction sites of solute and solvent.[6,7] α is the parameter to specify the "softness" of the λ_{LJ} dependence of the LJ component and was set to 0.5. The initial state (λ_{LJ} = 0, λ_{elec} = 0) corresponds to the pure solvent and the isolated solute, for which the solute and solvent are decoupled in the generation of the statistical ensemble. The final state (λ_{LJ} = 1, λ_{elec} = 1) refers to the solution system of interest with fully coupled solute-solvent interaction. The simulation was performed at $\lambda_{\mathrm{LJ}} = 0, 0.1, 0.2, \ldots, 0.9$, and 1.0 with λ_{elec} = 0 and at $\lambda_{\mathrm{elec}} = 0, 0.2, 0.4, 0.6, 0.8$, and 1.0 with $\lambda_{\mathrm{LJ}} = 1$. The MD setups were identical to those described in the main text, including the restraining potential for alanine dipeptide, and the run length was 10 ns at each set of λ_{LJ} and λ_{elec}.

The exact value of the (total) solvation free energy is listed in the row of "total (exact)". The deviation of the approximate free energy from the exact one is within 1.1 and 1.6 kcal/mol for the small solutes and for the four conformations of alanine dipeptide, respectively, and the preference order of the solvation free energy agrees well between the approximate and exact values. It is further seen that the order of the conformational preference is not affected by introducing the approximation, as noted at the end of the subsection Alanine Dipeptide.

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Small solutes

The definitions of the regions are given in Table 1 of the main text. C refers to the carbon atom in the methyl group of ethane, methylamine, methanol, and toluene, and Ph denotes the center-of-mass position of the six carbon atoms in the phenyl ring of toluene, aniline, and phenol. N is the amine nitrogen of methylamine and aniline, and O is the hydroxyl oxygen of methanol and phenol. The computed values for ethane were further averaged on the basis of symmetry.

Ethane

site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
	excluded volume	2.11	43.86 ± 0.03	0.00	2.82	0.00
	first shell	11.67	-2.20 ± 0.01	-5.86 ± 0.02	-0.78	-2.09 ± 0.01
C	second shell	26.38	-0.59	-0.58	-0.48	-0.47
	outer region	36.32	-0.10	-0.10	-0.11	-0.11
	sub-total	76.48			1.45 ± 0.01	-2.67 ± 0.01
	far-separated				-0.24	-0.25
total (with spatial decomposition)					2.66 ± 0.02	-5.58 ± 0.02
total (without spatial decomposition)					2.65 ± 0.02	-5.58 ± 0.02
total (exact)					1.82 ± 0.03	

Methylamine

site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
C	excluded volume	2.08	41.93 ± 0.03	0.00	2.66	0.00
	first shell	11.58	-3.11 ± 0.07	-7.32 ± 0.16	-1.10 ± 0.03	-2.59 ± 0.06
	second shell	26.24	-0.63 ± 0.01	-0.67 ± 0.03	-0.51 ± 0.01	-0.54 ± 0.02
	outer region	36.17	-0.11	-0.12 ± 0.01	-0.12	-0.13 ± 0.01
	sub-total	76.07			0.93 ± 0.03	-3.26 ± 0.07
N	excluded volume	1.36	42.44 ± 0.06	0.00	1.76	0.00
	first shell	2.18	-47.57 ± 0.34	-138.22 ± 0.73	-3.16 ± 0.02	-9.19 ± 0.05
	second shell	13.95	-5.00 ± 0.06	-6.64 ± 0.14	-2.13 ± 0.03	-2.83 ± 0.06
	outer region 1	22.40	-0.56 ± 0.02	-0.75 ± 0.04	-0.39 ± 0.01	-0.51 ± 0.03
	outer region 2	36.17	-0.13 ± 0.01	-0.18 ± 0.01	-0.14 ± 0.01	-0.20 ± 0.01
	sub-total	76.06			-4.06 ± 0.03	-12.73 ± 0.06
	far-separated				-0.42 ± 0.01	-0.35 ± 0.03
total (with spatial decomposition)					-3.55 ± 0.04	-16.34 ± 0.06
total (without spatial decomposition)					-3.66 ± 0.03	-16.34 ± 0.06
total (exact)					-3.71 ± 0.07	

