

ADDITIONS AND CORRECTIONS

Christopher J. Fennell,* Alan Bizjak, Vojko Vlachy, Ken A. Dill, Sapna Sarupria, Sowmianarayanan Rajamani, and Shekhar Garde: Ion Pairing in Molecular Simulations of Aqueous Alkali Halide Solutions

Page 6782. Following the publication of “Ion Pairing in Molecular Simulations of Aqueous Alkali Halide Solutions”, we offer a correction and a comment. First, one of the sets of force field parameters we tested had errors. We show here new results with the corrected parameters. The corrections do not change the PMFs for ions with sizes similar to the surrounding water, to within error, but they do change the PMFs when the ions are much smaller or larger, like Li and I. Interestingly, the new results lead to better agreement with experiments that are captured in the so-called Volcano relationship or the Law of Matching Water Affinities of Collins. Second, however, our simulations remain unable to resolve whether certain salts associate in water, in part, as noted before, because of limitations in interpreting dielectric relaxation spectroscopy experiments. These new calculations also bring to light the importance of choices of mixing rules used in ion–water computer simulations.

We recently described extensive computer simulations of the pairwise PMFs of different ion types using different water models and different force field parameters.¹ After publication, Sarupria, Rajamani, and Garde noticed a flaw in the implementation of one of our sets of ion parameters. We describe here new results of those cases with the corrected parameters. Most of our previous tests were on OPLS ions. However, we reported also a few simulations using the ion parameters from Dang and Jensen and Jorgensen (JJ). There was an inadvertent error in our reporting of Dang parameters and their use in simulations. Specifically, in Table 1 of the original article we reported LJ parameters that are ion–SPC water values, not the ion–ion values we intended to report. The associated Supporting Information now gives the proper unmixed parameters. The association constants and PMFs in the original Supporting Information and the Dang ion potassium fluoride PMF in the original Figure 3 were calculated by inadvertently using the mixed parameters in place of the bare ion values. We have now corrected this. Association constants and PMFs using the correct values are now included in the associated Supporting Information.

What conclusions are affected from the original article? In our original calculations, the Dang ions showed less variability in their association behavior. Those simulated ions were primarily dissociated in solution. Using the proper LJ values shows a much richer ion-pairing behavior. First, however, the correction does not change the behaviors we reported for ions having sizes similar to that of water (e.g., K and F), as shown Figure 1a. Correspondingly, the resulting association constants before and after the parameter correction overlap within error. In contrast, for ions significantly smaller or larger than water (e.g., Li and I), the corrected parameters predict a very different behavior. The new calculations suggest that LiI pair is primarily dissociated in solution, as shown in Figure 1b.

The corrected Dang parameters give ion-pairing association constants more in line with experimental solubility trends for the alkali halides.² LiF is predicted to be insoluble and the

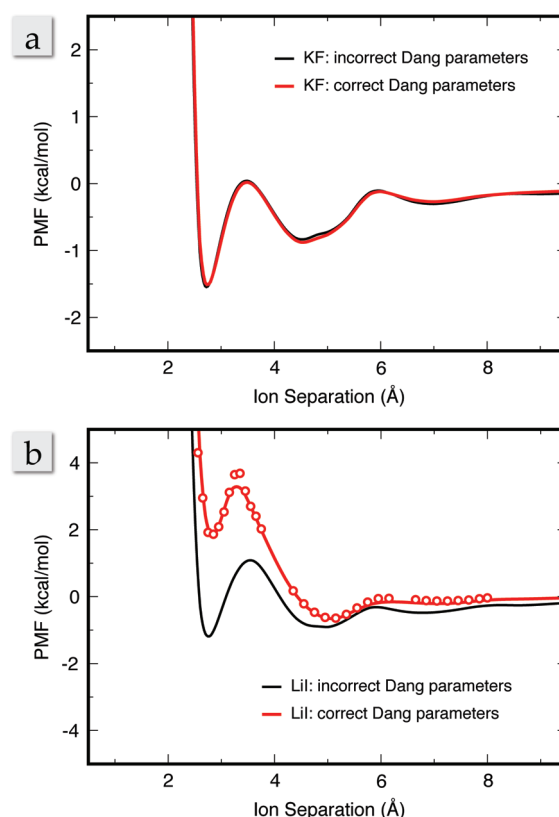


Figure 1. PMFs of (a) KF in TIP3P water and (b) LiI in SPC/E water using the incorrect LJ parameters of the original article and the correct Dang ion parameters. Similarly sized ions like K^+ and F^- show nearly no change in the PMF, while the dissimilarly sized Li^+ and I^- show distinctly different association behavior. The circles on the LiI plot are from a single 25 ns simulation at ~ 1 M salt concentration, showing the equivalence of extended simulations with the constraint technique used both here and in the original article.

resulting association constants for all water models are quite large (see the Supporting Information). All other salts remain dissociated in solution to varying degrees. The corrected Dang ion parameters predict ion–ion interactions that now follow the Law of Matching Water Affinities more closely than either the OPLS or JJ ions. Consider the changes in PMFs for iodide salts in TIP3P water for the OPLS and correct Dang ions shown in Figure 2. One expects increasing association of cations with iodide as the cation size is increased from lithium to cesium. This is not the case with the OPLS ions, as the CIP free energies in the PMFs actually increase. In contrast, the expected trend is readily apparent for the Dang ions where the decrease in the free energy of the CIP state is significant.

