Computational Modelling of Interfacial Properties of Droplets

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A thesis submitted in partial fulfillment of the requirements for the Doctor of Philosophy degree in Chemistry
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Abstract

Aqueous nanodroplets containing reactive species play an important role in atmospheric chemistry and technology. The presence of atmospheric aerosol particles and the chemical reactions they host plays a critical role in climate, visibility in the atmosphere, quality of air, and health. Man-made aerosols find applications in inkjet printing, electrospinning, electrospraying, and ionization methods used in mass spectrometry.

Despite their small size, these systems show complex chemical and physical behaviour because a significant portion of the system is occupied by a liquid-vapour interface. Interfaces are distinct regions characterized by large mass density gradients, shape fluctuations, particular orientation of molecules and curvature effects, especially in the lower-sized nanodroplets. Low temperature and charge are two additional factors that further enhance the complexity of physical chemistry in droplets. For example, supercooled droplets may still be liquid at 200 K or lower temperatures.

In this dissertation, atomistic modelling of aqueous nanodroplets containing ions and charged proteins are employed to study (a) the structure of the liquid-vapour interface; (b) interconversion reactions between solvent-separated and contact ion pairs, and (c) the rupture of the surface of highly charged droplets by emission of solvated ions. The results are scalable and extended to the microscale.

There are several important findings in the study. Firstly, the colder the aqueous droplets, the more likely is for the ion-pairing to take place near the surface where the thermodynamics and its kinetic is significantly different from those in the bulk solution. Secondly, new maxima in the number density of a single ion in aqueous droplets are detected that were not found in previous literature. Thirdly, for the first time the structure of the interface of a highly charged droplet and the size distribution of the progeny clusters emitted from the surface as a function of the ion type is identified.

The study of the ion-pairing as a function of temperature suggests possible ways for optimizing ionization methods used in native mass spectrometry. These studies open up new
directions in research such as modelling of cryo-preservation of macromolecules in droplets and exploration of the chemistry in conical geometries formed on the droplet surface for possible applications in catalysis.

Keywords: Droplet-Ion interactions, Charge-induced Instabilities, Electric Double Layer, Interfacial Phenomena, Ion Evaporation Model, Equilibrium Partition Model, Supercooled Droplets, Ion Pairing, Atmospheric Aerosols, Electrospayed Aerosols, Polarizable Model, Molecular Simulations
Summary for lay audience

Tiny water droplets containing ions, mainly sodium (Na\(^+\)) and chloride (Cl\(^-\)), are omnipresent in the environment and technological applications. Because of the presence of ions these droplets can be found at different charge states, such as neutral, lightly charged with one or a few ions, or highly charged with many ions. Moreover, these liquid droplets can be found at different temperatures. They can be found at room temperature in the surroundings of human action but they also participate in thundercloud processes in the upper troposphere, where the temperature may be as low as \(-70^\circ\)C.

Minuscule droplets at a low or neutral charge state are often encountered in the atmospheric aerosols in the lower troposphere where most of the human action takes place. The chemical and physical processes that occur in aerosols as well as the presence of aerosol particles themselves play a critical role in global climate, air pollution, visibility and health problems.

Highly charged droplets are encountered in thunderclouds, and in many technological applications such as inkjet printing, electrospinning, electrospraying, and ionization methods used in mass spectrometry. Modern experiments use small aerosol droplets as nano and micro-reactors, where tremendous acceleration of reactions may be achieved relative to that in the traditional “beaker” chemistry. The physical chemistry and reactivity of these small systems are much less understood relative to reactivity in large amounts of solution because these small systems have a large surface-to-volume ratio. A large surface implies that a large portion of the system is the vapour-liquid interface. Interfaces are complex regions because the system properties change as the system transitions from the neat liquid to the neat vapour phase.

In this thesis, I use molecular modelling to examine (a) the manner in which Na\(^+\) and Cl\(^-\) ions approach one another and dissociate in water droplets in the temperature range from supercooling (at approximately \(-70^\circ\)C) to room temperature (at approximately +25°C) and (b) the properties and the rupture of the droplet-vapour interface in highly charged droplets.

The computational results transform the analytical models that have been widely used in the fields of mass spectrometry so far.
The results of the studies allow us to propose methods to optimize experimental processes such as ionization methods used in mass spectrometry. These experimental methods are widely used in the medicine and pharmaceutical sector for the analysis of biological specimens.
Co-Authorship Statement

Section 2.4.1 is based on the article in preparation “Kwan, V.; Consta, S. Bridging Equilibrium and Dynamic Properties Between the Sub-nanometer and Marcoscopic Sized Charged Cluster.”. V. Kwan performed all of the simulations and data analysis for this section. The article was co-authored by V. Kwan and S. Consta.

Chapter 2 (exclude Section 2.4.1) is based on the accepted article “Kwan, V.; Maiti, S.; Saika-Voivod, I.; Consta, S. Salt Enrichment and Dynamics in the Interface of Supercooled Aqueous Droplets. J. Am. Chem. Soc., 2022, 144, 11148–11158” V. Kwan performed all of the simulations for this chapter and data analysis. S. Maiti (Mitacs Globalink research intern) replicated simulations and did benchmark calculations of droplet set-up of the simulations under the supervision of S. Consta and V. Kwan. V. Kwan wrote scripts and several codes for the data analysis. S. Consta developed the method and code for computing the diffusion coefficient in finite-sized systems and performed the relevant calculations using V. Kwan’s trajectories. I. Saika-Voivod provided some MD trajectories for pure supercooled droplets (using different software than what V. Kwan used) for comparisons with the simulations performed in this article and did a critical reading of the manuscript. The article was co-authored by V. Kwan and S. Consta.

Chapter 3 is based on the article “Kwan, V.; Consta, S. Bridging Electrostatic Properties Between Nanoscopic and Microscopic Highly Charged Droplets. Chem. Phys. Lett. 2020, 137238” and “Kwan, V.; Consta, S. Molecular Characterization of the Surface Excess Charge Layer in Droplets. J. Am. Soc. Mass Spectrom. 2021, 32, 33–45”. V. Kwan performed all the simulations and analysis for this chapter by writing scripts and codes. S. Consta developed the method and code for the droplet electric field that shows its fluctuations on the droplet surface and its average value. V. Kwan and S. Consta co-authored the manuscript.

Chapter 4 is based on the article “Kwan, V.; Consta, S. Conical Shape Fluctuations Determine the Rate of Ion-evaporation and the Emitted Cluster-size Distribution from Multi-charged Droplets. J. Phys. Chem. A, 2022, 126, 3229–3238” V. Kwan performed all the simulations and
relevant analysis for this chapter. V. Kwan wrote scripts and several codes for the data analysis. S. Consta wrote the code for the computation of the free energies for the ion-evaporation mechanism. V. Kwan and S. Consta co-authored the manuscript.
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CHARMM  Chemistry at Harvard Macromolecular Mechanics
COM     Centre of Mass
CIP     Contact Ion Pair
CPP     Cumulative probability profiles
EPM     Equilibrium Partitioning Model
ESI     Electrospray Ionization
IEM     Ion Evaporation Mechanism
LJ      Lennard-Jones
MALDI   Matrix-Assisted Laser Desorption/Ionization
MS      Mass Spectrometry
MICR    Maximum Ion Concentration Region
NAMD    Nanoscale Molecular Dynamics
NPB     Non-Linear Poisson-Boltzmann
OPLS-AA Optimized Potential for Liquid Simulations - All Atom
PB      Poisson-Boltzmann
PDB     Protein Data Bank
QLL     Quasi-Liquid Layer
RC      Reaction Coordinates
SECL    Surface Excess Charge Layer
SSIP    Solvent-Separated Ion Pair
SWM4-NDP Simple Water Model with 4-sites and Negative Drude Particle
TIP3P   Transferable Intermolecular Potential with Three Points
TIP4P   Transferable Intermolecular Potential with Four Points
VMD     Visual Molecular Dynamics
# List of Symbols

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<th>Symbol</th>
<th>Unit</th>
<th>Description</th>
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<tr>
<td>A</td>
<td>Å²</td>
<td>Surface area</td>
</tr>
<tr>
<td>C</td>
<td>mol/L</td>
<td>Concentration</td>
</tr>
<tr>
<td>C_b</td>
<td>mol/L</td>
<td>Bulk concentration</td>
</tr>
<tr>
<td>E</td>
<td>kcal/mol</td>
<td>Energy</td>
</tr>
<tr>
<td>E_{el}</td>
<td>kcal/mol</td>
<td>Electrostatic potential energy</td>
</tr>
<tr>
<td>E_{surf}</td>
<td>kcal/mol</td>
<td>Surface energy</td>
</tr>
<tr>
<td>K_{eq}</td>
<td>unitless</td>
<td>Equilibrium constant</td>
</tr>
<tr>
<td>k_B</td>
<td>J/K</td>
<td>Boltzmann’s constant</td>
</tr>
<tr>
<td>m</td>
<td>g</td>
<td>Mass</td>
</tr>
<tr>
<td>Q</td>
<td>e</td>
<td>Charge (of more than one atom)</td>
</tr>
<tr>
<td>Q_r</td>
<td>e</td>
<td>Droplet charge at Rayleigh limit</td>
</tr>
<tr>
<td>q</td>
<td>e</td>
<td>Charge (of a single atom)</td>
</tr>
<tr>
<td>R</td>
<td>Å</td>
<td>Radius</td>
</tr>
<tr>
<td>R_e</td>
<td>Å</td>
<td>Equimolar radius</td>
</tr>
<tr>
<td>r</td>
<td>Å³</td>
<td>Distance</td>
</tr>
<tr>
<td>T</td>
<td>K</td>
<td>Temperature</td>
</tr>
<tr>
<td>t</td>
<td>s</td>
<td>Time</td>
</tr>
<tr>
<td>U</td>
<td>kcal/mol</td>
<td>Potential of interactions</td>
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<tr>
<td>X</td>
<td>unitless</td>
<td>Rayleigh fissility parameter</td>
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<tr>
<td>ΔG‡</td>
<td>kcal/mol</td>
<td>Activation energy</td>
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<tr>
<td>ΔW</td>
<td>kcal/mol</td>
<td>Free energy difference</td>
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<tr>
<td>γ</td>
<td>N/m</td>
<td>Surface Tension</td>
</tr>
<tr>
<td>λ_d</td>
<td>Å</td>
<td>Debye length</td>
</tr>
<tr>
<td>λ_{PB}</td>
<td>Å</td>
<td>Decay length from the solution of the NPB equation in spherical coordinates</td>
</tr>
<tr>
<td>ρ</td>
<td>g/cm³</td>
<td>Mass density</td>
</tr>
<tr>
<td>φ</td>
<td>rad</td>
<td>Dipole angle</td>
</tr>
<tr>
<td>ε</td>
<td>unitless</td>
<td>Dielectric constant</td>
</tr>
<tr>
<td>ε₀</td>
<td>C² N⁻¹ m⁻²</td>
<td>Permittivity of free space</td>
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Chapter 1

Introduction

1.1 Motivation and Objectives

The prime interest in the study of interfacial phenomena stems from the fact that they are fundamental and omnipresent in all systems and surroundings. An interface forms between any two immiscible phases and it has physical and chemical properties differing from those of the bulk material on either side of the interface. For instance, electrochemistry occurs in the solid (electrode)-liquid interface, biological membranes have an interface with intracellular and extracellular fluids, the chemistry in atmospheric aerosols takes place mainly in their interface with vapour. One can distinguish interfaces between different physical phases such as liquid-vapour, but also between the same phases such as liquid-liquid (e.g. oil droplets in water). The phenomena that happen in the interface are very distinct relative to the bulk counterpart. For instance, the use of nanoparticles in various applications is resulted from their markedly different electronic and optical properties than their bulk counterpart due to their high surface-to-mass ratio.

Interfaces take many shapes: ranging from the planar surface between metal and electrolyte found in batteries and capacitors, to the curved surface found in droplets, to the irregular, rough surface between a zeolite and a liquid or vapour. When either one of the phases in the system is solid, the interface is considered as a rigid interface. This dissertation focuses on non-rigid interfaces such as droplet-air interfaces, where the fluctuating surface introduces additional
complexity to the system.

In the case where one of the phases carries excess charges, the interface will naturally become charged. The phase can be charged intentionally (e.g. by placing a charged strip of metal in an electrolytic solution, or by applying a high voltage to a spray of electrolyte to generate charged droplets) or naturally (e.g. droplets in thunderclouds are highly charged with electrons). Droplets with multiple charges carried by ions are ubiquitous in atmospheric aerosols\[1-4\], ionization methods used in native mass spectrometry and recently, they find applications as nanoreactors or micro-reactors for accelerating chemical reactions by orders of magnitude relative to their bulk solution counterparts\[5, 6\].

The focus of the thesis is on the study of the structure of a charged droplet-vapour (or vacuo) interface and of certain fundamental ion-pair interconversion reactions as well as of ion-release reactions that occur in the interface. Relations are made with the chemistry in atmospheric aerosols and (electro)sprayed droplets that are used in mass spectrometry analysis.

The water-air interface, even in the absence of ions, is charged. Even though the system is charge neutral, the interface is often polarized. To satisfy the law of conservation of charge, a layer with the opposite charge forms underneath the surface, which lead to the formation of an electric double layer. One can define the region where a local charge exists as the interface, which has different electrical properties than the bulk phase where there is no local charge.

There is a long-standing debate over the sign of the charge of the water-air interface and the magnitude of the surface charge. Molecular simulations and microscopic experiments have found that the water-air surface is positively charged from the preferential orientation of water molecules at the surface or surface preferential of transient positively charged ions such as the oxonium ions\[7-11\]. In contrast, macroscopic experiments have found that the water-air surface is negatively charged from the surface preferential of hydroxide ions\[12, 13\].

The interfacial properties of multiply-charged droplets are distinctly different from that of neutral liquid-vapour planar interfaces with dissolved ions. Planar liquid-vapour interfaces in the presence of ions have been extensively studied over several decades of research by exper-
Experimental and computational methods\[14-24\]. It is noted that the planar interfaces of a bulk solution are overall neutral. Differently from a bulk solution that is overall charge-neutral, droplets can be charged. The presence of the charge introduces effects in the system that are not present in a neutral planar interface or bulk solution.

Several fundamental features distinguish a charged droplet’s interface from that of a neutral planar interface. Firstly, when the charge-squared over the volume of a droplet is greater than a threshold value, instability may lead to the release of charge from a droplet’s surface that contains several ions or the formation of “star”-shaped droplets when all the charge is bound on a macroion (there is no free charge). Charge-induced instabilities do not appear in neutral interfaces. Secondly, when more than a single ion are present in a droplet, the droplet is a conductor and the ions with the excess charge are found closer to the surface while the counterions are in the interior. Therefore, the type of ions that are closer to the interface are those with the excess charge sign. On a neutral surface, the distance of the ions from the surface is determined mainly by the chemical interactions such as the effect of the ions in the Hydrogen-bonded network in an aqueous solution. Thirdly, when a sole simple macro(ion) is the charge carrier in a droplet, a fundamental force that affects its location arises from a confining harmonic potential centred at the droplet’s centre of mass. This effect was found by Consta et al. and has been named “electrostatic confinement\[25\]” (EC). Because of the finite size of a droplet, Consta et al. also considered the geometric confinement effect that works in the opposite direction to the EC and delocalizes the ion in the entire droplet. None of the above forces are present in a neutral planar or curved interface. Lastly, typical fluctuations in a charged droplet, regardless of its size, are conical protrusions on the surface, which are absent in a planar interface\[26\][27].
1.2 Objectives

The main objectives of this dissertation are:

1. Determine the location of the ions within a droplet, for droplets containing a single ion and droplets containing multiple ions.
2. Characterize the interface of a charged droplet with multiple ions in terms of ion concentration, nature of the ion, and charge distribution. Examine the scalability of the charge distribution to perform extrapolation of the results to droplet sizes that cannot be studied by molecular modelling yet.
3. Investigate release mechanisms of simple ions and macroions from the interface.
4. Study of the fundamental interconversion reaction between the contact ion-pair and the solvent separated ion-pair in droplets as a function of temperature. Examine the effect of supercooling on the equilibrium and dynamics of the reaction.
5. Assess existing analytical models that describe the charge distributions in droplets and the release of simple solvated ions from the droplet surface.

Some of the longer term objectives are

1. Enhance the understanding of the chemistry in atmospheric aerosols and their phase transformations.
2. In the field of mass spectrometry, relate the macroion (e.g. charged proteins, nucleic acids) charge state and conformation from the bulk solution to their state within charged droplets and finally to the gaseous state. [28,30]
3. Map out the possible charging mechanisms of macroions in droplets[27]
4. Suggest optimization steps to be implemented in ionization methods used for transferring macroions and their complexes from the bulk solution to the gaseous phase for mass spectrometry analysis[25].
5. Understand the reason that certain reactions are significantly accelerated in droplets relative to the bulk solution.
6. Develop analytical theories to generalize the results[31].
A necessary step to achieve these goals is to understand the charged droplet-vapour interface. These longer term goals have been partially achieved via the presented research and previous research performed in the Consta group.

In the next sections, the context of the studies, the fundamental structure of liquid interfaces, and the simulation methods used in these studies are presented.

1.3 Broader Context

The study of droplets is identical to the study of clusters. A cluster is an aggregate of molecules that can be found in the gaseous phase or in solution such as clusters of lipids in water. Depending on their size, they have been classified in the literature as microscopic (radius \( \leq 1.0 \) nm, which corresponds to a cluster size of approximately 190 H\(_2\)O molecules), mesoscopic (1.0 nm \(<\) radius \(<\) 50.0 nm ) and macroscopic (radius \(>\) 50 nm). Nano-droplets is a relatively newer term for mesoscopic clusters. Differently from the bulk solution, clusters have two parameters that can be varied: size and charge. A bulk solution is neutral and any of its properties do not change as a function of size. On the contrary, the physical properties and chemical reactivity of clusters (droplets) change with size and charge. A significant reason for the change of the properties with the size is the large surface-to-volume ratio that is inherent in finite-sized systems. Temperature is another parameter that affects the properties of a bulk solution and a cluster.

Clusters have been studied for many decades by computations\(^{[32,42]}\) and experiments\(^{[43–47]}\) (the references given are only indicative articles and they are to be considered only a small subset of the broad literature on clusters). The majority of studies has focused on clusters that contain up to a few hundred solvent molecules, a single ion with charge up to \(+3e\) (where \(e\) is the positive elementary charge) and at room or elevated temperature\(^{[31,36,48,49,49–53,53–57,57–66]}\). The study of larger clusters with macroions or multiple ions and at cold temperature are limited\(^{[52,54,67–71]}\). The reason that the larger clusters have been studied
much less is that in clusters, different from the bulk solution, all the interactions among the molecules are considered directly without truncation or Ewald summation methods that speed up the computations in the bulk solution. The inclusion of all the long-range interactions directly makes the computations very time-consuming. The study of cold clusters is even more time-consuming because these systems are characterized by slow dynamics. Conformational changes of macromolecules in clusters and the diffusion of macromolecules are also characterized by slow dynamics. A part of the research included in this thesis examines cold clusters at a temperature that is as low as 200 K, which is called supercooling.

One of the key questions that had not been understood in the literature over decades was that of the location of a single simple ion and single macroion (e.g. protein, nucleic acid or charged synthetic polymers) in droplets. Consta et al. developed a continuum model that shows the fundamental forces that determine the ion location[25]. The model considers a deformable droplet. It is the inclusion of the shape fluctuations that makes the model realistic, but on the other hand, complicated in its development.

In the model, the total energy of a droplet is written

\[ E = E_{\text{surf}} + E_{\text{el}} = \gamma A + E_{\text{el}} \quad (1.1) \]

where \( E_{\text{surf}} \) is the surface energy, \( E_{\text{el}} \) is the electrostatic energy, \( \gamma \) is the surface tension, and \( A \) denotes the surface area.

After a significant amount of algebra (found in the Supporting Information in ref.[25]), it is found that the energy (\( \Delta E_1 \)) related to the ion distance from the droplet’s centre of mass (COM) is given by

\[ \Delta E_1(||r||^2) = \frac{\varepsilon - 1}{4\pi\varepsilon_0\varepsilon(\varepsilon + 2)} \frac{Q^2}{R^3} ||r||^2 = K(\varepsilon)||r||^2 \quad (1.2) \]

where \( ||r||^2 \) is the distance of the ion from the droplet’s COM, \( \varepsilon \) is the dielectric constant of the droplet, \( \varepsilon_0 \) is the vacuum permittivity, \( Q \) is the charge of the ion and \( R \) is the radius of the droplet. The coefficient in front of \( ||r||^2 \) is denoted as \( K(\varepsilon) \). If the ion is localized in the center
of a droplet, the Gibbs-Boltzmann distribution of the ion positions is given by

\[
P(||r^2||)_{EC} = \frac{2}{\sqrt{\pi}} \left( \frac{K(\epsilon)}{k_B T} \right)^{3/2} ||r|| e^{-K(\epsilon)||r||^2/(k_B T)}
\]  

(1.3)

The theoretical analysis presented in the Supporting Information in ref. [25] is general and predicts not only the probability of finding the ion at a certain location but also it finds the threshold value of charge squared to volume ratio beyond which charge-induced instability develops resulting in the “star”-shaped droplets [72, 73]. It is noted that the model holds for dielectric droplets, which are droplets with a single simple ion or macroion. This theory allowed us to analyze the location of ions in supercooled droplets and to understand the location of macroions and simple ions in clusters (droplets).

The interfacial properties of multiple-charged droplets were not explored by atomistic modelling. However, in the field of mass spectroscopy, there is the qualitative model of C. Enke named the equilibrium partitioning model (EPM). EPM hypothesized the structure of the charged liquid droplet-vapour interface [74, 75]. The EPM model assumes similarity between the structure of a charged droplet and the electric double layer (explained in the next section) found on the surface of an electrode in contact with a solution. In the case of a droplet, the role of the electrode is assumed by the vacuo (or air). Thus, the model identifies two regions in a droplet. The outer region which is the excess charge region and an inner core region. Electrolyte and analyte ions partition between these two regions by establishing an equilibrium. The model infers that the species seen in the mass spectrum are those that make up the surface charge. Since EPM is a macroscopic model, it cannot readily provide the thickness of the outer layer and the amount of free charge present. The atomistic modelling performed in this research provides new information in that respect, that could not have been intuitively guessed.

**Rayleigh limit of a conductive charged droplet** The previous discussion was about dielectric droplets. Let us now consider a droplet containing a number of separate charges. These
separate charges can be simple ions or simple ions and macrorions. Those charges act as charge carriers, which render the droplet conductive. For a charged droplets with separate charges it is always energetically favourable to divide. However, the droplet may survive for a certain length of time. This duration depends on the charge squared to volume ratio for a certain value of the surface tension. When the ratio of the droplet charge squared to its volume is below a threshold value the droplet is in a metastable state. This threshold value is called the Rayleigh limit. A metastable states is a quasi-equilibrium state that lives long enough to be able to characterize it computationally or experimentally in a manner similar to that of an equilibrium state.

The droplet stability is characterized by the Rayleigh fissility parameter \( X \) given by

\[
X = \frac{Q^2}{64\pi^2\gamma\varepsilon_0 R^3}
\]  

(1.4)

where \( Q \) is the droplet charge, \( \gamma \) is the surface tension, \( \varepsilon_0 \) and \( R \) are the permittivity of vacuum, and \( R \) the radius of the droplet, respectively. When \( X = 1 \) the system is at the Rayleigh limit[76]. When \( X > 1 \), the system is above the Rayleigh limit and may spontaneously fragment, when \( X < 1 \) the system is below the Rayleigh limit and is stable with respect to small perturbation[73, 76–79]. The states at \( X < 1 \) are the metastable states discussed previously.

For a certain radius \( R \) and surface tension, one can find a value of charge, denoted by \( Q_r \) hereafter, such that \( X = 1 \). A droplet may have a charge \( Q \) that may be different from \( Q_r \). Thus, one can recast the Rayleigh fissility parameter by the ratio of charges squared as given in the second equality in Eq. 1.4

\[
X \approx \left( \frac{Q}{Q_r} \right)^2.
\]  

(1.5)

The consensus view for droplet fragmentation is that a highly charged micro-drop at \( X \approx 1 \) reduces its charge by emitting a jet of smaller progeny charged droplets (comprised solvent and ions)[80]. The jet release from the parent droplet is known as Rayleigh fission or Coulomb
The Rayleigh model is not only applicable to charge droplets, but it has also been used in the liquid drop model to describe the nuclear fission and in the conformational changes of charged macromolecules in the gaseous state and in solution. In the case of macromolecules, the cohesive forces (e.g., secondary structure, chain elasticity, entropic effect, and hydrogen bonding) replace the surface tension term in the model.

It has been suggested that when the radius of nanodrops is less than \( \approx 10 \) nm, the release of charge may take place before Rayleigh fission by emission of small clusters that contain solvated single ions. This is called the ion-evaporation mechanism (IEM).

### 1.4 Macroscopic Theory of Electric Double Layer

Historically, the bulk of the theory on charged interfaces focused on the behaviour of ions in an electrolyte in contact with a planar charged surface. In the case of a charged droplet, (i) the interface has a finite width, (ii) the charge at the interface stems from the fact that the droplet is a conductor carrying excess charges and (iii) the interface is curved.

The study of electric (interchangeable with electrical) double layers dates back to 1853, when Helmholtz put forth the idea of an electric double layer: a surface with positive electricity on one side and an equal amount of negative electricity on the other side, separated by an infinitesimally small distance.

In Helmholtz’s model, when an electrode with charge density \( \rho \) is placed in an electrolyte, the solvated ions form a layer at the electrode surface exactly balancing the charge on the electrode. This layer is commonly referred to as the stationary layer or the Helmholtz layer. All the unpaired ions are at some distance far away from the metal surface and play no part in the picture (effectively screened). In Helmholtz’s model, the ions are considered point particles. This is the simplest model for the spatial charge distribution at a metal-electrolyte interface. Helmholtz’s model, when applied to a charged droplet, corresponds to the macroscopic elec-
trostatic model of a conducting sphere, where all the charges are located on the surface and the electric field is discontinuous at the surface and the electric field in the interior is zero. It has been noted in J. D. Jackson’s textbook “at the microscopic level the charge is not exactly at the surface and the field does not change discontinuously”.

