

# Toward an Understanding of the Hofmeister Effect: A Computer Game with Dipoles and an Ion

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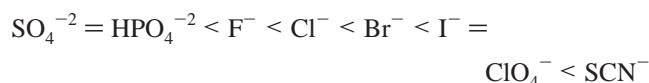
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The solvation of ions in dipolar lattice droplets has been studied using Monte Carlo simulations. It is found that for small dipoles the solvation behavior is similar to that expected from a dielectric model. For larger dipoles, large deviations from dielectric behavior are observed. For the larger dipoles, it is found that only the first layers solvate the ion and that the more-distant dipoles tend to reduce the solvation energy. The obtained results support the idea that there exist two regions in systems with large dipoles. In the region closest to the ion, the ordering of the dipoles is determined by the ion, and further away from the ion, a dipolar regime exists. Between these two regions, there is an interface region that is likely to be important to our understanding of the Hofmeister effect.

## Introduction

More than 100 years ago, the German physicists Lewith<sup>1</sup> and Hofmeister<sup>2</sup> independently showed that the addition of salt to water influenced many of the solubilizing properties of water in a way that could be understood by assuming that the ions could be ordered in a specific order and that an ion that influenced one property more than another ion also could be expected to influence other properties more. It was also shown that the difference in influence between different positive ions was small. The standard way to order some of the negative ions with increasing importance is



(There is obviously an ambiguity with respect to the words increasing and decreasing since only the sum of the contributions of the negative and positive ions can be determined and the individual importance contains a constant, undetermined contribution for all ions of a given charge.) The ordering of the ions is often named after Hofmeister as the Hofmeister series. The series is, however, sometimes also called the lyotropic series. Typical effects that follow these trends are heats of hydration of the alkali halides,<sup>3</sup> the entropy change upon the hydration of ions,<sup>4</sup> water activity coefficients,<sup>5,6</sup> ionic dilution entropy,<sup>7</sup> polymer cloud points,<sup>8,9</sup> polymer swelling,<sup>9</sup> and protein solubility.<sup>2</sup> The list above contains only part of the effects listed in the interesting review by Collins and Washabaugh,<sup>10</sup> where more references are given. This review lists 38 different observables that follow the trends predicted by the Hofmeister series. Despite the fact that the effects have been known for more than 100 years, no generally accepted explanations on a molecular level exist. It is, however, assumed that ions to the left in the list above are “supporting polar water structures”, and they are called structure makers or kosmotropes (the Greek word kosmos means order). Ions to the right in the list are supposed to destroy water structure and are called chaotropes or structure breakers. The  $\text{Cl}^-$  ion is said to have little effect

on the water structure, and the sign of many effects is said to change around the  $\text{Cl}^-$  ion.<sup>10</sup>

In their review article, Collins and Washabaugh suggest a molecular model for the Hofmeister effect based on these ideas. The key idea is to divide the water surrounding an ion into three different layers. In the first layer adjacent to the ion, the ordering of the water is determined by the ion. In the third layer, closest to the bulk, the structure is determined by the bulk, and in the intermediate second layer, the structure is determined by the two other layers. Each layer is believed to be one water molecule thick. Another essential ingredient in the model is that for the chaotropes the water molecules in the first layer are loosely bound whereas for the kosmotropes the water molecules in the first layer are strongly bound. These ideas are consistent with the views of some investigators<sup>11</sup> but are in disagreement with the views of others<sup>12</sup> who claim that the first hydration shell water molecules are always tightly bound. The actual model is complicated and involves the interaction between these different layers (shells) as well as the interaction between the first shell and the ion. A weak point in this model is that it is mainly qualitative and that it contains contributions with varying signs.

Ninham and Yaminski have suggested that part of the origin of the Hofmeister effect could be due to the dispersive interaction between molecules.<sup>13</sup> The importance of the Hofmeister effect for interfacial phenomena has been recently reviewed.<sup>14</sup>

In another rather recent work, Leberman and Soper<sup>15</sup> show using neutron diffraction measurements that ions dissolved in water affect the water structure in the same way as an increased pressure would. These authors also point out that different salts influence the structure to a different extent and that the magnitude of the structural changes follows the Hofmeister series.

In two recent all-atom Monte Carlo simulations of an ion dissolved in a water droplet, we have shown that the size and the polarizability of the ion influence its position in the droplet.<sup>16</sup> Ions with a larger radius and a large polarizability seem to prefer locations closer to the surface than ions with a smaller radius and a smaller polarizability.

These results are very controversial since they are in conflict with standard dielectric theory. If we regard the water droplet

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as a spherical drop of a dielectric medium, then we can show that the ion will be repelled by the surface. Using an image charge approximation and atomic units, this repulsion can be estimated from<sup>17</sup>

$$\Delta G_{\text{rep}} = (qa)^2(\epsilon - 1)/(2R(\epsilon + 1)(R^2 - a^2)) \quad (1)$$

where  $q$  is the charge,  $R$  is the radius of the droplet,  $a$  is the distance of the ion from the center of the droplet, and  $\epsilon$  is the relative dielectric permittivity of the medium in the droplet. (The free energy  $G$  in this equation will be given in atomic units.) If we use a droplet with a radius of 20. au (close to 1 nm) and assume a dielectric permittivity of water of 80, we can easily estimate that the ion is repelled by 4. kJ/mol when it is 5 au from the center. The corresponding values at 10 and 15 au are 21 and 82 kJ/mol, respectively.

The value 82 kJ/mol is significantly larger than the corresponding differences in the polarization energy originating from the polarizability of the ion. (Below, we show that this effect can be expected to be on the order of 10 to 20 kJ/mol.) Thus, it is possible to conclude that there must be effects other than the ion polarizability that are partly responsible for what was observed in the molecular simulations mentioned above. A major drawback of the all-atom-type modeling is that the effects that we are trying to model are small and the statistical accuracy of such calculations is rather low. The results obtained from the all-atom modeling mentioned above are, however, very anti-intuitive.

