



# Consensus on the solubility of NaCl in water from computer simulations using the chemical potential route

A. L. Benavides, J. L. Aragones, and C. Vega

Citation: The Journal of Chemical Physics **144**, 124504 (2016); doi: 10.1063/1.4943780 View online: http://dx.doi.org/10.1063/1.4943780 View Table of Contents: http://scitation.aip.org/content/aip/journal/jcp/144/12?ver=pdfcov Published by the AIP Publishing

Articles you may be interested in Temperature-dependent solubilities and mean ionic activity coefficients of alkali halides in water from molecular dynamics simulations J. Chem. Phys. **143**, 044505 (2015); 10.1063/1.4926840

Molecular dynamics study of salt–solution interface: Solubility and surface charge of salt in water J. Chem. Phys. **140**, 144705 (2014); 10.1063/1.4870417

Solubility of NaCl in water by molecular simulation revisited J. Chem. Phys. **136**, 244508 (2012); 10.1063/1.4728163

Solubility of KF and NaCl in water by molecular simulation J. Chem. Phys. **126**, 014507 (2007); 10.1063/1.2397683

Calculation of the melting point of NaCl by molecular simulation J. Chem. Phys. **118**, 728 (2003); 10.1063/1.1522375



teuse of AIP Publishing content is subject to the terms: https://publishing.aip.org/authors/rights-and-permissions. Downloaded to IP: 147.96.12.14 On: Wed, 30 Mar 2016 09:18:55

## THE JOURNAL OF CHEMICAL PHYSICS 144, 124504 (2016)



# Consensus on the solubility of NaCl in water from computer simulations using the chemical potential route

A. L. Benavides,<sup>1,a)</sup> J. L. Aragones,<sup>2,b)</sup> and C. Vega<sup>1,c)</sup>

 <sup>1</sup>Departamento de Química Física, Facultad de Ciencias Químicas, Universidad Complutense de Madrid, 28040 Madrid, Spain
 <sup>2</sup>Department of Materials Science and Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA

(Received 28 October 2015; accepted 29 February 2016; published online 23 March 2016)

The solubility of NaCl in water is evaluated by using three force field models: Joung–Cheatham for NaCl dissolved in two different water models (SPC/E and TIP4P/2005) and Smith Dang NaCl model in SPC/E water. The methodology based on free-energy calculations [E. Sanz and C. Vega, J. Chem. Phys. **126**, 014507 (2007)] and [J. L. Aragones *et al.*, J. Chem. Phys. **136**, 244508 (2012)] has been used, except, that all calculations for the NaCl in solution were obtained by using molecular dynamics simulations with the GROMACS package instead of homemade MC programs. We have explored new lower molalities and made longer runs to improve the accuracy of the calculations. Exploring the low molality region allowed us to obtain an analytical expression for the chemical potential of the ions in solution as a function of molality valid for a wider range of molalities, including the infinite dilute case. These new results are in better agreement with recent estimations of the solubility obtained with other methodologies. Besides, two empirical simple rules have been obtained to have a rough estimate of the solubility of a certain model, by analyzing the ionic pairs formation as a function of molality and/or by calculating the difference between the NaCl solid chemical potential and the standard chemical potential of the salt in solution. © *2016 AIP Publishing LLC*. [http://dx.doi.org/10.1063/1.4943780]

# I. INTRODUCTION

The study of salt solutions is relevant in different areas of knowledge. Salts are found in biological, geochemical, and industrial problems. For this reason, it is not surprising that many theoretical<sup>1–4</sup> and computer simulation studies have been devoted to the study of salt solutions. The study of NaCl solutions is particularly relevant as it is the main ionic component of sea water. A key ingredient when performing computer simulations is the choice of the intermolecular potential (i.e., force field). In the case of solutions, the force field should describe the interactions between the molecules of water, the interactions between the ions, and the cross interactions between the ions and the molecules of water.

Quite often, water is described by a simple rigid nonpolarizable model, and the ions are described as simple Lennard–Jones (LJ) charged centers. The parameters of the ion–ion interactions are usually determined to reproduce properties of NaCl in the solid phase,<sup>5</sup> while the parameters of the ion–water interaction are adjusted to reproduce some hydration properties<sup>6</sup> (enthalpies, free-energies) of the individual ions of the salt at infinite dilution or derivatives of the activity coefficient with respect to salt concentration.<sup>7,8</sup> In the last decade, it has become more obvious that phase equilibria can also be used to determine the parameters of the force field. In the particular case of water, the study of the vapor-liquid and liquid-solid equilibria has been proved to be very useful in designing intermolecular potentials.<sup>9</sup> One may wonder if a similar approach can also be useful in the case of ionic solutions. Several simulation works have studied ionic solutions.<sup>10-28</sup> Some of these works have used models that consider an explicit solvent and have been tested by comparing their predictions to some experimental properties. Solubility of salts in water is an interesting property to consider when developing force fields. However, solubility is not an easy problem using simulation studies, specially, when one considers an explicit solvent. That may explain why the study of the solubility for model potentials has not received much attention until very recently.

The first reported calculation of the solubility for an ionic system is the work of Ferrario *et al.*<sup>29</sup> for KF. Later on Sanz and Vega<sup>30</sup> determined the solubility for KF and NaCl. The solubility of NaCl was computed by Paluch *et al.*<sup>31</sup> Since there were some discrepancies between the results of Paluch *et al.* and Sanz and Vega,<sup>30</sup> even though both groups used the same force field, the problem was revisited by Aragones *et al.* in 2012.<sup>32</sup> Some years ago Smith and co-workers developed the osmotic ensemble Monte Carlo (OEMC), which allows to determine the concentration of the salt for a certain imposed value of the chemical potential and the solubility, using this route, for a number of different potential models.<sup>33,34</sup> Mester and Panagiotopoulos<sup>35,36</sup> have performed the calculation of

<sup>&</sup>lt;sup>a)</sup>On sabbatical leave from Departamento de Ingeniería Física, División de Ciencias e Ingenierías, Universidad de Guanajuato, Loma del Bosque 103, Col. Lomas del Campestre, CP 37150 León, Guanajuato, Mexico. Electronic mail: alb@fisica.ugto.mx

<sup>&</sup>lt;sup>b)</sup>Electronic mail: aragones@mit.edu

<sup>&</sup>lt;sup>c)</sup>Electronic mail: cvega@quim.ucm.es

the solubility of NaCl in water using different force fields. It is clear that the interest in obtaining the solubility of a salt dissolved in water by computer simulations has notoriously increased.<sup>31-46</sup> In some of these papers, the solubility was calculated by computing the chemical potential of the salt in the solid phase first, followed by a calculation of the chemical potential of the salt in solution at different concentrations (or in the case of the OEMC by performing one single simulation imposing the chemical potential of the solid phase). This is so because the chemical potential of NaCl in both phases, solid and solution, at equilibrium should be identical (chemical potential route). However, this is not the only way of determining the solubility. Another possibility is to use the direct coexistence method, in which a slab of salt is put in contact with water until equilibrium (at a certain T and p) is reached.<sup>47</sup> This approach was used by Joung and Cheatham,<sup>48</sup> Aragones et al.,<sup>32</sup> Kobayashi et al.,<sup>43</sup> Manzanilla-Granados et al.,<sup>46</sup> and Wiebe et al.<sup>45</sup>

What is the current status of the field? First, it is now clear that solubility changes dramatically from one force field to another. Second, the majority of the used force fields underestimate significantly the experimental value of the solubility of NaCl in water (even for models where polarization is included<sup>10,44</sup>). It is not yet clear what is the reason for that and further work is needed to understand that in more detail. In addition, it is clear that the solubility will be quite useful in the future to design good force fields for salt solutions. However, before this is achieved, there are some technical issues that need to be addressed. The solubility of a certain force field is unique and should not depend on the methodology used to determine it.

In Table I the solubility values of two popular force fields of NaCl in water (as described by the SPC/E model<sup>49</sup>) are presented. Results were obtained by different groups using different methodologies. The first issue to be addressed is that the solubility obtained from direct coexistence methods is generally much higher than the one obtained from the chemical potential route. This is certainly striking as in the past it has been shown that coexistence properties obtained from direct coexistence simulations<sup>50</sup> and from the chemical potential route were in quite good agreement for systems like hard spheres,<sup>47,51</sup> LJ,<sup>52</sup> water,<sup>53</sup> patchy colloidal models,<sup>54</sup> methanol,<sup>55</sup> hydrates,<sup>56,57</sup> or ionic melts.<sup>58</sup>

The SD/SPC/E solubility reported by different groups, by the chemical potential route, ranges from 0.6m to 0.9m, which is a reasonable agreement taking into account the expected uncertainty of the calculations. However, for the JC/SPC/E model,<sup>48,59</sup> the situation is not satisfactory. Moucka et al.<sup>37</sup> reported a solubility of 4.8(3)m using the generalized reaction field approach for the electrostatics in solution and the experimental value of  $\mu_s = -384.024$  kJ/mol. The value of 4.8*m* was also obtained by Aragones *et al.*<sup>32</sup> using Ewald sums. Later on Moucka et al.40 using the Ewald method reported a value of 3.64(20)m. Mester and Panagiotopoulos<sup>35</sup> reported a value of 3.59(4)m and later on of 3.71(4)m.<sup>36</sup> The values reported by Kobayashi et al.<sup>43</sup> range from 2.79m to 6.52m. Before studying in more detail the origin of the discrepancy of the solubility between the direct coexistence technique and the chemical potential route, it seems necessary to have a reliable value obtained from the chemical potential route.