![Electric Double Layer Theories](image)

**Figure 1.1: Illustration of various electric double layer theories.** Ions are represented with black circles, solvent molecules are represented with teal circles.

The theory of electric double layer have subsequently been modified by Gouy \[86, 88\], Chapman \[86, 89\], Stern \[86, 90\] and many others. In this section, a brief overview of the existing macroscopic theory of electric double layers is provided. Fig. 1.1 illustrates various electric double layer theories discussed in this section.

**The Poisson–Boltzmann Equation and Gouy–Chapman Theory**  The key equation of electrostatics is the Poisson equation expressed as

$$\nabla^2 \phi = -\frac{\rho}{\epsilon}$$  \hspace{1cm} (1.6)

where \( \nabla^2 \) is the Laplacian, \( \phi \) is the electric potential, \( \rho \) is the volume charge density and \( \epsilon \) is the dielectric permittivity of the medium.

Gouy \[86, 88\] and Chapman \[86, 89\] attempted to relate the Poisson Equation with Boltzmann distribution by writing the Poisson equation with a charge density that follows the Boltzmann distribution.
mann distribution.

For a system containing multiple ion species, the Poisson–Boltzmann equation is:

$$\nabla^2 \phi(r) = -\frac{1}{\epsilon} \sum_i c_{i,\infty} \exp\left[-\frac{z_i F \phi(r)}{RT}\right]$$  \hspace{1cm}(1.7)

where $\phi$ and $\epsilon$ have the same meaning as in Eq. 1.6, $c_{i,\infty}$ is the bulk concentration of species $i$, $z_i$ is the charge of species $i$, $F$ is the Faraday constant, $R$ is the ideal gas constant, and $T$ is the temperature.

Within the Poisson–Boltzmann framework, the local electrical potential is determined by the local concentration of ions.

In low electrolyte concentration limit (i.e. $z_i F \phi(r)/RT$ is very small), the approximation $\exp(z_i F \phi(r)/RT) = 1 - (z_i F \phi(r)/RT)$ can be made, which leads to the linear Poisson–Boltzmann equation. The solution of the linear Poisson–Boltzmann equation for a charged flat surface is:

$$\phi(r) = \phi_0 \exp(-\kappa r)$$ \hspace{1cm}(1.8)

where $\phi_0$ is the electric potential of the surface and $\kappa$ is the inverse of Debye length ($1/\lambda_D$) given by:

$$\kappa = \frac{1}{\lambda_D} = \sqrt{\frac{2z_i c_{i,\infty} F}{RT \epsilon}}$$ \hspace{1cm}(1.9)

The Debye length gives a characteristic width of the double layer. It also gives an estimate of the distance from the ion where its electrostatic effect is significant in a solution. In Chapter 3, a relevant parameter that describes the relative strength of the electrostatic interactions and the thermal diffusion in a charged droplet is presented, which is analogous to the Debye length.

As evident from Eq. 1.8, the electric potential of the system decreases exponentially away from the surface, which implies that the concentration of the oppositely charged ions also decreases with distance from the surface. This is often referred to as the diffuse double layer.
In this region, the ions are mobile as thermal motion is allowed. However, the electrostatic field arising from the charge of the electrode results in a preferential attraction for particles of opposite charge.

Like the Helmholtz model, the Gouy–Chapman model assumed that the ions are point charges and the dielectric permittivity is constant throughout the system. By incorporating thermal motion in the theory of double layer, the solution side of the double layer is no longer one molecule thick, but it extends into the bulk of the solution.

**Stern Theory**  
Stern\[86, 90\] modified the Gouy–Chapman theory to account for the finite volume occupied by ions. Stern also assumed that some of the ions may be bounded to the surface. According to Stern, the double layer can be split into two regions: (i) The Helmholtz layer near the surface with a thickness of the diameter of the ion and (ii) the diffuse layer from the first layer to the Debye length ($\lambda_D$). The electric potential of the Helmholtz layer decreases rapidly, while the electric potential of the diffuse layer decreases exponentially. The distance from the surface where the two meet is referred to as the shear plane, and the electric potential at the plane is referred to as the zeta ($\zeta$) potential. The zeta potential has important implications for the stability behaviour of a colloid.

The diffused double layer concept assumes that there is equilibrium between the adsorbed ion on the surface and those in the solution. This gives a specific charge to the surface due to preferential adsorption of ions of opposite charge and thus the concentration goes on decreasing with the distance and becomes same as that of the bulk solution.

In Chapter 3, I postulate that larger ions are more attracted to the interface in a charged droplet, which shares some similarity to the Stern theory.

**Grahame Theory**  
Considering that ions in solution are often surrounded by a solvation shell. Grahame\[86, 91\] incorporated the molecular detail of the solvent into the theory of double layers. The theory separated the Helmholtz layer into two layers – the inner Helmholtz layer, where the ions are partially solvated by the solvent as they are adsorbed onto the electrode, and
the outer Helmholtz layer, where the ions are fully solvated but remain at a fixed distance from the electrode.

Despite the difference between a metal-electrolyte interface and the water-air interface of a droplet, the macroscopic theory, in general, also holds for charged, curved, water-air interfaces given that the curvature of the interface is less than the Debye length. In Chapter 3, the solution of the non-linear Poisson–Boltzmann equation in spherical coordinates is compared to the computed ion concentration profile and the electric potential of a charged droplet.
1.5 General Methodology of the Molecular Modelling

This dissertation investigates ion- and microion-droplet interactions using atomistic molecular
dynamics (MD) methods. The studies focus on atomistic simulation of droplets up to a radius
of 7 nm and then generalize the result obtained to microscopic-sized droplets. In MD, classical
mechanics is used to describe the motion of atoms. This size is the largest size that can be
feasibly studied by atomistic MD with currently available computing power. MD simulations
can provide a glimpse into the time evolution of atomistic systems and one can monitor the
evolution of the droplets as if one observes the atomistic motions of the experiment through a
microscope. In this section, a brief overview of the key algorithm used in MD simulations is
provided.

Newton’s second law relates the applied force and the motion of the \(i\)-th particle in a \(N\)
particle system. This well-known equation reads:

\[
\mathbf{F}_i = m_i \ddot{\mathbf{r}}_i
\]  

(1.10)

where \(\mathbf{F}_i\) denotes the force acting on a particle \(i\), \(m\) is the mass of particle \(i\) and \(\ddot{\mathbf{r}}_i\) is its accel-
eration (second derivative of position with respect to time). If the work done on the particle
is path independent (i.e. conservative force), then it is also equal to the negative gradient of
potential energy expressed as:

\[
\mathbf{F}_i = -\nabla_i U \quad \text{or} \quad \ddot{\mathbf{r}}_i = -\frac{\nabla_i U}{m_i}
\]  

(1.11)

where \(\nabla\) denotes the gradient and \(U\) the total potential energy of the system.

The total potential energy \(U\) of the system is the sum of bonding and non-bonded energy.
The bonding energy part is written as the sum of potential energy contributions from bond
stretching, angle bending, dihedral energy and improper dihedral energy:

\[ U_{\text{bonded}}(r^N) = \sum_{\text{bonds}} k(r_{ij} - r_0)^2 + \sum_{\text{angles}} k_\theta(\theta_{ijk} - \theta_0)^2 + \sum_{\text{dihedral}} k_d(1 + \cos(n\phi + \psi)) \]  

(1.12)

where the bond stretching (first term) and angle bending (second term) terms are modelled as a harmonic oscillator, where a restorative force will coerce the bond length \( r_{ij} \) or bond angle \( \theta \) to return to their equilibrium position, \( r_0 \) and \( \theta_0 \), respectively. In the torsional energy term, \( n \) is the multiplicity term that determines the number of energy minima of the torsional energy term, \( \phi \) is the angle between the dihedral planes, and \( \psi \) is the phase shift term that determines the angle at which the dihedral energy is zero and \( r^N \) denotes collectively the spatial coordinates of all the atoms in the system. Note that in common molecular force fields, the factor of one-half in the harmonic oscillator equation is typically omitted for convenience.

The non-bonded interactions are expressed in the following equation:

\[ U_{\text{nonbonded}} = \sum_{i<j} \epsilon_{ij} \left[ \left( \frac{r_m}{r_{ij}} \right)^{12} - 2 \left( \frac{r_m}{r_{ij}} \right)^6 \right] + \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}. \]  

(1.13)

where \( r_{ij} \) is the distance between atom \( i \) and atom \( j \), \( r_m \) is the distance at which the LJ force is at the minimum between the two atoms, and \( \epsilon_{ij} \) is the depth of the potential well between the two atoms, \( \epsilon_0 \) is the permittivity of free space, \( q_i \) is the partial charge on atom \( i \).

The non-bonded interactions consist of (a) the LJ potential energy function, which is the first term in Eq. 1.13 and (b) the electrostatic interaction between a pair of charged atomic sites, which is the second term in Eq. 1.13. In the LJ function, the \( 1/r^{12} \) term approximates the repulsion between two atomic sites due to the Pauli exclusion principle and the \( -1/r^6 \) term approximates the London dispersion attractions.
1.5.1 Integration algorithm

The time evolution of the system with \( i \) particles can be calculated by solving a system of second-order ordinary differential equations (ODEs):

\[
\ddot{r}_i = \frac{F_i}{m_i} \quad (1.14)
\]

However, it is often impractical to do so, except for extremely simple systems. Instead, the solution is obtained by discretizing the system of ODEs and solving it numerically. The software NAMD\textsuperscript{[92]} (NAnoscale Molecular Dynamics) that I have employed, uses the velocity-Verlet integration scheme to advance the positions and velocities of the atoms in time. The velocity-Verlet algorithm is as follows\textsuperscript{[93]}

Given the initial position of the particle, initial velocity (which is randomized at the start of the simulation with respect to Boltzmann distribution) and the potential energy of the system (which can be used to calculate \( \ddot{r}(t) \))

1. Advance the position of the system by a time step (\( \delta t \))

\[
r(t + \delta t) = r(t) + \dot{r}(t)\delta t + \frac{\ddot{r}(t)}{2}\delta t^2 \quad (1.15)
\]

2. Advance the velocity of the system by half a time step (\( \frac{\delta t}{2} \))

\[
\dot{r}\left(t + \frac{\delta t}{2}\right) = \dot{r}(t) + \ddot{r}(t)\frac{\delta t}{2} \quad (1.16)
\]

3. Calculate \( \ddot{r}(t + \delta t) \) with \( r(t + \delta t) \) obtained in step 1

4. Advance the velocity of the system by another half a time step (\( \frac{\delta t}{2} \))

\[
\dot{r}(t + \delta t) = \dot{r}\left(t + \frac{\delta t}{2}\right) + \ddot{r}(t + \delta t)\frac{\delta t}{2} \quad (1.17)
\]
1.5.2 Droplet simulation in canonical ensemble

To simulate a droplet in the canonical (constant number of moles, volume and temperature) ensemble, the spherical boundary condition is used. The spherical boundary condition creates a virtual cavity where the droplet and the vapour molecules are contained in a finite space by applying a harmonic restoration force on molecules that go beyond the radius of the cavity. The spherical cavity is large enough to accommodate the surface fluctuations of the droplet. With the spherical cavity, the number of water molecules attached to the droplet remains constant after equilibration, as there are active exchanges of molecules between the liquid phase and the vapour phase.

The Langevin thermostat\cite{94} was used to maintain the system around the desired temperature. The Langevin equation is written as \cite{95}

\[
m_i \ddot{r}_i = -\nabla_i U - \gamma \dot{r}_i + R(t) \sqrt{\frac{2m_i \gamma k_B T}{\gamma}} \tag{1.18}
\]

where $\gamma$ is the Langevin damping coefficient and $R(t)$ is a stochastic force that satisfies the following conditions according to the fluctuation-dissipation theorem:

\[
\langle R(t) \rangle = 0 \quad \text{and} \quad \langle R(0)R(t) \rangle = 2m\gamma k_B T \delta(t) \tag{1.19}
\]

Where $\langle \cdot \rangle$ denotes the time-average of the value enclosed within and $\delta$ is the Dirac delta function. The strength of the thermostat is determined by $\gamma$, at $\gamma = 0$, the equation of motion reverts to the Newtonian equation of motion. The velocity-Verlet formation of the Langevin equation of motion is also referred to as the BBK algorithm (Brooks, Brünger, and Karplus). The detailed derivation can be found in Ref. \cite{95}.

1.5.3 Drude oscillator-based polarizable force field

Current empirical force fields tend to overestimate the electrostatic interaction between charged atoms, especially in interactions involving polyvalent ions\cite{96,97} or highly charged intrinsi-
cally disordered proteins (IDPs)\cite{98}. The source of this shortcoming is the missing electronic polarization in the models – when two charged atoms are in close proximity, the electron cloud around the atoms is distorted from its normal shape.

Several mean-field approaches have been suggested to remedy the shortcoming without treating the polarization explicitly, including the charge scaling method\cite{99}, using pair-specific non-bonded LJ parameter\cite{100} and by adding an extra $r^{-4}$ term to the Lennard-Jones potential function\cite{101, 102} to model the induced dipole moment interaction. It is important to note that these mean-field approaches only reproduce equilibrium properties.

Several methods exist for modelling induced polarization, including the Drude oscillator model\cite{103}, the polarizable point dipole model\cite{104} and the fluctuating charge model\cite{105}. In the Drude oscillator model, an auxiliary particle is attached to each polarizable atom via a harmonic spring, in essence, the electronic degree of freedom is being accounted for in an extended Lagrangian framework.

### 1.6 Outline of the Dissertation

The thesis is structured as follows:

*Chapter 2* presents the interconversion reaction of NaCl between the contact-ion pair (CIP) and the solvent-separated ion pair (SSIP) as well as the free-ion state in cold droplets. Direct computational evidence shows that the lower the temperature the closer to the surface the ion interconversion reaction takes place. In supercooled droplets the enrichment of the subsurface in salt becomes more evident. The stability of the SSIP relative to the CIP increases as the ion-pairing is transferred toward the droplet’s outer layers. In the free-ion state, where the ions diffuse independently in the solution, the number density of Cl$^-$ shows a broad maximum in the interior in addition to the well-known maximum in the surface. In the study of the reaction dynamics, a weak coupling between the interionic NaCl distance reaction coordinate and the solvent degrees of freedom is found, which contrasts the diffusive crossing of the free
energy barrier found in bulk solution modelling. The H$_2$O self-diffusion coefficient is found to be at least an order of magnitude larger than that in the bulk solution. I propose to exploit the enhanced surface ion concentration at low temperature to eliminate salts from droplets in native mass spectrometry ionization methods.

In Chapter 3, the location of ions within a charged droplet, for both droplets containing multiple ions is examined. The role of counterions play in the location of ions is also examined. The convergence of ion spatial distributions in aqueous droplets with diameter up to 16 nm ($\approx 6 \times 10^4$ H$_2$O molecules) using analytical theory and molecular dynamics is demonstrated. It is found that depending on the droplet size $\approx 55\% - 33\%$ of the ions (free charge) contributes directly into the droplet’s surface excess charge. The ion distribution convergence allows one to extrapolate the simulation results for nanoscopic droplets to larger sizes, which are still inaccessible to atomistic simulations. For the first time a molecular foundation on the equilibrium partitioning model of C. Enke is presented.

In Chapter 4, the mechanism of the ejection of ions from a charged droplet and its relationship to the structure of the interface is presented. The results are compared to existing cornerstone theories on ion-evaporation mechanism. In this chapter a systematic study of the emitted ion-cluster distribution in relation to their spatial distribution in the parent droplet using atomistic modelling is presented. It is found that in the parent droplet, multiple kosmotropic ions are buried deeper within the droplet than chaotropic ions. This differentiation in the ion location is only captured by a polarizable model. It is demonstrated that the emitted cluster-size distribution is determined by dynamic conical deformations and not by the equilibrium ion-depth within the parent droplet as the IEM models assume. Critical factors that determine the cluster-size distribution such as the charge sign asymmetry that have not been considered in models and in experiments are presented. It is argued that the existing IEM analytical models do not establish a clear difference between IEM and Rayleigh fission. A shift in the existing view for IEM is proposed from the equilibrium properties of the parent droplet to the chemistry in the conical shape fluctuations that serve as the centres for ion-emission. Consequently,
chemistry in the conical fluctuations may also be a key element to explain charge states of macromolecules in mass spectrometry and may have potential applications in catalysis.

The dissertation closes in Chapter 5 with a summary of the key results and an outlook of the new research directions generated by this research.
Bibliography


Chapter 2

Salt Enrichment in the Interface of a Supercooled Aqueous Droplet

This chapter is adapted from “Kwan, V.; Maiti, S.; Saika-Voivod, I.; Consta, S. Salt Enrichment and Dynamics in the Interface of Supercooled Aqueous Droplets. J. Am. Chem. Soc. , 2022, 144, 11148–11158” with permission from the American Chemical Society.

2.1 Introduction

Cold droplets are characterized by distinct physical properties relative to their room temperature counterparts. A notable example is the preservation within nanodroplets of the supercooled liquid state, in contrast to the bulk, where practically unavoidable crystallization prevents the liquid from existing in the temperature range of $T = 150$ K to $230$ K at $P = 1$ atm of pressure$^{[1-15]}$. In a broader context, the unique physical chemistry in small-volume cold systems has been demonstrated by the formation of new ice structures that cannot been seen in the bulk$^{[1-12, 16]}$.

Cold nano- and microdroplets have been studied through experiment and simulation in relation to crystallization and to their thermodynamic and structural properties $^{[17-29, 29, 30]}$. These cold nanoscopic systems have a surprisingly complex internal structure that varies with temperature and size, as revealed by computer simulations of the TIP4P/2005 model of water $^{[31-33]}$, which will be summarized in the context of the present study.
On cooling, and certainly by $T = 220$ K, the outer water layers can become significantly denser compared to the interior of the droplet. The interior core density continues to follow bulk values for the given $T$ and interior $P$. For droplets with number of molecules $N \geq 360$, the droplet interior exhibits a temperature of maximum density below which the density decreases, creating a density contrast between the lower density core and higher density (sub)surface, a contrast that sharpens with decreasing $T$. For $T \leq 200$ K, the density differences between core and subsurface exceed 5%. The above scenario means that simulated supercooled droplets (for $N \geq 200$) exhibit structural heterogeneity manifested by three radial regions: low-density interior, high-density subsurface (thickness $\approx 0.7–0.8$ nm) and surface (thickness $\approx 0.3$ nm). These regions are depicted in Fig. 2.1. This structure provides an interesting chemical environment that contrasts with that of a simpler nanodroplet at ambient conditions, where the density shows a decrease (mainly due to shape fluctuations) only at the liquid-vapour interface.

The exclusion of NaCl and other solutes by ice to its surface quasi-liquid layer (QLL) has been known for a long time [34–38]. This layer is the substrate for intense chemical reactivity. in an analogous manner, the surface and subsurface of cold aerosols may host similar reactivity[35, 39]. I present two examples that demonstrate the significance of the dynamics and thermodynamics of NaCl and other ions on the ice QLL. The first example is the effect of NaCl in the photolysis reactions of adsorbed polycyclic aromatic hydrocarbons[40, 41]. The presence of NaCl in QLL has been found to affect the kinetics of the photolysis reactions, but the manner in which it intervenes is still unknown. The second example is the enhanced activity of hydronium ions on ice surfaces detected by thermal desorption mass spectrometry[42, 43]. The experiments could not distinguish whether the activity was due to thermodynamic or kinetic factors[42, 43], which demonstrates the need to analyze both effects in order to understand the role of ions in reactivity. The interactions of salts and their dynamics in the outer layers of aerosols have not been explored yet at low temperature.

In this chapter, the fundamental interconversion reaction CIP $\rightleftharpoons$ SSIP between a pair of NaCl in mesoscopic clusters in the temperature range of 200–300 K is examined. The meso-
Figure 2.1: Typical snapshot of a supercooled droplet composed of \( N = 776 \) \( \text{H}_2\text{O} \) molecules and a sole \( \text{NaCl} \) ion-pair. Only the oxygen sites are depicted in the coloured shells. The \( \text{Na}^+ \) is depicted by the large red-coloured sphere, and the \( \text{Cl}^- \) by the blue-coloured sphere. The radii of the ions have been enlarged relative to the oxygen sites for clarity. Three regions are distinguished where the \( \text{H}_2\text{O} \) molecules are organized differently: (i) A bulk-like interior (orange-coloured) that extends from the droplet centre of mass (COM) to a distance \( r = R_B \). This region is characterized by a lower density and a better formed tetrahedral network than the outer layers. (ii) The subsurface region \( R_B < r < R_V \) (green-coloured), that is characterized by a higher density and lower degree of tetrahedrality than the interior. (iii) The surface region \( R_V < r < R_e \) (grey-coloured), where \( R_e \) is the equimolar radius. The determination of \( R_B \) and \( R_V \) is presented in Ref.[33] A few \( \text{H}_2\text{O} \) molecules (oxygen sites are depicted by small red-coloured spheres) are found at \( r > R_e \).
scopic clusters are also called nanodroplets, and hereafter the latter term will be used. The number density of the free ions, which is the state where the ions are not engaged in CIP or SSIP is also examined. Figure 2.2 illustrates the three different ion pairing configurations: contact (or intimate) ion pairs (CIP), solvent-separated ion pairs (SSIP) and free ion pairs. The meaning of SSIP and CIP and free ions is the same as that traditionally defined in the literature[44–46]. Note that the term “free ions” refers to the ions’ independent diffusive motion and not to lack of hydration.

Experiments and computations of NaCl ion pairs in clusters have been mainly performed in systems composed of up to a few tens of H$_2$O molecules. [47–57]. Fourier transform microwave spectroscopy[51] has shown that the distance between the ions in a NaCl pair increases by gradually adding up to 3 H$_2$O molecules and reaches the value of 2.9 Å, which is the contact ion pair (CIP) distance found in the bulk solution. Anion photoelectron spectroscopy[52] of clusters comprising NaCl and up to 12 H$_2$O molecules found that at 9–12 H$_2$O molecules, the CIP and SSIP (solvent-separated ion pair) formations are almost degenerate in energy. In larger clusters, characteristics different from those of minute or macroscopic sizes, such as the large shape fluctuations, prevail and may affect the reaction mechanisms. The experimental and computational studies of salt ion-pairing in larger clusters are more limited. Clusters of 150–400 H$_2$O molecules containing NaCl have been studied by X-ray photoelectron spectroscopy[58, 59].
Nanodroplets are characterized by a large surface-to-volume ratio. Thus, when they are neutral and sufficiently large, they may have commonalities with the ion-pairing features in planar interfaces. The NaCl ion-pairing in the planar water interface at room temperature has been extensively studied \([40, 46, 53, 60, 79]\). It has been found that the CIP and SSIP are stabilized differently in the interface from the bulk solution. There is a high degree of agreement that the ion dissociation is suppressed in the interface\([46, 68, 69]\) relative to bulk solution.

The study of ion-pairing in cold systems is more challenging because of the slow dynamics\([80, 81]\). The ion-pairing mechanism has been only recently explored in the premelting ice surface\([82]\). It has been found that the ice interface may play the dominant role in the reaction dynamics and that the dissociation dynamics of water molecules in the premelting layer differ significantly from those in bulk solution.

In this chapter, I use the example of NaCl in an aqueous nanodroplet to examine via molecular modelling how the water structure and dynamics at cooling, and more evidently at supercooling, affect the ion-pairing. Different from the simulations of ion-pairs in a planar interfaces\([46]\), where the ions are restricted to remain in the interface, in the droplet simulations the ions are free to explore the entire volume. I hypothesize that the colder the droplet, the more likely it is for the CIP to SSIP interconversion reaction to occur in the droplet subsurface and surface. I also hypothesize that the location may affect the equilibrium constant. As it will be discussed later, the salt enrichment of the interface at low temperature may be exploited to optimize the ionization conditions in mass spectrometry (MS).

### 2.2 Models and Simulation Methods

Equilibrium molecular dynamics (MD) simulations of aqueous nanodroplets (a) with a single NaCl pair, (b) multiple NaCl pairs, and (c) charged with multiple Na\(^+\) ions with a smaller number of Cl\(^-\) counterions and vice versa were performed.
The majority of the systems were composed of \( N = 776 \) H\(_2\)O molecules \( (R_e = 1.77 \) nm\). I selected a droplet of \( N = 776 \) H\(_2\)O to do the majority of the computations because this size is large enough to clearly distinguish the bulk-like interior of a droplet from the subsurface and at the same time this size is computationally feasible to be studied at low temperature and with a polarizable model. Simulation of \( N = 3000 \) H\(_2\)O molecules \( (R_e = 2.78 \) nm\) with the nonpolarizable force field were also performed for comparative reason. The MD simulations were performed using the software NAMD v2.14\[83\] and the trajectories were visualized using VMD 1.9.4a47\[84\].

The non-polarizable systems were modelled with the TIP4P/2005 water model \[85\] and the OPLS-AA ion parameters \[86\]-\[87\]. The polarizable systems were modelled with the SWM4-NDP water model \[88\] and the CHARMM-Drude ion parameters\[89\]. The equations of motion for the non-polarizable set of simulations were integrated with a time step of 2.0 fs and for the polarizable set model with 1.0 fs. The non-polarizable simulations were performed in the temperature range 200 K–300 K and the polarizable simulations in 260–300 K.

