

FULL PAPER

Challenges in predicting $\Delta_{\text{rxn}}G$ in solution: Hydronium, hydroxide, and water autoionizationShamneet Dhillon | Allan L. L. East 

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Abstract

Standard non-semiempirical continuum-dielectric orbital-based methods horribly overpredict, by 26–50 kcal mol⁻¹, the Gibbs energy for the water autoionization reaction $2 \text{H}_2\text{O}_{(l)} \rightarrow \text{H}_3\text{O}^+_{(aq)} + \text{OH}^-_{(aq)}$. Here, we demonstrate these errors, fully investigate the reasons for these errors, and show that the use of 4 explicit solvent within the continuum (the “semicontinuum,” “cluster-continuum,” or “hybrid” technique) can reduce the error of a standard continuum model from 50 to 2 kcal mol⁻¹. Results from pure cluster, pure continuum (several versions including semiempirical ones), and semicontinuum modeling are each presented and discussed. We recommend use of 3 waters around hydronium and 4 waters around hydroxide with standard continua whenever these ions are involved in reaction. To the possible surprise of some, time-consuming molecular-dynamics simulations are not needed to reproduce this problematic energy.

KEYWORDS

aqueous chemistry, cluster+continuum, continuum methods, explicit water, hydronium, hydroxide, ion product of water, K_w , semicontinuum, solvation

1 | INTRODUCTION

This article exposes the embarrassingly large errors of standard non-semiempirical continuum-dielectric orbital-based methods^[1] when applied to the water-autoionization Gibbs energy, thoroughly investigates these large errors, and shows what is required to correct the problem to chemical (~ 2 kcal mol⁻¹) accuracy. We are unaware of any published demonstration of the disastrous errors that can arise for this reaction from common continuum-dielectric methods. Past calculations of this energy, including those from molecular-dynamics simulations, will also be discussed, and recommendations are made for aqueous H_3O^+ and OH^- modeling.

Many others have observed that the undeniably crude continuum-dielectric approximation is particularly poor for aqueous ions, and have examined ways to improve upon it. Such improvements usually come in three general flavors: (i) they employ empirical parameters postcalculation,^[2–6] and/or (ii) they employ semiempirical parameters within the continuum-dielectric model (e.g., SMx models,^[5–9] as contrasted with PCM models^[10–12], and/or (iii) they employ explicit solvent molecules with the solute inside the continuum cavity^[3–6,13–16] (known variously as the semicontinuum,^[13] cluster-continuum,^[14] or “hybrid” technique). We prefer the ab initio point of view, and hence have an order of preference of iii > ii > i for these ideas. However, what is lacking among past semicontinuum applications [type (iii) studies] is a thorough examination of a challenging reaction-energy case with a variety of techniques. How fast (if at all) do semicontinuum results converge with respect to number of explicit solvent molecules added? Does this depend on the continuum-dielectric model used? Is the unfortunate dependence of results upon cavity radius^[17] mollified in semicontinuum modeling? Is any level of empiricism or semi-empiricism needed? This article is the first to delve this deeply into a case, a case with a disastrous 50 kcal mol⁻¹ error from an ordinary continuum-dielectric method, and we think this to be a very valuable contribution to the aqueous modeling community.

One past semicontinuum study is worthy of comment: the 2008 report of Bryantsev et al.,^[15] who examined the aqueous solvation Gibbs energy of H^+ and Cu^{2+} . For H^+ , there is a value from experiment of -265.9 kcal mol⁻¹ (1 M vapor \rightarrow 1 M solution).^[18] To reproduce it they used the COSMO continuum-dielectric model^[19] and semicontinua having up to 14 explicit water molecules, and found errors of {+23, +5, +4, +0.6, -0.5} kcal mol⁻¹ when using {1, 4, 6, 10, 14} explicit water molecules, respectively. This is a rare example of a semicontinuum study that went so

far as to demonstrate convergence with number of explicit solvent molecules added. Questions not addressed by their study, and addressed here, include the following: Will semicontinua energies reliably converge when other continuum-dielectric models are used? Do reaction energies also require 10 explicit water molecules to obtain 1 kcal mol⁻¹ accuracy, or will a cancelation of errors in the solvation energies allow for less waters to be used? Will semicontinua alone be able to eliminate the enormous 50 kcal mol⁻¹ error in an ordinary continuum calculation on water autoionization, or will other effects (nonelectrostatic terms, better electron correlation method, rigid-rotor-harmonic-oscillator terms, or ultimately semiempirical parameters or empirical corrections) be needed?

