Low density interior in supercooled aqueous nanodroplets expels ions to the subsurface

Shahrazad M. A. Malek,† Victor Kwan,‡ Ivan Saika-Voivod,†¶ and Styliani Consta∗,†‡

† Department of Physics and Physical Oceanography, Memorial University of Newfoundland, Canada, A1B 3X7
‡ Department of Chemistry, The University of Western Ontario, London, Ontario, Canada N6A 5B7
¶Department of Applied Mathematics, Western University, London, Ontario, Canada, N6A 3K7

E-mail: sconstas@uwo.ca

Abstract

The interaction between water and ions within droplets plays a key role in the chemical reactivity of atmospheric and man-made aerosols. Here we report direct computational evidence that in supercooled aqueous nanodroplets a lower density core of tetrahedrally coordinated water expels the cosmotropic ions to the denser and more disordered subsurface. In contrast, at room temperature, depending on the nature of the ion the radial distribution in the droplet core is nearly uniform or elevated towards the center. We analyze the spatial distribution of a single ion in terms of a reference electrostatic model. The energy of the system in the analytical model is expressed as the sum of the electrostatic and surface energy of a deformable droplet. The model predicts that the ion is subject to a harmonic potential centered at the droplet’s center of mass. We name this effect “electrostatic confinement”. The model’s predictions are consistent with the simulation findings for a single ion at room temperature but not at supercooling. We anticipate this study to be the starting point for investigating the structure of supercooled (electro)sprayed droplets that are used to preserve the conformations of macromolecules originating from the bulk solution.

Introduction

The spatial distribution of ions in droplets plays a decisive role in chemical reactivity in atmospheric and man-made aerosols. Applications of the man-made aerosols relevant to this study include spray-based ionization methods used in native mass spectrometry analysis1 and use of droplets as micro- (nano-) reactors for accelerating chemical synthesis.2–4 Aerosol droplets in the lower atmosphere carry a small charge determined by at most a few excess ions whereas droplets in thunderclouds and (electro)sprays are highly charged. In this article we show how a heterogeneous solvent structure in supercooled aqueous mesoscopic clusters charged with ions changes their spatial distribution relative to that at room temperature. Hereafter, we will use the term nanodroplets for these mesoscopic clusters.

The structure and stability of supercooled clusters composed of ionic species has fascinated scientists over several decades. Most of the experiments have been performed for clusters composed of a few tens of water molecules. Experiments have detected abun-
dance of certain “magic” cluster sizes associated with clathrate structures\textsuperscript{5} and have studied their reactivity in atmospheric chemistry.\textsuperscript{6} Many of these experiments have used Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry where dominant evaporative cooling of clusters over heating due to the absorption of black body radiation from the warmer walls of the apparatus\textsuperscript{5,6} has been reported. In certain FT-ICR experiments the temperature of clusters composed of 50-70H\textsubscript{2}O molecules is estimated to be 130 K-150 K. The hydration of ions in clusters at supercooling and elevated temperature in the last decade is actively investigated using infrared photodissociation spectroscopy.\textsuperscript{7–9} Moreover, supercooled droplets are used to preserve peptide conformations originating from the bulk solution in ion mobility and mass spectrometry experiments.\textsuperscript{1}

Most of the computational studies\textsuperscript{10–12,12–16,16–20,20–30} are for clusters at room or elevated temperatures, while there are relatively few computational studies\textsuperscript{15,17} of the supercooled clusters due to fact that they are notoriously challenging to be equilibrated. Voth and co-workers\textsuperscript{17} have investigated the location of a single Na\textsuperscript{+}, Cl\textsuperscript{−} and H\textsubscript{3}O\textsuperscript{+} ion in clusters of up to 100 H\textsubscript{2}O molecules in the temperature range of 100 K-450 K. They found that in supercooled clusters of 100 H\textsubscript{2}O molecules H\textsubscript{3}O\textsuperscript{+} and Na\textsuperscript{+} tend to reside within a few monolayers of the surface. At room and elevated temperature both the Na\textsuperscript{+} and Cl\textsuperscript{−} ions are found nearer to the center, while the H\textsubscript{3}O\textsuperscript{+} continues to be near the surface.

The spatial distribution of multiple ions in nanodroplets has been investigated less.\textsuperscript{31–33} Previously\textsuperscript{32,33} we reported atomistic simulations of the location of multiple ions in aqueous nanodroplets with diameter $\approx$ 2 nm - 16 nm at a temperature range of 300 K to 450 K. It was found that in droplets comprising $\approx$ 1000 H\textsubscript{2}O molecules, the radial ion distribution (measured from the droplet’s center of mass - COM) is almost uniform. As the droplet size increases, the distribution shows a distinct maximum in the outer droplet layers. The distribution decays almost exponentially toward the droplet’s COM. Toward the droplet exterior, the decay is determined by the ion size and shape fluctuations.\textsuperscript{32} The solution of the non-linear Poisson-Boltzmann equation for a spherical geometry\textsuperscript{34} is used as a reference model to compare with the atomistic simulations. The distributions of multiple ions and biological molecules such as peptides in supercooled droplets are still completely unknown.

The related question of the propensity of ions in a liquid-vapor planar interface has been studied over several decades.\textsuperscript{35–49} It is emphasized that the forces that determine the location of multiple ions in a planar interface are not the same as those in charged droplets regardless of their size. The reason is that the conductivity of the aqueous droplets drives the excess ions nearer to the surface and the counterions toward the interior.\textsuperscript{33} Another difference arises from the type of fluctuations that a droplet undergoes. Typical fluctuations in a charged droplet, regardless of its size, are the formation of conical protrusions, which are absent in a planar interface.\textsuperscript{50,51} These fluctuations may lead to release of ions from droplets. A single ion in a droplet is always subject to a harmonic potential centered to the droplets’ COM, as we show in this article. Such a force is not present in a planar interface. Detailed chemical interactions (e.g. charge transfer, solvent network) add one more layer of complexity in determining the ion position.

Here we study the radial distribution profiles of a single ion and multiple ions in relation to the solvent organization in supercooled aqueous clusters with sizes that vary from 100 H\textsubscript{2}O molecules (corresponding to a diameter of $\approx$ 1.8 nm) to 1100 (diameter $\approx$ 4.0 nm). Our recent computer simulations\textsuperscript{52} for pristine supercooled water clusters have revealed an anomalous, inverted radial density profile emerging for N $\geq$ 200 molecules at low temperature, in which a low-density core with relatively good tetrahedral ordering\textsuperscript{53} is surrounded by a high density subsurface. These observations have some commonalities with studies of nucleation within droplets and thin films.\textsuperscript{54–58} We hypothesize that the low density water core in supercooled droplets will differentiate the ion distribution from that at room temperature. This
hypothesis has not been explored earlier.\textsuperscript{17}

In order to obtain insight into the fundamental forces that determine the location of a single ion, we introduce a reference analytical model of a fluctuating droplet that contains a single ion. To our knowledge, such a reference model is still missing from the literature. In the model the energy of a fluctuating droplet is the sum of the electrostatic energy and surface energy. It predicts that an ion is always subject to a harmonic potential centered at the droplet’s COM. For this reason we name this effect “electrostatic confinement” (EC). The EC effect competes with the geometric confinement effect. We present the conditions under which the electrostatic confinement is more evident.