The composition of the systems that were simulated, their dimension and length of simulation time are presented in Table 2.1. Nanodroplets at \( T > 240 \) K were placed in a spherical cavity of radius 20.0 nm by using a spherical boundary condition\[33\]. Nanodroplets at \( T < 240 \) K were simulated in vacuo (without a spherical boundary condition) because they do not evaporate within the simulation time. The systems were thermalized with the Langevin thermostat with the damping coefficient set to 1/ps, 0.1/ps and 0.01/ps. The equilibrium properties were computed with damping coefficient of 1/ps, and I tested that they are independent of the value of the Langevin damping in the range of 1/ps–0.01/ps. All the simulation included a 0.2 \( \mu \)s equilibration period followed by a 1.0 \( \mu \)s– 3.0 \( \mu \)s production run, with configurations sampled every 0.1 ns.
Table 2.1: Description of systems studied. \( N \) denotes the total number of water molecules in the system, the asterisk next to the number of \( H_2O \) molecules denotes the runs with the SWM4-NDP polarizable model, “Ions” is the number and type of ions in the droplet, \( T \) (K) denotes the temperature of the system, \( N_d \) denotes the average number of water molecules that form the connected droplet, \( R_e \) denotes the equimolar radius of the droplet assuming 1 g/cm\(^3\) density, \( t_{run} \) is the production time of the system. For each system multiple runs have been performed with different Langevin coupling coefficient.
Table 2.2: Free energy differences ($\Delta W_{1,2}$) between the maximum and the minima in the free energy profiles shown in Fig. 2.4 (a) and Fig. 2.8 (a) for the non-polarizable model and the polarizable model, at various temperatures. BT denotes the free energy barrier top along the interionic distance reaction coordinate. In the third and fourth column, the number in parentheses is $\Delta W_{1,2}$ in units of $k_B T$, where $k_B$ is the Boltzmann constant. In the fifth column, $K_{eq}$ is the equilibrium constant for CIP $\rightleftharpoons$ SSIP. The statistical error in the free energy estimates is ±0.15 kcal/mol.

### 2.3 Equilibrium Properties of Supercooled Droplets

To examine how the particular structure of a cold droplet affects the ion-pairing I mainly study systems comprising $N = 776$ H$_2$O molecules and a sole NaCl pair in the temperature range of 200 K–300 K. Droplets with $N > 200$ H$_2$O have sufficient number of H$_2$O molecules to form a surface, subsurface and a bulk-like region allowing for the transferability of the results on ion solvation and ion-pairing to larger droplets. I model the systems with the non-polarizable TIP4P/2005 [85] water module and with the polarizable SWM4-NDP water model [88]. TIP4P/2005 allows one to model the systems at supercooling, but it lacks explicit treatment of electronic polarization. In previous research, it has been found that the SWM4-NDP model yields nonphysical water density at low temperature [33, 90, 91], and for this model, I can only study the trends in dynamic and equilibrium properties in the temperature range of 260–300 K. The non-polarizable model shows that the number of transitions between CIP and SSIP as well as between SSIP and the free ions (Fig. 2.3) are sufficient to provide good enough statistics to directly calculate free energy differences along the Na$^+$–Cl$^-$ interionic distance. Indicatively, at $T = 200$ K there are 7 transitions from CIP to SSIP within 2.8 µs, and...
at $T = 220$ K 10 transitions within 0.8 $\mu$s (Fig. 2.3). In Fig. 2.4(a) (for the non-polarizable model) the free energy along the $\text{Na}^+–\text{Cl}^-$ interionic distance at $T = 200$ K and 300 K are shown. The CIP is defined within the basin where the $\text{Na}^+–\text{Cl}^-$ interionic distance is in the range of 2.5–3.5 Å, the SSIP in 3.5–5.7 Å, and the free ion state when the interionic distance is $> 5.7$ Å. A SSIP may be easily formed (as is indicated by a very low free energy barrier along the interionic distance) by an encounter of the free ions in the course of their relative diffusive motion[44–46, 92]. The equilibrium constant for $\text{CIP} \rightleftharpoons \text{SSIP}$ and the free energy differences along the interionic distance are shown in Table 2.2. It was found that at $T = 300$ K the CIP is stabilized more than at 200 K and that at 200 K, the free energy difference between CIP and SSIP is smaller than at 300 K.

Figures 2.4(b) and (c) show the location at which the ion-pairing takes place at 200 K and 300 K, respectively. The free-ion configurations account for $\approx 70\%$ of the total number. It is found that the supercooled droplets with $N > 200$ exhibit heterogeneity that is manifested by three regions: a bulk-like interior, a subsurface, and a surface (Fig 2.1)[33]. In $N = 776$ the distances from the droplet’s COM that delimit these regions are $R_B = 7.4$ Å, $R_V = 14.8$ Å, and $R_e = 17.7$ Å (where $R_e$ denotes the equimolar radius), respectively. At 200 K, the CIP and SSIP show a distinct propensity to be in the middle of the subsurface. In contrast, at 300 K, the probability of forming CIP and SSIP is significant throughout the volume of the droplet but still with a slightly higher probability in the subsurface. To quantify the orientation of the ion-pairs, I consider the angle between the dipole moment of the CIP and SSIP (dipole moment is defined from the negative site to the positive site) and the vector defined from the droplet’s COM to the ion pair COM. At $T = 300$ K the orientation of the CIP spans all the angles, but at 200 K, the cosine of the angle peaks in the range of 0.0–0.2, which corresponds to an angle of 90–78° (Fig. 2.5). The orientation of the NaCl is clearly more pronounced within the polarizable model (Fig. 2.5).

The CIP orientation indicates a slight preference of the Cl$^-$ site toward the droplet’s surface. Even though Fig. 2.4 only shows the CIP $\rightleftharpoons$ SSIP equilibrium at two significantly different
**Figure 2.3:** Left: time evolution of the distance of each ion from the COM of the droplet. Right: time evolution of the distance between Na\(^+\) and Cl\(^-\). Simulations are performed with the non-polarizable model.
Figure 2.4: (a) Free energy for CIP $\Leftrightarrow$ SSIP interconversion reaction at 200 K and 300 K along the Na$^+$–Cl$^-$ interionic distance. (b) Distribution of Na$^+$ (red) and Cl$^-$ (blue) sites in the CIP, SSIP and free ions (F) basins at 200 K as a function of the distance from the droplet's COM (y-axis) (the profiles are not normalized by the volume of the spherical shell). (c) Same as (b) but at 300 K. The non-polarizable model is used.
temperatures, the propensity of the ions to be in the subsurface increases gradually as the temperature decreases as shown in Fig. 2.6 and Fig. 2.7. Specifically, I find that the non-polarizable model at 200 K more strongly expels Na$^+$ than Cl$^-$ (Fig. 2.6 (d)).

I think that the increased exclusion of the ions to the subsurface as temperature decreases is due to an improved H-bonded coordinated network in the droplet interior. The differences in the H-bonded network in the interior and subsurface in supercooled droplets have been presented in [33]. At supercooling, both the CIP and SSIP are mainly formed in the outer portion of the subsurface, where the dielectric constant is expected to be higher than that at 300 K. The higher dielectric constant at lower temperature may lead to a decrease in the free energy difference between the CIP and SSIP, which is consistent with the free energy profile at 200 K shown in Fig. 2.4. Figure 2.8 (a) shows the free energy of the interconversion between CIP and SSIP as a function of the NaCl interionic distance using SWM4-NDP model. The $K_{eq}$ values and the free energy differences are shown in Table 2.2. The striking feature is that the SSIP is formed with greater probability than the CIP. The free-ion configurations account for $\approx 85 - 87\%$ of the total production run. Figure 2.8 (b) and (c) show that the CIP is formed near the surface at 300 K and 260 K. The probability of encountering the ions in the interior and subsurface

Figure 2.5: Dipole moment orientation of NaCl ion pair. The dipole moment is defined from the negative site (Cl$^-$) to the positive site (Na$^+$). The angle $\phi$ is defined between the dipole moment and the vector that points from the droplet’s COM to the ion pair COM. (a) non-polarizable model (b) polarizable model.
Figure 2.6: Ion concentration profile of Na\(^+\) (red line) and Cl\(^-\) (blue line) in nanodroplets comprised \(N = 776\) H\(_2\)O molecules and a sole NaCl pair at (a) 300 K; (b) 240 K; (c) 210 K; (d) 200 K. The sole Cl\(^-\) (dotted blue) at 200 K is also shown for reference. The non-polarizable model is used.
Figure 2.7: Ion concentration profiles of Na\(^+\) and Cl\(^-\) sites (measured in units of concentration in the right y-axis), and H\(_2\)O density profiles (measured in units of g/cm\(^3\)) in the left y-axis) at various temperatures in droplets comprising \(N = 776\) H\(_2\)O molecules and a sole NaCl pair for the SWM4-NDP polarizable model is used.

decreases considerably relative to the non-polarizable model. The polarizable model finds the Cl\(^-\) to be nearer to the vapour-liquid interface than Na\(^+\). The closer proximity of Cl\(^-\) to the surface is in agreement with previous studies\([49, 53, 93-95]\) that have been performed at room temperature. The temperature effect, which has not been studied previously, shows that (a) the lower the temperature the higher the Cl\(^-\) concentration in the surface (see Fig. 2.8), (b) the free energy differences \(\Delta W_{1,2}\) (fourth column in Table 2.2) are not as sensitive to the temperature as for non-polarizable model. I attribute this reduced sensitivity to the fact that the polarizable model predicts the most probable location of the ions near the surface regardless of the temperature. The location does not change significantly with temperature.

Here, I point out a significant difference in the relative stability of CIP and SSIP between the present study and that of Dang et al. who studied the ion-pairing in the liquid-vapour planar interface using a different polarizable model\([46]\). In the Dang et al. case, the ion pair was confined in the Gibbs dividing surface of the planar interface\([46]\). It was found that the CIP is formed with a higher probability than the SSIP, whereas I find the opposite. I think that when the ion pair is confined in the Gibbs dividing surface both Na\(^+\) and Cl\(^-\) are partially solvated,
Figure 2.8: (a) Free energy for CIP ⇌ SSIP interconversion reaction at 200 K and 300 K along the Na⁺–Cl⁻ interionic distance. (b) Distribution of Na⁺ (red) and Cl⁻ (blue) sites in the CIP, SSIP and Free ions (F) basins at 260 K as a function of the distance from the droplet’s COM (y-axis) (the profiles are not normalized by the volume of the spherical shell). (c) Same as (b) but at 300 K. The polarizable model is used.
which promotes pairing due to the low dielectric constant environment. In our systems, the Cl\textsuperscript{−} lies on the surface, but the Na\textsuperscript{+} is well solvated at the borderline of the subsurface and surface or within the subsurface. The likelihood of the CIP formation relative to the SSIP may possibly decrease due to the particular requirements for the orientation of the H\textsubscript{2}O molecules near the interface.

In summary, even though the polarizable and the non-polarizable force fields show different locations of the ion-pairing at room temperature, both models indicate that the lower the temperature is, the farther from the droplet’s COM the ion-pairing takes place. The models are also in agreement in that the stability of the SSIP relative to the CIP increases as the ion-pairing is transferred toward the droplet’s outer layers and that when the CIP is formed, the Cl\textsuperscript{−} is found more in the exterior than when it is in the SSIP or free-ion form.

The consequences of the NaCl location for the reactivity of atmospheric aerosols are now discussed. Donaldson et al. have detected\cite{41} that brine exclusion to the surface quasi-liquid layer (QLL) of ice\cite{40, 96} affects the kinetics of photolysis reactions of adsorbed polycyclic aromatic hydrocarbons (e.g., anthracene, harmine). Similarly, it is expected that such organic molecules can also be adsorbed on aerosol surfaces. I suggest that the temperature-dependent spatial distribution of salts may be one of the factors that determine the photolysis kinetics in aerosols during different seasons or weather conditions. The precise mechanism in which the salts in the ice QLL affect the photolysis kinetics is still unknown\cite{41}. One possible deduction from spectroscopic measurements by Donaldson et al. is that brine exclusion to the surface may form a similar environment to that of a concentrated aqueous bulk solution, making the photolysis reactions have the same kinetics as that in the bulk solution. The relation between the structure of a supersaturated bulk salt solution to that of the salt-containing QLL is still to be examined. I think that this similarity may not hold for fine and ultrafine cold atmospheric aerosols where the subsurface and surface (which can be considered the counterpart of QLL on ice) may have different thicknesses from that of bulk ice. The present study shows that more generally, in ultrafine aerosols, a low temperature where H\textsubscript{2}O is still liquid may affect to a
different extent the brine concentration in the subsurface and the resulting ion-interconversion equilibrium constant and dynamics (described in the next section). Therefore, I expect that the kinetics of the photolysis reactions of organic compounds on fine and ultrafine atmospheric aerosols in the presence of salts may be determined by different factors from those on the ice surface.

Figure 2.9: Distribution of the number of oxygen sites in the first solvation shell surrounding the ion pair for the systems modelled by the polarizable model. From top to bottom: $T = 260$ K, 280 K, 300 K.
Solvation of CIP and SSIP  Here the solvation of CIP and SSIP using the SWM4-NDP model is discussed. The distribution of the number of H$_2$O molecules found in the closest hydration shell surrounding CIP and SSIP are shown in Fig. S8 in SI and the average values are presented in Table 2.3.

<table>
<thead>
<tr>
<th>$T$ [K]</th>
<th>CIP$_s$</th>
<th>CIP$_i$</th>
<th>SSIP$_s$</th>
<th>SSIP$_i$</th>
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<td>6.80</td>
<td>10.44</td>
<td>9.26</td>
</tr>
<tr>
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<td>6.56</td>
<td>10.18</td>
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</tr>
<tr>
<td>260</td>
<td>7.50</td>
<td>6.89</td>
<td>9.98</td>
<td>9.28</td>
</tr>
</tbody>
</table>

Table 2.3: Average number of oxygen sites in the first hydration shell surrounding the ion-pair. The averages correspond to the distributions shown in Fig. 2.9. The subscript $s$ and $i$ denote surface and interior, respectively.

In Table 2.3 the number of the oxygen sites were calculated within a distance of 3.9 Å from the Cl$^-$ ion or within 3.2 Å from the Na$^+$ ion. These distances are chosen to be the first minimum of the ion-oxygen radial distribution functions. I define the ion pair being on the surface (indicated by subscript $s$ in CIP and SSIP in Table 2.3) if one or both ions are further than 17 Å from the droplet’s COM (Note: $R_e = 17.7$ Å). I find that the ion-pairs located on the surface are solvated by $\approx 1.2$ fewer H$_2$O molecules than in the interior in the range of 260–300 K. The number of H$_2$O molecules in the nearest hydration shell decreases in the interior as the temperature decreases. I think that this decrease is due to the fact that the distance of 17 Å used to define the interior also includes the outer subsurface. At lower temperatures, the ions have a higher probability to be found in the outer subsurface region where they may experience reduced solvation. The SSIP basin (Fig. 2.8(a)) is wide and shows a fine structure of two small local minima. This structure is consistent throughout the temperature range 260–300 K and agrees very well with the structure observed in the potential of mean force (PMF) reported by Dang et al. using a different polarizable model[46]. As discussed later, this structure is consistent even in the presence of four NaCl pairs.

The fine SSIP structure is not seen by the non-polarizable models and even though it is present in the PMFs of Dang et al. they did not comment on it. The persistence of the fine structure indicates that it is a robust feature that I expect to be detected in spectroscopic signals.
Figure 2.10: (a) Distribution of oxygen sites (black dots) around the Na\(^+\) ion (red sphere), viewed from the centre of mass of the ion pair toward the Na\(^+\) ion for interionic distance 4.2–4.7 Å projected on a 2D image. Only oxygens within 3.2 Å of the sodium ion are included. It is noted that the chloride ion is hidden behind the view point and oxygen sites obscured by the Na\(^+\) are not shown. The oxygen distribution arises from the collection of many configurations in the MD trajectory. (b) Schematic representation of the oxygen position at this interionic distance. (c) and (d) are the same as (a) and (b), respectively but for interionic distance 4.7–5.2 Å.

The hydration of the SSIP states corresponding to the small local minima is shown in Fig. 2.10. I find that in the second local minimum the oxygen sites are nearer to the SSIP interionic distance (Fig. 2.10 (d)) than in the first minimum (Fig. 2.10 (b)), thus, they are the precursors of the dissociated free-ion state. The results show that the SSIP is not a single structure as it has often been assumed\[62\], but it may be composed of a multitude of short-living structures that in a stepwise manner lead to the dissociated free-ion state. These intermediate states may be viewed as probes of the dynamics of H\(_2\)O in different water models and in experiments.

### 2.4 Free Ions

In order to have a closer look at the free-ion state, I compare the Na\(^+\) and Cl\(^-\) number density with that of the sole ions using the polarizable model at 300 K as shown in Fig. 2.11. The free-
ion state is the most probable state of the ion pair (87\% of the total number of configurations). I find that the Na\(^+\) number density is higher in the interior, in agreement with previous research \cite{33, 97, 98}. I computed the number density of Cl\(^-\) at \(T = 300\) K as a function of the distance from the droplet’s COM. The number density shows two broad maxima. The basin of the one maximum near the surface extends from the subsurface to the surface region (1.2 Å-1.9 Å) and corresponds to a free energy minimum of 1.7 \(k_BT\) measured from the barrier top, which is located at 1.2 Å. This free energy estimate is in good agreement with the value of \(\approx 1.0\) \(k_BT\) reported by Caleman et al.\cite{97} at \(T = 293.15\) K, using a previous version of the polarizable model used in this study, in a cluster of radius equal to 1.1 nm, which corresponds to \(N \approx 190\) H\(_2\)O molecules. The value of this free energy as a function of the distance from the droplet’s COM is affected by shape fluctuations. The smaller the droplet, the larger the effect. Our free energy estimate (and that of Ref. \cite{97}) includes the contribution from the purely entropic effect due to the spherical geometry. If the free energy due to the geometric effect is subtracted, then the effect due to the ion-H\(_2\)O interactions equals 0.90 \(k_BT\). The \(N = 776\) droplet number density showed another broad maximum at 0.7 Å. The basin that is associated with it is in the range of 0.2–1.1 Å. It is likely, that the basin extends up to the droplet’s COM, but it is harder to distinguish that because of the larger statistical uncertainty near the centre. To our knowledge, the second maximum has not been previously discussed in the literature. The interior basin (0.2–1.2 Å) corresponds to a free energy basin that is more shallow than that on the surface, but it is wider, which indicates a substantial probability to encounter the Cl\(^-\) in the interior. The equilibrium constant is estimated directly by the number of configurations in the exterior basin over the interior is 3.2, however, the ratio of number densities in the two basins is estimate to be 1.1. The presence of Na\(^+\) increases slightly the residence time of the Cl\(^-\) on the surface, which decreases the number density of the Cl\(^-\) in the interior.
Figure 2.11: Ion concentration profiles of Na\(^+\) and Cl\(^-\) (measured in units of concentration in the right y-axis), and H\(_2\)O density profiles (measured in units of g/cm\(^3\)) in the left y-axis) at \(T = 300\) K in droplets comprising \(N = 776\) H\(_2\)O molecules and a sole NaCl pair. For reference, the concentration profile of a sole Cl\(^-\) in \(N = 776\) is included. The shaded area denotes the standard deviation calculated by block averaging over five equal segment. The polarizable model is used.

2.4.1 Revisiting the Theory of Electrostatic Confinement

The theory of electrostatic confinement states that when a sole simple macro(ion) is the charge carrier in a droplet, a fundamental force that affects its location arises from a confining harmonic potential centred at the droplet’s centre of mass. Equation \([1.3]\) gives the probability of finding the ion at some distance from the droplet’s centre of mass if the ion is localized in the centre of a droplet\([33]\):

\[ P(||r||^2)_{EC} = \frac{2}{\sqrt{\pi}} \left( \frac{K(\epsilon)}{k_B T} \right)^{3/2} \frac{||r||}{E} e^{-K(\epsilon)||r||^2/k_B T} = \frac{2}{\sqrt{\pi}} \kappa(\epsilon, T)^{3/2} ||r|| e^{-\kappa(\epsilon, T)||r||^2} \]  

(2.1)

where \(k_B\) is the Boltzmann constant, \(T\) is the temperature and \(\kappa(\epsilon, T)\) is

\[ \kappa(\epsilon, T) = \frac{K(\epsilon)}{k_B T} = \frac{\epsilon - 1}{4\pi\epsilon_0\epsilon(\epsilon + 2)} \frac{Q^2}{R^3 k_B T} \]  

(2.2)
where \( \varepsilon \) is the dielectric constant of the droplet, \( \varepsilon_0 \) is the vacuum permittivity, \( Q \) is the total charge of the droplet and \( R \) is the radius of the droplet.

It is very important to note that the theory of electrostatic confinement only holds when the ion is localized in the centre of the droplet. I propose that, in addition to the electrostatic confinement effect, the ions also have an affinity to the surface, the strength of the affinity is dependent on the ion-water and water-water interaction strength. Fig. 2.11 shows the concentration of Cl\(^-\) ion as a function of the distance from the center of mass of a droplet containing 776 H\(_2\)O modelled with the SWM4-NDP model. It is apparent that, near the surface of the droplet, the concentration profile resembles a gaussian distribution.

I model the contribution from the surface with a gaussian function. Where \( r_{\text{max}} \) is the distance from the center of mass where the ion is most concentrated, and \( s \) is a parameter to control the shape of the Gaussian function

\[
P(\|\mathbf{r}\|^2)_{\text{surf}} = \exp(-s(r - r_{\text{max}})^2)
\]  

The spatial distribution of a single ion in a droplet is a sum of the contribution of the surface potential and the contribution from electrostatic confinement

\[
P(\|\mathbf{r}\|^2) = A \cdot P(\|\mathbf{r}\|^2)_{\text{EC}} + B \cdot P(\|\mathbf{r}\|^2)_{\text{surf}}
\]

Fig. 2.12 shows the result of least squares fitting of Eq. 2.4 to the ion probability distribution obtained from the simulation of a single Cl\(^-\), Br\(^-\) and I\(^-\) in 190 H\(_2\)O or 776 H\(_2\)O modelled with the SWM4-NDP water model. There are five parameters to be fitted: \( A \) and \( B \), the relative contributions of the two effects, \( \kappa(\varepsilon, T) \), \( r_{\text{max}} \) and \( s \). The fitted curve shows qualitative agreement with theory. For I\(^-\), the surface effect dominates, while for Cl\(^-\), the electrostatic confinement effect and the surface effect are both presents. It appears that the surface effect is most dominant for larger anions, with Br\(^-\) exhibiting a small amount of electrostatic confinement effect. The surface effect seems to be absent in droplets containing cation. I speculate
Figure 2.12: Ion concentration profiles of Cl\(^-\), Br\(^-\), I\(^-\) sites at \(T = 300\) K for droplet comprise (a) 190 H\(_2\)O and 1 Cl\(^-\), (b) 776 H\(_2\)O and 1 Cl\(^-\), (c) 190 H\(_2\)O and 1 Br\(^-\), (d) 776 H\(_2\)O and 1 Br\(^-\), (e) 190 H\(_2\)O and 1 I\(^-\), (f) 776 H\(_2\)O and 1 I\(^-\). Black solid lines denote the computed concentration, black dashed lines denote the fitted concentration, red and blue dashed lines are the contribution from electrostatic confinement and the surface effect respectively. The polarizable model is used.
that, in molecular simulations, the water-air interface is positively charged, the interface repels cations and attracts anions. The electrostatic confinement effect appears to be most prominent in the larger droplet, which is explained by the distance separating the core region and the charged surface.

2.5 Droplets Containing Multiple Pairs of NaCl

To analyse the retention of salt in the interior of supercooled droplets, I also examined systems comprising 776 H$_2$O molecules and four NaCl pairs, using the polarizable model at 260 K and 300 K and the nonpolarizable model at temperatures from 300 K down to 200 K. The ion concentration profile (Fig. 2.13) and free energy profiles as a function of the interionic distance are shown in Fig. 2.14 and Fig. 2.15. The striking feature at lower temperatures is the increased Na$^+$ and Cl$^-$ concentration in the subsurface (distance from the COM > 1.2 nm) relative to that at 300 K. For SWM4-NDP the equilibrium constant as a ratio of configurations in the outer basin over the inner basin for Cl$^-$ is 12.2 at 260 K versus 3.3 at 300 K. This ratio for Na$^+$ is very similar at both temperatures and approximately equal to 0.84. The enrichment of the subsurface in ions at lower temperatures is attributed to the exclusion of the ions from the bulk-like interior due to a better coordinated H-bonded network. The reduced shape fluctuations may contribute to this increase as well. I find here that the internal H-bonded network is maintained even at a higher concentration of NaCl. It is interesting to note that Fig. 2.13 may create the impression that at room temperature the ions are deeper in the interior measured from the surface than at lower temperature. The depth of the ions from the surface is the same at the various temperatures. The visual misconception arises from the fact that the distance from the COM order parameter masks the droplet’s shape fluctuations. A comparison of the location of Na$^+$ and Cl$^-$ between the single pair in the droplet and the multiple pairs, shows that at higher NaCl concentration, the ions have a higher propensity toward the exterior. The free energy differences of CIP and SSIP (Fig. 2.14 and Fig. 2.15) are in excellent agreement with those for
the single NaCl (Fig. 2.8(a) and Table 2.2), which verifies the convergence of the runs.

![Graph showing ion concentration profiles and H2O density profiles at 260 K and 300 K.](image)

**Figure 2.13:** Ion concentration profiles of Na\(^+\) and Cl\(^-\) sites (measured in units of concentration in the right y-axis), and H\(_2\)O density profiles (measured in units of g/cm\(^{-3}\)) in the left y-axis) at 260 K and 300 K in droplets comprising \(N = 776\) H\(_2\)O molecules and a sole NaCl pair or 4 NaCl pairs. The SWM4-NDP polarizable model is used.

It is interesting to note that for several ions modelled with the nonpolarizable model, I have consistently found that near \(R_B\) the ion concentration shows a minimum. This unfavourable region indicates the presence of an energetic barrier, arising from the different quality of the H-bonded network, in the crossing of the ion from the subsurface to the interior. I think that the presence of the ions can be used to probe the local environments at the water interface and interior, and possibly to define the interface more precisely than any other order parameter.

Finally, I can examine the effect of the lower temperature on the location of the multiple ions in charged droplets, where ions of the same sign are in excess. I have studied droplets composed of 3000 H\(_2\)O molecules and 22Na\(^+\)+8Cl\(^-\) ions or 22Cl\(^-\)+8Na\(^+\) ions at \(T = 240\) and 300 K using the nonpolarizable model. Here I extend the studies of the effect of low temperature on the ion location and their ion-pairing in highly charged supercooled droplets.
Figure 2.14: Free energy for CIP ⇌ SSIP interconversion reaction at 200 K and 300 K along the Na$^+$–Cl$^-$ interionic distance for the nonpolarizable model system with 4 pairs of NaCl

Figure 2.15: Free energy for CIP ⇌ SSIP interconversion reaction at 260 K and 300 K along the Na$^+$–Cl$^-$ interionic distance for the SWM4-NDP system with 4 pairs of NaCl
Table 2.4: Integrated number density of the ions in the droplet interior, subsurface and surface in an aqueous droplet with $N = 3000$ H$_2$O modelled with the nonpolarizable model.

containing multiple ions. The key idea of surface enrichment of salts also appears in the highly charged droplets. I expect that a polarizable model will show an even higher enhancement of the surface concentration compared to that of the nonpolarizable model.