In the study presented here, when explicit water molecules are added to the water autoionization calculation, the same number n of explicit solvent molecules is added around each "solute:"



and in the case of semicontinuum calculations each hydrate cluster was placed inside a cavity in the dielectric-continuum model. Note that a reactant water molecule is designated a "solute" molecule (designated H₂O) and is distinct from the explicit "solvent" water molecules (designated W) in these calculations. Also note that the well-known equilibrium constant for this reaction, $K_{\text{W}} = [\text{H}^+][\text{OH}^-] = [\text{H}_3\text{O}^+][\text{OH}^-] = 1.0 \times 10^{-14}$ (M²) at 25 °C, converts to various ΔG° values depending on concentration convention:

$$\Delta G(55.35 \text{ M water} \rightarrow 1 \text{ M ions}) = - (0.001987)(298.15) \ln(10^{-14}) = + 19.1 \text{ kcal mol}^{-1}$$

$$\Delta G(1 \text{ M water} \rightarrow 1 \text{ M ions}) = - (0.001987)(298.15) \ln(10^{-14}/55.35^2) = + 23.9 \text{ kcal mol}^{-1}$$

The latter convention is assumed here to simplify comparison to computed results.

2 | METHODS

Unless otherwise noted, all computations use B3LYP/6-31+G(d) for electronic energies. Other basis sets tested were TZVP,^[20] 6-311++G(3d,3p),^[21] and aug-cc-pVQZ.^[22] Other electron-correlation approximations tested were MP2^[23] and CCSD(T).^[24] Various dielectric-continuum solvation models were tested: with Gaussian09 software^[25,26] we tested IEFPCM,^[10] CPCM,^[11] SCIPCM,^[12] IPCM,^[12] and SMD,^[8] and with Q-Chem software^[27] we tested SM8,^[7] SM12,^[9] and COSMO.^[19]

Gas-phase and gas-phase-cluster results report $\Delta E = \Delta_{\text{rxn}} E = E(\text{OH}^-) + E(\text{H}_3\text{O}^+) - 2 E(\text{H}_2\text{O})$ values using $E = E_{\text{electronic}}$ only. Continuum and semicontinuum results report ΔE values using electrostatic solvation terms only, that is, they use $E = \langle \Psi(f) | \hat{H} + \hat{V} / 2 | \Psi(f) \rangle$ only,^[1] except for SM8, SM12, and COSMO (and one IEFPCM test calculation) which included nonelectrostatic corrections. Most continuum-dielectric models claim to be producing a Gibbs energy G rather than an E ; regardless, it is implicitly assumed here that $\Delta E \approx \Delta G$ for this reaction. (This assumption was crudely tested (line 3 of Table 1, vide supra) and passed that test.) Continuum cavity surfaces for the solute molecules were consistently chosen to be overlapping-spheres using various definitions of van der Waals radii (i.e., not solvent-accessible or solvent-excluded surfaces), except for the isodensity-cavity models IPCM and SCIPCM.

Geometries used in all computations (including gas-phase ones) were B3LYP/6-31+G(d)/IEFPCM optimized geometries (Gaussian09 default IEFPCM: radii = UFF^[29] × 1.1). Figure 1 shows the cluster structures used (see Supporting Information for Cartesian coordinates of atoms). During testing of cluster choices (placement and orientation of the explicit water molecules), it became clear that, while ANY placement would drastically improve upon the 50 kcal mol⁻¹ error of not having any waters, there are some general principles that can further minimize errors: (i) Conserve the number of H-bonds introduced for reactants versus products. Here, when adding {1,2,3,4,7,10} explicit waters to each solute, {1,2,3,4,8,12} H-bonds were added. (ii) Conserve, as best as possible, the H-bonding ring strain introduced for reactants versus products. Here, we chose 10-atom rings consistently. (iii) Fill the first solvation shell first. To hydronium and hydroxide, these H-bonds are considerably stronger than

TABLE 1 Computed energies (E and ΔE) from various PCM methods, keeping cavity radii constant (UFF×1.1: $r_{\text{O}} = 1.925$ Å, $r_{\text{H}} = 1.587$ Å)