**Theory of Electrostatic Confinement**

Here, we present the key points of an analytical model that provides insight into the forces that determine the location of a single (macro)ion in a droplet. The details of the model are found in Sec. S1 in the SI. In the model we consider a charged dielectric droplet that may undergo shape fluctuations. The charge carrier can be a simple ion such as a Na\textsuperscript{+} or a single macroion with bound charge such as a protein or a nucleic acid. The energy of the charged droplet is written as the sum of the electrostatic energy and surface energy.

After some algebra (details are found in Sec. S1 in SI), it is found that the energy (denoted by $\Delta E_1$) related to the distance of the ion from the droplet’s COM is given by

$$\Delta E_1(||\mathbf{r}||) = \frac{\varepsilon - 1}{4\pi\varepsilon_0\varepsilon(\varepsilon + 2)} \frac{Q^2}{R^3} ||\mathbf{r}||^2$$  \hfill (1)

where $Q$, $R$ and $\varepsilon$ are the charge of the ion, the droplet radius and the relative dielectric constant of the solvent, respectively, $\varepsilon_0$ is the vacuum permittivity and $||\mathbf{r}||^2 = X_{\text{COM}}^2 + Y_{\text{COM}}^2 + Z_{\text{COM}}^2$ (where $X_{\text{COM}}, Y_{\text{COM}}, Z_{\text{COM}}$ are the coordinates of the droplet’s COM). The energy (1) has the functional form of a harmonic potential. From this point we would refer to this effect as “electrostatic confinement” (EC). We introduce the spring constant $K(\varepsilon)$ where

$$K(\varepsilon) = \frac{\varepsilon - 1}{4\pi\varepsilon_0\varepsilon(\varepsilon + 2)} \frac{Q^2}{R^3}.$$  \hfill (2)

In Fig. 1 we plot the value of the spring constant as a function of the relative dielectric constant for a droplet comprising 1000 water molecules and an ion. The electrostatic energy has two limiting cases $\varepsilon = 1$ and $\varepsilon = \infty$ when the electrostatic interaction of the ion with the droplet surface vanishes. In the former case the external and internal dielectric constants are equal and the droplet does not perturb the electric field of the ion. In the latter case the electrostatic field is localized in the vicinity of the ion and it is not affected by the droplet surface. As seen in the plot the maximum of the coefficient $K(\varepsilon)$ is attained at $\varepsilon = 1 + \sqrt{3} \approx 2.73$.

![Figure 1: Magnitude of the spring constant (Eq. 2) as a function of the relative dielectric constant $\varepsilon$. The values correspond to an ion of charge $Q = 1e$ in a droplet comprising 1000 water molecules and radius 19Å. The value of the potential has a maximum at $\varepsilon \approx 1 + \sqrt{3} \approx 2.73$.](image)

If the ion is localized in the droplet interior the Gibbs-Boltzmann distribution of the ion po-
Figure 2: Distribution of the distances of the COM of the cyclic peptide (grey colored histogram) measured from the droplet’s COM. The droplet radius is 3.8 nm and the charge of the peptide is 8e$^+$. The solid line is the gamma function fitted to the distribution using the maximum likelihood estimate (MLE). The inset shows a typical snapshot of the droplet composed of 8000 H$_2$O molecules (red colored) and the cyclic peptide (blue colored).

This probability distribution yields the radial concentration profile of the ion along the droplet radius. The expectation value of the square of the distance of the ion from the center of mass is given by

$$\langle \|r\|^2 \rangle = \frac{3}{2} \frac{k_B T}{K(\varepsilon)}.$$

The EC is more pronounced when the ion is localized at the center of the droplet, therefore we can write $\langle \|r\|^2 \rangle / R^2 \ll 1$. Analyzing Eqs. (2) and (4) we conclude that the effect will be more pronounced at low temperature, high charge, small radius and intermediate values of the dielectric constant. Small droplet with high

charge may undergo Rayleigh instability leading to the “star”-shaped droplets (see Fig. S2 in SI). If this is an issue in observations we need to increase the droplet radius while keeping constant the value of the Rayleigh parameter $X \sim Q^2 / R^3$. To illustrate the EC we model high charges by creating models of charged cyclic peptides. We could have used in the simulations a spherical ion with charge 8e$^+$ (or any other charge) instead of a cyclic peptide. The cyclic peptide is preferred because it is an effective way to create a large compact charge, which gives rise to realistic local electric fields that are not high enough to cause water dissociation. In experiments, a single ion with a high charge (e.g. 8e$^+$) may give rise to high local electric fields that may lead to water dissociation. The distribution of charge in a cyclic peptide does not cause this problem. DNA and RNA strands are other examples where the effect of the EC will be clearly observed. When a linear nucleic acid is used the droplet size should be large enough so that the linear geometry of the macroion does not affect the droplet’s spherical shape.

Using the maximum value of the $K$ parameter from Fig. 1 we obtain the estimate of the minimal dimensions of the excursions of the ion from its equilibrium position at the center of the droplet $\sqrt{\langle \|r\|^2 \rangle} \geq 12\text{Å}$. Therefore, for a droplet comprising 1000 water molecules and a single charge $Q = 1e$ the geometric confining effects should be taken into consideration.

In Fig. 2 the distribution of the distance of the center of mass of the peptide relative to the COM of the droplet is plotted. The droplet’s equimolar radius ($R_e$) is 3.8 nm and the charge is 8e$^+$. The distribution tapers off before reaching the droplet surface. Sampling proves to be a challenge in such systems. The simulation time should be much longer than the time for a molecule to diffuse the width of the droplet $D t_{\text{sim}} \gg R^2$. Typical values of the diffusion coefficient ($D$) are $\sim 10^{-9} \text{m}^2 \text{s}^{-1}$, hence the simulation time has to be in 10 ns 100 ns range at temperature $T = 300\text{K}$.

In summary, there is always a force on an ion toward the droplet’s COM. The electrostatic confinement effect is more pronounced for
an ion with a charge of at least $\pm 3e$ (where $e$ is the elementary positive charge) found in a droplet with a small radius. The radius size is equal or moderately larger than the radius at the Rayleigh limit. The Rayleigh limit is defined as the point where the electrostatic forces balance the surface forces. For a radius smaller than that at the Rayleigh limit, the droplet shows instability, which is manifested by “star”-shapes. The model can be extended further by including other factors such as the ion size and hydrophobic effects.

**Experimental: Models and Simulation Methods**

Here we present the main points of the computational methods. A detailed account of the methodology and parameters are found in Sec. S2 in SI. We performed equilibrium molecular dynamics (MD) simulations of aqueous nanodroplets charged with a single ion $\text{Na}^+$, $\text{Li}^+$, $\text{Cs}^+$, $\text{F}^-$, $\text{Cl}^-$, $\text{I}^-$, and multiple $\text{Na}^+$ ions. The droplets range in size from 100 H$_2$O molecules ($R_e = 0.87$ nm) - 1100 H$_2$O molecules ($R_e = 2.0$ nm). The temperature of the droplets was set at $T = 200$ K for supercooled droplets and at 300 K (room temperature) except for the 100-H$_2$O-molecule droplets that were simulated at 260 K instead of 300 K. The MD simulations were performed using GROMACS v4.6.1 and NAMD v2.14. The water molecules are modeled with the TIP4P/2005 (transferable intermolecular potential with four points) model. We selected the TIP4P/2005 because it reproduces well the density anomaly in liquid water, the liquid-gas surface tension over a broad range of temperatures and the liquid-gas coexistence line in the density-temperature plane. We also performed a number of simulations with a Drude oscillator-based polarizable model, where the H$_2$O molecules are represented with the SWM4-NDP model and the ions, Na$^+$ and Li$^+$ with the CHARMM Drude force field. The equations of motion for the TIP4P/2005 set of simulations were integrated with a time step of 2.0 fs and for the SWM4-NDP model with 1.0 fs. Each nanodroplet was placed in a closed volume so that it is in equilibrium with its vapor. The volume is large enough to accommodate the droplet’s shape fluctuations. The simulations were carried out in the canonical ensemble – constant number of molecules ($N$), volume, and $T$. The trajectories were visualized using VMD 1.9.4a47.