The study is relevant to native mass spectrometry (MS), where highly charged droplets, generated by spraying, are the intermediate carriers of analytes from the bulk solution to the gaseous state. These droplets disintegrate by solvent evaporation and fission events that release clusters containing solvated ions. The effect of evaporative cooling can be significant in a droplet’s lifetime and as discussed later, may be exploited to eliminate undesirable salt.

In native mass spectrometry (MS) droplets are heated up in order to quickly evaporate, but in this process ions may form undesirable adducts with the analytes. We propose that by initial cooling of a droplet instead of heating, or by introducing cycles of alternating heating and cooling during desolvation, the ions may accumulate near the surface. Cooling may also occur naturally via evaporation. Possibly, bombardment with other molecules may assist in the detachment of solvated ions or their salt complexes from the surface and reduce adduct formation at the latest stage of protein or other macromolecule desolvation.

I examine the example of a droplet composed $3 \times 10^3$ H$_2$O molecules with $22 \text{Na}^+ + 8\text{Cl}^-$ or $22 \text{Cl}^- + 8\text{Na}^+$. The systems are modelled by using the nonpolarizable model at 300 K and 240 K. Systems at 200 K were also modelled for over a microsecond time, but no motions of
the ions were observed. At $T = 240$ K the effect of the low temperature was demonstrated and still sampling of the slow dynamics was still feasible. Figure 2.16 shows the ion distributions at 240 K and 300 K. In droplets greater than a few thousand of H$_2$O molecules at room or elevated temperature the ions in excess show a maximum near the droplet surface and a slow decay toward the interior. The counterion distribution shows the opposite trend: it is higher in the interior, where the excess ion distribution decays and lower where the excess ion distribution has a maximum. This general trend is expected because the Poisson-Boltzmann equation solved for a sphere where the charge is accumulated on the surface predicts an exponential decay of the ions toward the interior\[99\]. In droplets with fewer than 1500 H$_2$O molecules the ion-in-excess distribution is almost uniform because (a) the characteristic length of the ion distribution decay is comparable with the droplet radius and (b) the ion distribution is affected by the droplet’s large relative shape fluctuations from the spherical shape\[99\].

At 240 K, there is a clear differentiation in the location of the Na$^+$ and Cl$^-$ relative to that at 300 K. The majority of the excess ions are accumulated in the subsurface.
I relate the findings to native mass spectrometry processes. In droplet-based ionization methods it is desirable to spray proteins from physiological solution (NaCl or KCl at concentration 150 mM) nevertheless, the formation of adducts of salts with proteins or other macromolecules prevents the use of these conditions. The formation of adducts is avoided by spraying from low ionic strength solutions (40–70 mM), where the ionic strength is provided by ammonium acetate that evaporates by creating volatile molecules NH$_3$ and CH$_3$COOH. Our study suggests that in supercooled droplets the majority of the simple ions may be expelled from the interior to the subsurface. The effect is less pronounced with the nonpolarizable model than with the polarizable model. I expect that at lower temperatures and with a polarizable model the accumulation of the ions in the surface and subsurface region will be more pronounced. Therefore, by initial cooling of a droplet instead of heating, the ions may accumulate near the surface. Possibly, bombardment with other molecules may assist in the detachment of solvated ions or their salt complexes from the surface.

2.6 Conclusion

The modelling of NaCl ion-pairing in aqueous nanodroplets shows that in colder droplets it is more likely to take place near the surface. In this location, the stability of the SSIP relative to the CIP increases. This is opposite to the results of bulk solution simulations\[46, 68, 69\]. The polarizable model shows a substantial stabilization of the SSIP relative to CIP not only at low temperature but also at $T = 300$ K. A side-result of modelling via SWM4-NDP (polarizable model) is an interior broad maximum in the number density for the Cl$^-$ ion in addition to the well-known maximum in the surface\[97, 98\]. This result indicates that the nonpolarizable force fields overemphasize the interior local maximum.

In the study of the reaction dynamics, a weak correlation between the interionic NaCl distance reaction coordinate and the solvent degrees of freedom is found. The reduced coupling is mainly attributed to the presence of Cl$^-$ near the surface and to the fast diffusion of H$_2$O
molecules. In contrast to bulk solution where the crossing of the free energy barrier (along the interionic distance) is diffusive, there are no significant re-crossings in droplets.

In atmospheric chemistry, there are important but still unanswered questions about how the structure of the salt-containing quasi-liquid layer (QLL) on ice affects the kinetics of photolysis reactions of adsorbed polycyclic aromatic hydrocarbons. Similar questions are expected about the role of NaCl in the photolysis reactions of adsorbed organic molecules on aerosols where their subsurface and surface can be considered the counterpart of QLL on ice. The present study provided thermodynamic and dynamic information to better understand the chemistry of salts in the outer layers.

Applications of this study are envisioned in the field of mass spectrometry. Because of the shift in the location of ion distributions and ion-pairing with temperature, I propose to exploit a cycle of alternating low and high temperature as a way to control the adduct formation with macromolecules in droplet-based ionization methods used in mass spectrometry. Natural evaporative cooling may also contribute to the decrease in the temperature of droplets. Bombardment of cold charged droplets with other molecules may be a possible way to remove Na\(^+\) ions from the salt enriched interface. Enhanced salt release from droplets that carry the analytes may considerably extend the capability of native mass spectrometry analysis because it may allow for the salinity of the parent bulk solution of a biological sample to be closer to a physiological concentration of NaCl or KCl. Protons are another major ionic species in charged droplets. Experiments and computations have detected enhanced proton activity on ice at 155 K. Molecular dynamics simulations predicted that the migration of surface-hydrated protons are \(\approx 2800\) times slower than that of bulk protons at 190 K because they can be locally trapped by the undercoordinated water molecules. Thus, it was deduced that the activity detected in experiments arises from the higher proton concentration. It has also been found that protons are excluded from the ice bulk because of poor solubility in ice. The present study and accumulated evidence from the literature supports the hypothesis that protons in cold aqueous droplets will also be expelled to the surface and their migration may
slow down due to local trapping. Therefore, the alternating cooling and heating of droplets may also provide a possible method of controlling the degree of protonation in proteins. I have shown that protonation and sodiation lead to different conformations of proteins\[103\], and therefore the migration of ions and their nature may also affect the conformations. The dynamics of the various processes involved, such as proton transfer migration rates as a function of temperature and rate of conformational changes of proteins, have to be examined in order to be able to control the chemistry of the proteins within droplets.

In summary, the expulsion of ions from the interior of a supercooled or ice droplet may be exploited in MS experiments in order to eliminate undesirable salts and control the charge states of biological macromolecules.

I envision that since it is possible for H\textsubscript{2}O in supercooled droplets to expel chemical species to the interface that otherwise reside in the interior at room temperature, the question of establishing a deeper relation between the solubility in supercooled H\textsubscript{2}O and ice\[35-38\] may be addressed.


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Chapter 3

Bridging Microscopic and Nanoscopic Properties


3.1 Introduction

In the last one and a half decades there has been a surge in the use of nano- and micro-drops in many applications in science and industry. Examples include dispersive liquid-liquid micro-extraction[1], micro- and nano-fluidity and acceleration of reactions in electrosprayed droplets[2–7]. Even though our ability to carry out chemical reactions on mass-scale in these minute volumes is rapidly growing, the knowledge of the reaction mechanisms of the dissolved species in the droplet environment is still limited.

In this chapter, we consider charged droplets in the aerosol phase for which we compute systematically the ion spatial distribution, surface excess charge, and electric field as a function of droplet size. Droplet sizes that are accessible to experimental scrutiny are atomistically modelled.
To our knowledge, this is the first study that addresses the convergence of electrostatic properties of nano-droplets and finds the portion of ions (free charge) that contributes to the surface excess charge. Moreover, for the first time, a molecular foundation on the equilibrium partitioning model of C. Enke\cite{8,9} is reported. In the computations, we use Na\textsuperscript{+} and Cl\textsuperscript{−} ions in aqueous droplets to demonstrate the effects. Nevertheless, the findings and the methodologies are transferable to any other ions and solvents.

The study is directly relevant to several aerosol-based experiments and to atmospheric chemistry\cite{10–12}. Such experiments include a recent development in the use of electro-sprayed droplets as reaction vessels \cite{2–6} and droplet-based ionization techniques used in native mass spectrometry\cite{13}. Finding the ion distribution is the first step to establishing the ion-evaporation mechanism (IEM)\cite{14–16}, and the equilibrium partitioning model of C. Enke\cite{8,9}, which are broadly used to explain the selectivity effectiveness of electrospray ionization mass spectrometry (ESI-MS). IEM and Enke models have been inferred by the analysis of mass spectrometry data. Our study provides the thus far missing knowledge of a droplet’s molecular structure.

A lot of experience has been obtained over many decades from the molecular modelling of related systems such that of ions near a planar interface\cite{17–21} and from the electrical double layer studies in electrochemistry and colloidal science\cite{22,23}. These systems are overall neutral, thus the findings may not be directly transferable to charged droplets.

Native mass spectrometry often relies on the use of charged droplets to carry analytes from a sample into the gaseous phase\cite{13,24–33}. The charged droplets may originate from a liquid solution or from a solid matrix as in the recently developed matrix-assisted ionization (MAI) technique\cite{34,35} that combines features of matrix-assisted laser desorption/ionization (MALDI) and electrospray ionization (ESI). These droplets comprise solvents, analytes, ions and possibly other additives. The initially sprayed droplets disintegrate as they are directed in their motion by an electric field through higher to lower pressure compartments. The purpose of the process is the release of analyte as free as possible from adducts and solvent molecules.
In order to explain the mass spectra abundances, intuitive macroscopic models of the droplet fragmentation kinetics, its structure and the effect of solvent evaporation have been developed over many decades [8, 14, 15, 36-43]. Despite the considerable amount of research that has been performed, the structure of charged droplets is still not completely analyzed and the mechanisms of charging of macroions are still under investigation.

We dissect the droplet structure using atomistic modelling to find the mechanisms of charging of macromolecules in spray-based methods used in native mass spectrometry and explain the acceleration of reactions in microdrops [2-6, 44]. [45] computed ion distribution profiles and compared them with our analytical theory that combines main factors that determine these distributions [45]. These factors include a decay length of the ion distribution that arises from the solution of the non-linear Poisson-Boltzmann (NPB) equation for a rigid spherical droplet, shape fluctuations and the size of the ions. In the same article [45] we developed a methodology on how to compute the average and instantaneous electric field on the droplet surface using the multipole expansion method of electrostatics [45].

We have found a bi-layer structure of an aqueous charged droplet by using atomistic modelling, as shown in the schematic in Fig. 3.1. Two regions are distinguished: an inner droplet region (bounded by the inner dotted circle) where the total charge arising from ions, hydrogen and oxygen sites of water molecules is zero and an outer region that carries the surface charge. Fig. 3.1 also depicts a schematic representation of water density (blue line), radial distribution of simple ions with positive and negative charge (red lines) and the total charge distribution (solid black lines) that arises from the ions, hydrogen and oxygen sites of water.

We have found that in the presence of Na\(^+\) or Cl\(^-\) ions, the total droplet excess charge is located in an outer layer with thickness of 1.5–1.7 nm. Computations of various droplet sizes comprised H\(_2\)O and Na\(^+\) or Cl\(^-\) ions showed that the percentage of ions in this layer depends on the droplet size. In droplets with diameter < 4 nm, ≥ 55% of the total number of ions (Na\(^+\) or Cl\(^-\)) that corresponds to a concentration of ≥ 0.08 ± 0.03 M, residing in SECL. In droplets with diameter > 16 nm, the proportion is ≤ 24%, which corresponds to a concentration of
Figure 3.1: Schematic representation of a bi-layer structure of a droplet (represented by circles) as determined by atomistic simulations of aqueous droplets. The horizontal axis measures distance from a droplet’s centre of mass (COM). The perpendicular axis to the horizontal divides the schematic into two parts where the radial distribution of the positive ions is shown in the right semi-circle and that of the negative ions in the left semi-circle. The crossing of the axes is at the droplet’s COM. The water mass density is shown by solid blue line, the ion radial distribution normalized by the volume of the spherical shell by a red line and the total charge distribution (arising from H, O, ions) by a solid black line. The inner dotted black line marks the onset of the building-up of the charge distribution and the outer dotted line is the droplet’s boundary at a water density $\approx 5 \times 10^{-4}$ g/cm$^3$, where the charge density decreases to zero. The grey ring delimits the maximum ion concentration region (MICR) for which details are provided in the text.
≤ 0.03 ± 0.01 M. The concentrations reported here have been estimated by dividing the moles of ions with the volume of the spherical shell where they reside. We note that SECL includes the droplet surface fluctuations, which leads to partial occupancy of the volume of the spherical shell with solvent. If we divide the moles of ions in SECL with the volume of the average number of H₂O molecules in the spherical shell, then the concentration of the ions in the outer layers is higher, but still, the new concentration is not dramatically higher than those estimated by using the entire spherical shell.

The thickness of the outer layer is determined by the width of the charge distribution profiles as shown by the black line in Fig. 3.1. We have also found that the thickness of the layer is invariant with droplet size. The two droplet regions (Fig. 3.1) are in agreement with the assumption of the bi-layer droplet structure used in the equilibrium partitioning model (EPM) of C. Enke[8, 9]. EPM assumes two regions in a droplet, a core region, and an outer region that has the surface charge. Electrolyte and analyte ions partition between these two regions by establishing an equilibrium.

Our computational bi-layer droplet structure is in agreement with the assumptions of the equilibrium partitioning model (EPM) of C. Enke[8, 9]. EPM assumes two regions in a droplet, a core region, and an outer region that has the surface charge. Since EPM is a macroscopic model, it cannot readily provide the thickness of the outer layer and the amount of free charge present, thus our molecular modelling provides complementary information in that respect. Enke points out that the surface excess charge layer is a “different phase” in the droplet where distinct chemistry takes place. Here, we propose that within the framework of EPM one may consider that the important region for chemical reactivity is extended beyond SECL to include the region where the concentration of the ions is still significant.

Our study provides complementary insight into the equilibrium partitioning model (EPM)[8, 42] of C. Enke by unravelling the molecular structure of the surface excess charge layer of droplets using molecular dynamics. In addition, certain insights will be obtained on the ion-evaporation mechanism (IEM)[14, 15, 36]. Our findings are also relevant to the usage of
droplets as micro-reactors for accelerating chemical reactions \cite{2-4,44} and electrification phenomena in atmospheric aerosols \cite{10,12}.

The partitioning of the species in the inner and outer droplet regions can be inferred by a fitting of experimental data. Differently from the IEM which treats the dynamics of the droplet dissociation events, the equilibrium partitioning model focuses on the “process that determines the relative abundance of the species making up the surface excess charge.” The model infers that the species seen in the mass spectrum are those that make up the surface charge. Since EPM is a macroscopic model, it cannot readily provide the thickness of the outer layer and the amount of free charge in this layer, thus our molecular modelling provides complementary information in that respect. Enke points out that the surface excess charge layer is a “different phase” in the droplet where distinct chemistry takes place. We think that this difference is justified by the charge variation in this layer, mass density variations and different dielectric responses relative to the core region.

In Section 3.5, we show that the percentage of ions in SECL depends on its nature. In the presence of macromolecules, it is possible that SECL has a thickness of 2.0 nm. Depending on the nature of the ion SECL may not hold the highest concentration of ions. We identify the maximum ion concentration region (MICR), which partially overlaps with SECL. The combination of these two regions may be responsible for distinct chemistry in droplets because this broader region is characterized by higher ion concentration than a bulk analogue, surface fluctuations that may couple with the reaction mechanisms\cite{7}, the existence of free surface that may facilitate the reaction\cite{7} and distinct molecular structure, which is more pronounced as the droplet becomes smaller.

In Section 3.6, we addressed the question of the convergence of electrostatic properties in droplets. A systematic study of a variety of droplet sizes and the use of scaling, allowed us to find universal behaviour for the maximum of the ion distribution as a function of droplet size and extrapolate data to larger droplet sizes that cannot be studied by atomistic modelling thus far. By extrapolation, we found that the relative droplet shape fluctuations become negligible
for droplet radius greater than $\approx 10$ nm.

## 3.2 Systems and Simulation Methods

We performed equilibrium molecular dynamics (MD) simulations of charged aqueous droplets with Na$^+$, Cl$^-$ and model hydronium\[46] ions. A typical snapshot of a system comprised H$_2$O molecules, Cl$^-$ and Na$^+$ ions is shown in Fig. 3.2 Table 1 shows the systems that have been studied and their characteristics. The simulations were performed by using the software NAMD version 2.12\[47]. Newton’s equation of motion for each atomic site was integrated using the velocity-Verlet algorithm with a time step of 1.0 fs. The trajectories were analyzed using VMD 1.9.2\[48]. The water molecules were modelled with the TIP3P (transferable intermolecular potential with 3 points)\[49] -CHARMM water model and the ions with the CHARMM36m\[50, 51] force field.

The large number of studies on the Eigen\[52] and Zundel\[53] complexes of water with hydronium ion in small clusters are indicative of the challenges in modelling and experiments\[54–74]. Because of the large size of the droplets that we study, we model the hydronium ions by an empirical model, where the parameters were taken from [46]. We address the following questions: (i) Is there enough space on the droplet surface to accommodate the Eigen “pyramids”. (ii) Does the particular structure of the Eigen complex, differentiate its location in a droplet relative to that of Na$^+$ ions?

Simulation of a droplet comprised 3500 H$_2$O molecules modelled with the TIP4P/2005 water model\[75] and the OPLS-AA ion parameters\[76, 77] is performed to ensure the results are force field independent.

All the forces were computed directly without any cut-offs. Equilibrium simulations in NAMD were set by placing the droplet in a spherical cavity of radius 20.0 nm by using spherical boundary conditions. The cavity was sufficiently large to accommodate the shape fluctuation of the droplet. The droplet will eventually reach vapour pressure equilibrium. The systems
were thermalized with the Langevin thermostat with the damping coefficient set to 1/ps. In the estimation of the Rayleigh limit the surface tension value for TIP3P at $T = 300$ K is taken to be 0.0523 N/m and at $T = 350$ K is taken to be 0.0432 N/m\cite{78} for a planar interface. For TIP4P/2005 at $T = 350$ K surface tension is taken to be 0.0619 N/m\cite{78}. The analysis of the droplet electric field and potential is done with in-house methodology and software, of which details are presented in the article of Kwan et al.\cite{45}.

The production runs of the $2 \times 10^4$ and $3 \times 10^4$ H$_2$O-molecule drops were for 40 ns, following a 10 ns equilibration time and that of 880 and 3500 H$_2$O-molecule clusters for 150 ns and 50 ns, respectively. The production run for the $6 \times 10^4$ H$_2$O-molecule drop was 8.5 ns.

<table>
<thead>
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<th>$R_e$</th>
<th>$Q_r$</th>
<th>$R_r$</th>
<th>$r_{\text{max}}$</th>
<th>$X$</th>
<th>Range</th>
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<td>1.2±0.1-2.6</td>
<td>3.3±0.6</td>
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<td>46.0</td>
<td>5.90</td>
<td>5.10-5.15</td>
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<td>5.2±0.1-6.8</td>
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<td>46.0</td>
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<td>5.10-5.15</td>
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<td>1.92</td>
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<td>0.95</td>
<td>1.3±0.1-2.8</td>
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<td>$3 \times 10^4$</td>
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<td>6.08</td>
<td>46.0</td>
<td>5.90</td>
<td>5.10-5.15</td>
<td>0.91</td>
<td>5.2±0.1-6.8</td>
<td>14.7±2.1</td>
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<tr>
<td>$3 \times 10^4$</td>
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<td>6.08</td>
<td>46.0</td>
<td>5.90</td>
<td>5.10-5.15</td>
<td>0.91</td>
<td>5.2±0.1-6.8</td>
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<td>1.2±0.1-2.6</td>
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<td>16Cl$^-$</td>
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<td>20.6</td>
<td>3.37</td>
<td>2.65-2.70</td>
<td>0.85</td>
<td>2.4±0.1-3.8</td>
<td>10.6±1.2</td>
</tr>
<tr>
<td>3500$^\dagger$</td>
<td>15I$^-$</td>
<td>2.95</td>
<td>20.6</td>
<td>3.37</td>
<td>2.65-2.70</td>
<td>0.85</td>
<td>2.4±0.1-3.8</td>
<td>10.6±1.2</td>
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<td>880</td>
<td>1Na$^+$</td>
<td>1.88</td>
<td>7.9</td>
<td>1.56</td>
<td>0.00-0.80</td>
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<td>880</td>
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<td>1.56</td>
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<td>0.02</td>
<td>1.3±0.1-2.5</td>
<td>0.3±0.1</td>
</tr>
</tbody>
</table>

Table 3.1: Systems studied, characteristic dimensions and number of ions in the SECL. $n_{\text{H}_2\text{O}}$ denotes average number of water molecules and $n_i$ number of ions in the droplets during the production runs. $R_e$ [nm] is the equimolecular radius, computed by using density of the TIP3P model at 350 K to be 0.9539 g/cm$^3$. $Q_r$ ($e$) is the charge estimated at the Rayleigh limit using radius $R_r$. $r_{\text{max}}$ [nm] is the distance from the droplet centre of mass (COM) to the maximum of the ion concentration profile. $R_r$ [nm] is the Rayleigh radius ($X = 1$) for charge equal $n_i$. $X$ is the fissility parameter of the simulated droplet (Eq. 1.4). “Range” [nm] denotes the interval defined from the droplet COM in which the surface excess charge is located. Details are presented in the text. $n_{\text{out}}$ denotes the number of ions in the SECL. $^\dagger$ denotes the systems where the TIP4P/2005 water model is used.
In addition, we also performed molecular dynamics simulation of a cholera toxin pentamer with the RCSB PDB ID 1JR0 at the charge state of +25e in an aqueous droplet comprised \( \sim 2 \times 10^4 \) TIP3P water molecules and 15 Na\(^+\) ions at \( T = 350 \) K. The protomers in the pentameric structure are identical and the protein assembly overall has a toroidal shape. We studied three systems: i) with no counterions, ii) with 18 pairs of NaCl, which correspond to a counterion concentration of 50 mM and iii) with 36 pairs of NaCl, which correspond to a counterion concentration of 100 mM. The radius of the droplet is 5.6 nm and the total charge of the system is +40e.

The dimension of a droplet (with or without ions) is often measured by the equimolecular radius \((R_e)\) (values for various systems are found in Table 3.1). This radius is determined from the zero adsorption condition. If the vapour density is approximated to zero, \( R_e \) can be given as:

\[
R_e = \left( \frac{3N}{4\pi \rho^j} \right)^{1/3}
\]  

where \( N \) is the number of molecules in the droplet, \( \rho^j \) is the density of the bulk liquid.

### 3.3 Charge Distribution in Droplets with a Single Ion

In order to obtain insight into the solvent structure in charged droplets, I will examine an aqueous droplet with 880 H\(_2\)O molecules and a single Na\(^+\) (droplet diameter \( \approx 4 \) nm). The solvation of a single ion has been extensively studied in the context of the Born model. Figure 3.3 (a) shows the radial ion distribution of a droplet comprised \( \approx 880 \) H\(_2\)O molecules and a single Na\(^+\) or single Cl\(^-\). The error bars for Na\(^+\) in (a) is not shown for clarity, they are of the same magnitude as for Cl\(^-\). The profiles in Fig. 3.3 (a) have been normalized by dividing the raw histogram data with the volume of a spherical shell \( \left( \frac{4}{3} \pi [(r + dr)^3 - r^3] \right) \) where \( r \) is the distance from the droplet COM.

Figure 3.3 (b) and (c) depict the non-normalized charged distribution of a pristine aqueous droplet and that in the presence of a single Na\(^+\) ion and a single Cl\(^-\) ion, respectively. Fig-
Figure 3.2: Typical snapshot of a droplet that comprises $\approx 3 \times 10^4$ TIP3P water molecules (red oxygen site, white hydrogen site), 23 Cl$^-$ ions (green spheres) and 67Na$^+$ ions (blue spheres).

Figure 3.3 (b) shows that for a pure $\approx 880$ H$_2$O droplet the charge distribution in the interval [14.0±1 Å, 18.0±1 Å] (negative trough) integrates to $\approx -3.25e$ and in the interval [19.0±1 Å, 25.0±1 Å] (positive peak) integrates to $\approx +3.21e$. The total charge over the undulation is $\approx 0.0e$ as expected. The same figure shows that in the presence of a Na$^+$ ion, solvent polarization appears in the droplet interior. Hereafter, the local charge of the solvent will be referred to as the polarization charge. This is not surprising since the Na$^+$ ion has a significant probability to be in the droplet interior. The integral of the polarization charge from the droplet COM to 17.0 ± 1 Å is $\approx -3.76e$ and under the positive peak yields $\approx +3.75e$. Thus, differently from the pure H$_2$O, in the presence of a single Na$^+$ ion the negative polarization is spread over a much broader interval (because of the ion diffusion) and it is $\approx 0.5e$ lower from that of pure H$_2$O. The total charge distribution (arising from H, O, Na$^+$) is also shown in Fig. 3.3 (b). The integral over 14.0±1 Å–17.0±1 Å (negative trough) yields $\approx -2.8e$ and the integral over 18.0±1 Å–25.0±1 Å, $\approx 3.76e$. These differences show that the Na$^+$ ion partially compensates
Figure 3.3: (a) Single Na\(^+\) and Cl\(^-\) ion concentration profiles (normalized, left y-axis) in a droplet comprised \(\approx 880\) H\(_2\)O molecules. The density of water is shown by the solid black line (right y-axis). (b) Radial charge distributions (i.e. the average local charge in the shell \((r, r + 0.5\text{Å})\)) of the same size droplet as in (a) of a pristine droplet shown by the red solid line, of the water only (polarization charge) in the droplet with a single Na\(^+\) ion by the blue dotted line and the total (H, O, Na\(^+\)) by the blue solid line. (c) same as (b) but for Cl\(^-\). The bin size is 1.0 Å. Error bars are not shown in (b) and (c) for clarity.
the negative trough of the pure water, which integrates to $\approx -3.25e$ vs $\approx -2.8e$ in the presence of the ion. When the ion is in the droplet interior, the ion charge is compensated as indicated by the total charge of zero in the interior. The integral of the charge distribution (comprised O, H sites) of the single ion compensates the positive ion when integrated up to 8 Å. In the outer droplet layers, the ions appear with higher probability (not normalized) at $\approx 13\text{Å}$ which is the distance at which the charge undulation starts to build up. The charge compensation will take place up to 20 Å–21 Å. This distance corresponds to the top of the positive peak in Fig. 3.3 (b). Beyond this peak the density of water molecules is negligible, and the few water molecules form islands on top of the interior solvation shells. Figure 3.3 (c) is the same as Fig. 3.3 (c) but for a Cl$^-$. A distinct feature is that the positive peak in the charge distribution of pristine water is reduced in the presence of the Cl$^-$. ion.