In this work, we will repeat the calculations leading to the solubility of both, SD/SPC/E and JC/SPC/E models, using the same methodology that was described in our previous works (2007, 2012), but now using much longer runs by taking advantage of the possibility of implementing this methodology with the GROMACS<sup>60</sup> package. After revisiting the problem, we have found that the re-computed values of the solubility are in very good agreement with those reported by Moucka *et al.*<sup>40</sup> and by Mester and Panagiotopoulos.<sup>36</sup> Since these

Model	Authors		Method	$m_s \; (\mathrm{mol} \; \mathrm{kg}^{-1})$	
JC/SPC/E	Joung and Cheatham <sup>48</sup>	2009	Direct coexistence method	7.27(7)	
	Moucka <i>et al.</i> <sup>37</sup>	2011	Chemical potential route	4.0(2) <sup>a</sup>	
	Aragones et al. <sup>32</sup>	2012	Chemical potential route	4.8(3)	
	Aragones et al. <sup>32</sup>	2012	Direct coexistence method	5.5(4)	
	Moucka <i>et al.</i> <sup>40</sup>	2013	Chemical potential route	3.64(20)	
	Kobayashi et al.43	2014	Direct coexistence method	6.20	
	Mester and Panagiotopoulos <sup>35</sup>	2015	Chemical potential route	3.59(4)	
	Mester and Panagiotopoulos <sup>36</sup>	2015	Chemical potential route	3.71(4)	
	Manzanilla–Granados et al. <sup>46</sup>	2015	Direct coexistence method	5.9(3)	
	This work	2015	Chemical potential route	3.71(25)	
SD/SPC/E	Aragones et al. <sup>32</sup>	2012	Chemical potential route	0.9(4)	
	Aragones et al.32	2012	Direct coexistence method	1.9(4)	
	Moucka <i>et al.</i> <sup>40</sup>	2013	Chemical potential route	0.61	
	Mester and Panagiotopoulos <sup>35</sup>	2015	Chemical potential route	0.61(1)	
	Mester and Panagiotopoulos <sup>36</sup>	2015	Chemical potential route	0.63(1)	
	This work	2015	Chemical potential route	0.68(08)	
JC-SPC/E-ion/TIP4P/2005	This work	2015	Chemical potential route	3.49(28)	
9					

TABLE I. Solubility  $m_s$  for JC/SPC/E, SD/SPC/E, and JC-SPC/E-ion/TIP4P/2005 models at p = 1 bar and at T = 298 K or T = 298.15 K, according to the case. Ewald sums were used in all calculations.

<sup>a</sup>This value was obtained from a linear interpolation for the Ewald summation chemical potential results presented in Figure 6, in the work of Moucka *et al.*<sup>37</sup> in conjuction with the experimental solid chemical potential value  $\mu_s = -384.024$  kJ/mol.

three groups have now quite similar values of the solubility, even though they compute the chemical potential of the salt in water using different approaches, this strongly suggests that the solubility, at least for these two potential models, is firmly established. The reason why it is different from that obtained from direct coexistence simulations should be investigated in the future. Finally, we shall consider three interesting issues.

First, since the JC/SPC/E model is the best model available so far when predicting the solubility (although still far from the experimental value), we shall consider the possibility of replacing the SPC/E model of water by TIP4P/2005<sup>61</sup> while keeping the ion–ion interactions and using Lorentz–Berthelot (LB) rules<sup>62,63</sup> to describe the ion-water interactions. A similar study was presented by Moucka *et al.*<sup>33</sup> by using a hybrid JC-TIP4P-Ew-ion/TIP4P/2005 force field. It will be shown that the solubility is not affected too much by replacing SPC/E by TIP4P/2005 water, as found by Moucka *et al.*<sup>33</sup> with the other water model replacement.

Second, we will consider the problem of ion pair formation. It is difficult to determine the number of ionic pairs from experiments, whereas it is relatively straightforward from simulations. It will be shown that for the models considered in this work, the number of ionic pairs is of about 0.075 when the ions concentration reaches the value of the solubility. This empirical rule may be quite useful to have a first rough of the solubility of a certain force field.

Third, after analyzing some of the results for the models considered in this work and some others, we provide a simple prescription to estimate the solubility value of a model force field by calculating only the difference between the NaCl solid chemical potential and the standard chemical potential of the salt in solution.

#### **II. METHODOLOGY**

The solubility can be determined by calculating the chemical potential of the salt (composed of ions X and Y) in the solid phase,  $\mu_{XY}^{solid}$ , and the chemical potential of the salt into the solvent,  $\mu_{XY}^{solution}$ , as a function of the composition of the solution. For some particular conditions of temperature, *T*, and pressure, *p*, the solubility can be then obtained by determining at which composition the chemical potential of the salt is identical to that of the pure solid, i.e., solving the equality:  $\mu_{XY}^{solid} = \mu_{XY}^{solution}$ .

The chemical potential of the salt in the solid phase can be easily calculated, for instance, with the Einstein crystal method<sup>64</sup> or with the Einstein molecule method.<sup>65–68</sup> Thus, the main problem in the determination of the solubility is the calculation of the chemical potential of the salt in solution,

$$\mu_{XY}^{solution} = \left(\frac{\partial G_{solution}}{\partial N_{XY}}\right)_{T,p,N_w},\tag{1}$$

where  $G_{solution}$  is the total Gibbs free-energy of the solution,  $N_{XY}$  is the number of salt molecules in solution, and  $N_w$  is the number of solvent molecules. From thermodynamics, the solution Gibbs free-energy can be expressed as

with  $A_{solution}$  being the solution Helmholtz free–energy, p the pressure, and V the volume. Therefore, the problem reduces to obtain  $A_{solution}$  and  $pV_{solution}$  varying  $N_{XY}$  while keeping  $N_w$  constant and use them in Eq. (1) to compute  $\mu_{XY}^{solution}$ .

By selecting a fixed number of solvent molecules, temperature and pressure, NpT molecular dynamics simulations can be used to obtain the  $pV_{solution}$  term, and the volume and density for different salt concentrations. The solution Helmholtz freeenergy can be then computed following the methodology described by Aragones *et al.*,<sup>32</sup> where  $A_{solution}$  is expressed as the sum of two contributions,

$$\frac{A_{solution}}{k_B T} = \frac{(A_{solution}^{id} + A_{solution}^{res})}{k_B T}$$
$$= N_w \ln \left(\rho_W \Lambda_b^3\right) + 2N_{XY} \ln \left(\rho_{XY} \Lambda_b^3\right)$$
$$- N_w - 2N_{XY} + \frac{A_{solution}^{res}}{k_B T}, \tag{3}$$

where  $k_B$  represents the Boltzmann's constant and  $A_{solution}^{id}$  term corresponds to the Helmholtz free-energy of an ideal ternary mixture (X, Y, and w). In this work, the de Broglie thermal wavelength of all species was settled to  $\Lambda_b = 1$  Å, and the internal partition function of all species to one to be consistent with the choice made in previous works for the estimation of the Helmholtz free-energy of NaCl in the solid phase. The term  $A_{solution}^{res}$  is a residual term that is not known and can be calculated by Hamiltonian integration. With this method, the XY solution is transformed into a pure reference system, for which  $A_{ref}^{res}$  is known. The transformation of the salt solution into a pure reference fluid can be done by introducing a coupling parameter  $\lambda$  in the Hamiltonian of the system,

$$U(\lambda) = \lambda U_{ref} + (1 - \lambda)U, \qquad (4)$$

so that when  $\lambda = 1$ , the particles of the system interact through a reference potential and when  $\lambda = 0$ , one recovers the original salt solution. Then, the residual free-energy of the solution can be obtained from Hamiltonian integration as

$$A_{solution}^{res} = A_{ref}^{res} + \int_0^1 \langle U - U_{ref} \rangle_{N,V,T,\lambda} d\lambda = A_{ref}^{res} + A^{integral}.$$
(5)

The integrand in this equation can be obtained for a certain composition, temperature and several values of  $\lambda$  (from 0 to 1) by using NVT simulation runs at the equilibrium density of salt solution. This density can be taken from the NpT simulation data previously performed to compute the pV term, or by a suitable fit to the density as a function of  $N_{XY}$  from those NpT simulations. For each concentration, having obtained the integrand for each  $\lambda$  value considered, a Simpson numerical integration program was used to compute the integral. Once the integral has been evaluated and we have  $G_{solution}$  for each concentration, there are several ways to compute the chemical potential of NaCl in solution, Eq. (1), as, for example.

1. To make a polynomial fit to  $G_{solution}$  as a function of the number of salt molecules  $N_{\text{NaCl}}$ , as done by Sanz and Vega in 2007. This is certainly not a good option as was discussed elsewhere.<sup>32</sup>

Reuse of AIP Publishing content is subject to the terms: https://publishing.aip.org/authors/rights-and-permissions. Downloaded to IP: 147.96.12.14 On: Wed, 30 Ma

2. To make a polynomial quadratic fit to  $G_2 = A_{solution}^{res}$ +  $pV_{solution}$  as a function of concentration, which is then substituted in the analogous equation to Eq. (2),  $G_{solution}$ =  $A_{solution}^{id}$  +  $G_2$ , to obtain a complete analytical expression for  $G_{solution}$  for each concentration; this route will be referred hereafter as fit  $G_2$  (see Aragones *et al.*<sup>32</sup> for details). This is a much better option and in general provides the correct value of the solubilities except when the solubility of the model is very small and falls in the Debye-Hückel regime (we shall return to this point later).

In any case, of course, regardless of the procedure used to analyze the free energies, it is necessary that the statistical uncertainty of  $A_{solution}^{res}$  to be small. In that respect, in retrospective our runs of 2007 were too short (by a factor of 80), and those of 2012 were short (by a factor of 20) when compared to those presented in this work. In addition, in this work, we have introduced another procedure to analyze the  $G_{solution}$  results to compute the chemical potential of NaCl in solution, which will be referred hereafter as fit  $G_{solution}$ . It is inspired in the procedure already implemented<sup>30</sup> in 2007 to determine the activity coefficient of the salt. We shall describe it now.