To analyze the features of the radial distribution (concentration) profiles of the ions in relation to the water structure, we use several parameters: (a) the density of water as determined from the Voronoi volumes associated with each water molecule, denoted by $\rho_T(r)$ (where $r$ denotes the distance from the droplet’s COM); (b) the tetrahedral order parameter, denoted by $q_T(r)$, and (c) the distance to the fifth nearest neighbor O of a given O atom denoted by $d_5$.

The parameter $q_T(r)$ is defined as follows. Initially, the tetrahedral order parameter, at the level of a single particle is defined as,

$$q_i = 1 - \frac{3}{8} \sum_{j=1}^{3} \sum_{k=j+1}^{4} \left[ \cos \psi_{jik} + \frac{1}{3} \right]^2,$$

where $\psi_{jik}$ is the angle between an oxygen atom $i$ and its nearest neighbor oxygen atoms $j$ and $k$ within a distance of $r_{cut} = 0.35$ nm. The radial function $q_T(r)$ as the average value of $q_i$ for all molecules within a spherical shell enclosed within $r \pm \Delta r/2$, where $\Delta r = 0.05$ nm. Similarly, we report results for $d_5(r)$, the average distance to the fifth O neighbor for O atoms located in the same spherical shell centered at $r$. We note that we find sometimes slight, but no significant differences for $\rho(r)$, $\rho_w(r)$, $q_T(r)$ and $d_5(r)$ whether an ion is present or not, and therefore use well-sampled data for these quantities for pure water taken from previous studies.

**Results**

**Single ion**

The main idea of the present article is that the low-density tetrahedral network that forms at
sufficiently low $T$ in the core of sufficiently large nanodroplets tends to expel certain ions to the relatively higher-density and more disordered subsurface. Fig. 3 illustrates this structure for the case of an $N = 776$ nanodroplet. The density structure of the nanodroplet is approximately the same for the nanodroplet whether it contains a single, several or no ions. Using a $N = 776$-Na$^+$ nanodroplet as an example, it is found that at 200 K, the $0 < r < R_B = 7.4$ Å region includes on average 57.14 oxygen sites yielding a number density $33.66 \pm 0.15$ nm$^{-3}$. The subsurface, $R_B < r < R_V = 14.8$ Å includes on average 410.62 O sites yielding a number density $34.56 \pm 0.15$ nm$^{-3}$. At 300 K, the density in the core is $34.38 \pm 0.15$ nm$^{-3}$ and in the subsurface $34.14 \pm 0.15$ nm$^{-3}$, and thus the difference at 200 K is inverted and significantly larger than at 300 K.

A more quantitative description is provided in Fig. 4, which shows the relation of the water structure and the probability density of the ion at 300 K (red curves) and 200 K (black curves). Fig. 4 (a) shows the H$_2$O radial density ($\rho(r)$) using the physical volume. Even though $\rho(r)$ profiles are typically used to identify a cluster’s boundary, they may mask certain features. The decrease in the density profile close to the cluster’s boundary masks the role of the shape fluctuations. Also, the fact that the profiles are built around the cluster’s COM, which is not one of the molecular entities in the system, may overemphasize the layered structure of the solvent at supercooling. In larger particles (e.g. aerosols) the plot will provide the average density of the droplet as a function of radius and layering will not be present. For this reason, we use additional measures of the solvent structure such as the Voronoi volume, $q_T$ and $d_5$. Note that for $r < 0.2$ nm, good statistics are difficult to obtain for all radial quantities, and results in this regime are quite noisy. The density using the Voronoi volume ($\rho_V(r)$) is also shown in Fig. 4 (a). The main feature of $\rho_V(r)$ is that it decays rapidly for surface atoms – those with large Voronoi volumes that extend outside the nanodroplet. To define a surface region we find $R_V$ such that $\rho_V(R_V) = \rho(R_e)$. Given this, approximately two thirds of the molecules at $r = R_V$ have unbounded Voronoi volumes. In panel (b) we show a close-up of $\rho_V(r)$. While monotonically decreasing with $r$ at large $T$, at low $T$, $\rho_V(r)$ is approximately constant for $r < R_B$ and then increases to a maximum at $r = R_P$. We choose $r = R_P$ as a representative feature of the subsurface, which now by default occupies $R_B < r < R_V$. Panels (c) and (d), showing $q_T(r)$ and $d_5(r)$, respectively, likewise show a bulk-like core with uniform properties for $r < R_B$ and a more disordered subsurface. The parameter $d_5$, a more indirect measure of the quality of the tetrahedral network, shows
Figure 4: Structure of pristine water droplet, single Na$^+$ and single F$^-$ distributions for $N = 776$ at $T = 200$ K (black line) and $T = 300$ K (red line). Shown as functions of $r$ are (a) density $\rho$ and density determined from Voronoi volumes $\rho_v$; (b) a close up of $\rho_v$; (c) tetrahedral order parameter $q_T$; (d) distance of the fifth O neighbor $d_5$; (e) Na$^+$ concentration, $C_{Na}$, for a single ion, which for 200 K includes results from starting the ion at the centre (in) and at the surface (out); and (f) same as (e) but for F$^-$. In panel (b), $R_P$ marks the maximum in $\rho_v$, a feature representative of the subsurface at low $T$. The horizontal bars in panel (e) approximate the spatial extent of $C_{Na}$ for 200 K (brown) and 300 K (red), and appear in Fig. 5. See details in the text.

| C$\rho$ [mol L$^{-1}$] | $C_{Na}$ [mol L$^{-1}$] | $R_P$ | $R_V$ | $R_e$ |
|------------------------|------------------------|-------|-------|-------|
| 0.2                    | 0.2                    | 0.2   | 0.2   | 0.2   |

Na$^+$ concentration $C_{Na}$ at 200 K (black line) and 300 K (red line) as obtained from starting the ion near the centre and starting near the surface are compared – thus showing the degree of equilibration we achieve. At $T = 300$ K, $C_{Na}(r)$ is approximately constant in the interior of the droplet, and begins to decay within the subsurface, becoming small by $R_V$ and decaying to zero significantly before $\rho(r)$ does. At room temperature the Na$^+$ concentration profile is consistent with the EC model. Because of the low charge, the geometric confinement effect dominates over the force toward the droplet’s COM. For this reason, the Na$^+$ radial distribution does not distinctly peak at the droplet’s COM, but it appears to be almost uniform.

Fig. 4 (e) shows a significant difference in $C_{Na}(r)$ at low $T$. Rather than being uniform, $C_{Na}(r)$ has a peak located within 0.2 nm from $R_P$. Thus, we see that in a nanodroplet with a heterogeneous radial density, as determined by $\rho_v(r)$, the single Na$^+$ ion tends to reside in the highest density environment for most of the time. This tendency is consistent with the fact that for constant $T$ and polarization factor (degree of dipole ordering),$^{78}$ the dielectric constant increases with increasing density.