To unravel the mechanism behind the attraction between the ion and the interface, we have undertaken a set of lattice calculations. The advantage of lattice calculations is that they are much faster and easier to analyze, and it is consequently easier to obtain accurate statistical averages and to vary important parameters. The drawbacks are the lack of mobility for the particles and that there is no possibility to vary the size (radius) of the ion relative to that of the dipoles.

**Method and System.** The starting point for the lattice modeling is a primitive cubic lattice. At each lattice point ( $i, j, k$ ), a dipole of fixed magnitude but with varying orientation is placed. All lattice points further away from origin than a given distance (3 or 4) are deleted from the calculation. In the first set of calculations, one of the dipoles is removed from the lattice, and an ion is placed in its position. A system defined in this way is determined by two dimensionless quantities  $\mu^2/(kTr^3)$  and  $\mu q/(kTr^2)$ . To map the results to the real world, one needs to identify a length and an energy scale in the system. Here we have chosen to identify  $kT$  with 0.001 energy unit. The reason for this is that this is close to the value for  $kT$  at room temperature in atomic units. The system we want to model is primarily water, and the water–water distance in liquid water is close to 3 Å. Using this, one can easily verify that the water dipole moment in the gas phase, which is around 1.8 D, equals 0.06 in lattice units and that a unit charge in the real world corresponds to a charge of close to 0.4 in the lattice. The purpose of the modeling is qualitative, so the exact values are of no importance.

Using a system like the one described above, we have performed Monte Carlo simulations to unravel the thermodynamics of the ion solvation in the lattice. In the first set of calculations, the goal was to calculate the variation of the system energy as a function of the position of the ion. In these calculations, a standard Monte Carlo procedure as suggested by Metropolis<sup>18</sup> was used. The dipoles were rotated one by one to a new random orientation on a spherical calotte surrounding the old orientation in such a way that the acceptance probability

in the Monte Carlo procedure was close to 0.5. The energy of the system was evaluated without any truncation of the interaction potentials. After an equilibration procedure where each dipole was typically rotated 3500 times, we started to accumulate data. Typically, each dipole was moved between 500 000 and 2 000 000 times in the production part of the calculations. The lower value is relevant to the small dipoles of 0.01, and the higher value applies to dipoles larger than 0.05. Data were sampled each time when all dipoles had been moved five times. We have estimated the statistical uncertainty by independent simulations, and the statistical uncertainty in the estimates is well below  $0.5kT$ . For the smaller dipole moments (less than 0.05), the uncertainty is less than  $0.1kT$ .

In another set of calculations, we calculated the free energy needed to move a charge from the center of the lattice to another lattice point. This was done in the following way. We performed an ordinary Monte Carlo simulation of the studied system with the ion at a fixed position. During the simulation, we calculated the energy needed to remove a charge of  $dq$  or the energy gained by increasing the charge by the same amount. During the simulations, we accumulated

$$\Delta\Omega = 1/N \sum \exp(-\beta\Delta U_i) \quad (2)$$

where  $\Delta U_i$  is the energy change in the system calculated when the charge is changed by  $dq$ ,  $\beta$  is  $1/kT$  where  $k$  is the Boltzmann constant, and  $T$  is the absolute temperature. The sum is evaluated over  $N$  conformations, and  $\Delta\Omega$  is the ratio between the partition function obtained with the original charge and the partition function that is relevant to the system with the modified charge.<sup>19</sup> The free-energy change  $\Delta A$  for the process can be obtained from

$$\Delta A = -kT \ln(\Delta\Omega) \quad (3)$$

where  $k$  is the Boltzmann constant. Using eqs 2 and 3, it is possible to calculate the free-energy change associated with the modification of the charge in a given position from  $q$  to  $q - dq$ . In principle, it should be possible to remove the entire charge  $q$  in one step. However, better statistics are obtained by performing the removal of the charge in steps. In the actual calculations, we calculated the free energies related to the addition/removal of charges of 0.025 and 0.05. To obtain the free energy related to the deletion of a charge of 0.4 (close to 1. in real charge units), we thus studied systems with charges of 0.0, 0.05, 0.1, 0.35, and 0.4. From such a series of calculations, it was possible to obtain three different estimates of the free energy associated with the removal of charge 0.4. We could either add the free energies associated with the removal of charge 0.05 from from charges 0.05, 0.1, 0.35, and 0.4 or add the free energies associated with the addition of charge 0.05 to charges 0.0, 0.05, 0.1, and 0.35.

The third alternative is to add the free energies associated with adding charge 0.025 to charges 0.0, 0.05, 0.1, and 0.35 to the energies associated with removing a charge of 0.025 from charges 0.05, 0.1, 0.35, and 0.4 with the proper sign. The three estimates obtained in this way typically differed by  $0.05kT$  and never differed more than  $0.4kT$ .

By the technique presented above, it is possible to calculate the free energy associated with a process where a charge is removed and a hole is created in the lattice. It is, however, more interesting to calculate the free energy associated with the process that replaces the ion with a dipole of the same magnitude as the lattice dipoles. To do this, we need to calculate the free energy associated with the removal of a dipole from a lattice filled with dipoles. Since the change of the free energy

associated with the removal of a dipole is smaller than that associated with the removal of an ion, we have chosen to remove the dipole in one step.