 $G_{solution}$  is an extensive property and therefore it can be expressed in terms of the chemical potentials as

$$G_{solution} = N_w \ \mu_w + N_{\text{NaCl}} \ \mu_{\text{NaCl}}. \tag{6}$$

 $G_{solution}$  is easily obtained from the simulation results as it has been previously discussed here. Moreover, the chemical potential of the NaCl in solution can be expressed in terms of the activity coefficient as

$$\mu_{\text{NaCl}} = \mu_{\text{NaCl}}^{\dagger} + 2RT \ln(m) + 2RT \ln(\gamma), \qquad (7)$$

where  $\mu_{NaCl}^{T}$  is the Henry's law (infinite dilution) standard chemical potential of the salt and  $\gamma_{NaCl}$  is the mean ionic coefficient (on the molality scale), which is a measure of the deviation of the salt chemical potential from the ideal solution. The activity coefficient can be described by the following empirical expression:

$$\ln(\gamma) = \ln(10) \left[ \frac{-AA\sqrt{(m)}}{1 + B\sqrt{(m)}} + \beta m \right],$$
(8)

which formally resembles the Davies's equation, often used to describe activity coefficients of real solutions.<sup>69</sup> In this expression, AA is related with the relative permittivity,  $\kappa$ , of the water model used in the calculations and temperature as  $AA = 1.824 \ 10^6 / (\kappa T)^{3/2}$ . As pointed out by Mester and Panagiotopoulos,<sup>35</sup> it is a good idea to choose AA in this way in order to recover the Debye-Hückel law,<sup>70</sup> which is exact at very low concentrations of the salt. This choice of AA, of course, will depend on the water model under consideration and it could be different from that of real water ( $\kappa = 78$ ). The corresponding AA values for the models considered in this work are presented in Table IV. For the JC/SPC/E and SD/SPC/E, we used the AA values from Table XIII in the work of Mester and Panagiotopoulos<sup>35</sup>, which considered a relative water permittivity of 73. For the JC-SPC/E-ion/TIP4P/2005, we calculated AA using the expression mentioned above with the relative water permittivity value of 58 obtained for the TIP4P/2005 water model by Vega and Abascal.9 In addition, by integrating the Gibbs-Duhem equation, it is possible to relate the parameters AA, B, and  $\beta$ , which describes the activity coefficient of NaCl, to the changes in the chemical potential of water. One then obtains, as shown by Moucka *et al.*,<sup>40</sup>

$$\mu_w = \mu_w^* - 2RTmM_w - RTM_w \ln(10) \left(\beta m^2 + \frac{2AA}{B^3 + B^4\sqrt{(m)}} + \frac{4AA\ln(B\sqrt{(m)} + 1)}{B^3} - \frac{2AA\sqrt{(m)}}{B^2} - \frac{2AA}{B^3}\right),\tag{9}$$

where  $\mu_w^*$  is the standard chemical potential of pure water and  $M_w = 0.018 \text{ kg mol}^{-1}$  its molar mass. Actually,  $\mu_w^*$  is trivially obtained from our calculations by simply dividing the Gibbs free energy of a pure water system (i.e., no ions) between the number of molecules of water. Therefore, in this route, the parameter AA is obtained from physical considerations and  $\mu_w^*$  from our calculations for pure water, and we just need three parameters, namely,  $\mu_{\text{NaCl}}^{\dagger}$ , B and  $\beta$ , to obtain  $G_{solution}$ .

# III. FORCE FIELD MODELS FOR NACL WATER SOLUTION

In order to study NaCl in water, we have considered three different force fields.

 JC/SPC/E. In this force field, water interactions are described through the SPC/E model.<sup>49</sup> The interaction between ions is described using the force field proposed by Joung and Cheatham (JC),<sup>59</sup> specially tailored for the case of the SPC/E water model. The LJ parameters of the crossed interactions between the ions and water are obtained using the LB combination rules. The parameters of this force field are provided in the supplementary material.<sup>71</sup>

- 2. *SD/SPC/E*. Again the SPC/E model is used to describe the water interactions, while the ion–ion and ion–water interactions are given by the Smith–Dang (SD) model.<sup>72,73</sup> The crossed ion–water interaction is determined from the LB combination rules. The parameters of this force field are also provided in the supplementary material.<sup>71</sup>
- 3. *JC-SPC/E-ion/TIP4P/2005*. Unlike the other two force fields, which have already been proposed and considered in the literature, this force field has never been studied before. In this force field water interactions are described by the TIP4P/2005 model, and the ion–ion interactions are identical to those used in the JC/SPC/E force field. The crossed LJ interaction between the ions and water

TABLE II. Parameters for the JC-SPC/E-ion/TIP4P/2005 force field. The parameters for the JC/SPC/E and SD/SPC/E are given in the supplementary material.  $^{71}$ 

LJ interaction	$\epsilon/k_B(\mathbf{K})$	$\sigma$ (Å)	Charge	q ( <i>e</i> )
	Joung-Cheat	ham TIP4P/20	05	
Na <sup>+</sup> –Na <sup>+</sup>	177.457	2.160	Na <sup>+</sup>	+1.0
Cl <sup>-</sup> -Cl <sup>-</sup>	6.434	4.830	Cl-	-1.0
Na <sup>+</sup> -Cl <sup>-</sup>	33.789	3.495		
Na <sup>+</sup> -O	128.604	2.659		
Cl <sup>-</sup> –O	24.488	3.994		
0–0	93.2	3.159		
			Н	0.5564
			М	-1.1128

is also obtained from the LB combination rules. The parameters of this new force field are presented in Table II. The motivation to consider this new force field is twofold. First, we want to determine how sensitive is the solubility to the choice of the particular water model used in the calculations (while keeping the ion-ion interactions). A general conclusion about this problem would require a case by case consideration. SPC/E and TIP4P/2005 were designed to describe the vaporization enthalpy of water only when including the polarization correction.<sup>49,61</sup> This similarity in the enthalpies could imply also similar solubilities. The second motivation was that having TIP4P/2005 instead of the SPC/E model would allow in the future to analyze in detail the effect of salt into properties as the maximum in density, surface tension, melting point, etc., where the performance of TIP4P/2005 for pure water is, in general, superior to that of the SPC/E model.

#### **IV. SIMULATION DETAILS**

For the three models considered in this work, NpT and free energy calculations were carried out with GROMACS.<sup>60</sup> All NpT simulations were performed at p = 1 bar, T = 298 K, using the Nosé-Hoover thermostat and the Parinello-Rahman barostat, both with a relaxation time of 2 ps. In the NpT runs, we used  $20 \times 10^6$  of MD steps with a 2 fs time step. Averages of properties were obtained from the last 20 ns of the run. The shape of the box was cubic and we used isotropic scaling in the NpT runs. The Lennard-Jones interactions were truncated at 0.9 nm and standard long range corrections (both for pressure and energy) were included. The particle-mesh Ewald summations<sup>74</sup> were used to treat the Coulomb interactions with a 4th-order interpolation function. The constraint algorithm was Lincs. Let us now describe the computational details of the free energy calculations. We have selected a pure Lennard-Jones fluid as the reference fluid,  $U_{ref} = U_{LJ}$ , which residual free energy,  $A_{ref}^{res}$ , was obtained from the Kolafa and Nezbeda equation of state.<sup>75</sup> The parameters of the LJ reference fluid used in all the calculations were  $\epsilon_{ref}/k_B = 78.2$  K and  $\sigma_{ref} = 3.14$  Å.

To compute the free energy of the NaCl solutions, we carried out simulations in the NVT ensemble to obtain the integrand in Eq. (5).

For the solubility estimation, the free energy was computed only up to a concentration slightly higher than the solubility reported for each model, 4.112m (20 NaCl) for the JC/SPC/E and JC-SPC/E-ion/TIP4P/2005 models, and 1.028m (5 NaCl) for the SD/SPC/E/ model.

Again, simulations were performed at 298 K using a Nose–Hoover thermostat<sup>76,77</sup> with a relaxation time of 2 ps and a time step of 2 fs. The calculations started with the original system (i.e.,  $\lambda = 0$ ) and we used in total 21 different values of  $\lambda$  to evaluate the integral of Eq. (5). The  $\lambda$  values considered were 0, 0.02375, 0.0475, 0.07125, 0.095, 0.14875, 0.2025, 0.31, 0.4175, 0.525, 0.6325, 0.74, 0.8475, 0.90125, 0.955, 0.9625, 0.97, 0.9775, 0.985, 0.9925, and 1. The selection of the  $\lambda$  spacing was chosen according to the integrand function in order to best reproduce it with an optimized number of  $\lambda$ 's (see the supplementary material<sup>71</sup>). For each value of  $\lambda$ , the initial configuration was taken from the last configuration of the previous (and smaller) value of  $\lambda$ . The integral of Eq. (5) was evaluated using the Simpson's integration method. For the JC/SPC/E and SD/SPC/E free-energy calculations, we used  $2 \times 10^6$  time steps (i.e., 4 ns) for each value of  $\lambda$ . In addition, for the JC/SPCE/E and SD/SPC/E, three to five independent calculations of the free energy were performed for each solution.

The purpose was to have accurate results to compare with those reported recently by Moucka *et al.*<sup>40,41</sup> and Mester and Panagiotopoulos<sup>36</sup> for these systems. In the case of the JC-SPC/E-ion/TIP4P/2005, we used only one free energy calculation per solution, but now using  $4 \times 10^4$  steps (i.e., 8 ns). In all cases, the average value of the integrand of Eq. (5) was obtained for each value of  $\lambda$  from the last 3 ns of the run (i.e., discarding the results of the first ns). The rest of simulation details in these free-energy calculations were identical to those of the NpT simulations, except that no barostat was considered.

## V. RESULTS

We will start our discussion by considering the JC/SPC/E model since for this model, there are more available solubility studies in the literature to compare with and it will help us to describe the application of the methodology that will be used later for the other two models. In this work, experimental density data were taken from a polynomial expression<sup>78</sup> and for the rest of properties we used Hamer and Wu<sup>79</sup> analytical expressions that are representative of the original experimental data.

#### A. JC/SPC/E

To evaluate the solubility, both the NaCl solid chemical potential and the NaCl chemical potential in solution are needed. For the former, we used the result obtained by Aragones *et al.*,<sup>32</sup>  $\mu_{\text{NaCl}}^{solid} = -384.12$  kJ/mol (using the reference state labeled as ref2 as will be discussed later). It is important to remark that the JC force field is a successful model

that reproduces almost exactly the experimental value of the chemical potential of the solid,  $\mu_{\text{NaCl,Exp}}^{solid} = -384.024 \text{ kJ/mol.}$ 

For the determination of the chemical potential of NaCl in solution, a fixed number of water molecules was used, namely,  $N_w = 270$ . Thus, the different concentrations considered were matched by changing the number of ions. We first performed NpT simulations of the NaCl solutions, from which the densities of the solutions were obtained (both in units of mass per unit of volume and number density of particles). In Fig. 1 the experimental density of the NaCl in water is compared to the simulation results for the JC/SPC/E force field at different molalities m (i.e., number of moles of NaCl per kg of water). As it can be seen, the density of the solutions varies smoothly with the salt concentration. In addition, this model reproduces the experimental densities at low and intermediate concentrations but overestimates them at higher concentrations, in agreement with available simulation data of other authors.