### 3.4 Effect of the Nature of the Ion on the Surface Excess Charge Layer: Maximum Ion Concentration Region

Figure 3.4 (a) shows the ion radial distribution of Cl$^-$ ions in droplets of $880\text{H}_2\text{O}$ molecules-6 Cl$^-$ ($X = 0.57$) and $3 \times 10^4 \text{H}_2\text{O}$ molecules-44 Cl$^-$ ($X = 0.91$) using the TIP3P model. The region where the surface excess charge is found has been highlighted. The outer boundary of the highlighting stripe is found where the density of water is $\approx 5 \times 10^{-4} \text{g/cm}^3$ and the inner boundary is where the surface excess charge starts to build-up (see also Fig. 3.1). The highlighted region contains 55% (concentration 0.082 mol/L) and 34% (concentration 0.034 mol/L) of total number of Cl$^-$ ions in droplet of $880$ and $3 \times 10^4 \text{H}_2\text{O}$ molecules, respectively. Note that the ion concentrations have been estimated by dividing the moles of ions with the volume of the spherical shell where they reside. SECL (the highlighted region in Fig. 3.4 (a)-(b)) is strongly affected by shape fluctuations, thus this outer region is not filled with solvent. We can also estimate the concentration of the ions by using the average volume of the $\text{H}_2\text{O}$ molecules in the highlighted region. Then the ion concentration is estimated to be higher in
Figure 3.4: (a) Cl\(^-\) concentration profiles and H\(_2\)O density vs distance from the droplet COM for droplets of 880 and 3 \(\times\) 10\(^4\) H\(_2\)O molecules at \(T = 350\) K. TIP3P model is used. (b) Same as (a) but for 16 Cl\(^-\) and 15 I\(^-\) in a droplet of 3500 H\(_2\)O molecules. TIP4P/2005 for water and OPLS parameters for the ions are used. The shaded area around the ion concentration denotes the standard deviation calculated by block averaging over five equal segments. The horizontal lines mark the bulk ion concentration \(C_b\). The vertical grey lines mark the Rayleigh radius, \(R_r\), for the amount of charge in the droplet and the equimolecular radius, \(R_e\) (values are presented in Table 3.1).

SECL, but still, it is not a dramatic change relative to the concentration profiles in Fig. 3.4 (a)-(b).

Figure 3.4 (b) is similar to (a) but for droplets comprised 3500 H\(_2\)O molecules and either 16 Cl\(^-\) ions or 16 I\(^-\) ions. It is reminded that these systems have been modeled by TIP4P/2005 model for H\(_2\)O and OPLS parameters for the ions. SECL with thickness in the range of 24±1 Å-38 Å contains 36\% of Cl\(^-\) ions which corresponds to a concentration of 0.056 mol/L and 54\% of I\(^-\) ions, which corresponds to 0.079 mol/L. Three interesting points arise from the study of these ion distributions. Firstly, the nature of the ion plays a significant role in the percentage of free ions in SECL (36\% of Cl\(^-\) ions vs. 54\% of I\(^-\) ions). Secondly, the different percentages of ions in SECL and the nature of the ions do not affect their thickness. Thirdly, the SECL thickness computed using TIP4P/2005 model is found to be 1.6 nm. We have found it in the range of 1.5–1.7 nm using the TIP3P water model. We conclude that the thickness of SECL shows low sensitivity to the force field parameters.
At this point, we discuss an intriguing observation that we made that allows us to identify the maximum ion concentration region (MICR) of a charged droplet and its relation to SECL. In previous articles, we introduced the decay length of the ion distribution that arises from solving the non-linear Poisson-Boltzmann equation (NPB) for a rigid spherical droplet[45, 90]. This length, which we denote it as $\lambda_{\text{PB}}$, looks in its form similar to the “Debye” length for neutral electrolytes. $\lambda_{\text{PB}}$ for monovalent ions are given by

$$\lambda_{\text{PB}} \approx \frac{\varepsilon k_B T}{\sigma}$$

where $k_B$ is Boltzmann constant, $T$ is temperature $T = 350$ K, $\varepsilon$ is the permittivity of water estimated using the dielectric constant 61.7 for $T = 350$ K and $\sigma = \frac{|Z|e^2}{4\pi R_e^2}$ for ions of charge $\pm 1e$, where $e$ is the charge of the electron and $|Z|$ is the absolute value of droplet charge in units of e. The values of $\lambda_{\text{PB}}$ for the droplets we study are presented in Table 3.2. The NPB finds that the ion distribution has its maximum value on the spherical surface and decays exponentially toward the droplet interior. The NPB considers a rigid sphere, thus it ignores the effect of shape fluctuations that appear in the outer layers of a droplet. If we consider the difference $r_{\text{max}} - \lambda_{\text{PB}}$ (shown in Table 3.2) I find a characteristic distance from the droplet COM, where the ion distribution has decayed from its peak value.

The bulk concentration $C_b [\text{M}]$ (shown in Table 3.2), here defined by simply dividing the moles of ions by the volume of a sphere with radius $R_e$. The $C_b$ concentration is shown by the horizontal line in Figs 3.4 (a)-(b). The intersection of the $C_b$ line with the radial ion distribution towards the droplet interior coincides with the point with abscissa $r_{\text{max}} - \lambda_{\text{PB}}$. We have made this observation consistently not only for the ion distributions presented in Fig. 3.4 (a)-(b). However, this is the first time we report our observation.

This observation shows that $\lambda_{\text{PB}}$, even though approximate, it defines a specific length of ion decay that has a solid theoretical foundation. The radial ion distribution at distance $> r_{\text{max}}$ is strongly affected by shape fluctuations. The $C_b$ line intersects this ion radial distribution in
Table 3.2: Systems studied, estimates of $\lambda_{PB}$ and ion concentrations. $n_{H_2O}$ denotes average number of water molecules and $n_i$ number of ions in the droplets during the production runs. $\lambda_{PB}$ [nm] is a characteristic decay length of the ion concentration that emerges from the solution of the non-linear Poisson-Boltzmann equation. Details for $\lambda_{PB}$ are presented in the text. $C_{MICR}$ [M] (where M stands for molarity) is the concentration of the ions in the maximum ion concentration region (details are presented in the text) and $C_{SECL}$ [M] is the concentration in SECL. $C_b$ [M] is the bulk ion concentration estimated by dividing the number of moles of ions by the volume of a droplet of radius $R_e$. “–” means that the quantity has not be defined for a certain droplet size (details are presented in the text). In all the systems the temperature is set at $T = 350$ K.

<table>
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<tr>
<th>$n_{H_2O}$</th>
<th>$n_i$</th>
<th>$\lambda_{PB} [\text{nm}]$</th>
<th>$C_{MICR} [\text{M}]$</th>
<th>$C_{SECL} [\text{M}]$</th>
<th>$C_b [\text{M}]$</th>
</tr>
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<tbody>
<tr>
<td>880</td>
<td>6Na$^+$</td>
<td>0.68</td>
<td>–</td>
<td>0.08 ± 0.03</td>
<td>0.360</td>
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<tr>
<td>880</td>
<td>6H$_2$O$^+$</td>
<td>0.76</td>
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<td>0.112 ± 0.001</td>
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<tr>
<td>5880</td>
<td>19Na$^+$</td>
<td>1.16</td>
<td>–</td>
<td>0.06 ± 0.02</td>
<td>0.167</td>
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<tr>
<td>2 $\times$ $10^4$</td>
<td>36Na$^+$</td>
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<td>0.04 ± 0.01</td>
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<td>1.08</td>
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<td>0.03 ± 0.01</td>
<td>0.078</td>
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<tr>
<td>880</td>
<td>6Cl$^-$</td>
<td>0.76</td>
<td>–</td>
<td>–</td>
<td>0.360</td>
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<tr>
<td>3500$^+$</td>
<td>16Cl$^-$</td>
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<tr>
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<td>1.08</td>
<td>0.103 ± 0.003</td>
<td>0.029 ± 0.003</td>
<td>0.078</td>
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In summary, we identify two significant regions in the charged droplets: (a) SECL (surface excess charge layer) is strongly affected by shape fluctuations. We expect that this is the layer from which ions are released in IEM. We have reported that shape fluctuations become neg-
ligible relative to the spherical shape at droplet radius greater than 10 nm. This droplet size coincides with that below which IEM is expected to dominate Rayleigh fission. Our results indicate that it is the concentration of ions in SECL that should enter the IEM kinetic equations and not the total ion concentration as has been used so far. The concentration of ions in SECL is estimated by using a volume that the average number of water molecules in the spherical shell is almost the same as that in the droplet core. (b) MICR (maximum ion concentration region) is the layer where there is an increased concentration of ions. There is an overlap between SECL and MICR, which is expected to increase with droplet radius.

Now we make the relation of MICR-SECL with the two-layer model in the EPM. EPM focuses on SECL because the model uses the analogy with the structure of a double layer that appears next to a charged surface. For droplets with radius < 10 nm we think that the active area of the droplet should be extended by $\lambda_{\text{PB}}$ in order to include MICR. If we consider a droplet of $10^5$ H$_2$O molecules, modelled by TIP3P at $T = 350$ K then the corresponding charge at the Rayleigh limit is $82.5 \, e$ and $R_e = 9.08$ nm, which yields $\lambda_{\text{PB}} = 1.29$ nm.

We have found that $\lambda_{\text{PB}}$ increases from 1.0 nm to 1.35 nm at $T = 350$ K in droplets of $R_e = 5.3$ nm ($2 \times 10^5$ H$_2$O molecules) to $R_e \approx 10$ nm, respectively (data are shown in Table 3.2). In tiny droplets of approximately $10^3$ H$_2$O molecules, MICR is extended to almost the entire droplet. It is straightforward to estimate the value of $\lambda_{\text{PB}}$ at any temperature, solvent dielectric constant and droplet size. Thus, it is reasonable to extend SECL by approximately 1.0 nm in order to define a distinct droplet region that encompasses the highest ion concentration, carries the excess charge and it is subject to shape fluctuations. In droplets with radius > 10 nm the relative shape fluctuations are small thus, for this droplet size, we expect MICR and SECL to overlap significantly.

The effect of the nature of the ions in their abundance in SECL is further examined in the cases of model hydronium ions and a protein complex. Figure 3.5(a) shows the distribution of “hydronium” ions in a droplet of $\approx 1000$ H$_2$O molecules and 6 ions at $T = 350$ K. The general features of the distribution are the same as that of the Na$^+$ ions but the hydroniums
reside much more in the outer water shells of the droplet than the Na\(^+\) ions; 80\% of hydronium ions reside in SECL vs. 55\% of Na\(^+\) ions. The thickness of the layer remains almost the same for the two types of ions. Even though the hydronium model omits important quantum effects it is demonstrated that it is possible for ions that carry features of the hydronium ion to have a much higher concentration in SECL than Na\(^+\) or Cl\(^-\) ions.

Figure 3.5: Droplet solvent density and hydronium ion radial distribution profile (upper panel). The Na\(^+\) radial distribution profile is included for comparison. The drop comprises \(\approx 880\) H\(_2\)O molecules and 6 H\(_3\)O\(^+\) ions at \(T = 350\) K. The total charge of the drop (lower panel). The black vertical line marks the onset of the surface excess charge layer. The shaded area denotes the standard deviation calculated by block averaging over five equal segments, each of \(4 \times 10^4\) configurations.

Figure 3.6 (a) shows a typical snapshot of 1JR0\(^{25+}\) in an aqueous droplet of \(2 \times 10^4\) H\(_2\)O molecules and several co-ions and counterions. In all the simulations 1JR0\(^{25+}\) resides off the
droplet COM. The charge distributions of aqueous droplets with various concentrations of simple ions shows that the surface excess charge layer has a thickness of \( \approx 2.0 \) nm (the onset of the negative value of the charge density is at 4.6 nm and the end value is at 6.6 nm where the water density becomes \( \approx 5 \times 10^{-4} \) g/cm\(^3\)). Therefore, in the presence of complex macromolecules SECL may be broader than that for simple ions.

Figure 3.6: (a) Typical snapshot of an aqueous droplets comprised \( 1JR0^{25+}, 14Na^+ \) ions and 36 pairs of NaCl. The water molecules are depicted in red, the Na\(^+\) ions in violet and the Cl\(^-\) ions in green. (b) Charge distribution measured from the droplet COM. The shaded area denotes the standard deviation calculated by block averging over five equal segments.

### 3.5 Structure of the Surface Excess Charge Layer

Figure 3.7 (a) shows that in the presence of positive ions in aqueous drops, SECL undulates (negative trough followed by a positive peak) and Fig. 3.7 (b) that for negative ions there is a single negative trough. The difference in SECL in the presence of cations and anions is explained as follows: We consider the orientation of the H\(_2\)O dipoles in pristine droplets as the reference structure. In a pristine droplet, there is an excess of hydrogen sites in the droplet periphery and thus, an excess of oxygen sites in the immediate (more in the interior) layer (Fig. 3.3 (b) and (c)) due to the presence of the interface. As a result the charge distribution shows undulation where a negative trough is followed by a positive peak. The cations enhance the presence of the hydrogen sites in the periphery and thus the undulation in SECL follows
Figure 3.7: (a) Radial charge density distribution in droplets containing Na\(^+\); (b) as (a) but for Cl\(^-\) ions. The shaded area denotes the surface excess charge layer. (c) \(<\cos \phi>\) as a function of the distance \(r\) from the droplet COM in droplets containing Na\(^+\) ions; (d) as (c) but for Cl\(^-\) ions.

Figure 3.8: Distribution of \(\cos(\phi)\) at selected distances from the droplet COM. The corresponding angles are shown on the top of the graphs. (a) \(880\text{H}_2\text{O} + 6\text{Na}^+\) ions and (b) \(880\text{H}_2\text{O} + 6\text{Cl}^-\) ions.
the same pattern as that of the pristine droplet. Differently, the presence of a single anion, as shown in Fig. 3.3 (c) has a significant effect in the lowering of the positive peak relative to that of a pristine aqueous droplet, while it does not affect the negative trough. Figure fig:c4s9 shows that the undulation in SECL approaches progressively a single trough as the number of negative ions increases. For one or two Cl\(^-\) ions, the undulation is maintained, but as the number of Cl\(^-\) ions increases, the charge distribution leads to one trough. The lowering of the positive peak arises from the change in the orientation of the water molecules.

The solvent polarization charge accompanies the free charge. The orientation of the water dipoles is directly related to the polarization charge. For this reason, we examine the distribution and the average value of \(\cos \phi\), where \(\phi\) is the angle between the \(\text{H}_2\text{O}\) dipole moment (directed from the oxygen site to the centre of the line that connects the two hydrogen sites) and the vector that points from the droplet centre of mass (COM) to the oxygen site of a water molecule. Figure 3.7 (c) and (d) show the average value \(\langle \cos \phi \rangle\) as a function of distance from the droplet COM for droplets of different size and sign of the ion’s charge. The corresponding distributions are shown in Fig. 3.8 (a) and (b) for a droplet of \(\approx 880 \text{H}_2\text{O}\) molecules including 6\(\text{Na}^+\) ions or 6\(\text{Cl}^-\) ions, respectively. The distributions are estimated in spherical shells of thickness 0.5 Å centred at the droplet COM. The combination of Fig. 3.7 (c)-(d) and Fig. 3.8 (a)-(b) show that for the smaller droplets of \(\approx 880 \text{H}_2\text{O}\) molecules, there is a solvent polarization in the interior, while in the larger droplets of \(\approx 3 \times 10^4 \text{H}_2\text{O}\) molecules, the polarization – still present – is less pronounced. The interior polarization arises from the fact that it is likely to find ions in the interior (Fig. 3.4). The larger the droplet, the lower the concentration of the ions, which explains the less pronounced polarization in the larger droplets. In SECL there are changes in the solvent polarization as indicated by the highlighted regions in Fig. 3.7.

For droplets with \(880 \text{H}_2\text{O}\) and 6 \(\text{Na}^+\) ions, there are three characteristic distances from the droplet COM, which appear in the SECL (see Fig. 3.7 (a)). These are: 11.0 ± 1.0 Å where the surface excess charge starts to build up, 14 ± 1.0 Å which is \(\approx\) at the minimum of the negative trough and 19±1.0 Å, which is \(\approx\) at the top of the positive peak. Beyond the 19 Å, the density of
Figure 3.9: Charge distribution in droplets comprised 880H₂O molecules and 1–6ClCl ions. (a) Ions only; (b) Water only; (c) Total (includes contributions from ClCl, H and O sites).
the water is considerably reduced and all the charge is polarization charge. At these distances, we examine the orientation of the H$_2$O dipole moment. All the graphs in Fig. 3.8 indicate that the angle distributions are quite broad, thus there is not a dominant angle. At $r = 14$ Å the preferred $\cos \phi$ values are in $-0.25 < \cos \phi < 0.75$ ($104.5^\circ < \phi < 41.5^\circ$) and at $r = 19$ Å $0.0 < \cos \phi < 0.75$ ($90^\circ < \phi < 41.5^\circ$). At $r = 19$ Å the probability of the negative $\cos \phi$ values have decreased considerably. In the presence of Na$^+$ ions, $\langle \cos \phi \rangle$ in the highlighted region (SECL) of Fig. 3.7 shows a small kink. A similar kink is not present in the droplets with Cl$^-$ ions. This difference in $\langle \cos \phi \rangle$ is associated with the different forms of the surface charge distribution in the ions of different charges: a single negative trough for Cl$^-$ ions vs an undulated charge distribution for Na$^+$ ions. The angle variations are less pronounced for the larger droplets because of the lower ion concentration. In the very outer region of $r > 19$ Å, the angle distribution becomes sharper. At this distance, the H$_2$O are polarized by the entire droplet charge and not by a specific ion.

Now we examine the ion charge compensation by the solvent molecules. It is often assumed that the charge of the ions is compensated by the solvent because of its high dielectric constant. This is generally true, but there are cases where this assumption may not hold.

We computed the radial distribution function ($g(r)$) between the Na$^+$ ions as shown in Fig. 3.10. The Na$^+$-Na$^+$ radial distribution function shows two significant peaks, at $\sim 3.7$ Å and $\sim 6.1$ Å that correspond to contact ion pairs (CIP) and solvent separated ion pair (SSIP), respectively[91–95]. The relative distance of the ions has an interesting effect on the compensation of the ion charge by the solvent molecules. If we have a single Na$^+$ in an aqueous droplet, we find that the integral of the charge up to 8.0 Å compensates for the charge of the ion. When we have 6Na$^+$ ions in a droplet of 880 H$_2$O molecules, the charge of the single ion is not compensated by the H$_2$O molecules found in a radius of 7.0 Å around the ion. The charge compensation should also include the other ions. We attribute the lack of charge compensation by the solvent to the small droplet size. In the smaller droplets, two Na$^+$ ions are very likely to be found at a distance < 1.4 nm, thus having their two immediate solvation shells
Figure 3.10: (a) Radial distribution function \((g(r))\) of \(\text{Na}^+\) ions in aqueous droplets as a function of distance \(r\) between any pair of ions. (b) Typical snapshot of a droplet of 880 H\(_2\)O molecules and 6 Na\(^+\) ions. Blue-colored H\(_2\)O molecules are found at \(r < 6\ \text{Å}\) from a Na\(^+\) centre. The thick red-colored H\(_2\)O molecules are at \(8\ \text{Å} < r < 6\ \text{Å}\). The shaded area denotes the standard deviation calculated by block averaging over five equal segment (only shown for 880 H\(_2\)O and \(2 \times 10^4\) H\(_2\)O). The thin red-colored H\(_2\)O molecules are the molecules that are not in the immediate vicinity of the ions. The snapshot shows in the encircled region the lack of sufficient solvation for charge compensation around the surface ions.

interacting. The effect is less pronounced in larger droplets. Charge compensation of the ions by the solvent may also not occur in ions that are very near the surface. In smaller droplets where the ion concentration is higher, the free charge that is near the surface may not be coordinated with a sufficient number of water molecules to compensate for its charge as shown in Fig. 3.10 (b). Our finding is also supported by the low dielectric constant of water detected under confinement\([96, 97]\).

### 3.6 Convergence of Ion Spatial Distributions

Below, we attempt to rationalize universal features of the charge density distribution in a droplet close to the Rayleigh limit. In Figure 3.11 (a) we show the ion distributions for five droplet sizes shown in Table 3.1. The profiles have been normalized by dividing the raw histogram data with the volume element of a spherical shell \(\frac{4}{3}\pi[(r+dr)^3 - r^3]\) where \(r\) is the distance from the
Figure 3.11: (a) Na\(^+\) concentration profiles vs distance from the droplet COM for aqueous droplets of various sizes at \(T = 350\) K. Standard deviation bars are sparsely shown for clarity purpose. The standard deviation is shown in Fig. 3.12. (b) Scaled plots of (a). The x-axis is scaled by \(R_r\) for the specific droplet charge state \((Q)\) and the y-axis by \(Q/R_r^3\) (data presented in Table 3.1).

Figure 3.12: Ion concentration profiles (left y-axis) and water density (right y-axis) in a droplet (a) for a droplet comprised \(\approx 3 \times 10^4\) H\(_2\)O molecules and either 44 Na\(^+\) ions or 44 Cl\(^-\) ions. (b) \(\approx 3 \times 10^4\) H\(_2\)O molecules, 44 Na\(^+\) ions and 23 NaCl pairs. The shaded area denotes the standard deviation calculated by block averging over five equal segments of \(4 \times 10^4\) configurations, separated by 0.2 ps.
droplet COM). We can recast Eq. [1.4] into the following form

\[
\frac{1}{(4\pi\varepsilon_0)^2} \frac{Q^2}{R^4} R = |E|^2 R = 4\varepsilon_0 \gamma X
\]

where \(|E| = Q/4\pi\varepsilon_0 R^2\) is the magnitude of the electric field on the surface of a spherical conductor with radius \(R\) (we remind that in this model all the charge lies on the surface and there are no shape fluctuations). Eq. [3.3] shows that the surface charge density, denoted hereafter by \(\sigma = \varepsilon_0|E|\) [98]. Hence, Eq. [3.3] becomes

\[
\sigma^2 = \frac{4\gamma X\varepsilon_0}{R}
\]

On the other hand, the surface charge density is computed by integrating the ion molarity \(n(x)\) from the surface of the droplet to the droplet centre

\[
\sigma = \frac{1}{4\pi R^2} \int_0^\infty dr 4\pi r^2 n(r)
\]

where the charge density is computed in units of \([\text{mol}] / [\text{m}]^2\). We note that \(n(r)\) is given by the non-linear Poisson-Boltzmann (PB) equation. \(n(r)\) drops sharply on the surface because of lack of shape fluctuations and decays towards the droplet COM. If the charge is localized near the surface of a droplet we may approximate the surface by a planar interface. The solution of the nonlinear PB equation relates the charge molarity on the surface of the droplet \(n(R)\) and the surface charge density (for details see [45])

\[
\sigma = \lambda_{PB} n(R)
\]

where \(\lambda_{PB}\) is a parameter emerging from the solution of the non-liner PB equation, that remarkably coincides with the Debye length of electrolyte with the ion molar concentration \(n(R)\). The “Debye length” scales as \(\lambda_{PB} \sim 1/\sqrt{n(r)}\), therefore, after some algebra we arrive at the re-
lation for the surface charge density derived from the solution of the nonlinear PB equation $\sigma^2 \sim n(R)$. Combining this result with Eq. 3.3, we arrive at the scaling for the maximum ionic concentration as a function of the droplet radius $n(R) \sim X/R$. The simulation data agree with the theoretical prediction (Eq. 3.3) that the surface charge density $\sigma$ decreases with the increase of the droplet radius as shown in Fig. 3.11(a). Figure 3.11(b) shows the scaled distributions, where the distance (x axis) in Fig. 3.11(a) has been scaled by $R_r$ shown in Table 3.1. The scaled distributions reveal an interesting behavior that is not evident in the non-scaled data (Figure 3.11(a)). The distributions of all droplet sizes apart from that of 880 H$_2$O molecules are very similar.

In the largest droplets comprising $6 \times 10^4$ H$_2$O molecules the scaled ion density decays faster than all the rest. The diminished magnitude of the relative shape fluctuations results in a sharper maximum of the ion density distribution. The larger relative shape fluctuations of the smallest droplets give rise to three features in the ion concentration profile. Firstly, the concentration profile of 880 H$_2$O molecules-6Na$^+$ ions appears to be much broader than those for the larger droplets. Secondly, the distance of $r_{\text{max}}$ from the droplet’s very outer surface where the water density is $5 \times 10^{-4}$ g/cm$^3$ becomes shorter as the droplet size increases. This distance is $\approx 1.7$ nm for the smallest droplet and $\approx 1.4$ nm for the largest droplet. $|R_e - r_{\text{max}}|$ follows the same trend: it is $\approx 1.0$ nm for the smallest droplet and $\approx 0.74$ nm for the largest droplet. In microscopic droplets the distance of the maximum of the ion distribution to $R_e$ (see Table 3.1) may become even shorter because of the reduced relative shape fluctuations. We estimated that the ratio of $r_{\text{max}}/R_r$ changes from 0.59 for droplets of 880 H$_2$O molecules to 0.92 for droplets of $6 \times 10^4$ H$_2$O molecules. The ratio of $r_{\text{max}}/R_r$ vs $R_r$ is shown in Fig. 3.13 where extrapolation of the data led to the intriguing observation that $r_{\text{max}}/R_r = 1$ when $R_r \approx 10$ nm. At this point, we relate our finding to IEM[14, 15]. The observation suggests that certain fluctuations in charge density (or shape since shape and charge density are intimately related) in droplets with radius less than 10 nm may be responsible for a faster release of solvated ions via IEM[14, 15] than a Rayleigh fission mechanism. The role of fluctuations has not been
considered in the original formulation of IEM\cite{14,15}. The specifics of Rayleigh fluctuations vs fluctuations underlying the IEM mechanism deserve a separate study.