The statistic obtained by a straightforward application of eqs 2 and 3 yields rather poor statistics for large dipoles (0.08–0.1), but it can be improved significantly by a small trick. Normally, one would sample  $\exp(-\beta\mu E \cos(\theta))$ , where  $E$  is the electric field acting on the dipole  $\mu$  and  $\theta$  is the angle between the field and the dipole. Formally, there is nothing that prevents us from using an algorithm where after having sampled a removal of the dipole, we move the same dipole to a new randomly generated Boltzmann weighted configuration and sample a new removal of the dipole. This means that what we should sample is the inverse of the Langevin partition function<sup>20</sup> for a dipole in a field  $E$  divided by  $4\pi$ . The factor  $4\pi$  appears since this is the partition function for the free dipole. Thus, we sample

$$\Delta\Omega = 1/N \sum 2\mu E_i / (\exp(\beta\mu E_i) - \exp(-\beta\mu E_i)) \quad (4)$$

as an estimate of the change in the partition function due to the removal of the dipole. Note that  $\mu$  and  $E_i$  are scalars in eq 4. The associated free-energy change is calculated as for the ion. By taking the free energy needed to remove an ion and subtracting the free energy needed to remove a dipole, one obtains the free energy for replacing an ion with a dipole. It is possible to obtain estimates of the uncertainty in the calculated free energies for removing a dipole by performing several simulations and calculating standard deviations in a standard way. To improve the accuracy of the estimates further, it is possible to use the symmetry of the system. For all positions except the site at the origin, there exist several symmetry-related sites. The free energy for removing a dipole from one site must naturally be the same as removing it from other symmetry-related sites. For all dipoles studied in this work except the dipole 0.1, the calculated standard deviations are smaller than  $0.3kT$ , which is the same accuracy that was obtained for the corresponding free energies of the ions. However, to obtain this accuracy, it was necessary to make 7.5 million displacements for the dipolar system with dipoles of 0.08. For the system with dipoles of 0.1, it was necessary to make more than 100 million displacements of each dipole, and we still obtained a standard deviation of only  $0.5kT$ .

## Results and Discussion

We have in the previous section outlined the formalism to calculate the changes in energy and free energy when a charge is moved out from the center of a lattice droplet to positions closer to the surface. In Figure 1a–f, we present the free-energy change associated with displacing an ion from the center to other lattice points for a droplet with radius 3.0. The position of a point along the  $x$  axis is given by the distance of the point from the origin (0, 0, 0). This means that the point 1, 0, 0 corresponds to an  $x$  value of 1.0. It should be noted that in order to separate the points 2, 2, 1 and 3, 0, 0, which both correspond to a distance of 3.0, the former point has been given a distance of 2.95, and the latter, a distance of 3.05. (This is, of course, arbitrary, but it makes some sense to assign a larger  $r$  value to the point 3, 0, 0 since it has only one nearest neighbor, whereas the site 2, 2, 1 has two nearest neighbors. Thus, one may say that the point 3, 0, 0 is more exposed to the surrounding.) The energies are given in units of  $kT$ . Four different charges (0.1, 0.2, 0.3, and 0.4) have been used. (The charge 0.4 almost corresponds to a real charge of 1.0.) The different panels a–f of Figure 1

correspond to lattice dipoles of 0.01, 0.02, 0.04, 0.06, 0.08, and 0.1, respectively. Figure 1a and b shows that systems made up of dipoles that are small show behavior that could be expected from a dielectric model. All ions are expelled from the surface and located in the center of the droplet. For the systems constructed from larger dipoles, three striking observations can be made.

(1) The smooth free-energy curves observed for the smaller dipoles are replaced by an oscillating behavior.

(2) Ions with small charges are expelled from the center of the droplet and are located at or close to the surface.

(3) The free energy needed to bring a charge from the center of the droplet to the surface is much smaller than that suggested by a dielectric model for the larger charges where the solvation of the ion could be expected to dominate over the dipolar structuring forces.

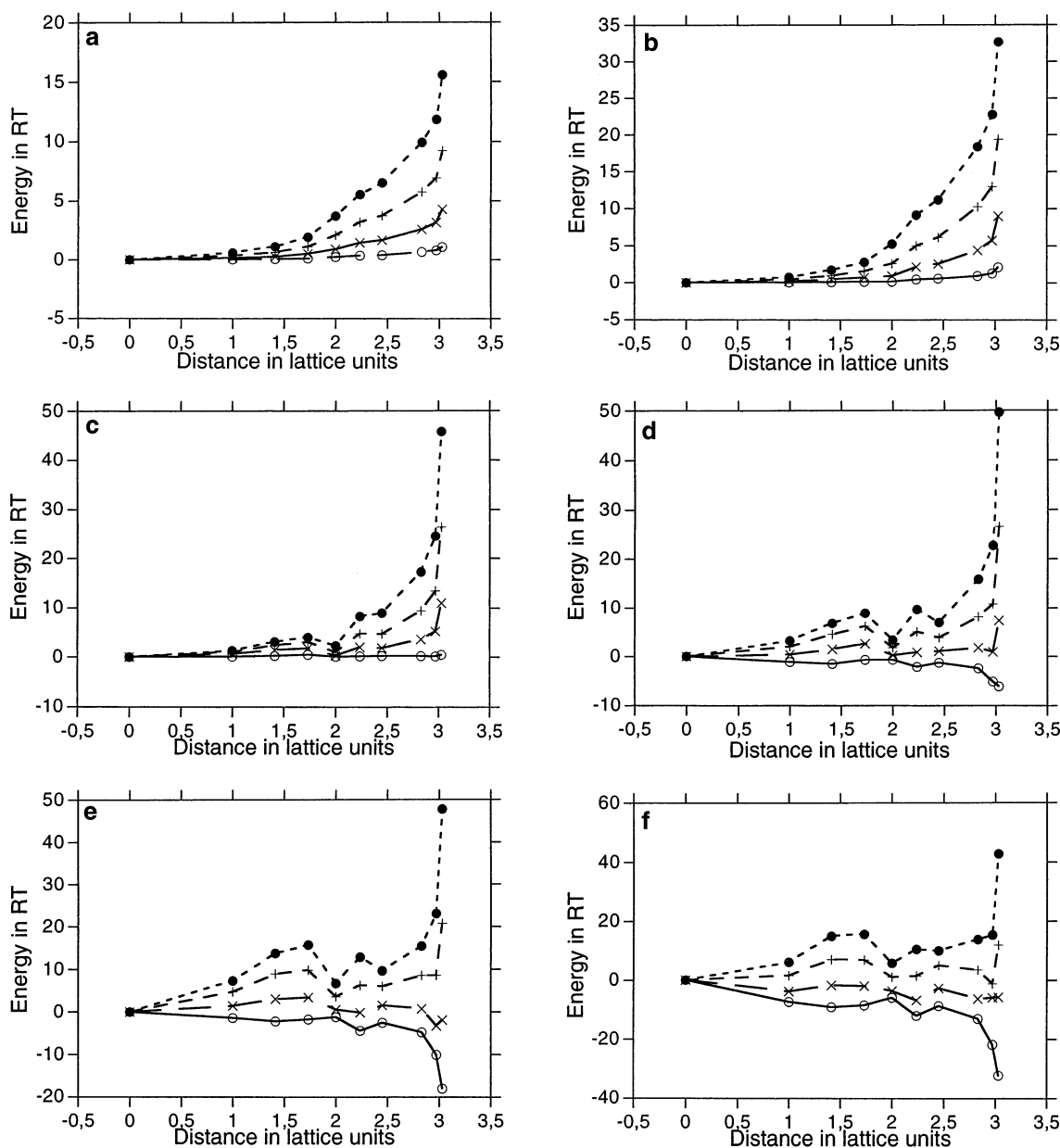
In Figure 2 a–c, we present a partition of the free energy of the system into an energetic ( $E$ ) and an entropic ( $-TS$ ) contribution as a function of the position of the ion (for charges 0.1 and 0.4) for dipoles 0.02, 0.06, and 0.10. The energies ( $E$ ) were obtained as the expectation values of the energy calculated in the simulations with the ion in a specific position. The  $TS$  terms were obtained from