Methanol

site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
C	excluded volume	2.06	41.72 ± 0.02	0.00	2.62	0.00
	first shell	11.54	-4.04 ± 0.10	-9.03 ± 0.22	-1.42 ± 0.04	-3.18 ± 0.08
	second shell	26.17	-0.66 ± 0.02	-0.79 ± 0.03	-0.53 ± 0.01	-0.63 ± 0.03
	outer region	36.10	-0.12 ± 0.01	-0.15 ± 0.02	-0.13 ± 0.01	-0.16 ± 0.02
	sub-total	75.87			0.54 ± 0.04	-3.97 ± 0.08
O	excluded volume	1.35	41.78 ± 0.05	0.00	1.72	0.00
	first shell	2.17	-64.31 ± 0.39	-165.30 ± 1.04	-4.26 ± 0.03	-10.94 ± 0.07
	second shell	13.90	-4.52 ± 0.07	-5.98 ± 0.14	-1.92 ± 0.03	-2.53 ± 0.06
	outer region 1	22.35	-0.56 ± 0.02	-0.79 ± 0.05	-0.38 ± 0.02	-0.54 ± 0.03
	outer region 2	36.10	-0.13 ± 0.01	-0.19 ± 0.02	-0.15 ± 0.01	-0.21 ± 0.02
	sub-total	75.87			-4.98 ± 0.05	-14.23 ± 0.11
	far-separated				-0.30 ± 0.02	-0.40 ± 0.03
total (with spatial decomposition)					-4.75 ± 0.03	-18.61 ± 0.06
total (without spatial decomposition)					-4.86 ± 0.03	-18.61 ± 0.06
total (exact)					-4.94 ± 0.04	

Toluene

site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
Ph	excluded volume	2.34	46.95 ± 0.01	-0.01	3.35	0.00
	first shell	20.66	-2.46 ± 0.07	-15.07 ± 0.15	-1.55 ± 0.04	-9.50 ± 0.09
	second shell	29.86	-1.26 ± 0.01	-1.30 ± 0.02	-1.15 ± 0.01	-1.19 ± 0.02
	outer region	30.64	-0.28	-0.30 ± 0.01	-0.27	-0.28 ± 0.01
	sub-total	83.50			0.39 ± 0.04	-10.96 ± 0.09
C	excluded volume	2.57	44.77 ± 0.02	0.00	3.51	0.00
	first shell	13.26	-4.74 ± 0.07	-11.43 ± 0.15	-1.92 ± 0.03	-4.62 ± 0.06
	second shell	28.77	-1.12 ± 0.01	-1.15 ± 0.02	-0.98 ± 0.01	-1.01 ± 0.02
	outer region	38.88	-0.18	-0.19 ± 0.01	-0.21	-0.22 ± 0.01
	sub-total	83.48			0.40 ± 0.02	-5.86 ± 0.05
	far-separated				-0.69 ± 0.01	-0.71 ± 0.02
total (with spatial decomposition)					0.10 ± 0.04	-17.53 ± 0.07
total (without spatial decomposition)					0.23 ± 0.03	-17.53 ± 0.07
total (exact)					-0.88 ± 0.05	

