

# Molecular Dynamics of Ion Formation from Charged Nanodroplets in Electrospray Ionization

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## Introduction

The mechanism of ion formation in electrospray ionization is the subject of continuing debate. One of the prominent descriptions of ion formation in electrospray ionization is based on continued division of supercharged droplets until a single ion remains in the residue (charge residue model) (1). In the competing model, the ions are directly ejected from the supercharged droplet (ion evaporation model) (2). According to recent analysis, both of these models have validity, although under different conditions. The ion evaporation model typically prevails for relatively small ( $m/z < 3,300$ ) solute ions (3,4), whereas the charge residue model seems to be valid for larger multiply charged species (5). Experimental evidence to decide between the ion evaporation model and the charge residue model is not readily available and is especially scarce for nanometer sized droplets. Classical molecular dynamics simulations promise a convenient way of dealing with the disintegration of nanodroplets of various charge states. Utilizing molecular modeling, we followed the gas-phase formation of glycine and glycine homologue ions from water nano-droplets. Molecular dynamics calculations were conducted on realistic nanodroplets to directly observe the prevailing charge reduction mechanism. This study showed that the mechanism of the detachment process for individual ions was associated with the formation of unstable surface protrusions containing one or a few ions. These protrusions could be viewed as the intermediate stage preceding ion ejection. The evaporated ion detached from the droplet accompanied by water molecules forming a cluster of one or two ions with approximately ten water molecules per ion.

## Methods

Following our experience with modeling matrix-assisted laser desorption ionization at the molecular level (6), simulations were performed using the CHARMM molecular modeling program. The CHARMM22 all-atom potential function was used for the peptides in combination with the TIP3P water model. The number of water molecules was varied from  $\sim 1,000$  to  $\sim 4,000$ . For each droplet size, the number of  $(\text{Gly})_n\text{H}^+$  ions ( $n=1,\dots,16$ ) was selected in the vicinity of the Rayleigh limit. This charge density led to at least one ion formation event during the first 100 ps of simulation.

No boundary conditions were employed as the droplet was placed in vacuum environment. We used various initial ion distributions inside the droplet to simulate different evolution periods and droplet formation conditions. The calculations were performed on a Sun Ultra Enterprise 4000 system, and on an SGI Origin 2000 computer. The results were analyzed using the gOpenMol visualization package on PC and SGI workstations.

## Results and Discussion

Initial testing of the model indicated very good agreement between the calculated radial distribution function for the water molecules and neutron diffraction data. Self-diffusion coefficients derived from the model also gave good agreement with experimental values. Our computer simulations showed that at the atomic scale, the surface of a charged nanodroplet was not smooth. Instead, it was fluctuating exhibiting significant irregularities. It was clear that macroscopic concepts like surface tension were not suitable for the description of nano-scale phenomena. Figure 1 shows the departure of a hydrated ion from the droplet at 34, 44 and 46 ps. At 300 K temperature, chains of water molecules could be observed on the droplet surface. The water chains were moving randomly, their length fluctuated between 2 and 7 molecules and were 1 to 2 molecules wide. It seemed that these water chains acted like tethers, facilitating the departure of ions. First, these chains dragged submerged ions to the droplet surface. Next, the ions moved from the surface along the water chain. Finally, the water chain broke while a few water molecules hydrated the departing ion. Increasing the number of ions, and consequently the overall charge of the droplet, resulted in the coexistence of the water chains with conical surface protrusions of various sizes. If a protrusion included an ion, it very likely became more localized on the droplet surface. The increase of protrusion height and the reduction of its base area often resulted in the detachment of the

protrusion from the droplet with the formation of a hydrated ion cluster. Our data clearly supported the ion evaporation model for these systems.