$$\Delta A = \Delta E - T\Delta S \quad (5)$$

The curves for the energies resemble the corresponding curves in Figure 1, indicating that the processes, at least for large charges, are to a large extent governed by the energy and that the entropy is of smaller importance. It also seems as if the entropic contribution to the free energy in general has an opposite sign to the energetic contribution. All observations made for the free-energy curves are also valid for the energy curves.

At this point, it seems appropriate to ask the question, how will the energy profile look if the droplet radius is increased to 4? In Figure 3 a–d, we present free energies, energies, and the entropic contribution ( $-TS$ ) to the free energies associated with the process of bringing the ion from the center of the droplet to different positions in the droplet for ions with magnitudes of 0.1, 0.2, 0.3, and 0.4. A dipole moment of 0.06 is used. The results show that the smaller ions are expelled to the surface in the same way as for the smaller droplet and that it is possible to find minima in the free-energy curves for the larger ions close to the surface but that ions in the region closest to the surface has a higher free energy than ions in the same region for the smaller droplet. The statistical uncertainty for these calculations has not been fully investigated, but it is highly unlikely that the errors are larger than  $1.5kT$  in the free energies and the energies. The accuracy in the  $-TS$  term, which is calculated from the energies and free energies, is obviously somewhat larger. We have avoided the more difficult systems with dipoles 0.08 and 0.1 since they would be too time-consuming. From Figure 3c–d, it seems clear, as it was for the system with radius 3, that the free energy for larger charges is dominated by the energy term and that there often is a smaller contribution to the free energy with an opposite sign from the entropy.

A question that may be of relevance for the understanding of these observations is, what is the solvation energy of an ion in the center of the lattice? By solvation energy, we mean here the energy change occurring when the lattice dipole in the center of the droplet is replaced by an ion. In Table 1, we present such data for a set of ions and for two dipole values (3 and 4) of the radius of the droplet. From Table 1, it is clearly seen that smaller ions act as hydrophobic particles could be expected



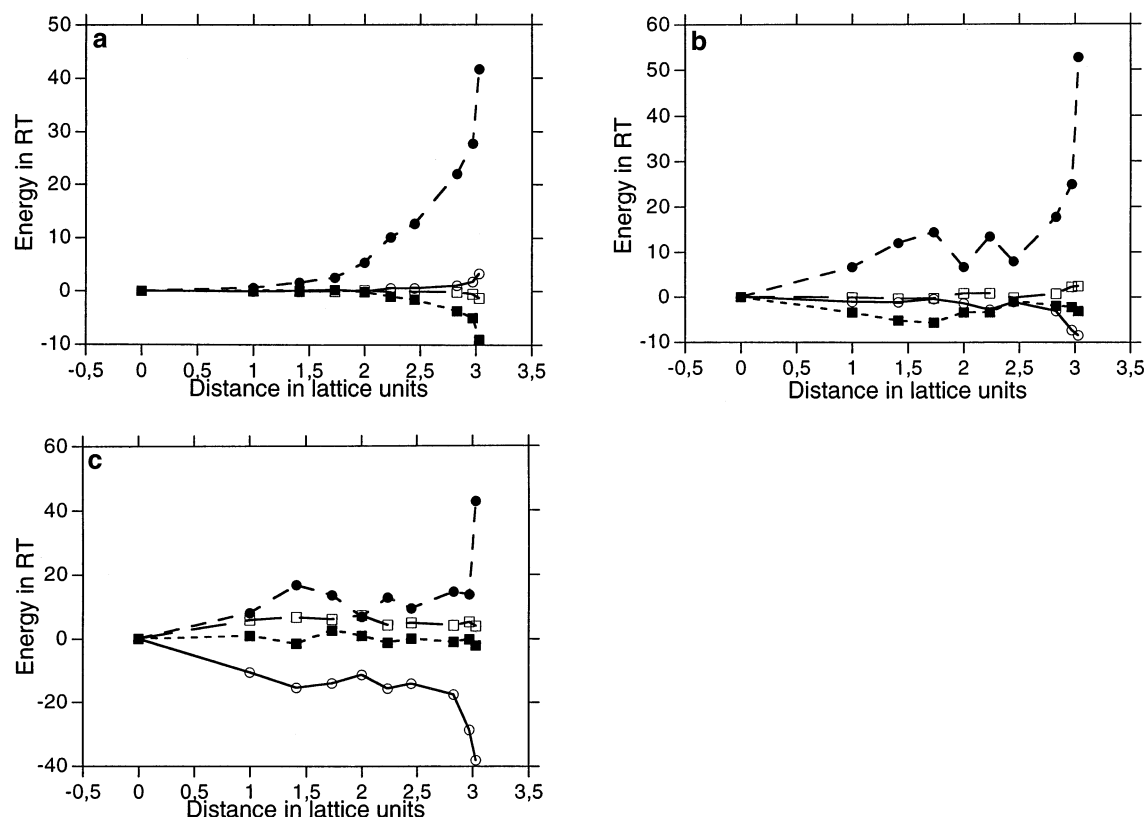
**Figure 1.** (a–f) Free-energy change in thermal units ( $kT$ ) related to the movement of ions with charges 0.1 ( $\circ$ ), 0.2 ( $\times$ ), 0.3 ( $+$ ), and 0.4 ( $\bullet$ ) from the origin to different positions in the lattice is shown. The different positions are specified by their distance from the origin of the droplet on the  $x$  axis. Note that the position 2, 2, 1 is given the distance 2.95 and that the position 3, 0, 0 is given the distance 3.05. Panels a–f corresponds to the dipoles 0.01, 0.02, 0.04, 0.06, 0.08, and 0.10, respectively. The radius of the droplet is 3.