Aniline

site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
Ph	excluded volume	2.29	47.15 ± 0.01	0.00	3.29	0.00
	first shell	20.37	-1.43 ± 0.07	-12.43 ± 0.14	-0.89 ± 0.04	-7.72 ± 0.09
	second shell	29.57	-1.27 ± 0.01	-1.34 ± 0.02	-1.14 ± 0.01	-1.21 ± 0.02
	outer region	30.39	-0.29	-0.31 ± 0.01	-0.27	-0.29 ± 0.01
	sub-total	82.62			0.99 ± 0.04	-9.22 ± 0.08
N	excluded volume	1.67	44.78 ± 0.03	0.00	2.28	0.00
	first shell	2.57	-23.66 ± 0.28	-93.42 ± 0.88	-1.85 ± 0.02	-7.32 ± 0.07
	second shell	15.57	-6.26 ± 0.05	-8.74 ± 0.10	-2.97 ± 0.02	-4.15 ± 0.05
	outer region 1	24.26	-0.89 ± 0.01	-1.03 ± 0.03	-0.66 ± 0.01	-0.76 ± 0.02
	outer region 2	38.56	-0.19 ± 0.01	-0.22 ± 0.01	-0.22 ± 0.01	-0.25 ± 0.02
	sub-total	82.63			-3.43 ± 0.02	-12.49 ± 0.07
	far-separated				-0.73 ± 0.01	-0.74 ± 0.01
total (with spatial decomposition)					-3.17 ± 0.02	-22.45 ± 0.05
total (without spatial decomposition)					-3.21 ± 0.02	-22.45 ± 0.05
total (exact)					-3.73 ± 0.04	

Phenol

site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
Ph	excluded volume	2.30	47.11 ± 0.02	0.00	3.30	0.00
	first shell	20.41	-0.99 ± 0.06	-11.62 ± 0.11	-0.62 ± 0.04	-7.23 ± 0.07
	second shell	29.61	-1.27 ± 0.02	-1.34 ± 0.03	-1.14 ± 0.01	-1.21 ± 0.03
	outer region	30.42	-0.29	-0.32 ± 0.01	-0.27	-0.30 ± 0.01
	sub-total	82.74			1.27 ± 0.04	-8.74 ± 0.08
O	excluded volume	1.68	43.83 ± 0.03	0.00	2.25	0.00
	first shell	2.57	-43.15 ± 0.29	-130.75 ± 0.68	-3.38 ± 0.02	-10.25 ± 0.05
	second shell	15.60	-6.31 ± 0.04	-9.05 ± 0.08	-3.00 ± 0.02	-4.31 ± 0.04
	outer region 1	24.29	-0.96 ± 0.02	-1.21 ± 0.04	-0.71 ± 0.01	-0.90 ± 0.03
	outer region 2	38.60	-0.21 ± 0.01	-0.27 ± 0.03	-0.25 ± 0.02	-0.32 ± 0.03
	sub-total	82.74			-5.10 ± 0.04	-15.77 ± 0.09
	far-separated				-0.73 ± 0.02	-0.84 ± 0.03
total (with spatial decomposition)					-4.56 ± 0.04	-25.35 ± 0.08
total (without spatial decomposition)					-4.63 ± 0.04	-25.35 ± 0.08
total (exact)					-5.29 ± 0.06	

Alanine dipeptide

Table 2 of the main text provides the definitions of the regions, and Figure 2 labels the C_1, N_1, C_2, C_3, and N_2 atoms in alanine dipeptide.