Approximation	$E(\text{H}_2\text{O})$ (au)	$E(\text{H}_3\text{O}^+)$ (au)	$E(\text{OH}^-)$ (au)	ΔE (au)	ΔE (kcal/mol)
iefpcm	-76.43125	-76.81601	-75.92938	0.11711	73.5
iefpcm with non-elec ^a	-76.42696	-76.81157	-75.92513	0.11721	73.6
iefpcm with RRHO G correc ^b	-76.42790	-76.80022	-75.93717	0.11841	74.3
iefpcm b3lyp/tzvp	-76.46842	-76.85961	-75.94620	0.13103	82.2
iefpcm b3lyp/6-311++G(3d,3p)	-76.46961	-76.85860	-75.96107	0.11955	75.0
iefpcm b3lyp/aug-cc-pvqz	-76.47857	-76.86840	-75.96932	0.11944	74.9
iefpcm mp2/aug-cc-pvqz	-76.35830	-76.74683	-75.85261	0.11716	73.5
iefpcm ccSD(t)/aug-cc-pvqz	-76.36985	-76.76057	-75.85873	0.12040	75.6
cpcm	-76.43061	-76.81603	-75.92944	0.11574	72.6

^a Using cav, rep, and dis flags for "nonelectrostatic" corrections^[28] in Gaussian09.

^b Using gas-phase rigid-rotor/harmonic-oscillator terms ("Gibbs energies," frequency run).