The thick horizontal bars shown in Fig. 4(e) measure the approximate extents of $C_{Na}(r)$ for low (brown) and high (red) $T$, and are drawn between $C_{Na}$ values of half the peak or plateau height. For 300 K, notwithstanding noise below $r = 0.2$ nm, the distribution extends to the center of the droplet, and so the left end point of the red bar is at $r = 0$. These horizontal bars are replotted vertically in Fig. 5 along with $R_B$, $R_P$, $R_V$ and $R_e$, for other nanodroplet sizes. The detailed Na$^+$ radial distribution profiles and the histograms of the raw data for the various droplet sizes are shown in Figs. S3 and S4, respectively, in SI. Fig. 5 shows the same trend in the structure of the H$_2$O and the location of the ions as found for $N = 776$. Measures of structure for low temperature ($T = 200$ K) as
those shown in Fig. 4 and in detail in Fig. S4 in SI are summarized in Fig. 5. The convergence of the trajectories for Na\(^+\) starting on the surface and the droplet’s COM is shown in Fig. S5 in SI. The surface thickness is estimated to be \(R_e - R_V \approx 0.3\) nm and the subsurface thickness \(R_V - R_B \approx 0.7 - 0.8\) nm for all sizes studied. It is noted that the cluster of \(N = 100\) does not show a tetrahedrally organized core.

Similarly to Na\(^+\), at 300 K, F\(^-\) (Fig. 4 (f)) and Li\(^+\) (Fig. S6 in SI) show higher concentration in \(0 < r < R_B\). Behavior consistent with our present study for F\(^-\) at 300 K has been reported in Ref.\(^{15,42}\) for clusters composed of 124-145 \(\text{H}_2\text{O}\) molecules. However, these systems are too small to show the effect of a core and subsurface in the ion location. We find that at 200 K, the maximum of the F\(^-\) concentration is shifted into the subsurface \(R_B < r < R_V\), and similarly for Li\(^+\).

In Fig. 6, we summarize how the concentration changes in the bulk core \((0 < r < R_B)\), subsurface \((R_B < r < R_V)\) and surface \((R_V < r < R_e)\) regions on changing \(T\) from 300 K to 200 K for ions other than Na\(^+\) in an \(N = 776\) nanodroplet. The details of the concentration profiles as a function of the distance from the droplet’s COM and the histograms of the raw data are shown in Figs. S6 and S7, respectively, in SI. Fig. 6 shows a significant decrease in the core concentration, and commensurate increase in the subsurface concentration, for Li\(^+\) and F\(^-\), and, to a lesser extent, for Cs\(^+\) as well. The larger anions Cl\(^-\) and I\(^-\) show no significant change.

In order to understand better the concentration changes at 200 K we discuss the direct observation of transition events between the core and subsurface at 200 K, which are shown in Figs. S8, S9, and 10 in SI. Li\(^+\) and F\(^-\) show only 1-2 events entering the core over a 2 \(\mu\)s (considering two MD trajectories of 1 \(\mu\)s each) production run, Cs\(^+\) shows 3-4 events and Cl\(^-\), I\(^-\) 5-6 events. During these rare events all the ions that we study are trapped within the core for at least 20 ns. Thus, differently from 300 K, where the large probability density in the core appears due to the frequent transitions between core and subsurface (Fig. S11 in SI), at 200 K, an increase in the probability density in the core appears due to the long residence time in this region.

The time evolution of the Cl\(^-\) transition events (Figs. S9 (a) in SI) does not show specific preference for the interior or the surface at both temperatures. A similar propensity for Cl\(^-\) ions was pointed out by Zhao et al.\(^{15}\) who performed simulations of halogen anions in a cluster of 124 \(\text{H}_2\text{O}\) molecules at room temperature and at supercooling using Born-Oppenheimer (BO) MD
simulations. In BO-MD the interactions are described by quantum density functional theory (DFT). The agreement between the results supports the validity of TIP4P/2005 to predict the location of the ions. The direct monitoring of the transitions, Fig. S9 in SI, shows that Cl$^-$ and I$^-$ interact more than the other ions with the border of the bulk core ($4.0 \ < r < 7.4 \ \text{Å}$) while in the subsurface, which may be the reason that allows them to make more frequent transition into the core than other ions. The Cs$^+$ ion, even though a chaotropic ion like Cl$^-$ and I$^-$, shows some features similar to Li$^+$, in that it does not frequently access the border of the bulk-like core as Cl$^-$ and I$^-$ do. In the rare transitions to the core, it remains trapped for a significant amount of time and for this reason its concentration profile appears bi-modal. A general observation from all the trajectories is that the crossing of the core is relatively faster than the residence time within the core, which indicates the presence of high potential energy barriers. The transition paths can be step-wise or rapid, which reflect the variety of pathways that can lead the ions in and out of the core region.

Now we examine the time correlation function for the exchange of the H$_2$O molecules surrounding F$^-$ in $N = 776$. Following the approach of D. Chandler in Ref. 79 we define a state variable, $N_A$ which is 1 if a H$_2$O molecule is within a sphere of radius 6.0 Å with center the F$^-$ ion and zero otherwise. Using this state variable we compute the correlation function $\langle N_A(t)N_A(0) \rangle$. The correlation functions at 300 K and 200 K are shown in Fig. 7. The correlation functions decay to the ratio of the number of H$_2$O molecules contained in the volume of radius 6.0 Å over the total number of molecules in the droplet. We find that the decay time at 300 K is 64 ps and at 200 K 10.7 ns. The ratio of the decay time at 200 K to 300 K is $\approx 200$ times larger than the ratio of the average velocities of the molecules at the two temperatures. The long residence time of the ions in the core and subsurface region is consistent with the decay time of the correlation function. Thus, in addition to structural and energetic factors that determine ion location, the two-orders-of-

magnitude slowing down in dynamics at low $T$ may be necessary to consider when time scales
relevant to an experiment become comparable to the decay time. Further complexities arise from the fact that dynamics at the surface and subsurface should be significantly faster than in the core. We have not addressed the radial dependence of the dynamics here, but we expect to address this in the future.

To test the effect of the force field in the different density regions, simulations were performed with a Drude oscillator-based force field,\textsuperscript{75} which uses the SWM4-NDP H\textsubscript{2}O model. The ion distribution profiles for a single Na\textsuperscript{+} and Li\textsuperscript{+} in an N=880 H\textsubscript{2}O droplet at 350 K and 200 K are presented in Fig. S14 and Fig. S15 in SI. At high temperature, similar to the runs with TIP4P/2005, the Na\textsuperscript{+} and Li\textsuperscript{+} radial distributions are uniform in the core and in part of the subsurface. The Li\textsuperscript{+} shows a preference toward the center. In both the TIP4P/2005 and SWM4-NDP the concentration of the ions starts to increase at 1.6 nm, which indicates that the depth from the surface is in good agreement between the two models. At low temperature it has been found that POL3 and SWM4-NDP are not suitable for ice-liquid simulation - they lead to a poor representation of ice.\textsuperscript{80,81}

We note here that the temperature in different molecular models may not correspond to the same physical state of the cluster. At 200 K, simulations of bulk solution have shown that SWM4-NDP is close to the point of maximum density of water.\textsuperscript{80,81} We have confirmed that even in clusters at 200 K the density is at its maximum. At 350 K, the density in the core is 32.79 ± 0.15 nm\textsuperscript{-3} and in the subsurface 32.39 ± 0.15 nm\textsuperscript{-3} while at 200 K, the density is 36.15 ± 0.15 nm\textsuperscript{-3} and 35.85 ± 0.15 nm\textsuperscript{-3}, respectively. Interestingly, both the Li\textsuperscript{+} and Na\textsuperscript{+} distributions using the polarizable model show their maximum in the subsurface, similarly to the TIP4P/2005. Disregarding the unrealistic nature of the density in the cluster for SWM4-NDP, this example demonstrates that there may be an optimal density for solvation of the ions.

