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Non-unique Lennard-Jones Parameter Problem with a Monatomic Cation

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In molecular mechanical force fields, a monatomic ion is represented as a charged van der Waals particle that interacts with all atoms of the molecular system. The Coulomb potential normally specifies the electrostatic interaction of the charge. The Lennard-Jones (LJ) potential expresses the pair-wise exchange-repulsion and dispersion interactions between atoms i and j with the well depth ε_{ij} and the distance $R_{\min,ij}$ at which the potential reaches the minimum. Following the Lorentz-Berthelot combination rule, the charge and the dispersion parameters, ε and $R_{\min}$, define the force field of a monatomic ion.[1]

The force field parameters are optimized to reproduce experimental findings through molecular simulations. Various experimental and theoretical data have been considered; a partial list includes the free energy of hydration, the entropy of hydration, the radial distribution function of water oxygen atoms around the ion, the lattice constant and the lattice energy of ionic crystals, osmotic coefficients, and geometric and energetic data from *ab initio* quantum mechanical calculations of monohydrates to water clusters of ions.[2-8] Unfortunately, it has been difficult to determine a unique set of force field parameters in most approaches even with multiple target observables. This communication elaborates the parameter correlation problem[9] and demonstrates that the non-unique parameters based on the hydration free energy can equivalently represent the thermodynamics of the a monoatomic cation.

The hydration free energies, ΔG_{hyd}, of monovalent cations are calculated by performing thermodynamic perturbation simulations of the ion solution. The system contains the ion at the origin of a water sphere of radius 1.6 nm under a solvent boundary potential.[10] The sphere includes 572 TIP3P[11] water molecules equilibrated at 298.15 K and 1 bar.

The calculation is performed in several steps. First, one mole of ideal gas of volume 0.024788 m^3 is confined into the volume of 0.001 m^3 at 298.15 K and 1 bar. The entropic contribution is $\Delta G_1 = -RT \ln(0.001/0.024788) = 7.958$ kJ mol^{-1}, where R is the gas constant and T is the absolute temperature. Second, the van der Waals particle with the distance parameter $R_{\min}$,, and $\varepsilon = 0.0$ is inserted at the center of a bulk water system. The hydration free energy ΔG_2 of the uncharged fictitious atom is calculated by thermodynamic perturbation with the soft core potential[12] where ε is increased to the value of the particle in steps of 41.84 J mol^{-1}. Third, the van der Waals particle of given $R_{\min}$ and ε is charged to +1e in 11 steps; 0.05, 0.15, 0.25, 0.35, 0.45, 0.55, 0.65, 0.75, 0.85, 0.95, and 1.0. The charging steps yield the free energy change ΔG_3 by using the weighted histogram analysis method.[13]

Langevin molecular dynamics at constant temperature and pressure is performed for 20 ps per each window with the time step of 1 fs. The last 17.5 ps of each window are used to compute the free energy change. The Langevin friction coefficient is set to 25 ps^{-1} for TIP3P oxygen atoms. The recommended nonbonding cutoff options are electrostatic switching and van der Waals switching functions with cut-on, cut-off, cut-nonbond distances of 1.8, 2.0 and 2.2 nm, respectively. O-H and H-H distances of water are fixed by applying the SHAKE constraint.[14] The dynamics trajectory is saved every 0.1 ps to calculate the radial distribution functions (RDFs). All calculations were performed with the CHARMM program version c35b1.[15]

ΔG_{hyd} of monovalent cations are obtained as a function of a range of LJ parameters: $R_{\min}$, spanning from 40 pm to 480 pm with the interval of 40 pm and ε spanning from 0.08368 kJ mol^{-1} to 1.00416 kJ mol^{-1} with the interval of 0.08368 kJ mol^{-1}. The experimental hydration free energy of the sodium ion[16] –365 kJ mol^{-1} is interpolated from the hydration free energy values to determine the distance parameter that pairs with the well depth parameter scanned from 83.68 J mol^{-1} to 1,004.16 J mol^{-1} with the interval of 83.68 J mol^{-1}. The cubic spline interpolation procedure yields a series of