The density as a function of the number of NaCl for all concentrations considered (N $_{\text{NaCl}}$  between 0 and 25) is well represented by a third-order polynomial in terms of the number of NaCl as

$$\rho(N/\text{\AA}^3) = r_0 + r_1 N_{\text{NaCl}} + r_2 N_{\text{NaCl}}^2 + r_3 N_{\text{NaCl}}^3, \quad (10)$$

where N is the total number of particles per unit volume,  $N = N_w + 2N_{\text{NaCl}}$ , and  $r_i$  are the fitting parameters tabulated in Table III.

We then performed the Hamiltonian integrations from the real system to the LJ reference system in the NVT ensemble at the equilibrium densities obtained from the NpT runs. The results of the Hamiltonian integration are presented in the supplementary material.<sup>71</sup> From these results we computed the Gibbs free energy of the solutions at the different concentrations considered. The chemical potential of NaCl in solution is then obtained from the derivative of the Gibbs free energy with respect to the number of NaCl molecules at *p*, T, and  $N_w$  constant (Eq. (1)). As already discussed in Sec. II, one possible approach is the route referred as fit  $G_{solution}$ , where the Gibbs free energies of the solutions are fitted to Eqs. (6)-(9); the parameters of this fit for the JC/SPC/E model



FIG. 1. Density versus NaCl molality for the JC/SPC/E and JC-SPC/Eion/TIP4P/2005 force fields compared to the experimental values (as indicated in the legend).

TABLE III. Coefficients for the polynomial fits to the number density  $\rho(N/Å^3)$  as a function of the number of NaCl molecules used in the solubility calculus for the three force fields considered in this work.

Model	$r_0 \cdot 10$	$r_1 \cdot 10^3$	$r_2 \cdot 10^5$	$r_3 \cdot 10^7$
JC/SPC/E	0.334 133	0.153 941	-0.235 243	0.141 983
SD/SPC/E	0.334 119	0.129 930	-0.25298	0.0
JC-SPC/E-ion/TIP4P/2005	0.333 482	0.172770	-0.308 400	0.268 313

are tabulated in Table IV. The absolute values of the standard chemical potential depend on the arbitrary choice of the de Broglie wavelength. In Table IV, the results labeled as ref1 correspond to a reference state where  $\Lambda_b = 1$  Å. To compare with the experimental results, where a difference reference state is chosen, it is necessary to add a constant,  $C_i$ . For the NaCl the value of the constant is  $C_{\text{NaCl}} = 386.8 \text{ kJ/mol}$ , whereas for water one should use  $C_w = -202.256 \text{ kJ/mol}$ (see Appendix B of Aragones et al.<sup>32</sup> for the justification of these constants). The chemical potentials consistent with the reference state are labeled as ref2 in Table IV.

The chemical potential of NaCl in the solid phase (green horizontal line) and in solution is presented in Fig. 2 as a function of molality. The solubility of NaCl in water is determined by the intersection of the two NaCl chemical potentials and is 3.71m. This recalculated solubility is now closer to the values reported by Moucka et al.<sup>40,44</sup> and Mester and Panagiotopoulos<sup>36</sup> showing the equivalence of the three methodologies. It is also shown in this figure that regardless of the procedure used to analyze the free energies of this work, fit to  $G_{solution}$  or to  $G_2$ , the same solubility is obtained. Therefore, the method used to fit the Gibbs free energies does not affect the value of the solubility, and one can even use finite differences to estimate the chemical potential,

$$\mu_{\text{NaCl}}\left(\frac{N_{\text{NaCl},2} + N_{\text{NaCl},1}}{2}\right)$$
$$= \frac{G_{\text{solution}}(N_{\text{NaCl},2}) - G_{\text{solution}}(N_{\text{NaCl},1})}{(N_{\text{NaCl},2} - N_{\text{NaCl},1})}, \quad (11)$$

where  $N_{\text{NaCl},1}$  and  $N_{\text{NaCl},2}$  are two selected numbers of NaCl in solution considered cases.

As it can be seen in Fig. 2, the chemical potential obtained from finite differences (magenta triangles) is fully consistent with that obtained from the other two routes to analyze the results (i.e., fit to  $G_2$  or fit to  $G_{solution}$ ). Notice that the predictions of three different groups using three different methodologies are now in agreement for both the solubility and the chemical potentials of NaCl in solution. The solubility calculated by these three groups for this model (i.e., 3.7m) is certainly lower than the experimental value (6.15m), which indicates deficiencies in the force field. In our calculus, we decided not to use results of  $G_{solution}$  at concentrations too much higher than those of the solubility to remove the possible risk of crystal precipitation of the supersaturated solution.<sup>21,82,83</sup> Notice that precipitation of the supersaturated solution would spoil the determination of the free energies, as when using Hamiltonian integration one should not have any phase transition along the integration. Until the issue of salt precipitation is clarified in a future work (i.e., the nucleation of

TABLE IV. Fit parameters for the solution chemical potential of the three models. In all cases, 270 molecules of water were used in the calculations. The chemical potentials are expressed in kJ/mol and the solubilities in mol/kg. In the line labeled with an asterisk, the standard chemical potential of the salt was obtained from the analysis of highly diluted solutions (using 2000 molecules of water instead of 270). Results labeled as ref1, use 1 Å for the thermal de Broglie wavelength. Results labeled as ref2 use the same reference state as used in experiments. The coefficient AA was obtained from the value of the temperature and of the dielectric constant of the considered water model. The standard chemical potential of water was obtained directly by dividing the Gibbs free energy of pure water between the number of water molecules. For the SD/SPC/E and JC-SPC/E-ion/TIP4P/2005, the value of B was fixed to 1.5 and was not optimized.

Model	AA	В	β	$\mu^{\dagger}_{ ext{NaCl}, \mathit{refl}}$	$\mu^*_{w,\mathit{refl}}$	$\mu^{\dagger}_{ ext{NaCl}, \mathit{ref2}}$	$\mu^*_{w,\mathit{ref2}}$	Solubility
JC/SPC/E	0.5677	1.5232	0.1126	-779.01(60)	-38.10(30)	-392.21(60)	-240.36(30)	3.71(25)
JC/SPC/E*	0.5677	0.9045	0.1352	-778.50*(60)	-38.10(30)	-391.70(60)	-240.36(30)	3.68(25)
SD/SPC/E	0.5677	1.5	0.1251	-767.55(60)	-38.10(30)	-380.75(60)	-240.36(30)	0.68(08)
JC-SPC/E-ion/TIP4P/2005	0.803	1.5	0.0922	-776.28(60)	-38.69(30)	-389.48(60)	-240.95(30)	3.49(28)

salt in a supersaturated solution<sup>84-86</sup>), we have decided to be on the safe side and used only  $G_{solution}$  results for concentrations slightly above the solubility limit. In any case, in Fig. 2 the indigo and orange dashed lines represent the extrapolation of our results to concentrations above the solubility limit. Good agreement is found with the estimates of the chemical potential of NaCl in solution reported by Moucka et al.<sup>40,44</sup> and Mester and Panagiotopoulos<sup>35</sup> for the supersaturated solution. It is worth to mention that Mester and Panagiotopoulos<sup>35</sup> have used the BAR method, implemented in GROMACS, for the free energy while we are using Hamiltonian integration, as implemented in GROMACS. Moucka et al.<sup>40,44</sup> have used the Monte Carlo with particle insertion method (OEMC). As it can be seen, the three methods give solubilities that are mutually consistent (within the statistical uncertainties) but at the moment we cannot say which method is the most efficient. In Figure 2 we also have included the Aragones et al.<sup>32</sup> results for the same model, where the solubility predicted was 4.8m. As it can be seen, the main reason for that was that our values of the chemical potential were low, due to insufficient equilibration. The message is that longer runs than those used



FIG. 2. NaCl chemical potential versus molality for the JC/SPC/E model as obtained from the results of this work using either the fit  $G_{solution}$  proposed in this work or the fit  $G_2$  proposed by Aragones *et al.*<sup>32</sup> This figure shows the equivalence of both methodologies. We also have included results of Mester and Panagiotopoulos<sup>35</sup> and Moucka *et al.*<sup>40</sup> Dashed curves represent an extrapolation of our results. The dashed–dotted curve represents the results from Aragones *et al.*<sup>32</sup> The solid NaCl chemical potential is represented by a horizontal line, from Aragones *et al.*<sup>32</sup> Experimental data (black curve) of Hamer and Wu<sup>79</sup> are also included. The estimated uncertainty in the chemical potential of NaCl in solution from this work is of 0.6 kJ/mol.<sup>71,80,81</sup>

in our previous work were needed to determine the chemical potential of the salt in solution with accuracy. We think a similar conclusion can be done for the Kobayashi *et al.*<sup>43</sup> solubility results.

Other interesting properties can be obtained form this chemical potential route as, for example, the excess chemical potential. In Figure 3 the excess NaCl chemical potential as a function of molality is presented together with Mester and Panagiotopoulos results.<sup>36</sup>

As it can be seen, the fit  $G_{solution}$  route, that accounts for the Debye-Hückel law, is able to reproduce the low concentration limiting behavior of Mester and Panagiotopoulos.<sup>36</sup> This behavior is not obtained if one uses the fit  $G_2$  route. Therefore, although the  $G_2$  route was able to provide a correct value of the solubility for this model, it does not provide accurate results of the chemical potential at low concentrations; the region where the excess chemical potential of the salt decreases with the concentration of the salt. For this reason, the fit  $G_{solution}$  route used in this work should be preferred, especially when dealing with salts with low solubilities or when one is interested in the low concentration of the chemical potential of the chemical potential of the chemical potential of the salt in solution. The variation of the salt is connected with



FIG. 3. NaCl excess chemical potential versus molality for the JC/SPC/E. Results of this work using the fit to  $G_{solution}$  (indigo continuous line) and using  $G_2$  fit (orange continuous line), Mester and Panagiotopoulos<sup>35</sup> (red solid circles) data, and experimental results<sup>79</sup> (black continuous line) are presented. Excess chemical potentials obtained as  $\mu_{exc,NaCl} = \mu_{NaCl} - 2RT \ln(\rho_{NaCl}\Lambda_b^3)$  with  $\Lambda_b = 1$  Å.

the variation of the activity coefficient (on the molarity scale) with the concentration. Details about how to relate the activity coefficient on the molality scale (used in this work) with that on the molarity scale are provided in the excellent review of Hamer and Wu.<sup>79</sup>

In Fig. 4(a) the water chemical potential as a function of molality obtained in this work is represented together with the results of Mester and Panagiotopoulos<sup>35</sup> and Moucka *et al.*<sup>40</sup> (as indicated in the legend). The agreement between the three different methods is good. Notice that we are including long range corrections and Mester and Panagiotopoulos<sup>35</sup> it seems they do not. Our calculations are for a temperature of 298 K which is slightly different from that considered for the other two groups (i.e., 298.15 K). In any case the standard chemical potentials of pure water obtained by the three groups,  $\mu^*_{w,ref2}$ , are in agreement (Mester and Panagiotopoulos:<sup>35</sup> –240.20(3) kJ/mol, Moucka *et al.*:<sup>41</sup> –240.30 kJ/mol and this work: -240.36(30) kJ/mol.)