α_{R}

site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
C_1	excluded volume	1.90	46.52 ± 0.03	0.00	2.70	0.00
	first shell	3.83	-13.19 ± 0.68	-67.24 ± 1.46	-1.54 ± 0.08	-7.85 ± 0.17
	second shell	8.07	-10.47 ± 0.22	-14.89 ± 0.47	-2.58 ± 0.05	-3.67 ± 0.12
	outer region 1	16.22	-2.32 ± 0.08	-3.18 ± 0.17	-1.15 ± 0.04	-1.57 ± 0.09
	outer region 2	25.46	-0.48 ± 0.02	-0.66 ± 0.04	-0.37 ± 0.02	-0.51 ± 0.03
	sub-total	55.48			-2.94 ± 0.14	-13.61 ± 0.29
N_1	excluded volume	0.83	45.57 ± 0.03	0.00	1.15	0.00
	first shell	0.86	-59.94 ± 0.99	-172.52 ± 2.64	-1.57 ± 0.03	-4.53 ± 0.07
	second shell	3.05	-17.40 ± 0.56	-26.85 ± 1.09	-1.62 ± 0.05	-2.50 ± 0.10
	outer region 1	7.18	-3.05 ± 0.09	-4.32 ± 0.18	-0.67 ± 0.02	-0.95 ± 0.04
	outer region 2	9.24	-0.54 ± 0.04	-0.79 ± 0.08	-0.15 ± 0.01	-0.22 ± 0.02
	sub-total	21.16			-2.86 ± 0.06	-8.19 ± 0.13
C_2	excluded volume	1.25	47.16 ± 0.02	0.00	1.80	0.00
	first shell	2.18	8.97 ± 0.69	-23.59 ± 1.47	0.60 ± 0.05	-1.57 ± 0.10
	second shell	4.43	-9.73 ± 0.37	-13.95 ± 0.75	-1.31 ± 0.05	-1.88 ± 0.10
	outer region 1	8.71	-1.94 ± 0.05	-2.25 ± 0.10	-0.52 ± 0.01	-0.60 ± 0.03
	outer region 2	13.48	-0.40 ± 0.04	-0.48 ± 0.07	-0.17 ± 0.01	-0.20 ± 0.03
	sub-total	30.05			0.40 ± 0.09	-4.25 ± 0.19
C_3	excluded volume	1.20	46.96 ± 0.02	0.00	1.72	0.00
	first shell	2.06	-62.47 ± 1.11	-156.79 ± 2.33	-3.92 ± 0.07	-9.85 ± 0.15
	second shell	6.96	-8.59 ± 0.23	-11.49 ± 0.47	-1.82 ± 0.05	-2.44 ± 0.10
	outer region 1	7.50	-1.44 ± 0.07	-1.97 ± 0.15	-0.33 ± 0.02	-0.45 ± 0.03
	outer region 2	10.46	-0.57 ± 0.04	-0.89 ± 0.08	-0.18 ± 0.01	-0.28 ± 0.02
	sub-total	28.18			-4.54 ± 0.10	-13.02 ± 0.20
N_2	excluded volume	1.37	46.53 ± 0.03	0.00	1.94	0.00
	first shell	1.80	2.08 ± 0.41	-60.57 ± 1.22	0.11 ± 0.02	-3.33 ± 0.07
	second shell	6.99	-10.54 ± 0.27	-22.22 ± 0.63	-2.25 ± 0.06	-4.74 ± 0.13
	outer region 1	17.48	-2.66 ± 0.09	-3.34 ± 0.19	-1.42 ± 0.05	-1.78 ± 0.10
	outer region 2	23.26	-0.49 ± 0.04	-0.69 ± 0.08	-0.35 ± 0.03	-0.49 ± 0.06
	sub-total	50.90			-1.96 ± 0.11	-10.33 ± 0.26
	far-separated				-1.51 ± 0.06	-2.00 ± 0.13
total (with spatial decomposition)					-13.43 ± 0.06	-51.43 ± 0.13
total (without spatial decomposition)					-13.85 ± 0.05	-51.43 ± 0.13
total (exact)					-14.99 ± 0.09	