Table 1. Calculated hydration free energies of the sodium ion[a]

ε	$R_{\min}/2$	ΔG_2[b]	ΔG_3[c]	ΔG_{hyd}[d]
0.0837	170.47	1.15	-371.37	-362.26
0.1674	162.63	0.82	-373.28	-364.50
0.2510	158.66	1.87	-372.25	-362.42
0.3347	154.30	1.91	-372.98	-363.10
0.4184	150.48	2.17	-375.99	-365.86
0.5021	149.23	2.72	-373.72	-363.04
0.5858	147.87	3.49	-379.01	-367.57
0.6694	145.58	4.14	-374.50	-362.39
0.7531	143.49	4.53	-378.40	-365.91
0.8368	143.05	5.25	-371.67	-358.46
0.9205	140.20	6.10	-380.88	-366.82
1.0042	138.72	6.60	-379.65	-365.10

[a]ΔG's and ε are in kJ mol^{-1} and $R_{\min}/2$ is in pm. [b]ΔG_2 is the free energy of the van der Waals sphere. [c]ΔG_3 is the free energy for the charging step from 0.0 e to +1.0 e. [d]$\Delta G_{\text{hyd}} = \Delta G_1 + \Delta G_2 + \Delta G_3$ is the total free energy of hydration including the entropic contribution, $\Delta G_1 = 7.958$ kJ mol^{-1}.

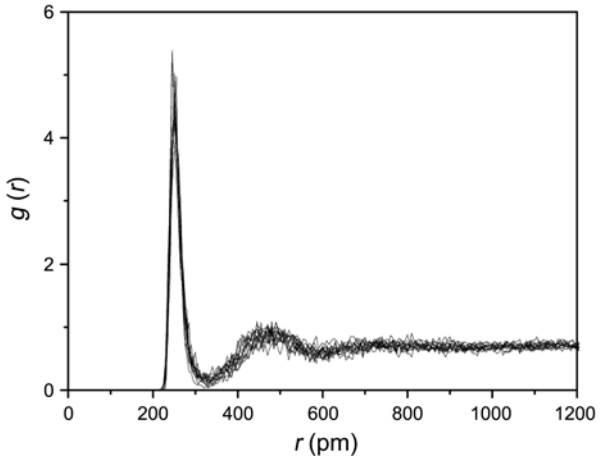


Figure 1. Ion-oxygen RDFs. All 12 RDFs are superimposed as they can hardly be distinguishable.

force fields with the distance parameter $R_{min}/2$ ranging from 139 pm to 170 pm as listed in Table 1.

The thermodynamic perturbation simulation creating the van der Waals atom results in ΔG_2. It shows unfavorable hydration of the uncharged atom up to 6 kJ mol^{-1}. The free energy change upon charging to +1e, ΔG_3, dominates the total ΔG_{hyd} and shows the trend of favorable hydration of smaller ions. For the 12 simulations, the ΔG_{hyd} of the sodium ion is averaged to −364 kJ mol^{-1} and the standard deviation is 2.5 kJ mol^{-1}.

The last 17.5 ps trajectory of the fully charged window is used to calculate RDFs. The RDFs of the water oxygen atoms around the ion are shown in Figure 1. All 12 RDFs are superimposed in the figure. The first peak position is at 250.5 ± 3.5 pm. The peak height is 4.69 ± 0.45 and the width at half-maximum is 26.3 ± 3.5 pm.

All RDFs are quantitatively indistinguishable, indicating that thermodynamic state functions that are directly calculated from the RDF are essentially identical, consistent with the ΔG_{hyd} values (Table 1). Therefore, no two experimental observables that are related to RDF may be used to assign a unique set of LJ parameters for a monatomic ion. Thus, if only ΔG_{hyd} values are taken into account, a wide range of LJ parameter pairs equally well represent the ion in molecular dynamics simulations.

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