to (i.e., they are expelled to the surface) in the more polar droplets. This is an expected behavior, but it is probably less expected that the solvation energy for an ion with unit charge (0.4 in the model that was used) is smaller in a droplet with radius 4 than in a droplet with radius 3 for dipoles that are 0.06 to 0.10. A possible explanation for this behavior could be that the energy needed to create a hole in the dipole lattice would have been larger in the droplet with radius 4 than in the droplet with radius 3. Table 1 indicates that this is not true. In fact, it is easier to remove a dipole from the larger droplet than from the smaller one. (The removal of a dipole is the same as replacing it with 0 charge.) The only possible explanation for the smaller solvation energy for the larger cluster is that the extra dipoles mainly interact with the dipoles in the smaller droplet and prevent them from solvating the ion. It is clear that this finding is in contradiction to what could be expected from simple dielectric theory, which predicts that the solvation energy grows as  $-1/R$  where  $R$  is the size of the droplet. However,

there are two conditions that must be valid for the dielectric theory to be valid. These are that the ion–dipole and the dipole–dipole interactions should be smaller than or on the order of  $kT$ . Neither of these conditions is fulfilled. (What it actually means is that the dipole–dipole interaction is so strong that clusters of dipolar particles are formed and that these pseudoparticles can be described as a dielectric medium. The studied system is too small to show this type of behavior.)

In the Introduction, we mentioned that all-atom Monte Carlo simulations of ions dissolved in water droplets showed that the polarizability of the ion was important to the ion's location in the droplet. The mechanism is obviously that the polarizability interacts with the electric field on the ion. One would thus expect positions with large electric fields to be favored by large polarizabilities. In Figure 4 a and b, we present data that clearly indicates that the field is larger for positions closer to the surface of the droplet both when the ionic charge is varied (Figure 4a) for a droplet radius of 3 and when the lattice dipole moment is





**Figure 2.** (a–c) Changes in the energy and entropic contributions ( $-TS$ ) to the free energy associated with the movement of ions with charges 0.1 and 0.4 from the origin to different positions in the lattice are shown. The different positions are specified by their distance from origin of the droplet on the  $x$  axis. Note that the position 2, 2, 1 is given the distance 2.95 and that the position 3, 0, 0 is given the distance 3.05. ○ indicates the energetic contribution for charge 0.1, and □ corresponds to the entropic contribution ( $-TS$ ) to the free energy for charge 0.1. ● and ■ have the same interpretation for charge 0.4. A droplet with radius 3 is studied. The dipole moments that are used are 0.02, 0.06, and 0.10 in a–c, respectively.