![Graph](image)

**Figure 3.13:** Ratio of $r_{\text{max}}/R_r$ as a function of $R_r$ for the droplets with Na\(^+\) at $T = 350$ K (Table 1) shown by circles. The line is for guiding the eye. Extrapolation of the line shows that $r_{\text{max}}/R_r = 1$ corresponds to $R_r \approx 10$ nm.

Counterions are commonly found in solutions. We examine the role of counterions and contrast it with systems without counterions. Figure 3.12 (a) shows the spatial ion distribution of droplets comprised $\approx 3 \times 10^4$ H\(_2\)O molecules, and either 44 Na\(^+\) ions or 44 Cl\(^-\) ions. The $r_{\text{max}}$ of the Cl\(^-\) ions is slightly more in the interior relative to the Na\(^+\) ions. Figure 3.12 (b) shows the ion distribution of a droplet comprised $\approx 3 \times 10^4$ H\(_2\)O molecules, 44 Na\(^+\) ions and 23 NaCl pairs. A main feature in Fig. 3.12 is that in a droplet with counterions the excess ions (Na\(^+\)) form an outer shell of higher concentration. The Cl\(^-\) ions are depleted from the region where the Na\(^+\) concentration is the highest and their concentration gradually increases toward the droplet centre. The location of the Cl\(^-\) ions is the result of the conducting character of the droplet, which dictates that the excess charge accumulates on the surface. If we scale the Na\(^+\) concentration in the presence of Cl\(^-\) ions the two concentrations with and without coun-
terions coincide. In the presence of counterions, the Na\(^+\) concentration (not scaled) appears to extend more toward the outer H\(_2\)O layers and to have a higher concentration in the interior. This behavior is attributed to the fact that in the presence of counterions the concentration of Na\(^+\) is higher in order to maintain the overall charge of the droplet the same as that without counterions. This increased outer concentration indicates that the surface is not saturated with free charge when only Na\(^+\) ions are present.

### 3.7 Surface Excess Charge and Electric Field

![Figure 3.14: (a) Charge distribution of a droplet (including H, O, ions) comprised 3 × 10\(^4\) H\(_2\)O molecules and either 44 Na\(^+\) ions or 44 Cl\(^-\) ions vs distance from the droplet COM (bin size 2.0 Å). (b) Colored shells centred at the droplet COM: yellow colored 0 Å < r < 50.0 Å, green colored 50.0 Å < r < 56.0 Å, grey colored 56.0 Å < r < 62.0 Å, red colored r > 62.0 Å.](image)

A relevant quantity to that of the ion spatial distribution is that of the surface excess charge. Figure 3.14 (a) shows the charge distribution of a droplet comprised 3 × 10\(^4\) H\(_2\)O molecules and either 44 Na\(^+\) ions or 44 Cl\(^-\) vs distance from the droplet COM (see also Fig. 3.17 for the polarization charge).

The onset of the building up of the charge is found at \(\approx 5.1 \pm 0.1\) nm, which is in the green region shown in Fig. 3.14 (b). At \(\approx 5.1\) nm the ion concentration is at its maximum value. For Na\(^+\) ions the charge distribution profile undulates at distance > 5.1 nm. The integral from 5.1 nm outward yields the total charge of the droplet (43\(e\)-44\(e\)). In Table 3.1 we have reported
Figure 3.15: Charge density (sum of Na\(^+\), oxygen, hydrogen sites), in aqueous droplets with Na\(^+\) ions as a function of droplet size.

Figure 3.16: Average radial potential of a droplet comprising 2 \times 10^4 \(\text{H}_2\text{O}\) molecules and 36 Na\(^+\) ions. Contribution from all the point charges (H, O, Na\(^+\)) is considered.
Figure 3.17: Charge distribution (in units of $e$) profiles in droplets comprised $3 \times 10^4 \text{H}_2\text{O}$ molecules and either $44\text{Na}^+$ ions or $44\text{Cl}^-$ ions. The vertical bars denote the standard deviation calculated by block averaging over five equal segments.
the range over which the integration is performed. The upper limit of integration is at the distance where the water density becomes $5 \times 10^{-4}$ g/cm$^3$. In our simulations and in experimental set-ups a droplet may be surrounded by vapour. As we have shown in previous work [45] this vapour is also polarized. Thus, the presence of the vapour may extend the surface charge but its contribution is insignificant. As shown in Table 3.1 the smallest droplet contributes $\approx 55\%$ of the free charge in the surface charge, while the largest droplets $\approx 37 - 33\%$. The error bars in the number of ions in the surface excess charge region are due to the uncertainty in the initial point of the interval over which the integration is performed. The error bars associated with the ion distribution and water density in this region are negligible because both have converged. The concentration of ions in the surface excess charge layer is also shown in Table 3.1. We remind here that the ion distribution is not uniform in the range of the excess surface charge (see Fig. 3.11). We note that the charge undulation is not unique to the positively charged droplets, but it also appears in an uncharged water droplet [80, 99]. In the presence of Na$^+$ ions, the charge undulation in pristine and positively charged droplet are in-phase but the building-up of the charge starts at a shorter distance relative to the uncharged case. The positive peak relative to that of the pristine water is higher because of the stronger orientation of the outer water molecules with the hydrogen sites pointing outwards. These water molecules are mainly found in the grey and red regions of Fig. 3.14 (b). The Cl$^-$ show only one negative trough in the charge distribution (Fig. 3.14 (a)), which is much broader than the negative trough of the Na$^+$ ions. The Cl$^-$ ions themselves enhance the negative trough of the pristine water molecules. The positive peak of the pristine water disappears because of the change in the orientation of the water molecules due to the overall negative charge of the droplet. Figure 3.15 shows the progression in the normalized charge distribution profiles as a function of droplet size for positive ions. The charge undulation becomes less pronounced with increased droplet size due to the decrease of the ion concentration as the droplet size increases.

In a previous work, Ahadi et al. [100] have placed the surface charge in charged droplets in the very outer periphery (water/vapour interface) of the droplet, where the density of water is
reduced substantially and does not include any free charge. It appears that Ahadi et al. attempt to define the droplet surface charge in the region where the total charge comprises only solvent polarization (no ions). We relate now the findings of Ahadi et al. with our plots. Figure 3.14 shows that for the droplet of 44 Na$^+$ ions, the integral of the charge from 6.18 nm (top of the positive peak) outwards, yields a charge very close to $+44e$. We have found the same for all the positively charged droplets shown in Fig. 3.15. This interval of integration corresponds to the red region in Fig. 3.14 (b) where there are no ions, thus this region appears to be close to Ahadi et al. assignment of the surface charge. Here we point out differences between assigning the surface charge in the very outer region vs the thick layer shown in Fig. 3.14. Firstly, since the outer positive peak for positive ions (Fig. 3.14 (a)) is very steep, the values of the charge in the outer droplet region is very sensitive to the starting point of integration. Secondly, because of the similarity of the charge undulation between pristine water droplets and positively charged droplets, the existence of positive charge (= total droplet charge) in the farthest water layers is not surprising. Differently, in the presence of Cl$^-$ ions, we cannot find an interval over which the integral yields the overall droplet charge located in the very outer water layers. For the Cl$^-$ ions we have to integrate over the range reported in Table 1. Thus, it is not evident that for both positive and negative ions we can find the total charge in the form of surface charge in the farthest water layers. Thirdly, the physical and chemical significance of the surface charge in the red region of Fig. 3.14(b) is not well defined because the outer “inert” solvent molecules cannot explain the mass spectrometry abundances. It is the presence of active species (ions and possibly other species) that play a critical role in the abundances. We emphasize here that the size of the standard deviation indicates that there are large charge fluctuations in the outer droplet layers, which may lead to the release of a solvated single ions or charge transfer processes to macroions (when macroions are present). The standard deviations in the definition of the droplet radius and charge density have not been considered in the article by Ahadi et al., hence the significant sensitivity of the periphery surface charge on the definition of the droplet radius has not been discussed.
Figure 3.16 shows the electrostatic potential of a droplet comprising $2 \times 10^4$ H$_2$O molecules and 36 Na$^+$ ions. At the vapour phase, the potential coincides with that of a point charge with $Q = 36e$. Inside the droplet, the potential can be well approximated by a constant value (within the error bars), which is the potential on the surface of the droplet. The potential raises in a region of 4.8–5.8 nm. This region starts from the minimum of the negative trough of the charge distribution (Fig. 3.15) and ends beyond the positive peak. The starting point of integration that yields the total droplet charge is the outer region found approximately in the middle of the “hump”. The starting point of integration at 5.9 nm where the dielectric and conducting behaviour differentiate, yields a charge (+4e) which is much less than the overall droplet charge.

At this point, it is in order to relate our findings with the equilibrium partitioning model of C. Enke. The model relates the analyte response using ESI-MS to the location of the analytes in a droplet[8, 9]. The Enke model assumes similarity between the structure of a charged droplet and the electric double layer found on the surface of an electrode in contact with a solution. In the case of a droplet, the role of the electrode is assumed by the vacuo (or air). Thus, the model identifies two regions in a droplet. The outer region which is the excess charge region and an inner core region. Electrolyte and analyte ions partition between these two regions by establishing an equilibrium. The model infers that the species seen in the mass spectrum are those that make up the surface charge. The foundation of the model is in agreement with the simulation findings presented here.

Now, we examine the electric field on the droplet surface. The shape fluctuations prevent a direct computation of the electrostatic potential and electric field on the droplet surface because of the large statistical errors[45, 101]. We have developed an approach (details are presented in Ref. [45]) to reconstruct the droplet surface and then compute the electric potential by using a multipole expansion. The normal component of the electric field for a droplet comprised $2 \times 10^4$ H$_2$O molecules and 36 Na$^+$ ions is shown in Fig. 3.18(a) and that of the same droplet size and charge, but with all the charge on a single ion is shown in Fig. 3.18(b). The electric field is...
computed for this specific droplet size over all its surface and over a number of configurations. The average electric field on the surface is 0.187 [V/Å] for both charge distributions, however in the conducting droplet (a), on 2% of the total area of the droplets used in the analysis the electric field magnitude is twice the average value but in the droplet (b) the fluctuations of the field are much smaller. This difference may be expected because in droplet (b) the charge is not transferred on the surface, thus the surface charge is close to that of pure water. Comparison with the findings by Kwan et al.\textsuperscript{[45]} for a conducting droplet of 1000 H$_2$O molecules and 8 Na$^+$ ions shows that the droplet electric field in the larger droplet decreases. This is expected since the larger the droplet, the lower the ion concentration. Moreover, the fluctuations of the electric field on the droplet surface decrease, which may explain the dominance of IEM in charged droplets with radius $\approx$10 nm\textsuperscript{[14–16]}. The average value of the electric field is in agreement with a range of values reported in experiments\textsuperscript{[43, 102]}. Our computations also show the magnitude of the fluctuations, which cannot be readily estimated in experiments.
3.8 Conclusions

The surface excess charge of droplets has raised much discussion in the field of native mass spectrometry since the seminal works of Iribarne and Thomson[14,15,36] and possibly earlier. Here for the first time, we dissected the nano-drop structure and we identified two important layers: the surface excess charge layer (SECL) and the maximum ion concentration region (MICR).

Using molecular simulations we have found that in the presence of simple ions the surface charge is found in an outer layer of thickness 1.5–1.7 nm. We emphasize that the surface charge arises from the combination of free charge (ions) and surface charge. The SECL thickness is invariant not only with respect to droplet size but also with respect to the nature of the simple ions and the fine details of different force fields. In the presence of macroions, the SECL may extend to 2.0 nm. The proportion of ions (free charge) in SECL depends on the nature of the ion and the droplet size. For the same droplet size, I\(^-\) and model hydronium ions show considerably higher concentration than the Na\(^+\) and Cl\(^-\) ions. In liquid nano-drops, SECL is strongly affected by shape fluctuations, and it does not have the highest ion concentration. Using the decay length (\(\lambda_{PB}\)) of the ion distribution that arises from the non-linear Poisson-Boltzmann equation, we were able to identify the maximum ion concentration region (MICR). In nano-drops MICR partially overlaps with SECL.

We showed that the structure of SECL changes with droplet size and sign of the ion’s charge. The positive ions create an undulated charge distribution (like the one for pure water) while the negative ions at very low concentrations exhibit an undulated charge distribution that progressively changes to a single trough when the ion concentration increases. The larger the droplet the lower the concentration of ions in SECL, thus the less pronounced is the effect of solvent polarization because of the presence of ions. In larger nano-drops, the number of hydrogen bonds per molecule is maintained high even in SECL. The relative larger shape fluctuations in droplets of a few nanometers diameter and the larger surface to volume ratio reduces the number of hydrogen bonds in comparison to the larger droplets. The structure of
SECL in smaller droplets indicates that the emission of ions from smaller droplets is more facile relative to larger droplets.

The new insights we obtained from this study are: (a) The maximum ionic concentration scaling is $n(R) \sim 1/R$, which allows us to infer the location of the maxima in larger droplets than those that can be simulated thus far. For droplets that range in size from several hundred to several tens of thousands of water molecules $|R_e - r_{\text{max}}|$ changes from approximately 1.0 nm for the smallest droplet to 0.74 nm for the largest droplet. (b) Scaling of the x-axis of the ion distributions by the Rayleigh radius of the droplet, reveals that for droplets with diameter, 7 nm (which is $\approx 6 \times 10^3$ H$_2$O molecules) to 16 nm the ion distribution profiles almost coincide. For the droplet of diameter 5 nm ($\approx 1000$ H$_2$O molecules) the Na$^+$ scaled concentration profile is broader than the other sizes. The profile for the smallest droplet is determined by the relative large shape fluctuations. (c) The presence of counterions plays a dramatic role in the manner in which the ions are distributed. The ions in excess are situated in the exterior while the counterions reside in the droplet interior. (d) We found that the surface excess charge comprises of $\approx 55\% - 33\%$ (decreasing from the smaller to the larger droplets) of the total number of ions and the solvent polarization charge. The thickness of the layer with the surface excess charge is 1.5–1.7 nm. This thickness appears invariant in all the droplet sizes we have studied. The amount of free charge in the surface excess charge region decreases with increasing droplet radius and converges with increasing droplet radius. Our findings are in agreement with the foundation of the equilibrium partitioning model of C. Enke[8, 9]. Computations of the droplet surface electric field show the magnitude of its fluctuations. We think that these fluctuations underlie the ion-evaporation mechanism. (e) Finally, our analysis indicates that at droplet radius $\approx 10$ nm the difference in values between $r_{\text{max}}$, $R_r$ and $R_e$ becomes negligible. Interestingly, this limit coincides with the droplet radius below which the ion evaporation mechanism dominates over the Rayleigh fission for droplet disintegration. We think that this coincidence is not fortuitous and requires further investigation of the droplet shape fluctuations.

We re-examine the relation of MICR-SECL with the bi-layer model in the equilibrium
partition model (EPM) of C. Enke. EPM focuses on SECL because the model uses the analogy with the structure of a solution double layer that appears next to a charged surface. For droplets with radius \(< 10\) nm we propose that the distinct region of the droplet may be extended by \(\lambda_{PB}\) in order to include MICR. We have found that \(\lambda_{PB}\) increases from \(1.0\) nm to \(1.35\) nm at \(T = 350\) K for a droplet radius from \(5.3\) nm \((2\times10^5\) H\(_2\)O molecules\) to \(\approx 10\) nm, respectively. In tiny droplets of approximately \(10^3\) H\(_2\)O molecules, MICR is extended to almost the entire droplet. The combination of MICR and SECL may create a droplet layer of approximate thickness of \(3.0\) nm that is characterized by higher ion concentration, it is subject to shape fluctuations and especially in the smaller droplets, the solvent polarization leads to large variations in the number of hydrogen bonds from the droplet interior to its surface. In a previous article[45], we have found the radial distribution of a charged polyhistidine of various charge states in a charged aqueous droplet. Comparison of the radial distribution of a polyhistidine with the combined SECL-MICR width reported here suggests that proteins may access MICR, at least in droplets with dimensions of several nanometers in diameter. Consequently part of a protein, or of a macromolecule in the more general case, can be exposed to a higher concentration of free ions and differently oriented solvent, which may affect its charge state.

IEM and the EPM give emphasis on different aspects of droplet chemistry that may explain the abundances in the mass spectra. The former focuses on the kinetics of ion evaporation and the latter on the equilibrium structure of the droplet. At a first glance, IEM and EPM may appear disjoint mechanisms. However, it is possible to combine them, by using the concentration of ions in SECL as input in the kinetic equation of IEM. We remind that the model in IEM of Iribarne and Thomson considers the total number of ions in the droplet. Fluctuations may create the electric field for ion emission and may lead to ion release much below the Rayleigh limit. The smaller the droplet, the larger the relative shape fluctuations, the more likely the ion to escape much before the Rayleigh limit. The inclusion of shape fluctuations and thus, the fluctuations in the electric field would provide missing components in IEM. In atmospheric aerosols where the droplets are charged much below the Rayleigh limit, the IEM will be the
mechanism to be followed for droplet disintegration.

In continuum models for electrosprayed droplets, it has been often assumed that the ionic charge is compensated by the solvent\cite{36}. We have found that this may not be the case in smaller droplets with diameter $< 4$ nm and high concentration of ions. In this case, the ion charge is not compensated only by the solvent surface charge but by the total charge that includes both solvent and other ions. Thus, there are correlations in the locations of the ions and for this reason, we cannot assume that the energy of the single ion is not affected by the presence of the others as it has been assumed in variations of the IEM model\cite{36}. In droplets with diameter $> 4$ nm the assumption of the energy independence of the single ion should be also tested because of the high ion concentration due to counterions and multiply charged macroions.

The next step in this study is to examine the concentration of a mixture of ions in the surface excess charge layer. The abundance of the ions in the surface excess charge region may change as a function of their overall percentage ratio in the droplet. Moreover, the emission of ions will change the droplet composition, thus there may be a redistribution of ions in the outer shell. It is also to be examined in future work whether the preference for the release of certain types of ions is determined by the composition of the surface excess charge layer in combination with the shape fluctuations. The effect of the nature of the solvent in the ion distribution and the role of the quadrupole moment in the surface charge are also questions to be investigated.
Bibliography


BIBLIOGRAPHY


Chapter 4

Conical Shape Fluctuations Determine the Rate of Ion Evaporation and the Emitted Cluster Size Distribution from Multi Charged Droplets

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4.1 Introduction

Droplets with multiple charges carried by ions are ubiquitous in atmospheric[1–4] and man-made aerosols. Man-made aerosols are most frequently produced using electrospray techniques and find numerous applications that include electrospinning[5], ionization methods coupled to mass spectrometry (MS), and fabrication of nanoparticles with non spherical geometries[6]. The disintegration mechanism of droplets may determine the location of the charge in evaporating cloud droplets[2] and plays a key role in determining the charge state of macromolecules detected in MS and the shapes of nanoparticles. Droplet fission is a complex multi-stage mechanism affected by the composition of the droplets and the ambient conditions. Solvent evapo-
ration is typically the slowest process driving the disintegration punctuated by violent progeny droplet release events.

It has been argued that the release of charge from droplets may occur via a Rayleigh instability[7] or the ion evaporation mechanism[8, 9] (IEM). The Rayleigh mechanism proceeds through the spontaneous formation of a jet when the electrostatic forces overcome the surface tension forces[7, 10–12]. Hereafter, the droplet charge at the Rayleigh limit, where the surface forces are equal to the electrostatic forces will be denoted as $Q_R$.

The release of the progeny droplets in Rayleigh instability have been detected in experiments[13–25]. The consensus is that a highly charged microdroplet containing multiple ions at a critical value of charge squared to volume ratio releases a tail of smaller progeny charged droplets that reduce significantly the charge of the parent droplet but carry away only a small amount of the mass of the parent droplet.

On the other hand, IEM is considered to take place via single uncorrelated events where a cluster containing a sole solvated ion is released. Hereafter, I will call these released clusters “ion clusters” in order to distinguish them from the train of progeny droplets released in a jet formed due to Rayleigh instability. The consensus is that the single ion clusters can be released from a parent nano droplet before the onset of the Rayleigh instability[8, 9, 26, 27]. The process can be written as

$$[(H_2O)_{m+k} I_{N+1}]^{(N+1)\pm} \xrightleftharpoons{} [(H_2O)_m I_N \cdots I(H_2O)_k]^{(N+1)\pm\dagger} \xrightleftharpoons{} [(H_2O)_m I_N]^{N\pm} + [I(H_2O)_k]^{\pm}$$

(4.1)

where $I^\pm$ represents the ion, $[(H_2O)_{m+k} I_{N+1}]^{(N+1)\pm}$ is the parent droplet, $[I(H_2O)_k]^{\pm}$ is the ion cluster, and $[(H_2O)_m I_N \cdots I(H_2O)_k]^{\dagger}$ the transition state at the barrier top of a free energy surface in the space of certain reaction coordinates[28, 29] (RCs).

Since IEM is considered to take place in nano droplets with a radius of approximately 10 nm its direct experimental detection has been challenging and as a result there are continuous efforts for its verification[8, 30–33]. In a recent article[31], Williams et al. observed
ion-emission from electrospayed droplets with mass ranging from 1 to 10 MDa (which corresponds to 55,000–550,000 water molecules) at the charge state of $\approx +50–300e$ (where $e$ denotes the positive elementary charge). The mean charge loss at an emission event is $1.1e$, which implies that the majority of the emission events correspond to the loss of a single charge, with rare occurrences of a loss of double or triple charge. The average mass loss from the droplet is between 0 and 4 kDa with 2–4 kDa measurement uncertainty, which corresponds to an average loss of up to 220 H$_2$O molecules with uncertainty in the range of 110–220 H$_2$O molecules. Therefore, even these sensitive and elegant experiments cannot directly observe the fragmentation mechanism at the point it occurs and the resulting cluster size distribution.

The fundamental IEM analytical models have been laid out in the seminal works of Iribarne and Thomson[8, 26], and Fenn–de la Mora–Labowsky [9, 27]. Both models include droplet’s surface energy and Born solvation energy of the ions in a very similar manner to that used by J. J. Thomson to describe nucleation in the presence of charged species[34]. The droplet shape fluctuations are not taken into account in these models. Details of the models are presented in the following section.

Figure 4.1 shows a schematic representation of the free energy profile for process 1 as a function of a collective RC and typical snapshots of the emission of a solvated ion from the parent droplet. The RC couples the distance of a departing ion from the remaining ions in the parent droplet to the droplet shape. Such an RC was devised in our previous work and was used to compute the free energy profiles for droplet fragmentation due to their high charge[28, 29]. Figure 4.1(a) shows a compact almost spherical droplet that may lead to (b)-(c), where the ion enters a conical shape fluctuation (see also Fig. 4.2). Figure 4.1(d) shows bridging H$_2$O strings that may form at a later stage of the process that finally lead to (e) where the droplet fragments and releases the ion-cluster.

After the barrier, there is no reversible path of fission (shown by the dashed line in Fig. 4.1). In addition, the fission is a multi-channel process since the emitted cluster may contain a variable number of H$_2$O molecules and rarely in larger droplets of two or three ions[31].
Figure 4.1: Schematic of a free energy profile along a collective RC that couples the location of the ions with the droplet shape. Typical snapshots of a departing ion-cluster from a droplet comprised 880 H$_2$O molecules and 6 Na$^+$ ions along the RC path are shown. $\Delta G^\ddagger$ denotes the free energy difference between the compact droplet at the minimum and the transition state at the barrier top. The dashed line in the free energy profile marks that beyond the barrier top the process is irreversible and it is a multi-channel reaction. See text for details.

Figure 4.2: Snapshots of the droplet at various stages of ion evaporation. (a) Formation of the cone (b) ion entering the cone.
The key point in the fragmentation events is the conical fluctuation at the transition state. These conical fluctuations and possible later string formations were captured in our previous works [28, 29, 35]. Later works also found the string formations [36] but not the role of the conical fluctuations.

In previous simulations we showed that the location of the conical shapes is not related to the location of the ions [35]. The computed $\Delta G^\ddagger$ represents the probability of finding system configurations with conical fluctuations [37, 38]. The free energy barrier is broad and it may possibly include a small minimum that corresponds to the entering of the ion in the cone and the onset of the departure of the ion-cluster from the parent droplet. In the analytical models [8, 9], the free energy barrier is attributed to the attractive interaction between the induced charge in the parent droplet and the departing ion-cluster. The induced charge has the opposite sign from that of the departing ion-cluster and it is estimated in the existing models [8, 9] by using the method of image charge for a planar conducting surface [39]. According to the computed free energy profiles [37, 38] and the present simulations this attractive interaction may not be as was considered in the previous analytical models [8, 9] because the ion-cluster departs from the tip of a conical shape that has different electrical characteristics from that of a spherical conducting droplet [40]. An attractive interaction but not of the nature and the magnitude assumed in the analytical models [8, 9], may be still present at the barrier top and it may determine to some extent, the degree of difficulty for the system to cross the barrier. Regardless of whether the ion cluster emission is attributed to a Rayleigh instability or IEM, the following questions have not been addressed so far: (a) a systematic study of the relation between the type of ion and the emitted cluster size distribution from the parent droplet; (b) calculation of empirical parameters, such as the ion depth from the droplet surface, that enter the existing IEM models; (c) an assessment of the IEM models when the simulation estimated parameters are used; (d) the effect of the polarizable versus non-polarizable solvent models on the ion location in droplets and the emitted cluster size distribution.

I hypothesize that distinct conical shape fluctuations in highly charged droplets contain-
ing multiple ions determine the ion emission free energy barrier height and the cluster size
distribution.