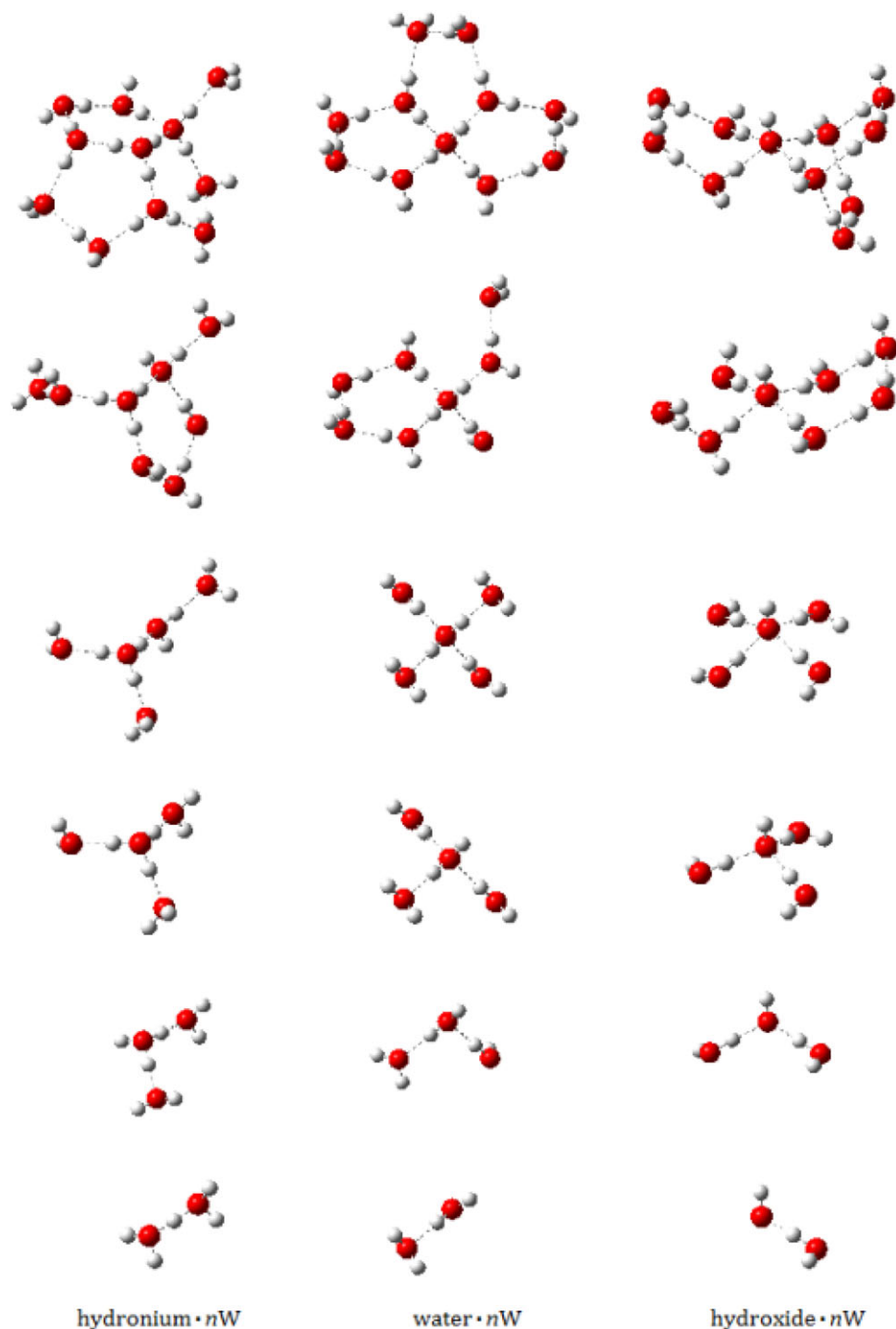


FIGURE 1 Optimized cluster structures used for computations

H-bonds between first and second solvation shells, and should be explicitly accounted for if dealing with a reaction in which these ions are consumed or produced (e.g., acid-catalyzed reactions). (iv) Do not explicitly solvate the unbasic lone pair of H_3O^+ or the unacidic H atom of OH^- ; stable results are obtained if the minor solute-solvent interactions are left to the continuum to handle.

3 | RESULTS

3.1 | Results with no explicit waters

Our “base” result for comparisons is the default continuum (SCRF) method of Gaussian09: IEFPCM, cavity radii = $\text{UFF} \times 1.1$ ($r_{\text{O}} = 1.925 \text{ \AA}$, $r_{\text{H}} = 1.587 \text{ \AA}$). With B3LYP/6-31+G(d) optimization it gives $73.5 \text{ kcal mol}^{-1}$ for the autoionization energy. The gas-phase B3LYP/6-31+G(d) result is

TABLE 2 Computed energies (E and ΔE) from Gaussian09's isodensity-cavity models

Continuum model ^{a,b}	$E(\text{H}_2\text{O})$ (au)	$E(\text{H}_3\text{O}^+)$ (au)	$E(\text{OH}^-)$ (au)	ΔE (au)	ΔE (kcal/mol)
scipcm 21x12, iso=.0004 (default)	-76.43130	-76.84101	-75.90116	0.12042	75.6
ipcm 21x12 iso=.0004	-76.43018	-76.83775	-75.90223	0.12037	75.5
ipcm 10x05, iso=.001 (default)	-76.43467	-76.84991	-75.92467	0.09476	59.5
ipcm 22x12, iso=.001	-76.43344	-76.85322	-75.92157	0.09209	57.8
scipcm 10x05, iso=0.001	-76.43575	-76.86315	-75.90690	0.10144	63.7
scipcm 21x12, iso=0.001	-76.43575	-76.86161	-75.90692	0.10298	64.6

^a The "m x n, iso = " notation: m x n refers to the number of grid points per atom in the ϕ and θ directions, while iso is the value (electrons/bohr³) of the electron density for the cavity surface.

^b The older IPCM method performs cavity isodensity updates *after* each SCF cycle, and can be considered an outdated approximation to the fully self-consistent SCIPCM method.

224 kcal mol⁻¹ while the true answer (see Introduction) is 23.9 kcal mol⁻¹. While this continuum method reduces the error from the gas-phase estimate by 150 kcal mol⁻¹, the remaining error is still shockingly large (50 kcal mol⁻¹).

Table 1 demonstrates that this large error is not due to the approximations made for basis set, electron correlation, neglect of nonelectrostatic terms (cavitation/repulsion/dispersion), neglect of rigid-rotor-harmonic-oscillator Gibbs-energy terms from a frequency calculation,^[30] nor choice of IEFPCM over the conductor-like CPCM.