When interested in colligative properties, it is crucial to determine the water activity in the solution.<sup>87</sup> The water activity as a function of molality is shown in Fig. 4(b) together with the Mester and Panagiotopoulos<sup>35</sup> and Moucka *et al.*<sup>40</sup> results. Again the three methodologies provide similar results.

Let us now turn to another interesting property, the NaCl activity coefficient. In Fig. 5 we present the natural logarithm of the mean activity coefficient,  $\ln\gamma$ , as a function of molality. Our results exhibit the same tendency of those from the works of Mester and Panagiotopoulos<sup>35</sup> and Moucka *et al.*<sup>44</sup>

An accurate determination of the activity coefficient is even more challenging than an accurate determination of the chemical potential. The explanation of this apparent paradox is that to estimate  $\gamma$  one needs not only accurate values of the chemical potential, but also accurate values of the standard chemical potential of the salt,  $\mu^{\dagger}_{NaCl}$ . As it was discussed by Sanz and Vega,<sup>30</sup> the value of  $\mu^{\dagger}_{NaCl}$  is related to the excess value of the chemical potential of the salt in solution at infinite dilution. Therefore, to estimate  $\gamma$  with high accuracy, both  $\mu_{NaCl}$  and  $\mu^{\dagger}_{NaCl}$  should be known with high accuracy. For the



FIG. 5. NaCl natural logarithm of the mean activity coefficient,  $\ln \gamma$ , versus molality at 298 K and 1 bar for the JC/SPC/E. Results of this work using  $\mu_{\text{NaCl}}^{\dagger} = -391.70 \text{ kJ/mol}$  (dotted–dashed curve) and  $\mu_{\text{NaCl}}^{\dagger} = -392.21 \text{ kJ/mol}$  (dotted curve) are presented. We have also included Moucka *et al.*<sup>44</sup> (dashed curve) and Mester and Panagiotopoulos<sup>35</sup> (red solid circles). Black solid line represents experimental data of Hamer and Wu.<sup>79</sup> The estimated uncertainty in  $\ln \gamma$  from this work<sup>71,80,81</sup> is 0.17. We have included two points (magenta squares) with their uncertainty to illustrate the error bars on our results at high concentrations.

JC/SPC/E, the values of  $\mu_{\text{NaCl}}^{\dagger}$  (using ref2) reported by Moucka *et al.*,<sup>40</sup> Mester and Panagiotopoulos<sup>36</sup> and in this work are -391.28, -391.70(20), and -392.21(60) kJ/mol, respectively, while the experimental value is -393.13 kJ/mol. Although the results from the different groups are in reasonable agreement the discrepancies seem to be larger than for the chemical potential at finite concentrations. These discrepancies are related to finite size effects in the estimation of  $\mu_{\text{NaCl}}^{\dagger}$ . The methodology described in this work requires to fix the number of molecules of water from the very beginning of the calculations. When using 270 molecules of water, the smallest amount of NaCl that one may have (i.e., one molecule) yields a concentration of 0.206*m*. Since  $\mu_{\text{NaCl}}^{\dagger}$  depends on a property at infinite dilution,<sup>30</sup> one may suspect that  $\mu_{\text{NaCl}}^{\dagger}$  is affected



FIG. 4. (a) Water chemical potential versus molality for the JC/SPC/E model. (b) Water activity versus molality for the JC/SPC/E, SD/SPC/E, and JC-SPC/E-ion/TIP4P/2005 models. Results of this work for the JC/SPC/E model (indigo continuous line), SD/SPC/E (orange continuous line), and JC-SPC/E-ion/TIP4P/2005 model (green continuous line) and their extrapolation predictions (dashed lines) are presented. We have included the work of Mester and Panagiotopoulos<sup>35</sup> ((a) red solid circles and (b) continuous line), Moucka *et al.*<sup>40</sup> (a) blue solid circles and (b) continuous line) and Hammer and Wu<sup>79</sup> (black continuous line) results. Activity of water obtained from  $\mu_w = \mu_w^* + RT \ln(a_w)$ .

by finite size effects (i.e., by the smallest concentration that can be sampled by a certain number of water molecules). To analyze this point in more detail, we have performed new calculations for the JC/SPC/E using 2000 molecules of water and five different concentrations (results are given in the supplementary material<sup>71</sup>),  $N_{\text{NaCl}} = 0, 1, 2, 3, 4$ .

The results for  $G_{solution}$  of these diluted solutions with 2000 molecules of water were fitted using a slightly modified version of the Davies equation<sup>69</sup> (see the supplementary material<sup>71</sup>), and the new  $\mu_{\text{NaCl}}^{\dagger}$  was -391.70(60) kJ/mol which is closer to Mester and Panagiotopoulos,<sup>35,36</sup> -391.70(20) and -391.60(20) who considered in their calculations at high dilution up to 5000 molecules of water. We then fitted the results of G<sub>solution</sub> for 270 molecules of water by imposing  $\mu_{N_{2}Cl}^{\dagger}$  obtained from the simulations of highly diluted solutions in the fit rather than leaving it as free parameter. The results of the fit are presented in Table IV. The activity coefficients computed in this way are also plotted in Fig. 5 (dashed-dotted line). As it can be seen, the agreement with the predictions from Moucka et al.44 and Mester and Panagiotopoulos36 improved. It should be mentioned that with this new fit, the value of the solubility is not modified and one obtains a value of 3.68(25), very close to the value of 3.71(25)m obtained using only the results from the 270 molecules of water study. In summary, when having a small number of molecules of water,  $\mu_{\text{NaCl}}^{\dagger}$  should be considered as a fitting parameter, which provides a reasonable initial guess for the standard potential of the salt. However, since the determination of  $\mu_{NaCl}^{\dagger}$  is affected by finite size effects, an accurate determination of the activity coefficient requires an accurate determination of  $\mu_{\text{NaCl}}^{\dagger}$ , which requires to use systems with a large number of water molecules. Nevertheless, the solubility and the chemical potential at finite concentrations seem to be hardly affected by the system size. In fact, the results of this work using 270 molecules of water are consistent with those of Mester and Panagiotopoulos<sup>36</sup> who used in most of the cases 500 molecules of water. It is clear from the discussion above that our approach to estimate activity coefficients has large error bars, and to reduce them one needs both longer runs (to reduce the error in the determination of chemical potentials at finite concentrations) and larger systems (to improve the predictions at infinite dilution required to estimate the standard chemical potential).

#### B. SD/SPC/E

The densities obtained from the NpT simulations for this model for all the concentrations considered (number of NaCl between 0 to 7) can also be as expressed in terms of the number of NaCl as a third-order polynomial. In Table III the polynomial fit constants are presented. Again, the solid NaCl chemical potential used in this work was obtained by Aragones *et al.*,<sup>32</sup>  $\mu_{\text{NaCl}}^{solid} = -384.07 \text{ kJ/mol}$ . The free energies obtained for this model from Hamiltonian integration are presented in the supplementary material,<sup>71</sup> and the parameters of the fit to  $G_{solution}$  are given in Table IV. For the activity coefficient, it is found that the value of B is commonly close to  $B = 1.5.^{79}$  The same was true for the JC/SPC/E model. For this reason and to reduce the number of parameters, we use the value

B = 1.5 in the fit. We checked that this choice was quite good and that the fit did not improve significantly by allowing this parameter to be adjustable.

The chemical potentials of NaCl in the solid phase and in solution as a function of molality are shown in Fig. 6. The intersection of the two phase NaCl chemical potentials occurs at 0.68*m* in good agreement with Moucka *et al.*<sup>40</sup> and Mester and Panagiotopoulos.<sup>36</sup> In this figure, we have included the results of Mester and Panagiotopoulos<sup>36</sup> and the experimental data. In addition, estimated values of the chemical potential of NaCl in solution using the finite differences method were included as an additional test of our prediction. As it can be seen, the agreement between both simulation methodologies is very good. It should be pointed out that the solubility would be 0.65m if the value -384.28 kJ/mol reported by Moucka et al.<sup>40</sup> was used for the chemical potential of the solid. As it can be seen, the SD/SPC/E model predicts a solubility one order of magnitude smaller than the experimental value. Thus, although the SD/SPC/E model describes fairly well the densities of the NaCl solutions, it fails in the prediction of the solubility value. So, a model that describes very accurately the densities of the NaCl solutions does not necessarily predict good solubilities.

For this model, we predicted in 2012 a solubility (from free energy calculations) of 0.9m, which is only slightly higher than the one reported here. Again, it seems that using longer calculations, the solubility decreases, and good agreement with the results of other groups is also obtained using this methodology.

In Fig. 7 the ln  $\gamma$  as a function of molality is shown for the SD/SPC/E model. Although our results should be taken with care as the standard chemical potential of the salt was obtained from the simulations using 270 molecules of water, the agreement with Mester and Panagiotopoulos<sup>35,36</sup> is good. In Fig. 4 we have included the water activity for this model and found that the results are similar to those of the JC/SPC/E model.



FIG. 6. NaCl chemical potential for the SD/SPC/E model versus molality of this work (indigo continuous line) and its extrapolation (indigo dashed line). Also shown: Mester and Panagiotopoulos<sup>35</sup> (red solid circles), Moucka *et al.*<sup>40</sup> (blue solid squares), finite difference method predictions (magenta triangles up), and experimental data (black continuous line) of Hamer and Wu.<sup>79</sup> The estimated uncertainty in the chemical potential of NaCl in solution from this work<sup>71,80,81</sup> is of 0.6 kJ/mol.