### 4.2 A Critical View of the IEM Models

In order to show how the simulation results complement the existing IEM models, I describe
the main points of the models and assess their assumptions. The construction of the Iribarne-
Thomson model, pertinent to Eq. [4.1] includes the following elements: first, the Born solvation
energy[34, 41–44] of a ion cluster ([I(H2O)k]± in Eq. [4.1]) transferred into a neutral droplet
under the condition that the radius of the ion cluster (rc), is much smaller than the radius of the
parent droplet (R); second, the energy of transferring the ion cluster within a charged droplet,
at depth di from the surface; third, the interaction of [I(H2O)k]± with the induced charge via the
image charge method; and lastly, the change in the surface area is taken to be 
\[ -4\pi\gamma r_c^2 \]
where \( \gamma \) denotes the surface tension, under the assumptions that the surface of 
\( [(H_2O)_{m+k}I_{N+1}]^{(N+1)±} \) (parent droplet) and \( [(H_2O)_mI_N]^{N±} \) are the same. Using these elements, the free energy as a
function of the distance of [I(H2O)k]± (ion cluster) from the droplet surface is estimated. The
free energy difference (\( \Delta G^\ddagger \)), between the barrier and the solvated ion within the parent droplet
(\( [(H_2O)_{m+k}I_{N+1}]^{(N+1)±} \)) is estimated to be
\[
\Delta G^\ddagger \approx e^2 \left( \frac{N}{R + x_m} \frac{x_m}{4x_m} \right) - \left( \Delta G_S^\ddagger + \frac{Ne^2}{R - d_i} \right) 
\]
where \( e \) is the positive elementary charge, and \( x_m \) is the position of the free energy barrier given
by
\[
x_m = R/(2N^{1/2} - 1) 
\]
and \( \Delta G_S^\ddagger \) is the Born solvation energy expressed as
\[
\Delta G_S^\ddagger = -4\pi\gamma r_c^2 - \frac{e^2}{2r_c} \left( 1 - \frac{1}{\varepsilon} \right) \approx -4\pi\gamma r_c^2 - \frac{e^2}{2r_c} 
\]
where \( \varepsilon \) is the dielectric constant.

The next step of the model is to approximate the rate constant of ion-evaporation by the total disintegration rate constant of the droplet. The rate constant yields an estimate for \( \Delta G^\ddagger \), that is then used in Eq. 4.2 to compute \( R \) (the radius of the parent droplet).

The model relies on several approximations. Some of the more debatable ones are listed below.

(1) The rate constant of the ion-evaporation is greater or equal to that of the solvent rate constant. This is a reasonable assumption for the droplet to be found below the Rayleigh limit and thus, allow for IEM to take place. However, the average rate constant, which is proportional to \( \langle e^{-\Delta G^\ddagger/kT} \rangle \) (where \( k \) is the Boltzmann constant) does not equal the \( e^{(-\Delta G^\ddagger)/kT} \), where \( \langle \Delta G^\ddagger \rangle \) is estimated in Eq. 4.2.

(2) \( \Delta G^\ddagger \) (Eq. 4.2) is only of electrostatic nature thus, it does not consider any fluctuations that lead to ion cluster evaporation. However, the energy terms for the activation energy assume a specific geometry of a droplet at the barrier. We can understand the role of the fluctuations by gaining insight from the Rayleigh model[7, 10–12], which includes the fluctuations at the onset of instability. These fluctuations include both electrostatic and surface energy terms. Since the droplet disintegration occurs below but still near the Rayleigh limit, it is expected that surface fluctuations will also play a role in the IEM mechanism.

(3) The radius of the emitted cluster equals the depth \( d_i \) that the ion is found within the droplet. This assumption is not supported by the simulation results presented in the next sections.

The model of Fenn–de la Mora–Labowsky recognizes that the droplet geometry (surface terms) at the barrier top may play a significant role, but the electrostatic problem is not trivial to solve. Moreover, in Ref. [9] it is intuitively recognized that the \([I(H_2O)_k]^\pm\) cluster may be far from spherical. Unfortunately, the complexity of the problem only allows for the treatment of the departing \([I(H_2O)_k]^\pm\) cluster as a sphere or a semi-sphere. In this model, the surfaces of \([(H_2O)_{m+k}I_{N+1}]^{(N+1)\pm}\) (parent droplet) and \([(H_2O)_mI_N]^{N\pm}\) are taken to be different, which adds a
correction term to the free energy barrier.

The Fenn–de la Mora–Labowsky model predicts that there is only a narrow window (or no window at all) of conditions where small ion clusters may evaporate. They conclude that the improved ion-evaporation model may under-predict the rate of ion evaporation in part because of substantial over-prediction of Born solvation energy.

4.3 Models and Simulation Methods

I performed equilibrium molecular dynamics (MD) simulations of charged aqueous droplets with multiple ions (Na⁺, Li⁺, Cl⁻, Cl⁺, I⁻, I⁺, F⁻ and Cs⁺) and droplet evaporation runs in order to sample ion cluster emission events. Simulations of droplets with a sole ion (Na⁺, Li⁺, Cl⁻, I⁻, F⁻, guanidinium) in a droplet composed of 880H₂O molecules were also performed to use them as reference systems. Model ions with different radii in an aqueous droplet were simulated in order to examine the relation between the ion radius and its location in an aqueous droplet. The details of the systems are presented in Table 4.1 and 4.2. The simulations were performed by using the software NAMD version 2.14[45].

The systems were modelled with polarizable (SWM4-NDP) and the non-polarizable (TIP4P/2005) force fields. In the polarizable model, the water molecules were represented with the SWM4-NDP model[46] and the ions were represented with the CHARMM Drude force field[47, 48]. The SWM4-NDP model is a five site model with four charge sites and a negatively charged Drude particle connected to the oxygen atom, while the ions are modelled with one charge site and a negatively charged Drude particle. To access the effect of the electronic polarization included in the polarizable model in the ion location and in the emitted clusters, simulations were also performed with the TIP4P/2005 model[49] as a comparison.

The Newton’s equation of motion for each atomic site was integrated using the velocity-Verlet algorithm with a time step of 1.0 fs for the systems with SWM4-NDP and 2.0 fs for the systems with TIP4P/2005. The trajectories were analyzed using VMD 1.9.4a47[50]. Equilib-
Equilibrium simulations in NAMD were performed in the canonical ensemble by placing the droplet in a spherical cavity of 10 nm radius using the spherical boundary conditions in order to maintain a vapour pressure equilibrium. All the forces were computed directly without any cut-offs. The temperature was controlled by the Langevin thermostat. NAMD utilizes a dual Langevin thermostat to freeze the Drude oscillators while maintaining the warm degrees of freedom at the desired temperature[51]. The systems were thermalized with the Langevin thermostat at 350 K for the warm degrees of freedom and at 1 K for the Drude oscillators. The damping coefficient for the Langevin thermostat was set to 1/ps. The ion cluster emission simulations (Table 4.2) were performed in vacuo with constant energy MD starting from thermalized droplets at $T = 300K$. For each ion, 50–100 simulations from different initial conditions were performed. The surface tension of SWM4-NDP has been reported[46] to be $67 \pm 4 \text{ mN/m}$ at $T = 298.15 \text{ K}$ and of TIP4P/2005 to be $69.3 \pm 0.9 \text{ mN/m}$ at $T = 300 \text{ K}$ and $61.9 \pm 1.3 \text{ mN/m}$ at $T = 350 \text{ K}[52]$.

<table>
<thead>
<tr>
<th>$M_{\text{H}_2\text{O}}$</th>
<th>Ions</th>
<th>$T$ (K)</th>
<th>$R_e$ (nm)</th>
<th>$t_{\text{run}}$ (ns)</th>
</tr>
</thead>
<tbody>
<tr>
<td>880 TIP4P/2005</td>
<td>6 Na$^+$, 6 Li$^+$</td>
<td>350</td>
<td>1.73</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>6 Cl$^+$, 6 Cl$^-$</td>
<td>350</td>
<td>1.73</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>6 I$^-$, 6 I$^+$</td>
<td>350</td>
<td>1.73</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>6 ions with varying radius</td>
<td>350</td>
<td>1.73</td>
<td>50</td>
</tr>
<tr>
<td>880 SWM4-NDP</td>
<td>1 Na$^+$, 1 Li$^+$</td>
<td>350</td>
<td>1.73</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>1 Cl$^-$, 1 I$^-$</td>
<td>350</td>
<td>1.73</td>
<td>100</td>
</tr>
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<td></td>
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<td>350</td>
<td>1.73</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>1 guanidinium$^+$</td>
<td>350</td>
<td>1.73</td>
<td>100</td>
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<tr>
<td>880 SWM4-NDP</td>
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<td>350</td>
<td>1.73</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>6 Cl$^-$, 6 I$^-$</td>
<td>350</td>
<td>1.73</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>6 Cs$^+$, 6 F$^-$</td>
<td>350</td>
<td>1.73</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 4.1: Composition and parameters of droplets. The number ($M_{\text{H}_2\text{O}}$) of H$_2$O molecules and the model used are shown in the first column. The second column shows the number and type of ions embedded in the droplet. The third column shows the temperature ($T$) that the simulations were performed. The fourth column shows the equimolar radius, $R_e$, and the fifth column the duration of the simulation run ($t_{\text{run}}$).
Chapter 4. Conical shape fluctuations

<table>
<thead>
<tr>
<th>$M_{\text{H}_2\text{O}}$</th>
<th>Ions</th>
<th>$T$ (K)</th>
<th>$R_e$ (nm)</th>
<th>$t_{\text{run}}$ (ns)</th>
<th>$n_{ej}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>880 TIP4P/2005</td>
<td>6 Na$^+$, 6 Cl$^-$, 6 Cl$^+$, 6 I$^-$, 6 I$^+$ 16 Na$^+$, 16 Cl$^-$</td>
<td>350</td>
<td>1.73</td>
<td>10</td>
<td>50</td>
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<tr>
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<td></td>
<td>350</td>
<td>2.82</td>
<td>10</td>
<td>25</td>
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<tr>
<td>880 SWM4-NDP</td>
<td>6 Na$^+$, 6 Li$^+$, 6 Cs$^+$ 6 Cl$^-$, 6 I$^-$, 6 F$^-$</td>
<td>300</td>
<td>1.73</td>
<td>10</td>
<td>50</td>
</tr>
</tbody>
</table>

Table 4.2: Composition of the parent droplet and parameters of the evaporation runs. The number ($M_{\text{H}_2\text{O}}$) of H$_2$O molecules and the model used are shown in the first column. The second column shows the number and type of ions embedded in the parent droplet. The third column shows the temperature ($T$) that the simulations were performed. The fourth column shows the equimolar radius $R_e$ of the parent droplet, the fifth column the duration ($t_{\text{run}}$) of the constant energy run in vacuo, and the sixth column the number of $n_{ej}$ events collected.

<table>
<thead>
<tr>
<th>Model</th>
<th>Multiple ions</th>
<th>$\sigma$ [Å]</th>
<th>$d_I$ [Å]</th>
<th>$n_1 (r_1$ [Å])</th>
<th>$n_2 (r_2$ [Å])</th>
<th>$\langle n_c \rangle$</th>
<th>$\langle r_c \rangle$ [Å]</th>
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<td>880 H$_2$O</td>
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<td>6.0</td>
<td>5.9 (3.2)</td>
<td>24.2 (5.5)</td>
<td>12.4</td>
<td>4.4</td>
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<tr>
<td></td>
<td>Cl$^-$</td>
<td>4.42</td>
<td>5.5</td>
<td>7.2 (3.8)</td>
<td>31.5 (6.1)</td>
<td>18.0</td>
<td>5.1</td>
</tr>
<tr>
<td></td>
<td>Cl$^+$</td>
<td>4.42</td>
<td>4.5</td>
<td>10.3 (4.3)</td>
<td>31.7 (6.4)</td>
<td>8.8</td>
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<tr>
<td></td>
<td>I$^-$</td>
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<td>3000 H$_2$O</td>
<td>Na$^+$</td>
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<td>24.2 (5.5)</td>
<td>12.4</td>
<td>4.4</td>
</tr>
<tr>
<td>TIP4P/2005</td>
<td>Cl$^-$</td>
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<td>7.2 (3.8)</td>
<td>31.5 (6.1)</td>
<td>16.5</td>
<td>4.9</td>
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<td>880 H$_2$O</td>
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<td>6.0</td>
<td>4.0 (2.6)</td>
<td>19.8 (5.2)</td>
<td>13.2</td>
<td>4.5</td>
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<td>23.7 (5.5)</td>
<td>12.6</td>
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</tr>
<tr>
<td></td>
<td>Cs$^+$</td>
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<td>9.7 (4.0)</td>
<td>31.7 (6.2)</td>
<td>13.0</td>
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<td>F$^-$</td>
<td>4.39</td>
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<td>Cl$^-$</td>
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<td>20.4 (6.4)</td>
<td>13.8</td>
<td>5.5</td>
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</table>

Table 4.3: Parameters that characterize the ion location in the parent droplet, and the emitted ion cluster size. The first column shows the number of H$_2$O molecules in the parent droplet and the water model used and the second column shows the type of ions embedded in the droplet. The third and fourth columns report $n_1$ and $n_2$, which are the average numbers of H$_2$O molecules in the first and second hydration shell of the ions, respectively. These coordination numbers have been estimated from the ion-H$_2$O radial distribution functions (RDFs) (Fig. 4.4). The ion-O distance where the first and second minimum in the RDFs are found are shown in parentheses next to $n_1$ and $n_2$. In the fifth column the distance of the maximum of the ion distribution from the droplet’s equimolar radius (Fig. 4.3), $d_I$, is reported. In the sixth column, $\langle n_c \rangle$ is the average number of H$_2$O molecules in $[I(H_2O)_k]^+$ (see also Fig. 4.9 for the cluster size distribution) and in the seventh column, $\langle r_c \rangle$ is the $[I(H_2O)_k]^+$ average radius estimated from the integral of the ion-oxygen RDF (Fig. 4.4).
4.4 Depth of Ions in a Droplet

Figure 4.3 (a) and (b) shows the radial probability distribution of six ions in droplets composed of 880 H$_2$O molecules ($R_e = 1.73$ nm), modelled using TIP4P/2005 and SWM4-NDP (polarizable model) at 350 K. The charge $Q_R$ at the Rayleigh limit for this droplet size at $T = 350$ K is $8e$. Both models show that the ion concentration is slightly higher near the droplet surface relative to the interior, which is expected because of the conducting nature of the system\[53].

However, there are a number of significant differences in the distributions that depend on the nature of the ions. SWM4-NDP clearly differentiates the position of the Na$^+$ and Cl$^-$ ions, by showing that the Cl$^-$ maximum is closer to the droplet surface than Na$^+$. On the contrary, TIP4P/2005 shows a slight shift of the Na$^+$ distribution closer to the surface than the corresponding Cl$^-$ distribution. Figure 4.3 shows that a sole I$^-$ and Cl$^-$ in a droplet, modelled by SWM4-NDP, have a significant probability to be found near the surface, and similarly, the multiple ions also reside in the same location. For a sole Cl$^-$, I have found that in addition to the well-known maximum of the number density on the droplet surface, there is also a significant broad maximum in the droplet interior\[54]. In the presence of multiple ions the maximum near the surface is maintained but as expected the interior maximum disappears. Thus, for the chaotropic ions (Cl$^-$ and I$^-$) the location of the multiple ions is the same as that of the single ion in the droplet’s subsurface or surface.
Figure 4.3: Ion concentration profiles and water density profiles as a function of the distance from the droplet’s COM for (a) TIP4P/2005 systems (b) SWM4-NDP systems at $T = 350$ K. Note that the density of water is different in (a) and (b), possibly due to different surface fluctuations. (c) Sole ion number density and H$_2$O density in a droplet of 880 SWM4-NDP H$_2$O molecules. The vertical lines mark the droplet’s equimolar radius ($R_e$).
Ion-H$_2$O RDFs (Fig. 4.4) show that the first and second hydration shells of the multiple ions (Table 4.3) are the same as those of the sole ion when it resides in the droplet’s outer layer where there is the surface excess charge (55) (see the fifth and sixth columns in Table 4.4). The surface excess charge layer for the single and multiple ions are shown in Fig. 4.5.

<table>
<thead>
<tr>
<th>System</th>
<th>Ion type</th>
<th>$n'_1$ ($r_1$ [Å])</th>
<th>$n'_2$ ($r_2$ [Å])</th>
<th>$n''_1$ ($r_1$ [Å])</th>
<th>$n''_2$ ($r_2$ [Å])</th>
</tr>
</thead>
<tbody>
<tr>
<td>880 H$_2$O</td>
<td>Na$^+$</td>
<td>5.9 (3.2)</td>
<td>24.8 (5.5)</td>
<td>5.9 (3.2)</td>
<td>23.6 (5.6)</td>
</tr>
<tr>
<td>TIP4P/2005</td>
<td>Li$^+$</td>
<td>5.3 (3.1)</td>
<td>21.7 (5.2)</td>
<td>4.9 (2.8)</td>
<td>18.6 (5.1)</td>
</tr>
<tr>
<td>Sole Ion</td>
<td>Cl$^-$</td>
<td>7.1 (3.8)</td>
<td>28.3 (5.9)</td>
<td>6.9 (3.8)</td>
<td>25.2 (5.8)</td>
</tr>
<tr>
<td></td>
<td>I$^-$</td>
<td>7.2 (4.1)</td>
<td>30.6 (6.1)</td>
<td>7.1 (4.2)</td>
<td>24.8 (6.2)</td>
</tr>
<tr>
<td>880 H$_2$O</td>
<td>Na$^+$</td>
<td>5.9 (3.2)</td>
<td>25.9 (5.6)</td>
<td>5.9 (3.2)</td>
<td>23.6 (5.6)</td>
</tr>
<tr>
<td>TIP4P/2005</td>
<td>Li$^+$</td>
<td>5.3 (3.1)</td>
<td>22.0 (5.2)</td>
<td>5.0 (2.9)</td>
<td>18.6 (5.1)</td>
</tr>
<tr>
<td>Multiple Ions</td>
<td>Cl$^-$</td>
<td>7.0 (3.8)</td>
<td>31.1 (6.0)</td>
<td>6.8 (3.7)</td>
<td>25.4 (5.8)</td>
</tr>
<tr>
<td></td>
<td>I$^-$</td>
<td>7.0 (4.0)</td>
<td>31.2 (6.1)</td>
<td>7.0 (4.2)</td>
<td>23.7 (6.2)</td>
</tr>
<tr>
<td>880 H$_2$O</td>
<td>Na$^+$</td>
<td>5.5 (3.2)</td>
<td>21.7 (5.3)</td>
<td>4.3 (3.1)</td>
<td>20.1 (5.4)</td>
</tr>
<tr>
<td>SWM4-NDP</td>
<td>Li$^+$</td>
<td>4.0 (2.6)</td>
<td>20.0 (5.2)</td>
<td>4.0 (2.7)</td>
<td>16.9 (5.1)</td>
</tr>
<tr>
<td>Sole Ion</td>
<td>Cl$^-$</td>
<td>6.6 (3.8)</td>
<td>30.0 (6.1)</td>
<td>6.2 (3.8)</td>
<td>22.1 (6.0)</td>
</tr>
<tr>
<td></td>
<td>I$^-$</td>
<td>7.7 (4.2)</td>
<td>28.6 (6.1)</td>
<td>6.1 (4.3)</td>
<td>20.1 (6.4)</td>
</tr>
</tbody>
</table>

Table 4.4: Ion-H$_2$O RDF parameters for a sole ion and multiple ions in a droplet composed of 880H$_2$O molecules. I distinguish two regions in the droplet, an internal, marked by the superscript $I$ and an external, marked by $E$. The external region is the surface excess charge layer. The first column describes the system and the second column describes the type of ions. The third and fourth columns show $n'_1$ and $n'_2$, which are the average coordination numbers of H$_2$O molecules in the first and second solvation shell of the ion, respectively, when the ion resides in the internal region. The first and second minimum in the RDFs are shown in parentheses next to $n'_1$ and $n'_2$. The fifth and sixth columns are the same as the third and fourth columns, respectively but when the ion resides in the surface excess charge layer. These coordination numbers have been estimated from the RDFs (Fig. 4.6 and Fig. 4.7).

The hydration of the multiple ions in the excess surface charge layer and interior is also shown in Table 4.4. The first hydration shell of the multiple ions has a reduced number of H$_2$O molecules relative to the sole ion in the interior. Therefore, the chaotropic ions Cl$^-$ and I$^-$ may be partially solvated, which indicates that they are located on the droplet–vapour interface.

For a group of kosmotropic ions (Li$^+$ and Na$^+$) there is an evident difference in the location of the sole ion and the multiple ions. Among the ions that were examined, many sole ions (Li$^+$, Na$^+$, F$^-$ and guanidinium) have higher number density near the centre and a lower number
Figure 4.4: (a) Ion–Oxygen radial distribution function, and (b) coordination number for the SWM4-NDP modelled systems. (c) Ion–Oxygen radial distribution function, and (D) coordination number for the TIP4P/2005 modelled systems.
Figure 4.5: (a) Charge cumulative distribution of the SWM4-NDP systems with cations, (b) Charge cumulative distribution of the SWM4-NDP systems with anions (c) Charge cumulative distribution of the SWM4-NDP systems with a sole cation. For comparison the charge distributions with TIP3P are also included.
density in the subsurface. Sole Ion-H\textsubscript{2}O RDFs computed in the interior and in the surface excess charge layer of the droplet are shown in Fig. 4.6 and Fig. 4.7.

Here, I define the interior of the droplet to be the volume with radius less than 12.0 Å from the centre of mass of the droplet. I calculated the ion-oxygen and ion-hydrogen RDF and coordination number for ions in the interior of the droplets and ions in the exterior of the droplet. I found in the case of the small ions (F\textsuperscript{−}, Li\textsuperscript{+}) there is little difference in the coordination number in the first solvation shell between the two regions, yet for the medium-sized ions (Na\textsuperscript{+}, Cl\textsuperscript{−}), there is a small difference in the first solvation shell, and finally, for the large ions (I\textsuperscript{−}), there is a significant difference in the coordination number within the first solvation shell. In other words, large ions are less solvated when they are located in the surface-excess charge layer (SECL).

Anion-O RDF shows a larger difference between interior and exterior ions, relative to the anions-H RDF. The RDF suggests that even if the ions are surrounded by fewer H\textsubscript{2}O molecules closer to the surface, the H\textsubscript{2}O molecules of the first solvation shell orient differently from the interior H\textsubscript{2}O and may contribute to both of their hydrogen sites to the immediate coordination of the anion.

The kosmotropic ions (Na\textsuperscript{+}, Li\textsuperscript{+}) show the two immediate hydration shells to the ion to be very similar to those of the sole ion in the interior (see the fifth and sixth columns in Table 4.4). Therefore, multiple kosmotropic ions (Li\textsuperscript{+}, Na\textsuperscript{+}) are found on the average at least two layers of H\textsubscript{2}O molecules within the droplet.

I emphasize that the ion distributions (Fig. 4.3 (b)) show that the ions are not equivalent in their degree of solvation. The hump of the distribution has a width of at least 3.0 Å, which indicates that the degree of solvation of the ions in the outer layers varies by at least one solvation shell.

In order to obtain further insight into the location of the multiple ions and in particular, in the interplay between ion-solvent and solvent-solvent interactions, I performed simulations of an aqueous droplet with ions of the same charge $+1e$ but different diameter. All the ions have
Figure 4.6: Radial distribution functions (RDF) for (a)-(b) Li$^+$ and (c)-(d) Na$^+$. 

(a) Interior Li$^+$-O RDF VS SECL Li$^+$-O RDF
(b) Interior Li$^+$-H RDF VS SECL Li$^+$-H RDF
(c) Interior Na$^+$-O RDF VS SECL Na$^+$-O RDF
(d) Interior Na$^+$-H RDF VS SECL Na$^+$-H RDF
Figure 4.7: Same as Fig. 4.6 but for F\(^{-}\), Cl\(^{-}\), I\(^{-}\).
the same depth of the Lennard-Jones energy well as that of a Na\(^+\) ion. Figure 4.8 shows the ion charge density effect in its location. The number density of every ion shows a trend in its depth as a function of the ion radius. Ions with diameter smaller or larger than that of Na\(^+\) move closer to the surface than Na\(^+\). The ion with diameter twice that of Na\(^+\) is found the farthest out. The ions with diameter less than Na\(^+\) are strongly solvated such as Li\(^+\) ion, and for this reason they have to be treated as effectively larger ions due to their closely bound first solvation shell\([56-61]\). In conclusion, in droplets with multiple ions, the size alone of the \(+1e\) ions differentiates the depth in which they can be found.

![Figure 4.8: Radial probability distribution of model ions that each carries a charge +1e and radius a multiple of \(\sigma\), where \(\sigma\) represents the diameter of a Na\(^+\) ion. The ions are found simultaneously in a droplet comprised 880 TIP4P/2005 H\(_2\)O molecules.](image)

**4.5 Emitted Cluster Size Distribution**

Here, I aim to answer the following questions:
1. What is the size of the departing ion cluster immediately after its emission?

2. How does the size of the ion cluster depend on the nature of the ion?

3. Does the location of the ions in the parent droplet affect the size of the emitted ion cluster?

4. Does the size of the parent droplet affect the size of the emitted ion cluster?

5. Do polarizable and non-polarizable models yield different cluster size distributions?

6. How do the simulation results compare with the predictions of the existing ion-evaporation models?

Figure 4.9: Box plot of the cluster size distribution immediately after emission. The distributions were computed with the TIP4P/2005 model and SWM4-DP. The vertical line between the box boundaries marks the median. The average values of the cluster size for the various ions are shown in Table 4.3.
Figure 4.9 shows the ion cluster size distribution immediately after emission. Table 4.3 shows the average cluster size in terms of the average number of \( \langle n_c \rangle \) of \( \langle r_c \rangle \). The average radius only provides a rough estimate of the cluster size because their shapes are not spherical. \( \langle r_c \rangle \) is estimated by the ion-H\(_2\)O RDF instead of using the equimolar radius.