P_{II}

site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
C_1	excluded volume	1.93	46.68 ± 0.04	0.00	2.75	0.00
	first shell	3.97	-14.85 ± 0.36	-70.08 ± 0.86	-1.80 ± 0.04	-8.49 ± 0.10
	second shell	8.39	-9.34 ± 0.19	-12.48 ± 0.40	-2.39 ± 0.05	-3.19 ± 0.10
	outer region 1	16.88	-2.09 ± 0.05	-2.68 ± 0.11	-1.08 ± 0.03	-1.38 ± 0.06
	outer region 2	26.46	-0.42 ± 0.02	-0.53 ± 0.05	-0.34 ± 0.02	-0.43 ± 0.04
	sub-total	57.63			-2.86 ± 0.08	-13.49 ± 0.17
N_1	excluded volume	0.87	45.64 ± 0.04	0.00	1.21	0.00
	first shell	0.97	-46.62 ± 0.87	-145.31 ± 2.03	-1.38 ± 0.03	-4.30 ± 0.06
	second shell	3.56	-16.11 ± 0.40	-25.37 ± 0.83	-1.75 ± 0.04	-2.75 ± 0.09
	outer region 1	8.57	-2.38 ± 0.10	-2.88 ± 0.21	-0.62 ± 0.03	-0.75 ± 0.05
	outer region 2	11.18	-0.39 ± 0.03	-0.45 ± 0.06	-0.13 ± 0.01	-0.16 ± 0.02
	sub-total	25.15			-2.68 ± 0.07	-7.96 ± 0.16
C_2	excluded volume	1.21	46.98 ± 0.02	0.00	1.73	0.00
	first shell	1.92	14.23 ± 0.73	-17.26 ± 1.44	0.83 ± 0.04	-1.01 ± 0.08
	second shell	3.73	-9.88 ± 0.33	-14.59 ± 0.68	-1.12 ± 0.04	-1.66 ± 0.08
	outer region 1	7.11	-1.98 ± 0.06	-2.13 ± 0.13	-0.43 ± 0.01	-0.46 ± 0.03
	outer region 2	10.76	-0.42 ± 0.04	-0.46 ± 0.09	-0.14 ± 0.01	-0.15 ± 0.03
	sub-total	24.73			0.88 ± 0.07	-3.28 ± 0.15
C_3	excluded volume	1.10	47.55 ± 0.02	0.00	1.60	0.00
	first shell	1.61	-60.33 ± 0.80	-160.48 ± 2.17	-2.96 ± 0.04	-7.88 ± 0.11
	second shell	4.97	-8.72 ± 0.23	-10.57 ± 0.49	-1.32 ± 0.03	-1.60 ± 0.07
	outer region 1	5.11	-1.38 ± 0.08	-1.61 ± 0.18	-0.22 ± 0.01	-0.25 ± 0.03
	outer region 2	6.95	-0.48 ± 0.04	-0.61 ± 0.10	-0.10 ± 0.01	-0.13 ± 0.02
	sub-total	19.74			-3.01 ± 0.07	-9.86 ± 0.16
N_2	excluded volume	1.45	46.10 ± 0.03	0.00	2.04	0.00
	first shell	2.08	-11.71 ± 0.51	-80.20 ± 0.79	-0.74 ± 0.03	-5.09 ± 0.05
	second shell	8.27	-10.83 ± 0.39	-22.15 ± 0.84	-2.73 ± 0.10	-5.59 ± 0.21
	outer region 1	21.03	-2.31 ± 0.04	-2.83 ± 0.08	-1.48 ± 0.03	-1.81 ± 0.05
	outer region 2	28.19	-0.36 ± 0.03	-0.45 ± 0.06	-0.31 ± 0.02	-0.39 ± 0.05
	sub-total	61.02			-3.23 ± 0.10	-12.88 ± 0.19
	far-separated				-1.36 ± 0.05	-1.33 ± 0.12
total (with spatial decomposition)					-12.26 ± 0.08	-48.80 ± 0.14
total (without spatial decomposition)					-12.75 ± 0.08	-48.80 ± 0.14
total (exact)					-13.28 ± 0.12	