FIG. 7. NaCl natural logarithm of the mean activity coefficient,  $\ln \gamma$ , versus molality at 298 K and 1 bar for the SD/SPC/E. This work (indigo continuous line) and the work of Mester and Panagiotopoulos<sup>35,36</sup> (red solid circles and blue solid diamonds).

# C. JC-SPC/E-ion/TIP4P/2005

For this new model, the densities obtained from the NpT runs can be fitted very well to a third-order polynomial in terms of the number of NaCl. The coefficients of the fit are presented in Table III. In Fig. 1, the density is shown as a function of molality. As for the JC/SPC/E model, this model overestimates the experimental density, specially at high concentrations. Free energies for this model obtained from the Hamiltonian integration runs are presented in Table V.

For the solid NaCl chemical potential, we used the result obtained by Aragones *et al.*,<sup>32</sup>  $\mu_{\text{NaCl}}^{solid} = -384.12 \text{ kJ/mol}$ . Since the ion–ion interactions are identical in the JC/SPC/E and JC-SPC/E-ion/TIP4P/2005 force fields, also the chemical potential of the NaCl in the solid phase. In Fig. 8 the chemical potentials of NaCl for this model and for the JC/SPCE both in solution and in the solid phase are presented together with the experimental data. The intersection of the solution chemical potential model with the solid chemical potential occurs at 3.49*m*. Thus, the solubility of this new force field is almost equivalent to that of the JC/SPC/E, 3.71*m*, although 0.2*m* smaller, which confirms our working hypothesis that one should not expect big differences in the solubility when replacing the SPC/E model of water by the TIP4P/2005 model while keeping the ion–ion interactions. Since Joung and Cheatham<sup>59</sup> proposed a force field for



FIG. 8. NaCl chemical potential versus molality for the JC-SPC/Eion/TIP4P/2005 model of this work (indigo dashed line) and our extrapolated predictions (indigo dashed line) and for the JC/SPC/E model (orange continuous line) and our extrapolated predictions (orange dashed line). The solid NaCl chemical potential is shown as a green horizontal line and the experimental data<sup>79</sup> are presented with a black continuous line. We have also included finite difference method predictions (magenta triangles up).

many salts in SPC/E water, it seems that replacing SPC/E by TIP4P/2005 (while keeping the ion-ion interactions) and using the LB combination rules will yield similar results. Joung and Cheatham<sup>59</sup> also proposed a force field for NaCl in TIP4P–Ew water.<sup>88</sup> Since TIP4P/2005 and TIP4P-Ew are quite similar in many respects (i.e., both models do also incorporate the Berendsen correction to the vaporization enthalpy), it is also likely that the solubility will be quite similar when replacing TIP4P-Ew by TIP4P/2005 in the calculations (while keeping the ion-ion interactions and using LB combination rules for the ion-water interactions). In fact, Moucka et al.<sup>33</sup> have already shown some evidence of this. Notice though that the JC/TIP4P-Ew ion force field does not seem to be very accurate as it predicts a solubility of about 1.4m and recently Mester and Panagiotopoulos have obtained the same value.33,35 Remind that the solubility of the JC/SPC/E was of about 3.71m and the experimental value is about 6.14m. For this reason, it seems that the ion-ion interactions are better described by the JC/SPC/E force field. In summary, one should not expect big changes in the solubility of a model when replacing SPC/E by TIP4P-Ew or TIP4P/2005 (when keeping the ion-ion interaction and using the LB combination rules). After all, these models incorporate the Berendsen

TABLE V. Free-energy components of JC-SPC/E-ion/TIP4P/2005 solutions at 298 K and 1 bar. All the solutions have 270 water molecules. Energies are given in kJ per mole. The number density  $\rho = N/V$  is given in particles per Å<sup>3</sup>, where  $N = N_w + 2N_{\text{NaCl}}$ . The chemical potential of NaCl is given in kJ per mole of NaCl.

N <sub>NaCl</sub>	ρ	G <sub>solution</sub>	A <sup>integral</sup>	$\mathbf{A}_{LJ, \textit{ref}}^{\textit{res}}$	pV <sub>solution</sub>	A <sup>id</sup> solution	m (mol kg <sup>-1</sup> )	$\mu^{solution}_{ ext{NaCl}, ref2}$
0	0.033 348	-10 447.39(30)	-8951.18(30)	1447.16	0.49	-2943.86	0.000	-∞
1	0.033 518	-11238.51(60)	-9724.47(60)	1480.43	0.49	-2994.96	0.206	-399.58(60)
2	0.033 682	-12022.91(60)	-10497.58(60)	1513.49	0.49	-3039.31	0.411	-396.45(60)
5	0.034138	-14365.65(60)	-12816.78(60)	1611.34	0.49	-3160.70	1.028	-391.95(60)
12	0.035 024	-19795.28(60)	-18209.14(60)	1830.35	0.51	-3416.99	2.466	-386.70(60)
15	0.035 336	-22 113.95(60)	-20513.24(60)	1919.83	0.51	-3521.06	3.084	-385.09(60)
17	0.035 526	-23 657.11(60)	-22046.46(60)	1978.02	0.52	-3589.19	3.495	-384.11(60)
20	0.035785	-25967.49(60)	-24341.36(60)	2063.22	0.52	-3689.87	4.112	-382.75(60)

Reuse of AIP Publishing content is subject to the terms: https://publishing.aip.org/authors/rights-and-permissions. Downloaded to IP: 147.96.12.14 On: Wed, 30 Ma

polarization correction in their design. It is also true that, at least with respect to the solubility, the force field proposed by JC for SPC/E water yields the best estimate, although still lower than the experimental value.

For comparison of the effect of using a different water model in the force field of the salt solution, in Fig. 9 the NaCl natural logarithm of the mean activity coefficient,  $\ln \gamma$ , versus molality at 298 K and 1 bar is shown for the JC-SPC/Eion/TIP4P/2005 and the JC/SPC/E models. It can be seen that JC-SPC/E-ion/TIP4P/2005 is in better agreement with the experimental data than the JC/SPC/E model, especially above 2.2m. At very low concentrations, the opposite is true (due to the fact that the dielectric constant of TIP4P/2005 deviates more than SPC/E from the experimental value). The dielectric constant of these two models is lower than the experimental value, so the initial decrease of the activity is too pronounced. Although our results for the activity coefficient of the JC-SPC/E-ion/TIP4P/2005 should be taken with care as the standard chemical potential of the salt was obtained from the simulations using 270 molecules of water, it is clear that activity coefficient of this model is lower than that of the original JC/SPC/E model. In Fig. 4(b) we have included the water activity for this model and found that at high concentrations it is somewhat closer to the experimental values.

### D. Ionic pairs

We have also investigated the ionic pairs formation (a cation and an anion in direct contact in the solution) at different concentrations for the three models considered in this work. The number of ionic pairs (per ion)  $n_{ionic-pairs}$  was obtained using the cation–anion radial distribution,  $g_{Na^+-Cl^-}$ (r), in the solution obtained from the NpT runs and integrating it up to the first minimum (located at a distance of  $r_{min}$ ) as<sup>15,89</sup>

$$n_{ionic-pairs} = 4\pi \rho_{Na^+} \int_0^{r_{min}} r^2 g_{Na^+-Cl^-}(r) dr, \quad (12)$$



FIG. 9. NaCl natural logarithm of the mean activity coefficient, ln  $\gamma$ , versus molality at 298 K and 1 bar for the JC-SPC/E-ion/TIP4P/2005 model shown as indigo dashed line. Results for the JC/SPC/E are also presented, using two values for  $\mu^{\dagger}_{\rm NaCl}$ , one obtained from the study of diluted solutions having 270 molecules of water and the other one obtained from the analysis of diluted solutions having 2000 molecules of water. Experimental data (black solid curve) of Hamer and Wu<sup>79</sup> are also included.

where  $\rho_{Na^+}$  is the  $Na^+$  number density, obtained as

$$\rho_{Na^+} = \left(\frac{N_{Na^+}}{V}\right). \tag{13}$$

In Fig. 10, the results for the number of ionic-pairs are presented. As expected, the number of ionic pairs increases as the solution becomes more concentrated for the three models considered in this work.

# E. Two simple empirical rules to estimate the solubility of a model

After analyzing the solubility of these models and the ionic pairs formation, we found an empirical prescription to estimate the solubility of a certain force field at room T and p. As it can be seen from the figure, the concentration at which the number of ionic pairs (per ion) is close to 0.075 (i.e., about 7% formation) is very close to the solubility of the considered model. At least this prescription works very well for the three models considered in this work. This is an efficient rule for testing models. To have an idea of the advantage of using this rule to test models, we can compare the time that it takes to get the information for the ion pairing criteria with the time that it takes to obtain the solubility by Hamiltonian integration; NpT calculations for 8 different concentrations take one day using a cluster with eight CPUs. Free energy calculations for 8 solutions (for just one model) take 24 days in a cluster with 8 CPUs. The CPU used was an Intel Xean X5680 with a clock frequency of 3.33 GHz.

Another simple empirical rule is related with the difference between the NaCl solid and the standard dissolution chemical potentials of different models and the solubility of each model. As can be seen in Fig. 11, the solubility of the considered models is approximately given by

$$m_s = 1.552 + 0.275 \ (\mu_{\text{NaCl}}^{solid} - \mu_{\text{NaCl}}^{\dagger}).$$
 (14)



FIG. 10. Number of ionic pairs versus molality for the JC/SPC/E, SD/SPC/E, and JC-SPC/E-ion/TIP4P/2005 models. The horizontal line corresponds to 0.075 ionic pairs value. The star symbols with the corresponding model colors (see legend) show the solubility of the three models obtained in this work. The continuous lines with the corresponding model colors (see legend) are simple polynomial fits to the number of ionic pairs as a function of molality to guide the eye.

Reuse of AIP Publishing content is subject to the terms: https://publishing.aip.org/authors/rights-and-permissions. Downloaded to IP: 147.96.12.14 On: Wed, 30 Mar



FIG. 11. Solubility as a function of the difference between the NaCl solid chemical potential and the NaCl standard dissolution chemical potential for the JC/SPC/E, SD/SPC/E, JC-SPC/E-ion/TIP4P/2005, JC/TIP4P-Ew,<sup>35</sup> AH/BK3, <sup>10,44,90,91</sup> KBI-SPC/E, <sup>7,36,92</sup> and SD-BMHTF-SPC/E<sup>35,93-96</sup> models (see legend). The dashed green line is just to guide the eye and show the linear data correlation. The star symbol shows the NaCl experimental solubility.