Why is there such a difference in the ion pairing behavior between the OPLS and Dang ions? Both sets of ions have been independently parametrized with the goal of reproducing experimental ion hydration data,^{3–5} and ion pairing behavior is not directly considered in these fitting processes. Only recently have investigations into ion pairing behavior led to detailed assessment of the specific ion parameters.^{1,6–10}

A key conclusion from our present simulations is the importance of the Lennard-Jones mixing rules, which differ for

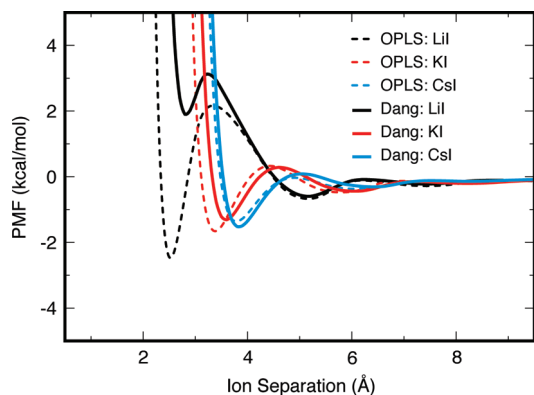


Figure 2. PMFs of LiI, KI, and CsI in TIP3P water using the OPLS ion parameters (dashed lines) and Dang ion parameters (solid lines). The OPLS ions show a shallowing of CIP depth with increasing ion size, and the association constants integrated from these PMFs are the same within error. In contrast, the Dang ions demonstrate the increasing association of iodide with larger cations clearly, consistent with the Law of Matching Water Affinities.

the different ion parameter sets. There are two main choices made: geometric or arithmetic mixing rules. OPLS and Åqvist ion–water parameters use the geometric mean to choose the size parameters (σ).^{3,11} In contrast, the AMBER force field and Dang ion–water parameters choose parameters using the arithmetic mean for σ .^{5,12–14} For species, such as ions, that have net formal charge, the electrostatic interactions are large enough that how these mixed σ values are determined become important and can lead to unexpected behavior such as ion aggregation in aqueous solution.^{6,8}

Is there a correct choice of mixing rules? In the simulation of hard-spheres, or theories of primitive or restricted primitive models of ion solutions,^{15–18} use of an arithmetic mean for the ion–ion σ is more physical and more appropriate because it respects the excluded volume of the individual ions. At contact, the separation distance will be the sum of the independent ion radii, and an arithmetic mean will capture this exactly. For soft spheres of the various molecular mechanics force fields, comparisons to experimental quantities tend to drive the acceptance of a select set of parameters or techniques. For ion pairing, the scarcity of definite experimental numbers makes such determinations challenging. Recent comparisons to Setchenow coefficients and conductance data show that the OPLS ion model is good.^{7,9}

We find here that the Dang treatment with its arithmetic mean mixing rules are better able to reproduce the experimental trends captured in the Law of Matching Water Affinities.^{2,19–21} Suggestions by Auffinger et al. are similar for the AMBER force field,⁶ and recent calculations of osmotic coefficients with the Dang ions appear to confirm the experimental viability of some of these salt combinations.²² Thus, the use of arithmetic mixing rules that properly account for the excluded volumes of ions appears to be important for consistency with experiments.

Finally, we note that our new simulations still do not resolve whether LiCl, LiBr, or other lithium salts should associate in solution. In the original manuscript, we stated that aggregates observed in recent studies^{9,23} are likely an artifact of chosen

modeling parameters. OPLS and JJ anions associate with lithium or not, depending on what water model is used. In contrast, lithium ions dissociate from the Dang anions, irrespective of the water model. Unfortunately, experiments are not decisive enough to fully resolve this issue. The dielectric relaxation spectroscopy (DRS) experiments discussed in the original manuscript, like conductivity experiments, require model-dependent interpretation.^{24,25} Whether two ions are paired or not cannot be determined in a model-free way. Because of the fit to the model used by Wachter et al.,²⁵ the association constants determined by DRS are not directly comparable to those we calculate here.

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Supporting Information Available: Updated version of Figure 9 of original manuscript. Table of ion association constants. Figures of corrected potential of mean force plots. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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