Regarding the relation of the subsurface structure in a droplet to that of a planar surface we note that densification at supercooling also occurs for a planar interface.\textsuperscript{57,82} In the temperature range of our study, the clusters are still in the liquid state. The experiments of Pradzynski et al. have shown the possibility of ice formation in clusters composed of several hundreds of water molecules.\textsuperscript{7} The authors estimated that the temperature of the clusters is 90 K-115 K. We expect that in order to see a phase transition in the systems that we study, we should decreases the temperature below 200 K. In the analysis of surface layers it will be challenging to distinguish small-particle surface melting from size-dependent melting.\textsuperscript{83}

The expulsion of the ions from the core is reminiscent of brine rejection from ice, where upon crystallization ions are expelled into the liquid.\textsuperscript{84,85} While liquid water lacks the long-range order of the crystal, the low-density form of the liquid, like ice, possesses a network structure, characterized by a first sharp diffraction peak in the structure factor arising from a high degree of tetrahedrality.\textsuperscript{86–88} The value of $qT$ of deeply supercooled liquid water is comparable to that of ice.\textsuperscript{53,84} For nanodroplets, the more disordered and denser subsurface appears to play the role of liquid water in usual brine rejection at freezing. We expect that the dynamics and the precise steps of the ion rejection mechanisms from the low-density core in nanodroplets will be different from those in bulk ice. It is noted that in simulations of brine rejection,\textsuperscript{84} Na\textsuperscript{+} is rejected faster than Cl\textsuperscript{−}, with Cl\textsuperscript{−} being more than twice as likely to be incorporated into the crystal lattice, an observation not dissimilar to what we see in terms of Cl\textsuperscript{−} remaining in the low-density liquid nanodroplet core, although sampling equilibrium distributions in the case of brine rejection is certainly more difficult.

**Multiple Na\textsuperscript{+} ions**

Figure 8 shows the radial distributions of multiple ions at $T = 300$ K and 200 K in droplets comprising 1100 H\textsubscript{2}O molecules. The same plot for a system of 776 H\textsubscript{2}O molecules - 5 Na\textsuperscript{+} ions is shown in Fig. S16 in SI. At $T = 300$ K the distributions (for 1100 and 776 H\textsubscript{2}O molecules) are almost uniform with an incipient broad maximum appearing in the outer layers of the
Note that in the larger droplets the effect of the counterions in $\lambda_{PB}$ has also to be considered.\textsuperscript{34} Evidently, the higher temperature will lead to a slower ion decay. For 1100 H$_2$O - 8 Na$^+$ ions at $T = 300$ K the distribution decays (toward the droplet’s COM) as an exponential function fitted by $0.40 \exp(-(1.37 - r)/1.3)$, where $\lambda_{PB} \approx 1.3$ nm (note: to convert from $n(r)$ in nm$^{-3}$ to $C_{Na}(r)$ in mol/L, one should multiply $n(r)$ by 10/6.022). Equation 7 with dielectric constant of water equal to 75, yields $\lambda_{PB} \approx 0.8$. In droplets of up to a few thousands of water molecules the effect of shape fluctuations is significant, therefore, we interpret the value of $\lambda_{PB}$ only in a qualitative manner. A value of $\lambda_{PB}$ in the range of 0.8 nm (theoretical estimate)-1.3 nm (from fitting) is comparable in magnitude with the droplet radius ($R_e = 2.0$ nm), which indicates that the radial distribution function will decay slowly toward the COM. The predicted slow decay is indeed found in the simulations. The ion distribution at $T = 200$ K decays in a way that cannot be analyzed using the NPB predictions at the lower temperature. The multiple ions similarly to the single ion are expelled from the drop’s core and their distribution shows a maximum at the same location as the single ion (Fig. 8). The distribution shows two peaks at a distance 0.52 nm and at 1.5 nm. The lower intensity peak at 0.52 nm corresponds to a single ion that exchanges location with the outer ions (found at $\approx 1.5$ nm). The mobility of the inner ion indicates that the appearance of the two peaks is not due to a metastable state.

**Conclusions**

We found that in supercooled aqueous droplets, a heterogeneous solvent structure leads to a different ion radial distribution relative to that at a room temperature. Specifically, we demonstrated that the interior tetrahedral network that forms at supercooling expels cosmotropic ions (Na$^+$, Li$^+$, F$^-$) from the core region to the more disordered subsurface. The radial distribution of chaotropic ions (Cl$^-$, I$^-$, Cs$^+$) appear to be affected less by the presence of the bulk-
structured core. They also spend most of the time in the subsurface from where they make rare incursions to the core region. Once inside the core, they reside there for a significant amount of time.

The atomistically simulated ion radial distributions are supported by a reference analytical model that predicts the location of an ion in a fluctuating droplet. The theory finds that an ion (regardless of its nature) is always subject to a harmonic potential centered at the droplet’s center of mass. This electrostatic confinement effect is more pronounced for certain droplet dimension and charge of the ion. In the supercooled nanodroplets the model predictions deviate from the simulated ion distributions due to the specific organization of the solvent that is currently not included in the analytic model.

We expect the effect of the heterogeneity in the solvent structure to appear even in the larger droplet sizes. In microdroplets, where thermodynamics of the phase transitions will be similar to that in the bulk solution, ice may form in the interior and then the ions will be expelled most likely in a similar manner to the brine rejection from bulk ice. In a planar surface, where liquid layers cover ice, the dependence of the thickness and ordering of the liquid surface layer on temperature has been studied for several decades.\textsuperscript{89,90} A similar investigation for the subsurface and surface layers is still missing for the nanodroplets.

The present study opens up the discussion on several questions. Evaporative cooling of droplets is a process that has been reported to be important in a droplet’s lifetime in ionization methods used in native mass spectrometry. The implications of the distribution of multiple ions in the subsurface in a Rayleigh fission and ion-evaporation mechanism have to be examined. A conical deformation is a key structure in the mechanism of ion emission.\textsuperscript{51} An intriguing question is whether the formation of a conical deformation in the droplet that emits ions is affected by the low density liquid at supercooling or an ice interior. A related question is whether the Rayleigh limit of a supercooled droplet changes since the conducting region for certain ions is restricted to the subsurface and surface instead of exploring the volume of the entire droplet. A study on these questions will be relevant to atmospheric chemistry, native mass spectrometry and the physics of jets.