The chemical potentials in this expression are given in kJ/mol.

As long as the NaCl solid chemical potential and the NaCl standard chemical potentials of a model are known, we can have an idea of their solubility at room T and p. The NaCl chemical potential can be obtained, for instance, by using the Einstein crystal methodology<sup>64</sup> or the Einstein molecule method.<sup>65–68</sup> The standard chemical potential of the salt in solution can be calculated by using highly diluted solutions and one of the three methodologies mentioned in this work. Interestingly, the correlation is successful in describing the results for a polarizable model of NaCl in water.<sup>10,44,90,91</sup> The experimental solubility is out of the correlation line of these models. This correlation seems to be valid for other 1:1 salts solutions, as long as the salt crystal structure is NaCl type, as, for example, NaI and KCl. For instance, for the JC/SPC/E models of NaI and KCl, the solubility predicted by this linear correlation would be 7.85 and 2.39, respectively, in good agreement with the calculated values by Mester and Panagiotopoulos: 367.75m and 2.65m.

When designing force fields for electrolytes in water, usually hydration properties at infinite dilution (as, for instance, the standard chemical potential) are used as target properties. However the results of Fig. 11 show that the solubility is rather controlled by the difference between the chemical potential of the solid and the standard chemical potential of the salt in solution. Besides since the number of ionic pairs found at a certain concentration is controlled by the solubility (see Fig. 10), one may conclude that this difference of chemical potentials is also controlling the number of ionic pairs in solution.

## **VI. CONCLUSIONS**

In this work, we have computed the solubility of several models of NaCl in water using computer simulations. The chemical potential of the solid phase was obtained from Einstein crystal calculations. The chemical potential of the salt in water was evaluated by performing Hamiltonian integration following the same approach that was described in our previous work. The main difference with respect to our previous work is that much longer runs are used here (possible since we used now the efficient MD program Gromacs) and the way of analyzing the results for the total Gibbs free-energy of the system. The solubility predictions obtained in this work for both the SD/SPC/E model and the JC/SPC/E models are in good agreement with the results of Moucka *et al.*<sup>40</sup> and Mester and Panagiotopoulos.<sup>35</sup> This is gratifying as for these two models, the results of three different groups, using different approaches, are mutually consistent. Therefore, these results can be regarded as a benchmark for solubility calculations of NaCl in water.

The solubility of the two first models considered in this work is significantly lower than the experimental one. In fact the solubility value found for the SD/SPC/E, 0.68(08)m, is about ten times lower than the experimental value (i.e., 6.14m). For the JC/SPC/E the solubility is 3.71(25)m, which is 40% below the experimental value. It is not clear why most of the potential models proposed so far for NaCl in water underestimate the solubility with respect to the experimental value (which may explain why the number of ionic pairs is usually high in simulation studies<sup>97,98</sup>). Clearly some further work is needed to understand the origin of that. In any case it is clear that there is room for improvement when designing force fields for sodium chloride solutions.

It is interesting to point out that these two models use the same model to describe water interactions (in fact they use the respectable SPC/E model) while they differ significantly in the prediction of the solubility (the solubility of JC/SPC/E being six times larger than that of SD/SPC/E). That illustrates that when describing the solubility, "chemistry" rather than "physics" matter. At low concentrations the variation of the activity coefficient (which is related to the variation of the excess chemical potential) can be described by the Debye-Hückel law, and the limiting constant of this law depends only on temperature and of the value of the dielectric constant of the solvent (i.e., of physical variables). Since both models use the same model of water, they behave in a similar way in this "physical" regime. However, their solubility differs significantly due to "chemical" differences (contained implicitly in the force field), as they differ in the value of the chemical potential of the solid, in the value of the standard chemical potential of the salt in solution (which is related to the excess chemical potential of the salt at infinite dilution) and on the activity coefficients at medium and high concentrations. These are "chemical" differences. It is rather naïve to expect to understand the problem of the solubility of NaCl in water, by focusing only on a physical variable, i.e., the dielectric constant of the solvent.

Since the results of the JC/SPC/E seem to be reasonable, we have analyzed the possibility of replacing the SPC/E model of water by the TIP4P/2005. It has been found that the predictions of the density and of the solubility change very little with this replacement. The solubility, although reasonable, is again low as compared to the experimental value. There may be certain advantages in having a reasonable NaCl model (with a not too low solubility) which uses the TIP4P/2005 instead of SPC/E. For instance, studies related with cryoscopic effects (i.e., the change in the melting point of ice due to the presence of salt) will be much easier when using TIP4P/2005 as the melting point of this model is of about 252 K, and the dynamics at this temperature will be faster than that of SPC/E water at its melting point (for this model the melting point is of 215 K). Second, there is high interest in understanding the behavior of water at low temperatures (i.e., supercooled water). Since TIP4P/2005 describes very well the properties of water at low temperatures (including the maximum in density), it seems reasonable to use this model in combination with a reasonable model of NaCl. It seems that the JC-SPC/E-ion/TIP4P/2005, although far from perfect, can be a reasonable choice.

Finally we have determined the number of ionic pairs (per ion) as a function of the salt concentration. We found empirically that when the concentration of the salt is close to that of the solubility, the number of ionic pairs is of about 0.075. At least this rule seems to work for the three models considered in this work (and it remains to be studied if the rule holds or not for other models of NaCl in water). The advantage of this rule is that it allows to estimate the solubility of a force field from cheap NpT runs (necessary to determine the number of ionic pairs) and not from expensive chemical potential calculations. Notice that these rules only apply at room T and p. In any case, there is no a free lunch, and this rule is only approximated, as the only rigorous way of determining the solubility is by equating the chemical potential of the salt in the solid phase with that of the salt in the solution. In any case it may be useful as a rough first guess. Also we have found another approximated prescription relating the solubility to the difference between the chemical potential of the solid and the standard chemical potential in solution. Although this prescription is approximated since it does not include the activity coefficient, it holds reasonably well.

There is still a final conclusion. The solubility of the models SD/SPC/E and JC/SPC/E obtained from the chemical potential route by three different groups (differing only in the way the chemical potential is obtained) is mutually consistent and in good agreement. However the values obtained from this route are entirely different from those obtained from direct coexistence simulations. It is clear that both techniques should provide the same value of the solubility. The reason of this discrepancy is not clear and should be investigated in more detail in future studies.

# ACKNOWLEDGMENTS

We thank Dr. J. L. Abascal for helpful discussions. A. L. Benavides thanks support from CONACYT (México) (Convocatoria 2014 de Estancias Sabáticas Nacionales, Estancias Sabáticas al Extranjero y Estancias Cortas para la Consolidación de Grupos de Investigación and Project Nos. 152684 and ECOS 232871). This work was funded by the Spanish Ministry of Education [Grant No. FIS2013/43209-P] and by UCM/Santander Grant No. 910570.

- <sup>1</sup>E. Waisman and J. L. Lebowitz, J. Chem. Phys. 52, 4037 (1970). <sup>2</sup>L. Blum, Mol. Phys. 30, 1529 (1975).
- <sup>3</sup>D. Levesque, J. J. Weis, and G. N. Patey, J. Chem. Phys. 72, 1887 (1980).