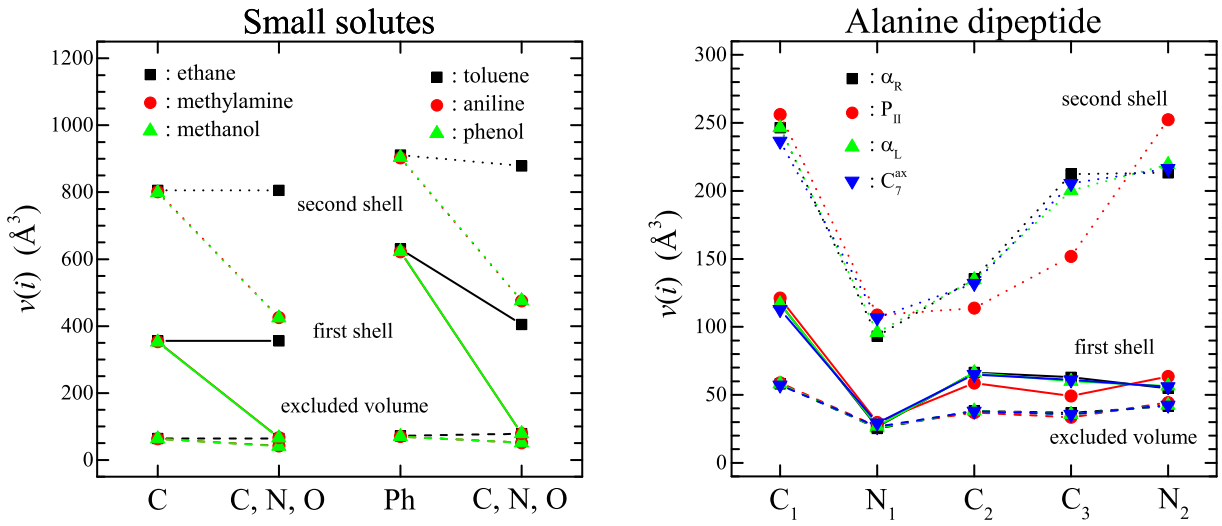
α_{L}

site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
C_1	excluded volume	1.90	46.66 ± 0.02	0.00	2.70	0.00
	first shell	3.83	-16.48 ± 0.60	-75.48 ± 1.35	-1.93 ± 0.07	-8.82 ± 0.16
	second shell	8.07	-11.00 ± 0.33	-15.58 ± 0.72	-2.71 ± 0.08	-3.83 ± 0.18
	outer region 1	16.22	-2.55 ± 0.07	-3.58 ± 0.14	-1.26 ± 0.03	-1.77 ± 0.07
	outer region 2	25.45	-0.57 ± 0.03	-0.83 ± 0.06	-0.44 ± 0.02	-0.64 ± 0.05
	sub-total	55.47			-3.63 ± 0.13	-15.06 ± 0.27
N_1	excluded volume	0.84	45.79 ± 0.02	0.00	1.17	0.00
	first shell	0.88	-65.33 ± 0.72	-168.32 ± 1.56	-1.75 ± 0.02	-4.52 ± 0.04
	second shell	3.14	-16.17 ± 0.62	-24.52 ± 1.17	-1.55 ± 0.06	-2.35 ± 0.11
	outer region 1	7.40	-2.87 ± 0.12	-4.19 ± 0.24	-0.65 ± 0.03	-0.95 ± 0.05
	outer region 2	9.54	-0.50 ± 0.05	-0.75 ± 0.10	-0.15 ± 0.01	-0.22 ± 0.03
	sub-total	21.80			-2.92 ± 0.09	-8.03 ± 0.16
C_2	excluded volume	1.25	46.77 ± 0.02	0.00	1.78	0.00
	first shell	2.17	11.10 ± 0.70	-19.42 ± 1.40	0.73 ± 0.05	-1.29 ± 0.09
	second shell	4.41	-9.54 ± 0.48	-13.84 ± 1.04	-1.28 ± 0.06	-1.86 ± 0.14
	outer region 1	8.66	-2.06 ± 0.11	-2.49 ± 0.23	-0.54 ± 0.03	-0.66 ± 0.06
	outer region 2	13.40	-0.48 ± 0.05	-0.63 ± 0.11	-0.19 ± 0.02	-0.26 ± 0.04
	sub-total	29.89			0.50 ± 0.12	-4.06 ± 0.24
C_3	excluded volume	1.17	47.24 ± 0.02	0.00	1.69	0.00
	first shell	1.96	-76.17 ± 0.58	-186.29 ± 1.44	-4.55 ± 0.03	-11.14 ± 0.09
	second shell	6.56	-9.85 ± 0.29	-13.69 ± 0.57	-1.97 ± 0.06	-2.74 ± 0.11
	outer region 1	7.03	-1.59 ± 0.11	-2.24 ± 0.23	-0.34 ± 0.02	-0.48 ± 0.05
	outer region 2	9.77	-0.67 ± 0.08	-1.06 ± 0.16	-0.20 ± 0.02	-0.32 ± 0.05
	sub-total	26.49			-5.38 ± 0.08	-14.67 ± 0.18
N_2	excluded volume	1.39	46.32 ± 0.03	0.00	1.96	0.00
	first shell	1.85	-4.80 ± 0.29	-68.24 ± 0.74	-0.27 ± 0.02	-3.85 ± 0.04
	second shell	7.19	-10.15 ± 0.50	-21.23 ± 1.04	-2.23 ± 0.11	-4.66 ± 0.23
	outer region 1	18.02	-2.54 ± 0.08	-3.24 ± 0.18	-1.39 ± 0.05	-1.78 ± 0.10
	outer region 2	24.01	-0.42 ± 0.03	-0.55 ± 0.06	-0.31 ± 0.02	-0.40 ± 0.05
	sub-total	52.46			-2.23 ± 0.15	-10.69 ± 0.32
	far-separated				-1.58 ± 0.12	-2.15 ± 0.24
total (with spatial decomposition)					-15.28 ± 0.06	-54.69 ± 0.10
total (without spatial decomposition)					-15.71 ± 0.05	-54.69 ± 0.10
total (exact)					-16.91 ± 0.08	