We anticipate our study to provide the starting point for investigating the structure of the supercooled droplets containing unstructured peptides and complexes of ions. Several possible scenarios are envisioned that may affect the charge states of macromolecules. On the one hand, if a macromolecule and simple ions are expelled to the subsurface, the macromolecule will be exposed to a higher concentration of ions and different structure of solvent than that at room or elevated temperature. Thus, their charge state and release mechanism will be determined by the distinct chemical features of the subsurface. On the other hand, if a macromolecule is trapped in a glassy core its diffusion toward the surface will be delayed and its exposure to ions will be altered, which will in turn affect its charge state. We envisage that studies in this direction will assist in interpreting ion mobility-mass spectrometry data on the detection of the conformations of macromolecules originating from the bulk solution and will provide insight into the chemistry of atmospheric aerosols.

Supporting Information

(S1) Derivation of the electrostatic confinement (EC) model and comparison with atomistic simulations of an ion in a droplet. (S2) Details of the computational methods and models. (S3) Water density and structure, and single Na\textsuperscript{+} radial concentration for various droplet sizes (S4) Evidence of the convergence of the simulation data, and radial probability density (concentration) profiles for \(\Gamma^-\), \(\text{Cl}^-\), \(\text{F}^-\), \(\text{Li}^+\), \(\text{Cs}^+\) in room temperature and supercooled nanodroplets. (S5) Radial distribution functions for ion-Oxygen of \(\text{H}_2\text{O}\) and ion-Hydrogen of \(\text{H}_2\text{O}\). (S6) Radial probability density (concentration) profiles of ions in supercooled and room temperature nanodroplets using a polarizable molecular model. (S7) Multiple-ion radial concentration profiles in supercooled and room
Acknowledgments

S.C. thanks Prof. D. Frenkel, Department of Chemistry, University of Cambridge, UK, and Dr. Anatoly Malevanets, The University of Western Ontario for discussions on the stability of charged systems. Professor D. Russell, Department of Chemistry, Texas A & M University is thanked for pointing out the variable temperature ESI source and the role of cold droplets in transferring the protein conformations for MS analysis. V.K. acknowledges the province of Ontario and the University of Western Ontario for the Queen Elizabeth II Graduate Scholarship in Science and Technology. I.S.-V. thanks the Departments of Applied Mathematics and Chemistry at Western University for sabbatical hosting. We acknowledge the financial support from Natural Sciences and Engineering Research Council (Canada). Computational resources were provided by ACENET and Compute Canada.

References

(1) Raab, S. A.; El-Baba, T. J.; Woodall, D. W.; Liu, W.; Liu, Y.; Baird, Z.; Hales, D. A.; Laganowsky, A.; Russell, D. H.; Clemmer, D. E. Evidence for Many Unique Solution Structures for Chymotrypsin Inhibitor 2: A Thermodynamic Perspective Derived from vT-ESI-IMS-MS Measurements. J. Am. Chem. Soc. 2020, 142, 17372–17383.

(2) Bain, R. M.; Pulliam, C. J.; Cooks, R. G. Accelerated Hantzsch electrospray synthesis with temporal control of reaction intermediates. Chem. Sci. 2015, 6, 397–401.

(3) Ingram, A. J.; Boeser, C. L.; Zare, R. N. Going beyond electrospray: mass spectrometric studies of chemical reactions in and on liquids. Chem. Sci. 2016, 7, 39–55.

(4) Sahraeian, T.; Kulyk, D. S.; Badu-Tawiah, A. K. Droplet Imbibition Enables Non-Equilibrium Interfacial Reactions in Charged Microdroplets. Langmuir 2019, 35, 14451–14457.

(5) Lee, S.-W.; Freivogel, P.; Schindler, T.; Beauchamp, J. Freeze-dried biomolecules: FT-ICR studies of the specific solvation of functional groups and clathrate formation observed by the slow evaporation of water from hydrated peptides and model compounds in the gas phase. J. Am. Chem. Soc. 1998, 120, 11758–11765.

(6) Schindler, T.; Berg, C.; Niedner-Schatteburg, G.; Bondybey, V. E. Heterogeneously catalyzed hydrolysis of chlorine nitrate: Fourier-transform ion cyclotron resonance investigations of stratospheric chemistry. J. Chem. Phys. 1996, 104, 3998–4004.

(7) Pradzynski, C. C.; Forck, R. M.; Zeuch, T.; Slaviček, P.; Buck, U. A fully size-resolved perspective on the crystallization of water clusters. Science 2012, 337, 1529–1532.
(8) Stachl, C. N.; Williams, E. R. Effects of temperature on Cs+ (H2O) 20 clathrate structure. *J. Phys. Chem. Lett.* 2020, 11, 6127–6132.

(9) Cooper, R. J.; DiTucci, M. J.; Chang, T. M.; Williams, E. R. Delayed onset of crystallinity in ion-containing aqueous nanodrops. *J. Am. Chem. Soc.* 2016, 138, 96–99.

(10) Lu, D.; Singer, S. J. Ion solvation in model polar clusters. *J. Chem. Phys.* 1996, 105, 3700–3714.

(11) Gorlova, O.; DePalma, J. W.; Wolke, C. T.; Brathwaite, A.; Odbadrakh, T. T.; Jordan, K. D.; McCoy, A. B.; Johnson, M. A. Characterization of the primary hydration shell of the hydroxide ion with H2 tagging vibrational spectroscopy of the OH−-(H2O) n= 2, 3 and OD−-(D2O) n= 2, 3 clusters. *J. Chem. Phys.* 2016, 145, 134304.

(12) Herce, D. H.; Perera, L.; Darden, T. A.; Sagui, C. Surface solvation for an ion in a water cluster. *J. Chem. Phys.* 2005, 122, 024513.

(13) Perera, L.; Berkowitz, M. L. Ion solvation in water clusters. *Z. Phys. D Atom Mol. Cl.* 1993, 26, 166–168.

(14) Thaunay, F.; Ohanessian, G.; Clavaguera, C. Dynamics of ions in a water drop using the AMOEBA polarizable force field. *Chem. Phys. Lett.* 2017, 671, 131–137.

(15) Zhao, Y.; Li, H.; Zeng, X. C. First-principles molecular dynamics simulation of atmospherically relevant anion solvation in supercooled water droplet. *J. Am. Chem. Soc.* 2013, 135, 15549–15558.

(16) Hagberg, D.; Brdarski, S.; Karlström, G. On the solvation of ions in small water droplets. *J. Phys. Chem. B* 2005, 109, 4111–4117.

(17) Burnham, C. J.; Petersen, M. K.; Day, T. J.; Iyengar, S. S.; Voth, G. A. The properties of ion-water clusters. II. Solvation structures of Na+, Cl-, and H+ clusters as a function of temperature. *J. Chem. Phys.* 2006, 124, 024327.

(18) Makov, G.; Nitzan, A. Solvation and ionization near a dielectric surface. *J. Phys. Chem.* 1994, 98, 3459–3466.

(19) Fifen, J. J.; Agmon, N. Structure and spectroscopy of hydrated sodium ions at different temperatures and the cluster stability rules. *J. Chem. Theory Comput.* 2016, 12, 1656–1673.

(20) Galib, M.; Baer, M.; Skinner, L.; Mundy, C.; Huthwelker, T.; Schenter, G.; Benmore, C.; Govind, N.; Fulton, J. L. Revisiting the hydration structure of aqueous Na+. *J. Chem. Phys.* 2017, 146, 084504.

(21) Perera, L.; Berkowitz, M. L. Structure and dynamics of Cl-(H2O) 20 clusters: The effect of the polarizability and the charge of the ion. *J. Chem. Phys.* 1992, 96, 8288–8294.