Of the PCM parameters amenable to improvement, those for cavity shape and size are commonly targeted. Table 2 presents results from isodensity-cavity models. An isodensity value of 0.0004 reproduces the ΔE values of Table 1; a larger value (which shrinks the cavity volumes) reduces the 50 kcal mol⁻¹ error by 10-15 kcal mol⁻¹. Returning to overlapping-sphere cavities, we tested various other choices for sphere radii from the literature (Table 3), generating a variety of results. The trend is that ΔE falls as the cavities are shrunk, because the solvent gets "closer" to the solutes, which dramatically stabilizes the ions (products) relative to neutrally charged solutes (reactants). The arbitrariness of the choice of radii, and the well-known^[17] sensitivity of continuum-model results to such choice, is disturbing, but in addition we point out that *none* of these choices in Table 3 (except for the outdated UAHFx1.2 choice with its uncomfortably small anions) give reasonable answers for ΔE (errors > 20 kcal mol⁻¹).

Table 4 presents results from other popular continuum models, compared with IEFPCM results run with the same cavity radii. The SMD result (49 kcal mol⁻¹) halved the error of default IEFPCM, but the improvement is entirely due to its choice of cavity radii (line 3 of Table 4) and is still in error by 25 kcal mol⁻¹. The COSMO result (50 kcal mol⁻¹) also halved the error of default IEFPCM, with 14 kcal mol⁻¹ improvement due to its cavity choice and another 9 kcal mol⁻¹ improvement due to undetermined contributions in the COSMO solvation model. The SM8 and SM12 results (26 and 27 kcal mol⁻¹) are the only reasonable ones here (+3 kcal mol⁻¹ error), with most of its improvement (relative to default IEFPCM) due to particularly small cavities, but an additional 18 kcal mol⁻¹ improvement due to the incorporation of extra semiempirical parameters meant to correct for first solvation shell effects like hydrogen bonding. (Note that Klamt accounts for first solvation shell effects with a different philosophy, recommending that COSMO be supplemented by an extra calculation, COSMO-RS,^[39] which accounts for the molecularity of the solvent; like SM8/SM12 it also uses experimental information to determine values for additional parameters.)

TABLE 3 Computed reaction energies (ΔE) using various choices for cavity radii $r(\text{O})$ and $r(\text{H})$

Continuum model	ΔE (kcal/mol)	$r(\text{O}), r(\text{H})$ (Å)
iefpcm, radii: UFF \times 1.1 (e.g., G09) ^a	73.5	1.925, 1.587
iefpcm, radii: UA0 \times 1.0 (e.g., G03) ^b	67.0	(1.85, 1.95, 2.05) for (OH ⁻ , H ₂ O, H ₃ O ⁺)
iefpcm, radii: COSMO ^c	59.3	1.720, 1.300
iefpcm, radii: Bondi \times 1.0 (e.g., SMD) ^d	49.7	1.520, 1.200
iefpcm, radii: NewBondi \times 1.0 (e.g., Q-Chem) ^e	46.7	1.520, 1.100
iefpcm, radii: SM8 (e.g., SM8, SM12) ^f	44.3	1.520, 1.020
iefpcm, radii: UAHF \times 1.2 (e.g., G98) ^g	29.3	(1.548, 2.016, 1.812) for (OH ⁻ , H ₂ O, H ₃ O ⁺)

^a Universal Force Field radii^[29] scaled by 1.1; the default in Gaussian09.^[25]

^b United Atom radii (There is no literature reference for the UA0 radii. D. J. Fox (Gaussian Inc., private communication) reports that the UA0 algorithm is to take the UFF radius for a nonhydrogen atom and add 0.1 * n_H to unite attached H atoms, with no correction for ion charge.) unscaled [$r(\text{O}); r(\text{H})=0$]; the default in Gaussian03.^[31]

^c Radii used in COSMO.^[19b]

^d Bondi radii,^[32] used in SMD for these particular atoms.^[8]

^e updated Bondi radii,^[33] used as default in Q-Chem's^[27] PCM algorithm.

^f Radii used in SM8^[7] and SM12.^[9]

^g United Atom for Hartree-Fock radii^[34] scaled by 1.2 [$r(\text{O}); r(\text{H})=0$]; the default in Gaussian98.^[35]

TABLE 4 Computed energies (E and ΔE) comparing SMD, COSMO, SM8, and SM12 continuum models versus IEFPCM