Figure 4.9 shows that the most probable size of emitted Na\(^+\)-clusters comprises 10-13 H\(_2\)O molecules for SMW4-NDP and 10-15 H\(_2\)O molecules for TIP4P/2005, while the maximum size, which is of low likelihood, comprises 25–26 H\(_2\)O molecules. For Cl\(^-\), the cluster size distribution for both models is broader than that of Na\(^+\) and it is shifted toward larger sizes. The most probable sizes are found in the range of 16–23 H\(_2\)O TIP4P/2005 H\(_2\)O molecules and 13–21 H\(_2\)O SMW4-NDP H\(_2\)O molecules. Interestingly, the polarizable model and the non-polarizable model predict similar cluster size distributions. This indicates that the electronic polarization plays a relatively small role in the size of the detached cluster. For I\(^-\) (SWM4-NDP modelled), the most probable cluster size distribution is in the range of 10–15 H\(_2\)O molecules. Even though the I\(^-\) ion has a larger diameter than Na\(^+\) and Cl\(^-\) the most probable cluster sizes are shifted slightly toward larger sizes than Na\(^+\)-clusters when the polarizable model is used. When the non-polarizable model is used the opposite trend is observed. For testing purposes, I used model ions Cl\(^+\) and I\(^+\), which only differ from Cl\(^-\) and I\(^-\), respectively, in the charge sign (all modelled with the TIP4P/2005 set of parameters). The Cl\(^+\) and I\(^+\) clusters are smaller than all of the other ions, even though within the parent droplet Cl\(^+\) is solvated almost with as many H\(_2\)O molecules as Cl\(^-\).

It was very difficult to collect significant statistics for the F\(^-\) ions. Under the same conditions as for the other ions, the number of observed droplet fragmentations were very few, possibly because the F\(^-\) ions are solvated deeper inside the droplet (see \( d_t \) values in Table 4.3) than any other ions we examined. The few observed fragmentation events showed departing clusters with more H\(_2\)O molecules than Cl\(^-\) and I\(^-\). For the three negative ions (F\(^-\), Cl\(^-\), I\(^-\)) one may say that the larger the ion, the more is located on the surface, the smaller the average...
size of the departing cluster. Among the positive ions we examined, Cs\(^+\) clusters are almost of the same size as Li\(^+\), while those of Na\(^+\) appear slightly smaller. However, the values of \(d_1\) and \(\langle r_c \rangle\) shown in Table 4.3 are quite different. One reason for this difference may be the non-spherical shape of the departing ion-cluster. We think that the most important reason is that the ion-clusters are released from the surface excess charge layer of a droplet\([55, 62]\), which may include a part of the maximum of the concentration profile of the ions and it certainly includes the ions between the maximum and the droplet surface (described by the decaying part of the concentration profile toward the droplet surface). These outer ions are less solvated than the ions at the maximum of the concentration profiles and in the interior (Table 4.3 and Table 4.4).

The comparison among all the cluster size distributions shows that the number of \(\text{H}_2\text{O}\) molecules attached to the emitted ion is weakly correlated to the location of the maximum of the ion probability distribution (Fig. 4.3) within the droplet. It is mainly the dynamic process at the conical shape from where the ion is emitted that determines the cluster size and not the equilibrium solvation in the droplet interior. I think that there is a weak correlation between the inherent solvation properties of the ion and the emitted cluster sizes. Ions like I\(^-\) that show a clear propensity for reduced solvation (when I\(^-\) is the sole ion in the droplet and in a multiple-charged droplet) relative to Na\(^+\), Cl\(^-\) and other ions, are intuitively expected to carry fewer \(\text{H}_2\text{O}\) molecules when emitted than better solvated ions. Indeed, I see that I\(^-\)-cluster distribution has a longer tail toward smaller clusters than Cl\(^-\) and Na\(^+\).

Small emitted clusters have a number of configurations where the ion can be in the interior or partially solvated. These configurations have different strengths of ion-\(\text{H}_2\text{O}\) and \(\text{H}_2\text{O}-\text{H}_2\text{O}\) interactions\([63]\) that may affect the later lifetime of the emitted clusters.

The dramatic difference in the cluster size distributions between Cl\(^-\) and Cl\(^+\), and between I\(^-\) and I\(^+\), also suggests that the charge sign asymmetry may play a role in differences in the cluster size distributions between positive and negative ions. It was demonstrated that the ions that emitted ion clusters come from the SECL (see Chapter 3). Difference in the cluster size due to charge sign asymmetry has also been shown in the free energy profiles computed
as a function of the cluster size in the vapour-liquid nucleation of water in the presence of ions\cite{34,64,70}. Simulations of the water vapor to liquid nucleation have shown that at the minimum of the free energy profiles, negative ions give rise to a larger cluster and at the barrier top, the negatively charged critical nuclei lead to a lower nucleation barrier than the positive ions\cite{64}.

Simulations that have been performed with larger droplets of 3000 H\textsubscript{2}O molecules (Fig. 4.3 and Table 4.3) show that the parent droplet size does not affect significantly the cluster size distribution.

Interestingly, Iribarne and Thomson detected clusters of Na\textsuperscript{+}(H\textsubscript{2}O\textsubscript{25}) instead of Na\textsuperscript{+}(H\textsubscript{2}O\textsubscript{8–9}) as the minimization of the Born model predicts\cite{8}. They speculated that perhaps there is a special stability of the Na\textsuperscript{+}(H\textsubscript{2}O\textsubscript{25}) cluster. The simulations indicate that Na\textsuperscript{+}(H\textsubscript{2}O\textsubscript{25}) is the maximum cluster size that is released from a droplet. Another interesting comparison is that the experiments of Iribarne and Thomson found that the Na\textsuperscript{+} emitted clusters are larger than the Cl\textsuperscript{–} clusters, which is opposite from what the present simulations reveal. Iribarne and Thomson suggest that the initially released clusters may change their size in their path to detection.

We note that small emitted clusters have a number of configurations where the ion can be in the interior or partially solvated. These configurations have different strengths of ion–H\textsubscript{2}O and H\textsubscript{2}O–H\textsubscript{2}O interactions\cite{63} that may affect the later lifetime of the emitted clusters.

In summary, the depth of the ion within a droplet is weakly correlated to the size of the emitted ion cluster. For example, Na\textsuperscript{+} is emitted with significantly fewer H\textsubscript{2}O molecules than Cl\textsuperscript{–}, even though both ions are found in almost the same depth in the TIP4P/2005 modelled droplets. The lack of a clear correlation may be attributed to the fact that it is mainly the dynamic process at the conical shape from where the ion is emitted that determines the cluster size and not the equilibrium solvation in the droplet interior. The larger ion radius does not increase the number of H\textsubscript{2}O molecules that are carried with the ion. For example I\textsuperscript{–} carries fewer H\textsubscript{2}O molecules than Cl\textsuperscript{–}, even though I\textsuperscript{–} is larger than Cl\textsuperscript{–}. The charge sign asymmetry plays a significant role in the cluster size distribution. Singly charged negative ions (e.g. Cl\textsuperscript{–}) with
a comparable radius to the corresponding positive charged ions (Na\(^+\), Cl\(^+\)) are released with more H\(_2\)O molecules than the positive ions. Polarizable and non-polarizable models predict a similar cluster size distribution and average cluster size. The largest difference appears in I\(^-\), where the polarizable model shows a somewhat larger average number of H\(_2\)O molecules. The cluster size distributions show a weak dependence on the size of the parent droplet.

The relation between the depth of the ion in the droplet and the cluster size distributions has not been considered in the existing analytical IEM models and in the manner that IEM has been perceived so far. A detailed comparison between the analytical models and the simulation results is presented in the next section.

### 4.6 Comparison with the IEM Models

A natural limitation of the IEM models is that they cannot provide the cluster size distribution because of their continuum nature. As a result, it is not clear whether the minimization of the Born energy and surface energy used in the models provides the most probable cluster size or the average cluster size. Moreover, the models do not take into account the ion size (approximately equivalent to the size of a H\(_2\)O molecule), which plays a non-negligible role in clusters composed of approximately 10 or fewer H\(_2\)O molecules.

Here I compare the simulations with the Iribarne-Thomson model. Despite the model’s limitations, the agreement between the two for the expected size of the released ion–H\(_2\)O cluster is impressive considering the model’s simplicity. The Born model predicts that clusters of radius of 4 Å will be released, which correspond to \(\approx 8–9\) H\(_2\)O molecules by using equimolar radius equal to 4 Å. For the sodiated parent droplets the model prediction is near the most probable size range of 10–13 H\(_2\)O molecules (Fig. 4.9). For the chlorinated parent droplet, the model predictions are also relevant because simulations find that the smallest released Cl\(^-\)–H\(_2\)O cluster comprises 8–9 H\(_2\)O molecules, and shows the first maximum at 10 H\(_2\)O molecules. I attribute the difference between simulations and models to the fact that the model does not
consider the conical shapes on the droplet surface, which are the centres from where the ions are leaving. This particular geometry determines the number of H$_2$O molecules in the departing cluster instead of the spherical shapes used in the model.

Another factor to be examined in the interpretation of experimental ion cluster distributions is whether the emitted Cl$^-$-containing clusters may evaporate in their journey to MS detection, while the Na$^+$-containing cluster may increase in size by condensation. This suggestion is supported by the absolute value of H$_2$O–H$_2$O potential energy per H$_2$O molecule reported in Ref.[65]. It is found that in clusters of 20 and 30 H$_2$O molecules the H$_2$O–H$_2$O potential energy is smaller in the presence of Cl$^-$ than of Na$^+$.

Here I compare the results of simulations with those of Eq. 4.2. Iribarne and Thomson find the droplet radius $R$ at which ion-evaporation may occur as a function of $N$ by solving Eq. 4.2 for $R$, given $\Delta G^\ddagger$, $d_l$ and $\Delta G_o^\ddagger$. $\Delta G^\ddagger$ is taken to be $\approx 9$ kcal/mol by using the qualitative argument that this value leads to an observed overall disintegration rate of microseconds for droplet size of $\approx 10$ nm. Simulations provide a direct estimation of $\Delta G^\ddagger$ because the size of the emitted cluster and the depth of the ion can be computed (Table 4.3).

For the Na$^+$ emitted cluster, Eq. 4.4 yields a solvation energy of $-62.25$ kcal/mol when an average radius of 4.4 Å (Table 4.3) is used. Iribarne and Thomson use the solvation energy value of $-64$ kcal/mol which is near the value estimated by using the simulation input in Eq. 4.4. Note that the surface tension value of 70 mN/m for the SMW4-NDP model is used, while Ref. [8] uses 72 mN/m.

Entering the parameters of the ion depth and solvation energy in Eq. 4.2 I find that for a range of radii and charge below the Rayleigh limit, $\Delta G^\ddagger \leq 10$ kcal/mol (10 kcal/mol $\approx 4 kT$ at $T = 300$ K). In previous research, it was found that a barrier height of $4 kT$ may lead to a solvated ion release within several nanoseconds, which is a reasonable rate of ion evaporation within the droplet’s lifetime[28 29]. For example: $R = 10.0$ nm (that corresponds $Q_R = 123.5$) and $N = 100 – 123.5$, yield $\Delta G^\ddagger = 10.5 – 0$ kcal/mol. $R = 8.0$ nm (that corresponds to $Q_R = 88.4$) and $N = 66 – 82$, yield $\Delta G^\ddagger = 9.3 – 0.6$ kcal/mol. For the same system $N > 82$
yield $\Delta G^\ddagger < 0$. For $R = 5.0$ nm and $N = 25 - 31$ yield $\Delta G^\ddagger = 10.0 - 1.48$ kcal/mol.

I think that the negative values may indicate that the fragmentation occurs readily for charge above a threshold value. Thus, Eq. 4.2 finds the charge state of the droplet, above which $\Delta G^\ddagger < 10$ kcal/mol, and thus ion cluster release can occur before the Rayleigh limit.

For Na$^+$ ions, a range of charge with $\Delta G^\ddagger \leq 10$ kcal/mol can be also found at $R > 10$ nm differently from the estimate of Iribarne and Thomson that emission of single solvated Na$^+$ occurs up to $R = 8.4$ nm.

For the Cl$^-$ emitted cluster, Eq. 4.4 yields solvation energy $-69.3$ kcal/mol when the average radius of emitted cluster is taken to be $5.6$ Å (Table 4.3).

Ref. [8] uses the value of $-56$ kcal/mol based on thermodynamic estimates. Using average radius of emitted cluster $5.6$ Å and the depth $2.5$ Å Eq. 4.2 yields $\Delta G^\ddagger >> 10$ kcal/mol even at the Rayleigh limit. By trial and error, one can find a combination of depth and size of emitted cluster that may lead to $\Delta G^\ddagger \leq 10$ kcal/mol. However, these values do not agree with the parameters estimated in the simulations. Perhaps the disagreement is due to the fact the Cl$^-$ cluster size distribution is significantly broader than that of Na$^+$. Thus, the Na$^+$ cluster size average may represent better the distribution than the Cl$^-$ average value.

### 4.7 Conclusion

Existing models of the ion-evaporation mechanism relate the solvation of the ions in the parent droplet to the free energy difference at the transition state, and to the emitted cluster size. I found via atomistic modelling that in the parent droplet, multiple kosmotropic ions (e.g. Na$^+$, Li$^+$ and F$^-$) and weakly polarizable chaotropic ions (e.g. Cs$^+$) are solvated deeper within the droplet than polarizable chaotropic ions (e.g. Cl$^-$ and I$^-$). This differentiation in the ion location is only revealed by a polarizable model.

The key step in the ion evaporation are the conical shape fluctuations in the droplet surface. Ions may enter the conical shapes and then they may be emitted solvated within a cluster.
found a rather weak correlation between the depth of the ion within the parent droplet and the emitted ion-cluster size distribution. The lack of a clear correlation may be attributed to the fact that it is mainly the dynamic process at the conical shape from where the ion is emitted that determines the cluster size and not the equilibrium solvation in the droplet interior. I suggest a shift of focus from the depth of the ions in the parent droplet that appears in the models to the chemistry in the dynamic conical fluctuations. I showed that the charge sign asymmetry plays a critical role in the cluster size distribution. Singly charged negative ions (e.g. Cl$^-$ ions), which have a comparable radius to the positively charged ions (e.g. Na$^+$, Cl$^+$) are released with more H$_2$O molecules than the positive ions. A similar trend is found for the pair of I$^-$ and I$^+$. This trend due to the charge sign asymmetry is also supported by computations of free energy profiles as a function of the cluster size in the vapour–liquid nucleation of water. It has been found that negative ions give rise to a larger cluster size at the minimum of the free energy profiles than positive ions [34, 64–70]. I also showed that the size of the parent droplet does not significantly affect the cluster size distribution.

Simulation results oppose the assumptions of the existing IEM models on the relation of the ion depth within the droplet and the size of the emitted cluster. I note that the energetic factors that are considered in the IEM models may also apply to a Rayleigh mechanism, precluding a differentiation of the two mechanisms in the existing analytical models. Since the ion cluster departs from the tip of a conical shape that has different electrical characteristics from that of a spherical conducting droplet [40], the attractive interaction between the induced charge in the parent droplet and the departing ion cluster may be different from that assumed in the existing IEM analytical models.

In summary, the IEM can be described as ion cluster emission that may occur before the Rayleigh limit when (a) the free energy barrier for the appearance of the conical fluctuations is a few $kT$ and (b) the rate constant of the droplet radius reduction due to solvent evaporation is less or equal to that of the ion emission. Under these conditions, it is indubitable that IEM will take place because ion release from a multi charged droplet is always energetically favourable [12].
The geometry of the transition state and the factors that determine the emitted cluster size distribution is better presented via atomistic modelling than via analytical modelling.

A new analytical theory for IEM should focus on the conical fluctuations and reconsider the manner in which the attractive interaction between the induced charge in the parent droplet and the departing ion cluster is to be computed.

The active role of the conical fluctuations opens up a number of intriguing questions. A charged-residue mechanism has been supported as a mechanism for charging of macromolecules in droplets[71]. This mechanism is expected to take place when a compact macromolecule is surrounded by a few layers of H$_2$O molecules. It is to be examined whether frustration caused by the presence of the macromolecule prevents the formation of the conical fluctuations and as a result, the charge is transferred on the macromolecule. A significant complication in the atomistic modeling of these systems arises from their large size that makes the use of a polarizable model challenging.
Bibliography


Chapter 5

Summary and Conclusion

Liquid droplet-vapour interfaces show distinct structure and reactivity relative to bulk solution counterparts. In this thesis, key characteristics of the interfaces of aqueous droplets that had not been identified previously in the scientific literature were discovered. Differently from a bulk solution, droplets may be charged, and in reality, they are found at different charge states in nature and in technological applications. In these studies the charge carriers were ionic species such as simple ions or macroions. The most of the presented studies were for simple ions, but the author of the thesis has also studied the effect of macroions in research that has not been presented in this thesis. Three different charge states of droplets were examined: neutral, with a single ion and multiple ions.

Neutral aqueous droplets containing a pair or multiple pairs of NaCl are systematically simulated from supercooling to room temperature. A key finding of the study is that the colder the aqueous droplets the more likely is for the ion pairing to take place near the surface. At this location, the stability of the SSIP (solvent-separated ion pair) relative to the CIP (contact-ion pair) increases. This is opposite to the results of bulk solution simulations[1-3] where the formation of SSIP is suppressed in the interface. It was found that the equilibrium constant for $\text{CIP} \rightleftharpoons \text{SSIP}$ increases as the temperature decreases. In the study of the reaction dynamics, a weak coupling between the interionic NaCl distance reaction coordinate and the solvent degrees of freedom was found. The reduced coupling is mainly attributed to the presence of Cl$^-$ near the surface and to the fast diffusion of H$_2$O molecules. In contrast to bulk solution
where the crossing of the free energy barrier (along the interionic distance) is diffusive, there are no significant re-crossings in droplets. The ion pairing on the droplet interface is important for reactions in atmospheric aerosols. For example, photolysis of ozone may generate oxygen radical that via a series of reactions with aqueous NaCl droplets may lead to formation of Cl$_2$. The availability of Cl$^-$ on the droplet surface plays a key role in the formation of Cl$_2$. In the atmospheric chemistry field studies have reported that chemistry in brine might be more important than reactivity in completely frozen samples and that the presence of brine affects the photolysis rates of water-insoluble aromatics.

Droplets with a single ion are characterized by distinct interactions between that ion and the solvent, which are not present in a planar interface. I found that in droplets composed of at least several hundreds of H$_2$O molecules, the number density of a single Cl$^-$ and Br$^-$ shows a significant broad maximum in the droplet’s interior in addition to the well-known maximum in the surface. Moreover, I$^-$, which has the highest propensity for residing in the droplet’s surface, also shows a marginal broad maximum in the droplet’s interior. These results change the view about the location of the ions that was accepted in the literature for over a decade. Consta showed that a sole ion (simple or macrorion) in a droplet is always subject to a harmonic potential centered at a droplet’s center of mass. This effect was named “electostatic confinement” (EC). The force constant in this harmonic potential is proportional to the ratio of charge squared to droplet’s volume and to a more complicated function of the droplet’s dielectric constant. The EC effect is not so evident (even though present) in smaller nanodroplets with low charge, because EC competes with the geometric confinement that tends to spread the number density of the ion in almost all of the droplet’s volume. I advanced the theoretical study by showing how the interior maximum in the number density of Cl$^-$, Br$^-$ and I$^-$ is the result of EC.

The impact of this research is that for the first time in the literature I have the entire picture of ion (simple or macroion)- droplet interactions as a function of the ion’s charge. Consta et al. have found a threshold value of charge squared to volume ratio that above this value the charged
droplets take “star” shapes\[8\]. Below this threshold, EC along with the geometric confinement and possibly certain chemical effects such as charge transfer processes and solvent-solvent interactions, determine the ion location. This research completed the question on the single (macro)ion-droplet interaction by using a combination of molecular simulations and a general electrostatic-fluctuation theory that holds below and above the threshold value determined by the charge-squared to volume ratio of the droplet.

Lastly, *droplets containing multiple ions* also have their own distinct structure and chemistry. In these studies, the structure of charged droplets was dissected and the relation of the droplet structure and the ion-evaporation mechanism (IEM) was examined. These questions had not been systematically addressed in the literature for over fifty years because these relations cannot be directly detected in experiments. The surface excess charge layer (SECL) of a highly charged droplet was identified. SECL comprises ions (free charge) and solvent polarization (bound charge). It was found that in the presence of simple ions the thickness of SECL is invariant with respect to droplet size and the nature of the ions. In the presence of simple ions this layer has a thickness of $\approx 1.5 - 1.7 \text{ nm}$ but in the presence of macroions it may extend to $\approx 2.0 \text{ nm}$. The proportion of ions contained in SECL depends on the nature of the ions and the droplet size. For the same droplet size, $\text{I}^-$ and model $\text{H}_3\text{O}^+$ ions show considerably higher concentration than $\text{Na}^+$ and $\text{Cl}^-$ ions.

It is conceivable to consider that ion release will take place from SECL. The ion-evaporation mechanism is perceived to be a major pathway for disintegration of multi-ion charged droplets found in atmospheric and sprayed aerosols. However, the precise mechanism of IEM and the effect of the nature of the ions in the emitted cluster-size distribution had not been established despite its broad use in mass spectrometry and atmospheric chemistry over past half century. A systematic study of the emitted ion-cluster distribution in relation to their spatial distribution in the parent droplet using atomistic modeling was presented in this thesis. It was found that in the parent droplet, multiple kosmotropic ions are buried deeper within the droplet than chaotrophic ions. This differentiation in the ion location is only captured by a polarizable model.
It was demonstrated that the emitted cluster-size distribution is determined by dynamic conical deformations and not from the equilibrium ion-depth within the parent droplet as the IEM models assume. I discovered critical factors that determine the cluster-size distribution such as the charge sign asymmetry that were not considered in models and in experiments. It was argued that the existing IEM analytical models do not establish a clear difference between IEM and Rayleigh fission. A shift in the existing view for IEM is proposed from the equilibrium properties of the parent droplet to the chemistry in the conical shape fluctuations that serve as the centers for ion-emission. Consequently, chemistry in the conical fluctuations may also be a key element to explain charge states of macromolecules in mass spectrometry and may have potential applications in catalysis.

In conclusion, in all the studies the critical role of the surface in interconversion reactions of ion pairs and ion-cluster emission was demonstrated. In the presence of single ions, the electrostatic confinement effect explains the ion number density even in small nanodroplets. The use of a polarizable model is important for many aspects of the study. Certain characteristics of the location of the ions also emerge with non-polarizable model, but they are either less pronounced or incomplete. The polarizable modelling was used for droplets of up to 800 water molecules. However, I have found that droplets with a number of water molecules greater than 200 are sufficient large to form a surface, subsurface and a bulk-like region allowing for the transferability of the results on ion solvation and ion-pairing to larger droplets.

In atmospheric chemistry, there are important but still unanswered questions about how the structure of the salt-containing quasi-liquid layer (QLL) on ice affects the kinetics of photolysis reactions of adsorbed polycyclic aromatic hydrocarbons\cite{5, 9} such as anthracene and harmine. Similar questions are expected to hold about the role of NaCl in the photolysis reactions of adsorbed organic molecules on aerosols where their subsurface and surface can be considered the counterpart of QLL on ice. The present study provided thermodynamic and dynamic information to better understand the chemistry of salts in the outer layers.

These studies led us to propose optimization methods for the ionization techniques used in
mass spectrometry (MS). Specifically, in droplet-based ionization methods (e.g. electrospray, sonic spray, thermal spray) it is desirable to spray proteins from physiological solution (NaCl at concentration of 150 mM). Nevertheless, in the course of the droplet disintegration, the formation of adducts of salts with proteins or other macromolecules prevents the use of the physiological conditions in the initial bulk solution. The formation of adducts in MS is avoided by dissolving the proteins in low ionic strength solutions (40–70 mM), where the ionic strength is maintained by ammonium acetate and the solutions are cleaned as possible as from NaCl. The ammonium acetate in droplets evaporates by transforming into volatile molecules NH$_3$ and CH$_3$COOH. However, these ionic strength conditions are not representative of those in a biological cell and they may alter the conformation of a macromolecule relative to that in a biological sample. Understanding the location of ions in droplets may allow one to control better the ionic strength of the initial bulk solution. The present studies lead us to propose that when proteins are sprayed from a physiological bulk solution one may control the ion location by applying a cycle of cooling and heating during the droplet’s lifetime. In the experiments, heating of droplets is routinely applied in order to assist the droplet evaporation. Possibly initial cooling of a droplet instead of heating, or by applying an alternating cycle of heating and cooling may increase the ion concentration near the droplet surface. Bombardment with other molecules may assist in the detachment of solvated ions or their salt complexes from the droplet’s surface.

5.1 Outlook

These studies can branch out to many directions. Here, only a few of the directions are presented. Cryo-preservation is an intriguing field of research that finds applications in cryo-electron microscopy and ion-mobility experiments. For example, cryo-electron microscopy has proved extremely powerful in preserving the conformations of macromolecules. One of the computational directions is to study the structure of water and its diffusivity in the presence
of macromolecules at supercooled droplets and bulk solution.

In the thesis, I examined the ion-droplet and salt-droplet interactions in aqueous droplets as a function of temperature. The same questions in different solvents have not been investigated yet. I studied the reactivity of NaCl because of its central role in the planet’s life and climate. The study can be also extended to other salts, such as LiF, where both the ions show higher number density near the droplet’s center of mass. The question is how the lower temperature may affect the location where the ion-pairing is more likely to take place. The distinct physical chemistry that may occur in nanoconfined cold systems has been demonstrated by several authors, where depending on the dimensions of the confining environment and the degree of the hydrophilicity of the walls, new ice structures that cannot been seen in bulk solution have been observed\cite{10-22}. The effect of ions in the water phase diagram in nano-confinement is still to be explored.

Another possible research direction is the extension of the applicability of the Drude-based polarizable models to lower temperature. It was found in these studies that the H$_2$O Drude-based polarizable model showed non-physical structure in nanodroplets at low temperature. For this reason, the simulations with the polarizable model were performed up to 260 K. It is very important to correct the polarizable model so one can study supercooling of H$_2$O using models that take into account the electronic polarization.

Another direction that I envision to see developing is chemistry in the conical solvent shapes. Conical shapes such as Taylor cones may hide new chemistry mechanisms and possibly may have catalytic properties that have not been explored so far. This chemistry may find applications in electrochemistry and inkjet printing.
Bibliography


Appendix A

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2. **Kwan, V.;** Consta, S. Release of Macromolecules from Droplets - Validity Of the Born Model and the Role of the Conical Jets. *In Preparation 2022*