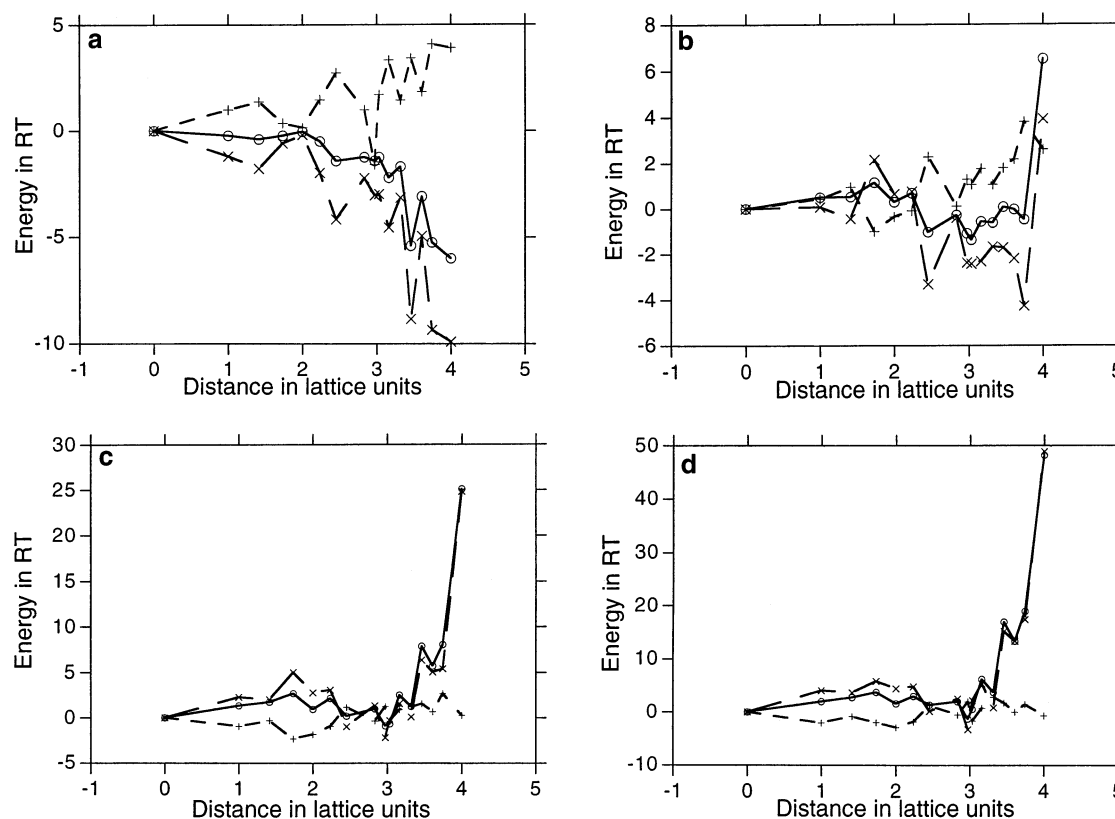
varied for a radius of 4 (Figure 4b). The data that is actually plotted in Figure 4 is  $dE/dP$ , that is, the derivative of the system energy as a function of ion polarizability evaluated at  $P = 0$ . Realistic ionic polarizabilities in the unit system used here vary from 0.05 to 0.3. This means that one can expect that points closer to the surface can get a relative stabilization from the polarizability, which is on the order of  $4kT$  to  $8kT$ .

We have presented a set of unexpected findings for the solvation of ions in droplets built from dipolar lattices. A suitable starting point for understanding these findings is the solvation energy of an ion in the center of a droplet, which was presented above. First, we note that the decrease in solvation energy with increasing size is in sharp contradiction to the prediction of dielectric models, which suggests that the solvation energy should increase with increasing size. The explanation must be that the dipoles that are added when the radius is increased from 3 to 4 interact strongly with the outer dipoles in the droplet with radius 3. This interaction prevents these dipoles from solvating the ion in an efficient way. An observation that supports this conclusion is that the largest solvation energy for an ion with charge 0.4 is obtained for dipoles with a magnitude between 0.04 and 0.06. For dipole moments smaller than that corresponding to the maximum solvation energy (0.05), the solvation energy increases with system size for ions with charge 0.4. For larger dipoles, a maximum in the solvation energy occurs when the size of the lattice is increased. The picture that emerges indicates that there are two important types of structures that need to be considered to understand the solvation of ions in highly dipolar media. The first structure is the structure that the ion tries to induce on the dipoles. In this structure, all dipoles are (on average) pointing toward (or away from) the ion. The

second structure is the structure that the dipoles would have preferred if left alone. In this structure, the dipoles are forming antiparallel bands. If the system is made larger, this tends to support the dipolar structure. This results in a smaller region where the ionic structure prevails and a smaller solvation energy.

To understand why the cavity formation (solvation of an ion with 0 charge) is easier in the larger droplet than in the smaller one, the analysis must be taken one step further. If we analyze the structures preferred in purely dipolar systems, we see that not all dipole–dipole interactions are attractive. One may also say that the orientations of some dipoles are in conflict with each other. These conflicts can naturally partly be reduced by the introduction of empty lattice sites but also by the surface of the droplet. The larger the droplet, the smaller the importance of the surface of the droplet, and an additional empty lattice site may be more important in relaxing the repulsive dipole–dipole interactions, leading to a smaller cavity-formation energy in the larger droplet.

This picture is not completely different from that used to explain the solvation properties of molecules in water. The molecules are classified as structure makers and structure breakers. We see here that an ion breaks the dipolar structure but forms another structure in its vicinity. It is likely that the empty cavity (ions with 0 charge) supports the dipolar structure by removing some of the repulsive interactions inherent in these structures. From this, we may conclude that a particle can be classified as a structure maker in two different ways.  $\text{SO}_4^{2-}$  is one example, where the likely explanation is that the ionic structure introduced by the doubly charged ion is larger than the dipolar structure destroyed by the same ion. The other extreme is a molecule such as  $\text{CH}_4$  (here modeled as an empty



**Figure 3.** (a–d) Free energies  $\circ$ , energies  $\times$ , and entropic contributions to the free energy  $+$  calculated for dipoles with magnitude 0.06 in a droplet with radius 4. Panels a–d corresponds to charges 0.1, 0.2, 0.3, and 0.4, respectively. The different positions are specified by their distance from the origin of the droplet on the  $x$  axis. Note that the position 2, 2, 1 is given the distance 2.95 and that the position 3, 0, 0 is given the distance 3.05.