C_7^{ax}

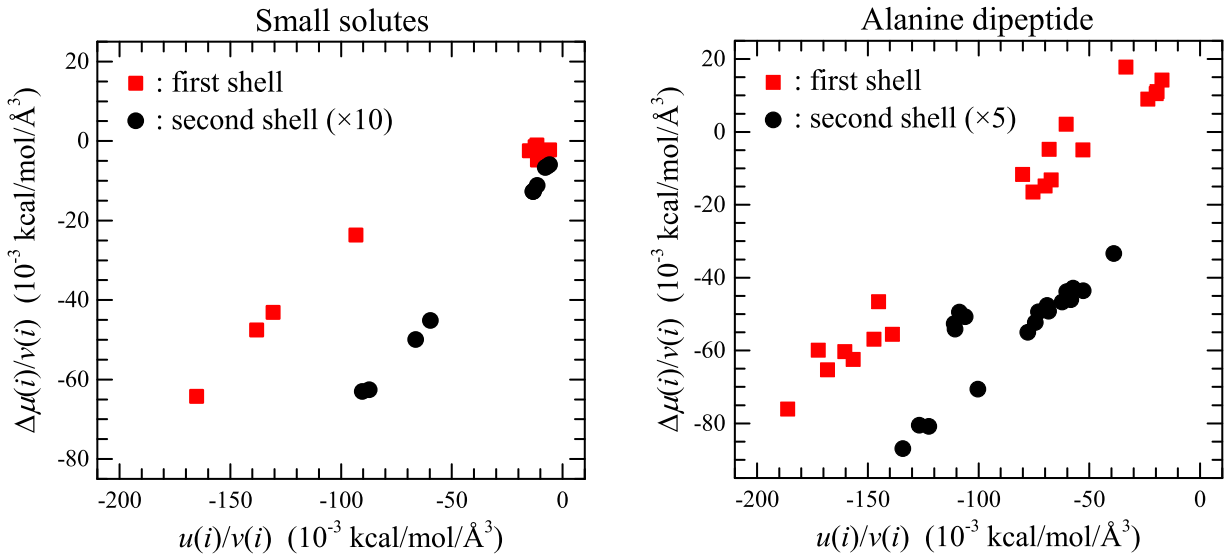
site in the solute	region	$\rho_0 v(i)$	$\Delta\mu(i)/v(i)$	$u(i)/v(i)$	$\Delta\mu(i)$	$u(i)$
C_1	excluded volume	1.87	46.93 ± 0.02	0.00	2.68	0.00
	first shell	3.69	-4.95 ± 0.40	-53.01 ± 0.90	-0.56 ± 0.05	-5.97 ± 0.10
	second shell	7.75	-9.21 ± 0.16	-11.69 ± 0.33	-2.18 ± 0.04	-2.76 ± 0.08
	outer region 1	15.53	-1.84 ± 0.03	-2.09 ± 0.05	-0.87 ± 0.01	-0.99 ± 0.03
	outer region 2	24.35	-0.36 ± 0.01	-0.41 ± 0.02	-0.27 ± 0.01	-0.30 ± 0.01
	sub-total	53.19			-1.20 ± 0.07	-10.02 ± 0.14
N_1	excluded volume	0.87	45.41 ± 0.02	0.00	1.21	0.00
	first shell	0.96	-56.92 ± 0.93	-147.32 ± 1.99	-1.67 ± 0.03	-4.31 ± 0.06
	second shell	3.49	-14.13 ± 0.34	-20.08 ± 0.61	-1.50 ± 0.04	-2.14 ± 0.07
	outer region 1	8.38	-2.20 ± 0.08	-2.80 ± 0.17	-0.56 ± 0.02	-0.72 ± 0.04
	outer region 2	10.91	-0.37 ± 0.03	-0.47 ± 0.06	-0.12 ± 0.01	-0.16 ± 0.02
	sub-total	24.61			-2.65 ± 0.05	-7.32 ± 0.08
C_2	excluded volume	1.24	47.05 ± 0.02	0.00	1.78	0.00
	first shell	2.13	10.48 ± 0.51	-19.81 ± 1.01	0.68 ± 0.03	-1.29 ± 0.07
	second shell	4.32	-8.78 ± 0.12	-12.05 ± 0.24	-1.16 ± 0.02	-1.59 ± 0.03
	outer region 1	8.46	-1.73 ± 0.04	-1.87 ± 0.10	-0.45 ± 0.01	-0.48 ± 0.02
	outer region 2	13.07	-0.38 ± 0.02	-0.44 ± 0.04	-0.15 ± 0.01	-0.18 ± 0.02
	sub-total	29.22			0.71 ± 0.05	-3.53 ± 0.10
C_3	excluded volume	1.17	46.99 ± 0.02	0.00	1.68	0.00
	first shell	2.00	-55.60 ± 0.54	-138.93 ± 1.11	-3.39 ± 0.03	-8.47 ± 0.07
	second shell	6.73	-6.68 ± 0.16	-7.80 ± 0.33	-1.37 ± 0.03	-1.60 ± 0.07
	outer region 1	7.25	-1.02 ± 0.05	-1.18 ± 0.11	-0.23 ± 0.01	-0.26 ± 0.02