- <sup>4</sup>L. L. Lee, Molecular Thermodynamics of Electrolyte Solutions (World Scientific, Singapore, 2008).
- <sup>5</sup>J. Anwar, D. Frenkel, and M. G. Noro, J. Chem. Phys. **118**(2), 728 (2003).
- <sup>6</sup>G. Hummer, L. R. Pratt, and A. E. Garcia, J. Phys. Chem. 100, 1206 (1996).
- <sup>7</sup>S. Weeransinghe and P. E. Smith, J. Chem. Phys. **119**, 11342 (2003).
- <sup>8</sup>M. Fyta and R. R. Netz, J. Chem. Phys. **136**, 124103 (2012).
- <sup>9</sup>C. Vega and J. L. F. Abascal, Phys. Chem. Chem. Phys. 13, 19663 (2011). <sup>10</sup>H. Jiang, Z. Mester, O. A. Moultos, I. G. Economou, and A. Z. Panagiotopou-
- los, J. Chem. Theory Comput. 11, 3802 (2015).
- <sup>11</sup>Z. R. Kann and J. L. Skinner, J. Chem. Phys. 141, 104507 (2014). <sup>12</sup>G. Lanaro and G. N. Patey, J. Phys. Chem. B 119, 4275 (2015).
- <sup>13</sup>M. Kohagen, P. E. Mason, and P. Jungwirth, J. Phys. Chem. B 120, 1454 (2016).
- <sup>14</sup>S. Reiser, S. Deublein, J. Vrabec, and H. Hasse, J. Chem. Phys. 140, 044504 (2014).
- <sup>15</sup>R. Hartkamp and B. Coasney, J. Chem. Phys. 141, 4275 (2014).
- <sup>16</sup>G. A. Orozco, O. A. Moultos, H. Jiang, I. G. Economou, and A. Z. Panagiotopoulos, J. Chem. Phys. 141, 234507 (2014).
- <sup>17</sup>J. S. Kim, Z. Wu, A. R. Morrow, and A. Yethiraj, J. Phys. Chem. B 116, 12007 (2012).
- <sup>18</sup>S. Deublein, J. Vrabec, and H. Hasse, J. Chem. Phys. **136**, 084501 (2012).
- <sup>19</sup>M. M. Reif and P. H. Hunenberger, J. Chem. Phys. 134, 144104 (2011).
- <sup>20</sup>D. Corradini, M. Rovere, and P. Gallo, J. Phys. Chem. B **115**, 1461 (2011).
- <sup>21</sup>F. N. Mendoza and J. Alejandre, J. Mol. Liquids 185, 50 (2013).
- <sup>22</sup>J. Vincze, M. Valisko, and D. Boda, J. Chem. Phys. 133, 154507 (2010).
- <sup>23</sup>D. Horinek, S. I. Mamatkulov, and R. R. Netz, J. Chem. Phys. 130, 124507 (2009).
- <sup>24</sup>R. C. DeMille and V. Molinero, J. Chem. Phys. **131**, 034107 (2009).
- <sup>25</sup>M. Patra and M. Karttunen, J. Comput. Chem. 25, 678 (2004).
- <sup>26</sup>S. Chowdhuri and A. Chandra, J. Chem. Phys. 115, 3732 (2001).
- <sup>27</sup>S. Koneshan and J. C. Rasaiah, J. Chem. Phys. **113**(18), 8125 (2000).
- <sup>28</sup>J. P. Brodholt, Chem. Geol. **151**, 11 (1998).
- <sup>29</sup>M. Ferrario, G. Ciccotti, E. Spohr, T. Cartailler, and P. Turq, J. Chem. Phys. 117, 4947 (2002).
- <sup>30</sup>E. Sanz and C. Vega, J. Chem. Phys. **126**, 014507 (2007).
- <sup>31</sup>A. S. Paluch, S. Jayaraman, J. K. Shah, and E. J. Maginn, J. Chem. Phys. 133, 124504 (2010).
- <sup>32</sup>J. L. Aragones, E. Sanz, and C. Vega, J. Chem. Phys. 136, 244508 (2012).
- <sup>33</sup>F. Moucka, M. Lisal, and W. R. Smith, J. Phys. Chem. B **116**, 5468 (2012).
- <sup>34</sup>M. Lisal, W. R. Smith, and J. Kolafa, J. Phys. Chem. B **109**, 12956 (2005).
- <sup>35</sup>Z. Mester and A. Z. Panagiotopoulos, J. Chem. Phys. **142**, 044507 (2015).
- <sup>36</sup>Z. Mester and A. Z. Panagiotopoulos, J. Chem. Phys. 143, 044505 (2015). <sup>37</sup>F. Moucka, M. Lisal, J. Skvor, J. Jirsak, I. Nezbeda, and W. R. Smith, J. Phys. Chem. B 115, 7849 (2011).
- <sup>38</sup>J. Alejandre, G. A. Chapela, F. Bresme, and J. P. Hansen, J. Chem. Phys. 130, 174505 (2009).
- <sup>39</sup>A. S. Paluch, S. Jayaraman, J. K. Shah, and E. Maginn, J. Chem. Phys. 137, 039901 (2012).
- <sup>40</sup>F. Moucka, I. Nezbeda, and W. R. Smith, J. Chem. Phys. **138**, 154102 (2013). <sup>41</sup>F. Moucka, I. Nezbeda, and W. R. Smith, J. Chem. Phys. 139, 124505 (2013).
- <sup>42</sup>F. Moucka, I. Nezbeda, and W. R. Smith, J. Chem. Theory Comput. 9, 5076 (2013).
- <sup>43</sup>K. Kobayashi, Y. Liang, T. Sakka, and T. Matsuoka, J. Chem. Phys. 140, 144705 (2014).
- <sup>44</sup>F. Moucka, I. Nezbeda, and W. R. Smith, J. Chem. Theory Comput. 11, 1756 (2015).
- <sup>45</sup>H. Wiebe, J. Louwersheimer, and N. Weinberg, Mol. Phys. **113**, 3176 (2015).
- <sup>46</sup>H. M. Manzanilla-Granados, H. Saint-Martin, R. Fuentes-Azcatl, and J.
- Alejandre, J. Phys. Chem. B 119, 8389 (2015). <sup>47</sup>J. R. Espinosa, E. Sanz, C. Valeriani, and C. Vega, J. Chem. Phys. 139, 144502 (2013).
- <sup>48</sup>I. S. Joung and T. E. Cheatham, J. Phys. Chem. B **113**, 13279 (2009).
- <sup>49</sup>H. J. C. Berendsen, J. R. Grigera, and T. P. Straatsma, J. Phys. Chem. 91, 6269 (1987).
- <sup>50</sup>A. J. C. Ladd and L. V. Woodcock, Mol. Phys. **36**, 611 (1978).
- <sup>51</sup>E. G. Noya, C. Vega, and E. de Miguel, J. Chem. Phys. **128**, 154507 (2008).
- <sup>52</sup>J. R. Morris and X. Song, J. Chem. Phys. 116, 9352 (2002). <sup>53</sup>M. M. Conde, M. A. Gonzalez, J. L. F. Abascal, and C. Vega, J. Chem. Phys.
- 139, 154505 (2013). <sup>54</sup>E. G. Noya, C. Vega, J. P. K. Doye, and A. A. Louis, J. Chem. Phys. 132,
- 234511 (2010). <sup>55</sup>D. G. Salgado and C. Vega, J. Chem. Phys. 132, 094505 (2010).
- <sup>56</sup>M. M. Conde and C. Vega, J. Chem. Phys. **133**, 064507 (2010).

- <sup>57</sup>V. K. Michalis, J. Costandy, I. N. Tsimpanogiannis, A. K. Stubos, and I. G. Economou, J. Chem. Phys. **142**, 044501 (2015).
- <sup>58</sup>J. L. Aragones, C. Valeriani, E. Sanz, and C. Vega, J. Chem. Phys. 137, 104507 (2012).
- <sup>59</sup>I. S. Joung and T. E. Cheatham, J. Phys. Chem. B **112**, 9020 (2008).
- <sup>60</sup>D. V. der Spoel, E. Lindahl, B. Hess, G. Groenhof, A. E. Mark, and H. J. Berendsen, J. Comput. Chem. **26**, 1701 (2005).
- <sup>61</sup>J. L. F. Abascal and C. Vega, J. Chem. Phys. **123**, 234505 (2005).
- <sup>62</sup>H. Lorentz, Ann. Phys. **248**, 127 (1881).
- <sup>63</sup>D. Berthelot, C. R. Acad. Sci. **126**, 1713 (1898).
- <sup>64</sup>D. Frenkel and A. J. C. Ladd, J. Chem. Phys. **81**, 3188 (1984).
- <sup>65</sup>C. Vega and E. G. Noya, J. Chem. Phys. **127**, 154113 (2007).
- <sup>66</sup>E. G. Noya, M. M. Conde, and C. Vega, J. Chem. Phys. **129**, 104704 (2008).
- <sup>67</sup>J. L. Aragones, C. Valeriani, and C. Vega, J. Chem. Phys. **137**, 146101 (2012).
- <sup>68</sup>J. L. Aragones, E. G. Noya, C. Valeriani, and C. Vega, J. Chem. Phys. **139**, 034104 (2013).
- <sup>69</sup>C. W. Davies, J. Chem. Soc. 2, 2093 (1938).
- <sup>70</sup>P. Debye and E. Hückel, Physikalische Zeitscrift **24**, 185 (1923).
- <sup>71</sup>See supplementary material at http://dx.doi.org/10.1063/1.4943780 for tables with simulation data involved in the calculus of the solution chemical potential.
- <sup>72</sup>L. Dang and D. E. Smith, J. Chem. Phys. **99**, 6950 (1993).
- <sup>73</sup>D. E. Smith and L. X. Dang, J. Chem. Phys. **100**, 3757 (1994).
- <sup>74</sup>U. Essmann, L. Perera, M. L. Berkowitz, T. Darden, H. Lee, and L. G. Pedersen, J. Chem. Phys. **103**, 8577 (1995).
- <sup>75</sup>J. Kolafa and I. Nezbeda, Fluid Phase Equilib. **100**, 1 (1994).
- <sup>76</sup>S. Nosé, Mol. Phys. **52**, 255 (1984).
- <sup>77</sup>W. G. Hoover, Phys. Rev. A **31** (1985).

- <sup>78</sup>P. S. Z. Rogers and K. S. Pitzer, J. Phys. Chem. Ref. Data **11**, 15 (1982).
- <sup>79</sup>J. Hamer and Y. C. Wu, J. Phys. Chem. Ref. Data 1, 1047 (1972).
- <sup>80</sup>W. R. Smith and R. W. Missen, Chem. Eng. Educ. **37**, 222 (2003).
   <sup>81</sup>Guidelines for Evaluating and Expressing the Uncertainty of NIST Measurement results, Appendix A: Law of Propagation of Uncertainty, http://www.
- nist.gov/pml/pubs/tn1297/appa.cfm, accessed May 02, 2016.
- <sup>82</sup>J. Anwar and P. K. Boateng, J. Am. Soc. **120**, 9600 (1998).
- <sup>83</sup>J. Anwar and D. Zahn, Angew. Chem., Int. Ed. 50, 1996 (2011).
- <sup>84</sup>J. Alejandre and J. P. Hansen, Phys. Rev. E 76, 061505 (2007).
- <sup>85</sup>D. Chakraborty and G. N. Patey, J. Phys. Chem. Lett. 4, 573 (2013).
- <sup>86</sup>N. E. R. Zimmermann, B. Vorselaars, D. Quigley, and B. Peters, J. Am. Chem. Soc. **137**, 13352 (2015).
- <sup>87</sup>W. R. Smith, F. Moucka, and I. Nezbeda, Fluid Phase Equilib. 407, 76 (2016).
- <sup>88</sup>H. W. Horn, W. C. Swope, J. W. Pitera, J. D. Madura, T. J. Dick, G. L. Hura, and T. Head-Gordon, J. Chem. Phys. **120**, 9665 (2004).
- <sup>89</sup>J. L. Aragones, M. Rovere, C. Vega, and P. Gallo, J. Phys. Chem. B 118, 7680 (2014).
- <sup>90</sup>P. T. Kiss and A. Baranyai, J. Chem. Phys. **138**, 204507 (2013).
- <sup>91</sup>P. T. Kiss and A. Baranyai, J. Chem. Phys. **141**, 114501 (2014).
- <sup>92</sup>M. B. Gee, N. R. Cox, Y. Jiao, N. Bentenitis, S. Weerasinghe, and P. E. Smith, J. Chem. Theory Comput. 7(5), 1369 (2011).
- <sup>93</sup>M. Tosi and F. Fumi, J. Phys. Chem. Solids 25, 31 (1964).
- <sup>94</sup>J. E. Mayer, J. Chem. Phys. 1, 270 (1933).
- <sup>95</sup>M. L. Huggins and J. E. Mayer, J. Chem. Phys. 1, 643 (1933).
- <sup>96</sup>F. Fumi and M. Tosi, J. Phys. Chem. Solids 25, 31 (1964).
- <sup>97</sup>P. Auffinger, T. E. Cheatham III, and A. C. Vaiana, J. Chem. Theory Comput. 3, 1851 (2007).
- <sup>98</sup>A. A. Chen and R. V. Pappu, J. Phys. Chem. B **111**, 6469 (2007).