**TABLE 1: Calculated Solvation Energies for Ions in Droplets with Radii 3 and 4 Obtained for Different Dipoles and Ions in Units of  $kT^a$**

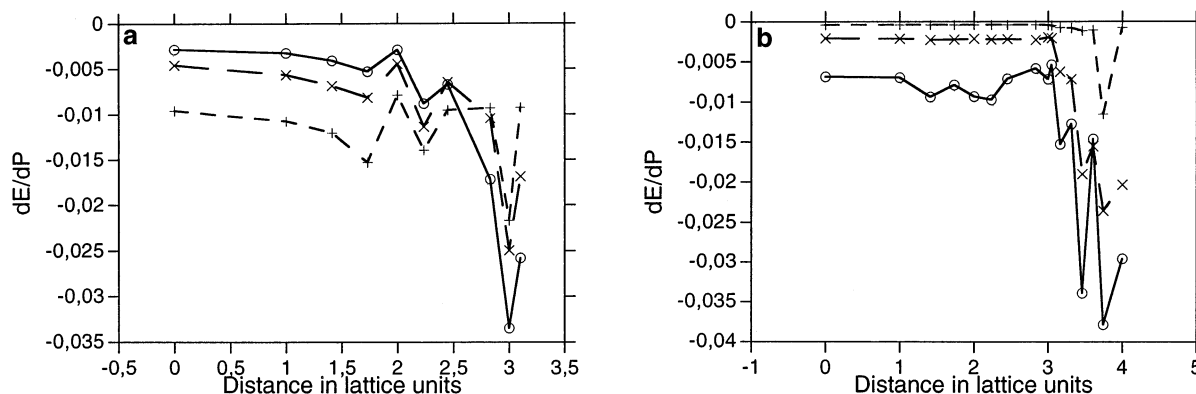
	$\mu = 0.01$	$\mu = 0.02$	$\mu = 0.04$	$\mu = 0.06$	$\mu = 0.08$	$\mu = 0.10$
$q = 0.0, r = 3$	0.1	0.6	5.3	17.1	32.7	54.4
$q = 0.0, r = 4$	0.1	0.6	5.6	16.7	31.5	51.9
$q = 0.1, r = 3$	-2.9	-5.5	-2.7	8.0	22.9	44.3
$q = 0.1, r = 4$	-3.1	-5.8	-2.1	8.9	22.8	42.8
$q = 0.2, r = 3$	-11.2	-21.6	-23.7	-15.7	-4.4	15.7
$q = 0.2, r = 4$	-12.1	-22.6	-22.7	-13.3	-2.3	16.7
$q = 0.3, r = 3$	-20.6	-44.3	-54.0	-49.5	-42.4	-26.1
$q = 0.3, r = 4$	-25.2	-47.8	-53.9	-46.6	-39.7	-23.4
$q = 0.4, r = 3$	-38.6	-74.7	-92.2	-91.8	-88.9	-76.3
$q = 0.4, r = 4$	-41.8	-79.5	-93.9	-89.6	-86.5	-73.6

<sup>a</sup> The solvation energy is calculated as the difference in energy between a dipolar lattice and a lattice where the central dipole is replaced with an ion.

lattice site), which creates structure by removing some of the inherent conflicts in the dipolar lattice, thereby promoting structure in the system. The structure-breaking particles are particles in which the sum of the induced ionic order and the reduced dipolar order adds up to a decrease in order. It should be noted that this discussion is a bit speculative since we have not calculated the entropy change associated with dissolving a hydrophobic particle in the dipolar droplet but only the entropy associated with transforming a dipole into a hydrophobic particle.

We are now in a position to understand the variation of the energy and free energy as a function of ionic position, ionic charge, and droplet size. We have seen above that the behavior of the energy and the free energy is almost the same for the larger charges. This means that the position of the ion is mainly determined by the energy, especially for the larger charges studied. For some systems, however, one can find significant contributions from the entropy to the free energy. If we start

by analyzing the results obtained for the smaller dipoles 0.01 and 0.02, we see that the general trends are exactly what could be expected from a dielectric cavity model in which either an ion or a dipole is placed in the cavity. In such a model, there would be a solvation energy for the ion and for the dipole. Both of these entities have a solvation free energy that decreases as the ion or dipole approaches the surface of the droplet. The ionic free energies are, however, much larger for all of the charges except for the case with an empty cavity (0 charge). This means that the position of the ion is the one that gives the maximum solvation energy for the ion (i.e., in the center of the droplet). However, for larger dipoles, there is a complicated interplay between the two types of structures discussed above. The forces favoring the ionic structure completely dominate for the smaller dipoles, but for the larger dipoles, the ions are capable of dominating only part of the system. Naturally, the larger the ionic charge is, the larger the region that is dominated by the ion, and the larger the dipole moment is, the larger the



**Figure 4.** (a, b)  $dE/dP$ , the derivative of the system energy with respect to the polarizability for the ion, is presented as a function of ionic position. The derivative is given in  $RT/(\text{lattice units})^3$ . The different positions are specified by their distance from the origin of the droplet on the x axis. Note that the position 2, 2, 1 is given the distance 2.95 and that the position 3, 0, 0 is given the distance 3.05. Panel a shows the variation of  $dE/dP$  for a lattice dipole of 0.07 for charges 0.2 (+), 0.3 (x), and 0.4 (O) and a droplet with radius 3. Panel b illustrates the variation with the size of the lattice dipoles for dipoles 0.01 (+), 0.05 (x), and 0.09 (O) for a droplet with radius 4 for an ion with charge 0.4.

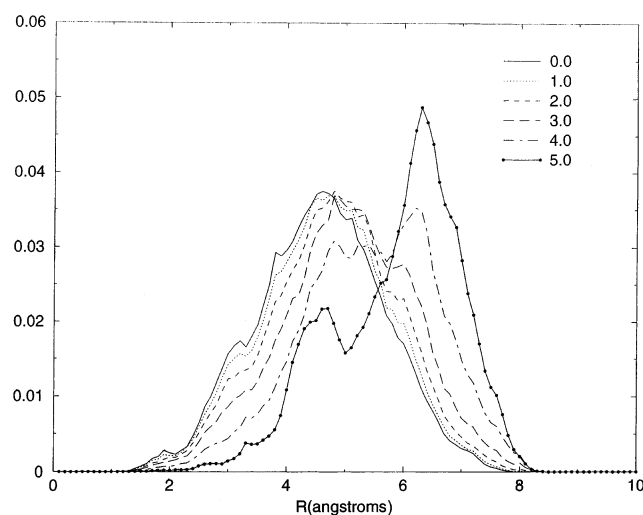
dipolar region is. The electric field at some sites in the boundary region between the two domains is smaller, and the dipoles at these sites will be relatively loosely bound. The system will try to reduce the interface between the two regions. This can be accomplished by moving the ion toward the surface of the droplet. This will naturally imply a worse solvation of the ion, but the interface region is reduced.