(22) Perera, L.; Berkowitz, M. L. Erratum: Many-body effects in molecular dynamics simulations of Na+ (H2O) n and Cl-(H2O) n clusters [J. Chem. Phys. 95, 1954 (1991)]. *J. Chem. Phys.* 1993, 99, 4236–4237.

(23) Perera, L.; Berkowitz, M. L. Many-body effects in molecular dynamics simulations of Na+ (H2O) n and Cl-(H2O) n clusters. *J. Chem. Phys.* 1991, 95, 1954–1963.

(24) Caleman, C.; Hub, J. S.; van Maaren, P. J.; van der Spoel, D. Atomistic simulation of ion solvation in water explains surface preference of halides. *Proc. Natl. Acad. Sci. U.S.A.* 2011, 108, 6838–6842.

(25) Werhahn, J. C.; Akase, D.; Xantheas, S. S. Universal scaling of potential energy functions describing intermolecular interactions. II. The halide-water and alkali
metal-water interactions. *J. Chem. Phys.* **2014**, *141*, 064118.

(26) Vaitheeswaran, S.; Thirumalai, D. Hydrophobic and ionic interactions in nanosized water droplets. *J. Am. Chem. Soc.* **2006**, *128*, 13490–13496.

(27) Harder, E.; Roux, B. On the origin of the electrostatic potential difference at a liquid-vacuum interface. *J. Chem. Phys.* **2008**, *129*, 12B613.

(28) Fracchia, F.; Del Frate, G.; Mancini, G.; Rocchia, W.; Barone, V. Force field parametrization of metal ions from statistical learning techniques. *J. Chem. Theory Comput.* **2018**, *14*, 255–273.

(29) Kwan, V.; Consta, S. Molecular Characterization of the Surface Excess Charge Layer in Droplets. *J. Am. Soc. Mass Spectrom.* **2021**, *32*, 33–45, PMID: 32597645.

(30) Duignan, T. T.; Mundy, C. J.; Schenter, G. K.; Zhao, X. S. Method for Accurately Predicting Solvation Structure. *J. Chem. Theory Comput.* **2020**, *16*, 5401–5409.

(31) Zdrali, E.; Okur, H.; Roke, S. Specific ion effects at the interface of nanometer-sized droplets in water: structure and stability. *J. Phys. Chem. C* **2019**, *123*, 16621–16630.

(32) Kwan, V.; Malevanets, A.; Consta, S. Where do the ions reside in a highly charged droplet? *J. Phys. Chem. A* **2019**, *123*, 9298–9310.

(33) Kwan, V.; Consta, S. Bridging electrostatic properties between nanoscopic and microscopic highly charged droplets. *Chem. Phys. Lett.* **2020**, 137238.

(34) Malevanets, A.; Consta, S. Variation of droplet acidity during evaporation. *J. Chem. Phys.* **2013**, *138*, 184312.

(35) Enami, S.; Colussi, A. J. Long-range specific ion-ion interactions in hydrogen-bonded liquid films. *J. Chem. Phys.* **2013**, *138*, 184706.

(36) Enami, S.; Colussi, A. J. Ion-Specific Long-Range Correlations on Interfacial Water Driven by Hydrogen Bond Fluctuations. *J. Phys. Chem. B* **2014**, *118*, 1861–1866.

(37) Jungwirth, P.; Tobias, D. J. Surface effects on aqueous ion solvation: A molecular dynamics simulation study of NaCl at the air/water interface from infinite dilution to saturation. *J. Phys. Chem. B* **2000**, *104*, 7702–7706.

(38) Omta, A. W.; Kropman, M. F.; Woutersen, S.; Bakker, H. J. Negligible effect of ions on the hydrogen-bond structure in liquid water. *Science* **2003**, *301*, 347–349.

(39) Ghosal, S.; Hemminger, J. C.; Bluhm, H.; Mun, B. S.; Hebenstreit, E. L.; Ketteler, G.; Ogletree, D. F.; Requejo, F. G.; Salmeron, M. Electron spectroscopy of aqueous solution interfaces reveals surface enhancement of halides. *Science* **2005**, *307*, 563–566.

(40) Knipping, E.; Lakin, M.; Foster, K.; Jungwirth, P.; Tobias, D.; Gerber, R.; Dabdub, D.; Finlayson-Pitts, B. Experiments and simulations of ion-enhanced interfacial chemistry on aqueous NaCl aerosols. *Science* **2000**, *288*, 301–306.

(41) Otten, D. E.; Shaffer, P. R.; Geissler, P. L.; Saykally, R. J. Elucidating the mechanism of selective ion adsorption to the liquid water surface. *Proc. Natl. Acad. Sci. U.S.A.* **2012**, *109*, 701–705.

(42) Petersen, P. B.; Saykally, R. J. On the nature of ions at the liquid water surface. *Annu. Rev. Phys. Chem.* **2006**, *57*, 333–364.
(43) Onorato, R. M.; Otten, D. E.; Saykally, R. J. Measurement of bromide ion affinities for the air/water and dodecanol/water interfaces at molar concentrations by UV second harmonic generation spectroscopy. J. Phys. Chem. C 2010, 114, 13746–13751.

(44) Smith, J. W.; Saykally, R. J. Soft x-ray absorption spectroscopy of liquids and solutions. Chem. Rev. 2017, 117, 13909–13934.

(45) Baer, M. D.; Mundy, C. J. Toward an understanding of the specific ion effect using density functional theory. J. Phys. Chem. Lett. 2011, 2, 1088–1093.

(46) Adel, T.; Ng, K. C.; Vazquez de Vasquez, M. G.; Velez-Alvarez, J.; Allen, H. C. Insight into the Ionizing Surface Potential Method and Aqueous Sodium Halide Surfaces. Langmuir 2021,

(47) Beck, T. L. The influence of water interfacial potentials on ion hydration in bulk water and near interfaces. Chem. Phys. Lett. 2013, 561, 1–13.

(48) Tobias, D. J.; Hemminger, J. C. Getting specific about specific ion effects. Science 2008, 319, 1197–1198.

(49) Tielrooij, K.; Garcia-Araez, N.; Bonn, M.; Bakker, H. Cooperativity in ion hydration. Science 2010, 328, 1006–1009.

(50) Consta, S.; Mainer, K. R.; Novak, W. Fragmentation mechanisms of aqueous clusters charged with ions. J. Chem. Phys. 2003, 119, 10125–10132.

(51) Kwan, V.; O’Dwyer, R.; Laur, D.; Tan, J.; Consta, S. Relation between Ejection Mechanism and Ion Abundance in the Electric Double Layer of Droplets. J. Phys. Chem. A 2021, 125, 2954–2966.

(52) Malek, S. M. A.; Poole, P. H.; Saika-Voivod, I. Thermodynamic and structural anomalies of water nanodroplets. Nat. Commun. 2018, 9, 2402.

(53) Malek, S. M. A.; Poole, P. H.; Saika-Voivod, I. Surface tension of supercooled water nanodroplets from computer simulations. J. Chem. Phys. 2019, 150, 234507.

(54) Johnston, J. C.; Molinero, V. Crystalization, melting, and structure of water nanoparticles at atmospherically relevant temperatures. J. Am. Chem. Soc. 2012, 134, 6650–6659.

(55) Nandi, P. K.; Burnham, C. J.; Futera, Z.; English, N. J. Ice-amorphization of supercooled water nanodroplets in no man’s land. ACS Earth Space Chem. 2017, 1, 187–196.