	outer region 2	10.11	-0.37 ± 0.02	-0.48 ± 0.04	-0.11 ± 0.01	-0.15 ± 0.01
	sub-total	27.26			-3.43 ± 0.05	-10.48 ± 0.11
N_2	excluded volume	1.39	47.58 ± 0.03	0.00	2.02	0.00
	first shell	1.83	17.83 ± 0.55	-33.59 ± 1.56	1.00 ± 0.03	-1.87 ± 0.09
	second shell	7.09	-9.90 ± 0.21	-21.76 ± 0.50	-2.14 ± 0.05	-4.70 ± 0.11
	outer region 1	17.72	-2.27 ± 0.04	-2.45 ± 0.08	-1.22 ± 0.02	-1.32 ± 0.04
	outer region 2	23.57	-0.34 ± 0.01	-0.36 ± 0.03	-0.24 ± 0.01	-0.26 ± 0.02
	sub-total	51.60			-0.60 ± 0.07	-8.16 ± 0.17
	far-separated				-1.11 ± 0.04	-1.22 ± 0.09
total (with spatial decomposition)					-8.28 ± 0.05	-40.75 ± 0.10
total (without spatial decomposition)					-8.87 ± 0.05	-40.75 ± 0.10
total (exact)					-9.85 ± 0.07	

Volumes $v(i)$ of the excluded-volume, first-shell, and second-shell regions



The lines connecting the data are drawn for eye guide, and are dashed, solid, and dotted for the excluded volume, first shell, and second shell, respectively. C, N, and O refer to the methyl carbon, amine nitrogen, and hydroxyl oxygen, respectively, and Ph is the center of the phenyl group. For ethane, the data are plotted both at "C" and "C, N, O" and the lines connecting them are horizontal. The data and line overlap between methylamine and methanol and between aniline and phenol.

Correlation plots between $\Delta\mu(i)/v(i)$ and $u(i)/v(i)$ in the first and second shells



In the second shell, $\Delta\mu(i)/v(i)$ and $u(i)/v(i)$ are multiplied by factors of 10 and 5 for the small solutes and for alanine dipeptide, respectively.