Continuum model	$E(\text{H}_2\text{O})$ (au)	$E(\text{H}_3\text{O}^+)$ (au)	$E(\text{OH}^-)$ (au)	ΔE (au)	ΔE (kcal/mol ^a)
SMD (Q-CHEM)	-76.43768	-76.84691	-75.94969	0.07876	49.4
SMD (Gaussian09)	-76.43659	-76.84658	-75.94894	0.07766	48.7
<i>iefpcm</i> , radii: Bondix1.0 (e.g., SMD)	-76.43972	-76.85010	-75.95011	0.07924	49.7
COSMO (Q-CHEM) ^b	-76.43739	-76.83691	-75.95761	0.08026	50.4
<i>iefpcm</i> , radii: COSMO	-76.43610	-76.83716	-75.94058	0.09445	59.3
SM8 (Q-CHEM)	-76.43772	-76.85590	-75.97798	0.04156	26.1
SM12 chelg ^c (Q-CHEM)	-76.43864	-76.85081	-75.98351	0.04295	27.0
SM12 mk ^c (Q-CHEM)	-76.43895	-76.85085	-75.98428	0.04277	26.8
<i>iefpcm</i> , radii: SM8 (e.g., SM8, SM12)	-76.44572	-76.86985	-75.95097	0.07063	44.3

^a The true Gibbs-energy change is 23.9 kcal mol⁻¹ (see Introduction).

^b Note that the ADF^[36] version of COSMO uses radii that differ from traditional COSMO.

^c SM12 results depend upon definition of partial charges; we report results from chelg^[37] and Merz-Kollman^[38] variants.

3.2 | Results with explicit waters

Table 5 presents results from incorporating explicit solvent water molecules in the calculations (Equation 1, Figure 1). The gas-phase cluster models (column 2 in Table 5) are terrible, with the $n = 10$ result still in error by 70 kcal mol⁻¹. However, semicontinuum modeling with Gaussian09's default method (IEFPCM) and radii (UFF \times 1.1; column 3) completely cured the 50 kcal mol⁻¹ error in default IEFPCM computations, with errors of 2 kcal mol⁻¹ at $n = 3$ and 1 kcal mol⁻¹ at $n = 4, 7$, and 10. It even cured the basis set error problem of TZVP^[20] (column 4), whose lack of diffuse functions caused a 7-9 kcal mol⁻¹ additional error for $n = 0$ (Table 1). It does not cure the dependence upon cavity radii, however (column 5 vs. column 3). Since the SM12 gave a very good $n = 0$ result, we wished to explore what it would do with explicit water use: the values become unstable beyond $n = 2$, but keep in mind that SM12 was parameterized to be used with only $n = 0$ or $n = 1$ and not meant to be used with large microsolvated clusters.

The default IEFPCM model in Gaussian09 converges rather robustly to the true answer as explicit waters are added inside the cavity. The default cavity radii (UFF \times 1.1) appear to be a fortunate choice in this regard.

4 | DISCUSSION AND CONCLUSION

The autoionization of water, as a challenging test reaction, was an excellent tool to contrast accuracies of various static (nondynamic) computational methods. Modeling this aqueous-phase free-energy of reaction via moderate microsolvation alone (up to 10 explicit water molecules) results in > 70 kcal mol⁻¹ error (Table 5). Using continuum-dielectric models without microsolvation produces values that vary dramatically with cavity size (Table 3), get worse if the orbital basis set lacks diffuse functions (TZVP result, Table 1) but stay rather insensitive to other model adjustments (Table 1). The semiempirical SM8 and SM12 continuum-dielectric methods, in the absence of explicit waters, predict the autoionization energy well (only 2-3 kcal mol⁻¹ too high).

The hybrid approach of semicontinuum modeling is able to reproduce the autoionization of water to within 2 kcal mol⁻¹, but only when used "appropriately." The presented results help to discern what is meant by "appropriately." The bare-bones IEFPCM model with default UFF \times 1.1 cavity radii was shown to converge robustly to the correct answer, with careful consideration of water placement (e.g., conservation of number of introduced H bonds), but at least $n = 3$ water molecules are needed to obtain good accuracy with it for this reaction. Large errors are had if less than 3 waters are provided (e.g., $n = 1$ gave 27 kcal mol⁻¹ error, Table 5, entry 51.1). In contrast, the semiempirical SM8 and SM12 models were

TABLE 5 Computed energies (ΔE) using explicit waters (microsolvation, Figure 1). The true free energy change is 23.9 kcal mol⁻¹ (see Introduction)