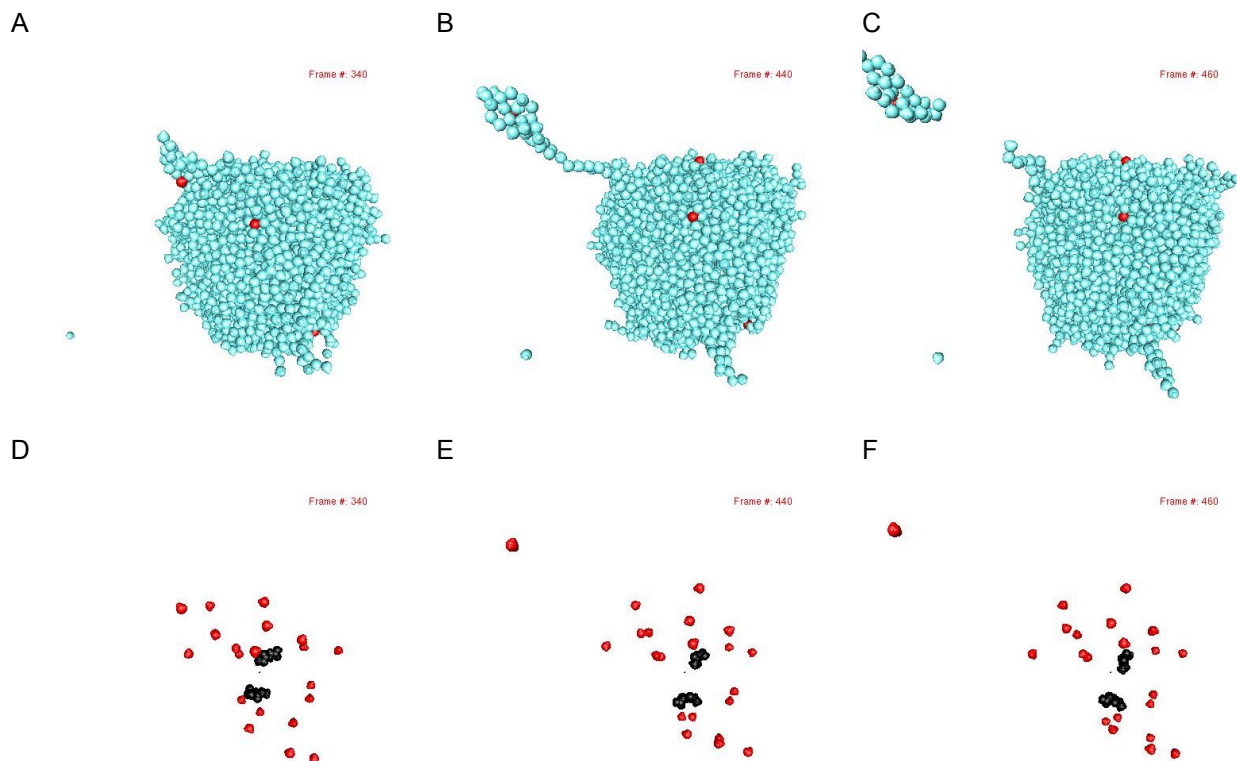


Figure 1. Detachment of a water cluster containing a single ion from a charged nanodroplet composed of 4300 water molecules (blue), 21 hydronium ions (red) and 2 diglycine ions (black). Snapshots were taken at 34 ps (panels A and D), 44 ps (panels B and E) and 46 ps (panels C and F). Ion distributions inside droplet are shown in panels D, E and F.

The occurrence and the frequency of surface protrusion formation was linked to the presence of ionic solutes in the droplet. Contrary to previous assumptions, however, the charged species did not have to be close to the surface in order to induce the formation of protrusions.

Studying the distribution of hydronium and protonated diglycine ions in the same nanodroplet we observed that diglycine ions aggregated near the center of the droplet, whereas hydronium ions stayed closer to the surface. This observation contradicted the conventional wisdom about expulsion of hydrophobic moieties from the center of aqueous droplets.

## Reference

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