There is a fundamentally different way of looking upon the problem of solvation of an ion in a molecular medium that might give some insight into the process. The starting point for this approach is a simple dielectric model of an infinite system. The potential experienced by the ion in such a model could be calculated from  $-q(\epsilon - 1)/(\epsilon r)$  (in atomic units). Here,  $q$  is the charge, and  $r$  is the cavity radius. As before,  $\epsilon$  is the dielectric permittivity. If we assume an infinite value for  $\epsilon$ , a charge of 0.4, and a radius of 1, we obtain a value for the potential of 0.4. A dipole with magnitude 0.1 situated 1 unit of length away from the ion creates a potential of 0.1 at the ion. This means that it is easy for the dipoles to create the potential required by the ion and that not all of the dipoles are oriented by the ion since this would create a far too attractive potential for the ion. Dipoles situated at some distance from the ion are thus free or almost free to interact with other dipoles. For dipoles located at intermediate distances from the ion, it may be that some are involved in solvating the ion whereas others are mainly interacting with other dipoles.

### Summary and Generalization to Real Systems

We have seen in the previous section that the solvation of an ion in a dipolar lattice shows a rich and unexpected behavior. We have also seen that this unexpected solvation behavior is a consequence of the interplay between what we can call ionic and dipolar ordered regions. We have further seen that hydrophobic particles may promote the dipolar order. This means that the studied model gives some sort of rationalization of the concepts of structure making and structure breaking of solutes in water. The most important conclusion made in this work is that the interplay between the ionic and dipolar solvation regions is very important to the explanation of the observations made by Hofmeister more than 100 years ago.

At this point, the crucial question appears: Has the observed behavior anything to do with what is observed in real systems in general and in water in particular? The first issue that must be considered is whether the observations made in this work can be found for an ion dissolved in water. We have previously



**Figure 5.** Probability of finding the ion at a given distance from the center of mass of a water droplet made from 50 molecules. The different curves corresponds to different polarizabilities varying from 0 to 5 au in steps of 1 au. The curves are easily identified by the fact that the ion is monotonically displaced toward the surface with increasing polarizability.

published results obtained from molecular dynamics (MD) simulations of an ion in water, where the interaction potentials have been constructed using the NEMO approach.<sup>16a</sup> We are presently extending that study using MC simulations instead of MD simulations to avoid problems with temperature stability. In Figure 5, we present graphs showing the probability of finding an ion at a given distance from the center of mass of the cluster for a cluster containing 50 water molecules. The different graphs in the Figure correspond to different polarizabilities of the ion. The other potential parameters are chosen to describe a chloride ion in water. Figure 5 indicates that the ion is moved toward the surface when the polarizability is increased. The graphs in Figure 5 also indicate that there seem to be two different types of solvated ions and that their relative population changes with increasing polarizability. The data shown in Figure 5 is presented to show that the phenomena similar to the ones observed for the model system can be observed also in all-atom simulations. A full account of these all-atom simulations will be given elsewhere.<sup>16b</sup>

To further answer the question of the applicability of the results presented in this work for real systems, we must analyze the approximations in the model.

By far the largest differences between the studied system and a real polar liquid are the fixed position for the dipoles and the fact that we have studied a droplet instead of the surface of bulk water. These approximations probably make the system more crystal-like. One can, however, argue that on the length scale of a few molecular diameters a polar liquid is also highly structured. It is likely that the effect of the translation of the particles will reduce the observed effect and that the observed behavior will be shifted to larger values for  $\mu^2/V$ , where  $\mu$  is the particle dipole moment and  $V$  is the particle volume. It is more difficult to have any definite opinion about the differences between the interface of a droplet and the interface of bulk water. It would naturally have been interesting to study larger droplets, but it is presently not possible to obtain good statistics for such systems. The computational time grows approximately with the cube of the droplet radius. We have also seen that an increase in system size naturally modifies the behavior but not in a drastic way. Moreover, it seems from comparison of the droplets with radius 3 and 4 that the hydrophobic nature of the ions is larger for the larger droplet. It is thus very likely that the behavior seen in the droplet will exist in a modified way close to real interfaces. Another important approximation is that the particles lack polarizabilities. The main effect of polarizability on the dipolar particles would have been to increase the effective dipole moment of a lattice site, which implied that the studied effects would have been observed for smaller  $\mu^2/V$  values. The effect of polarizability on the ion has been studied, and the main effect is that it will favor positions close to the droplet surface. The mechanism is that when the ion is solvated in or close to the center of the droplet its solvation is almost isotropic and a small electric field is found on the ion, whereas a position close to the surface implies a nonisotropic solvation with a larger electric field on the ion.<sup>16</sup> (The stabilization energy is proportional to the polarizability and the square of the electric field on the polarizability.) One could also ask the question, would a different lattice change the behavior? Since the mechanism for what is observed is general in the sense that it is based on the incompatibility of the solvent structure preferred by the ion and the inherent structure of the solvent, one must expect the effect to be applicable to all liquids, provided that they are polar enough. There are, however, several aspects of the ionic solvation that cannot be studied by a lattice model. It would be interesting to be able to study the influence of the size and shape

of the ion as well as what the effect of a quadrupolar moment associated with the dipole would be. These may be properties that are of importance to understanding the difference between positive and negative ions apart from the fact that negative ions have larger polarizabilities.

An appropriate concluding remark is that it would be interesting to investigate whether effects similar as those observed in water could also be observed in other liquids. This question has, as far as we know, not been addressed.

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