# of waters n	B3LYP 6-31+G(d) gas	B3LYP 6-31+G(d) <i>iefpcm</i>	MP2 TZVP <i>iefpcm</i>	B3LYP 6-31+G(d) <i>iefpcm</i> $\alpha = 0.6^a$	B3LYP 6-31+G(d) SM12 chelg
0	224.2	73.5	83.1	29.6	27.0
1	169.9	51.1	56.7	25.7	25.5
2	140.8	38.4	41.7	21.8	26.7
3	101.4	26.1	28.3	16.9	14.1
4	82.1	22.8 ^b	24.4 ^b	14.3	11.3
7	99.4	24.3	24.8	16.5	27.3
10	94.4	24.5	24.4	14.4 ^c	21.9

^a α is the scale factor upon UFF radii, here resulting in $r(\text{O}) = 1.0500$ and $r(\text{H}) = 0.8658$ Å.

^b This value is {22.1, 23.3, 23.2} with {M06-2x^[40]/6-31+G(d), ω B97X-D^[41]/6-31+G(d), B3LYP/aug-cc-pVQZ}, additional runs requested by a referee.

^c This value is still poor (19.0) with a milder $\alpha = 0.85$, that is, $r(\text{O}) = 1.488$ and $r(\text{H}) = 1.227$ Å.

designed to get the right answer without adding more than 1 explicit water molecule in the calculation, and hence should not be used with more than this (e.g., $n = 3$ with SM12 gave $-10 \text{ kcal mol}^{-1}$ error, Table 5, entry 14.1). The severe dependence on ΔE versus cavity size that exists with continuum modeling is damped with semicontinuum modeling but does remain (Table 5).

There are past examples of quantum-chemical prediction of the autoionization energy in the literature. In 2005 Zhang and Houk^[42] reported a surprisingly excellent value of $24.7 \text{ kcal mol}^{-1}$ from B3LYP/6-311++G(3d,3p)/CPCM//B3LYP/6-31G(d)/gas computation with Gaussian98 revision A.9, which used UAHFx1.2 cavity radii. We still have a copy of Gaussian98 revision A.9, and could reproduce their energies from their Cartesian coordinates. Certainly this value benefitted from the unusual and no-longer-favored UAHFx1.2 radii, but also note that Gaussian09 produces a value 5 kcal mol^{-1} higher with these radii (e.g., Table 3 last row for IEFPCM), due principally to differing $E(\text{OH}^-)$, and we suspect that Gaussian98 made a differing and now-outdated choice on what to do with the "outlying charge" issue.^[1,43] Next, in 2006 Slozil and Jungwirth^[44] obtained interesting values of 25 (MP2) and 28 (CCSD(T)) kcal mol^{-1} using two gas-phase clusters: $(\text{H}_2\text{O})_8 \rightarrow \text{H}_3\text{O}^+ \cdot 6 \text{ H}_2\text{O} \cdot \text{OH}^-$. Given that gas-phase clusters gave 70 kcal mol^{-1} errors in our work (Table 5), due to insufficient solvation of the ions, their good result may fortuitously arise from having the two ions so close to each other. Finally, we mention the autoionization free-energy results from simulations: Trout and Parrinello^[45] and Sprik^[46] both obtained 17 kcal mol^{-1} , from BLYP-based Car-Parrinello molecular dynamics (CPMD) with periodic replication of a 9.68 \AA -wide 32-water cell, and Warshel and coworkers^[47] obtained 18 kcal mol^{-1} from QM/MM simulations employing B3LYP for 7 explicit waters, molecular mechanics for further waters out to an 18 \AA sphere, and a dielectric continuum beyond that. While simulations in principle would be excellent ways to model solvation energies, these are significant underestimates which those authors ascribed to technical limitations.

In summary, the free energy of autoionization of water is modeled well by semicontinuum modeling of $2 \text{ H}_2\text{O} \cdot n\text{W} \rightarrow \text{H}_3\text{O}^+ \cdot n\text{W} + \text{OH}^- \cdot n\text{W}$ but is sensitive to cavity radii choice and water placement. SM12 with $n = 1$, as well as IEFPCM with default UFFx1.1 radii and $n \geq 4$ carefully placed waters (Figure 1), both reproduce the true answer to within 2 kcal mol^{-1} . Without explicit waters, most continuum-dielectric methods gave extremely poor results. We recommend such semicontinua whenever hydronium or hydroxide ions are involved in reaction.

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