(56) Li, T.; Donadio, D.; Galli, G. Ice nucleation at the nanoscale probes no man’s land of water. Nat. Commun. 2013, 4, 1–6.

(57) Haji-Akbari, A.; Debenedetti, P. G. Computational investigation of surface freezing in a molecular model of water. Proc. Natl. Acad. Sci. U.S.A. 2017, 114, 3316–3321.

(58) Hall, K. W.; Zhang, Z.; Burnham, C. J.; Guo, G.-J.; Carpendale, S.; English, N. J.; Kusalik, P. G. Does local structure bias how a crystal nucleus evolves? J. Phys. Chem. Lett. 2018, 9, 6991–6998.

(59) Rayleigh, L. XX. On the equilibrium of liquid conducting masses charged with electricity. Philos. Mag. 1882, 14, 184–186.

(60) Peters, J. Rayleigh’s electrified water drops. Eur. J. Phys. 1980, 1, 143.

(61) Hendricks, C.; Schneider, J. Stability of a conducting droplet under the influence of surface tension and electrostatic forces. Am. J. Phys. 1963, 31, 450–453.

(62) Consta, S.; Malevanets, A. Disintegration mechanisms of charged nanodroplets: novel systems for applying methods of activated processes. Mol. Simul. 2015, 41, 73–85.
(63) Consta, S. Manifestation of Rayleigh instability in droplets containing multiply charged macroions. J. Phys. Chem. B 2010, 114, 5263–5268.

(64) Berendsen, H. J. C.; van der Spoel, D.; van Druren, R. GROMACS: A message-passing parallel molecular dynamics implementation. Comput. Phys. Commun. 1995, 91, 43.

(65) Lindahl, E.; Hess, B.; van der Spoel, D. GROMACS 3.0: A package for molecular simulation and trajectory analysis. J. Mol. Model. 2001, 7, 306.

(66) van der Spoel, D.; Lindahl, E.; Hess, B.; Groenhof, G.; Mark, A. E.; Berendsen, H. J. C. GROMACS: Fast, Flexible and Free. J. Comput. Chem. 2005, 26, 1701.

(67) Hess, B.; Kutzner, C.; van der Spoel, D.; Lindahl, E. GROMACS 4: Algorithms for highly efficient, load balanced, and scalable molecular simulation. J. Chem. Theory Comput. 2008, 4, 435.

(68) Phillips, J. C.; Braun, R.; Wang, W.; Gumbart, J.; Tajkhorshid, E.; Villa, E.; Chipot, C.; Skeel, R. D.; Kalé, L.; Schulten, K. Scalable molecular dynamics with NAMD. J. Comput. Chem. 2005, 26, 1781–1802.

(69) Abascal, J. L. F.; Vega, C. A general purpose model for the condensed phases of water: TIP4P/2005. J. Chem. Phys. 2005, 123, 234505.

(70) González, M. A.; Valeriani, C.; Caupin, F.; Abascal, J. L. F. A comprehensive scenario of the thermodynamic anomalies of water using the TIP4P/2005 model. J. Chem. Phys. 2016, 145, 054505.

(71) Vega, C.; de Miguel, E. Surface tension of the most popular models of water by using the test-area simulation method. J. Chem. Phys. 2007, 126, 154707.

(72) Vega, C.; Abascal, J. L. F.; Nezbeda, I. Vapor-liquid equilibria from the triple point up to the critical point for the new generation of TIP4P-like models: TIP4P/Ew, TIP4P/2005, and TIP4P/ice. J. Chem. Phys. 2006, 125, 034503.

(73) Lamoureux, G.; Harder, E.; Vorobyov, I. V.; Roux, B.; MacKerell, A. D. A polarizable model of water for molecular dynamics simulations of biomolecules. Chem. Phys. Lett. 2006, 418, 245–249.

(74) Yu, H.; Whitfield, T. W.; Harder, E.; Lamoureux, G.; Vorobyov, I.; Anisimov, V. M.; MacKerell, A. D.; Roux, B. Simulating Monovalent and Divalent Ions in Aqueous Solution Using a Drude Polarizable Force Field. J. Chem. Theory Comput. 2010, 6, 774–786, PMID: 20300554.

(75) Luo, Y.; Jiang, W.; Yu, H.; MacKerell, A. D.; Roux, B. Simulation study of ion pairing in concentrated aqueous salt solutions with a polarizable force field. Faraday Discuss. 2013, 160, 135–149.

(76) Humphrey, W.; Dalke, A.; Schulten, K. VMD: Visual Molecular Dynamics. J. Mol. Graphics 1996, 14, 33–38.

(77) Chau, P. L.; Hardwick, A. J. Mol. Phys. 1998, 93, 511.

(78) Aragones, J. L.; MacDowell, L. G.; Vega, C. Dielectric Constant of Ices and Water: A Lesson about Water Interactions. J. Phys. Chem. A 2010, 115, 5745–5758.

(79) Chandler, D. Introduction to modern statistical mechanics; New York, Oxford University Press, 1987.

(80) Gladich, I.; Roeselová, M. Comparison of selected polarizable and nonpolarizable water models in molecular dynamics simulations of ice I h. Phys. Chem. Chem. Phys. 2012, 14, 11371–11385.

(81) Muchova, E.; Gladich, I.; Picaud, S.; Hoang, P. N.; Roeslova, M. The Ice-Vapor Interface and the Melting Point of Ice
I h for the Polarizable POL3 Water Model. 
*J. Phys. Chem. A* 2011, **115**, 5973–5982.

(82) Vrbka, L.; Jungwirth, P. Homogeneous freezing of water starts in the subsurface. *J. Phys. Chem. B* 2006, **110**, 18126–18129.

(83) Peters, K. F.; Chung, Y.-W.; Cohen, J. B. Surface melting on small particles. *Appl. Phys. Lett.* 1997, **71**, 2391–2393.

(84) Tsironi, I.; Schlesinger, D.; Späh, A.; Eriksson, L.; Segad, M.; Perakis, F. Brine rejection and hydrate formation upon freezing of NaCl aqueous solutions. *Phys. Chem. Chem. Phys.* 2020, **22**, 7625–7632.

(85) Vrbka, L.; Jungwirth, P. Brine rejection from freezing salt solutions: A molecular dynamics study. *Phys. Rev. Lett.* 2005, **95**, 148501.

(86) Elliott, S. R. Medium-range structural order in covalent amorphous solids. *Nature* 1991, **354**, 445–452.

(87) Shi, R.; Tanaka, H. Distinct signature of local tetrahedral ordering in the scattering function of covalent liquids and glasses. *Sci. Adv.* 2019, **5**, eaav3194.

(88) Saika-Voivod, I.; Smallenburg, F.; Sciortino, F. Understanding tetrahedral liquids through patchy colloids. *J. Chem. Phys.* 2013, **139**, 234901.

(89) Wei, X.; Miranda, P. B.; Shen, Y. Surface vibrational spectroscopic study of surface melting of ice. *Phys. Rev. Lett.* 2001, **86**, 1554.

(90) Sánchez, M. A.; Kling, T.; Ishiyama, T.; van Zadel, M.-J.; Bisson, P. J.; Mezger, M.; Jochum, M. N.; Cyran, J. D.; Smit, W. J.; Bakker, H. J. et al. Experimental and theoretical evidence for bilayer-by-bilayer surface melting of crystalline ice. *Proc. Natl. Acad. Sci. U.S.A.* 2017, **114**, 227–232.