



# Molecular Dynamic Simulation of ESI droplet fragmentation in MS vacuum stages

Physical & Theoretical  
Chemistry

University of Wuppertal

Leonie Grashoff, Clara Markert, Walter Wißdorf, Thorsten Benter

## Introduction

Recent research [1] has demonstrated that liquid charged droplets generated by Electrospray Ionization (ESI) penetrate deeply into the vacuum systems of commercial mass spectrometers (MS). A significant fraction of the ion signal detected in the mass analyzer is suspected to originate from those droplets. Therefore, the droplet fragmentation and bare ion generation process takes in part place under medium or high vacuum conditions and potentially strong electric fields. The aspiration of droplets into the devices can have adverse effects for the performance, due to contamination by comparably large amounts of solvents.

To get to an improved understanding of the complex ion generation process from charged droplets, classical molecular dynamics (MD) simulations are used to create a microscopic model of the dynamics of collisions between charged droplets and background gas under vacuum conditions. The calculations allow the estimation of internal temperature changes and fragmentation dynamics of liquid droplets at such conditions. Since the dynamics of the droplets are largely unknown, molecular dynamics (MD) simulations help to rationalize experimental observations.

## Methods

Moltemplate is used for particle ensemble set up, while the force field based MD simulations are performed with the open source code LAMMPS. Simulated liquid nanodroplets of various composition, with circa 1000 individual molecules, are set up and heated with a numerical thermostat function with different heating rates. The heating leads to evaporation and fragmentation processes. The resulting fragmentation patterns are analyzed with cluster analysis methods. The visualization and simulation of the trajectory analysis is carried out using Ovito in combination with custom Python programs.

Periodic boundary conditions are used for the simulation box to imitate a large system with small computational effort. During the simulation, the temperature of the simulated system is controlled by a Nosé-Hoover thermostat. The force field OPLS (Optimized Potentials for Liquid Simulations) is used in this work. It allows, with custom modifications, simulations of peptides in liquid solvents. OPLS is chosen since the force field is suitable for describing liquid solvents used in the ESI process.

## Droplet Heating and Fragmentation

Figure 1 shows the fragmentation of simulated solvent droplets depending on the composition of the chemical system or other factors like temperature.

The left panel shows two simulations with the same solvent, number of solvent molecules and temperature but differing number of ions and thus differing charge. The panel shows that with higher charges, the same droplet fragments faster.

The blue graph depicts a sudden decline at about 100 ps. This is where the droplet splits into two comparably large fragments. This phenomenon is frequently observed in the simulations.

The right panel shows how the same droplet evaporates differently depending on the temperature. With higher temperatures the droplet evaporates into single molecules or small clusters of just a few molecules.

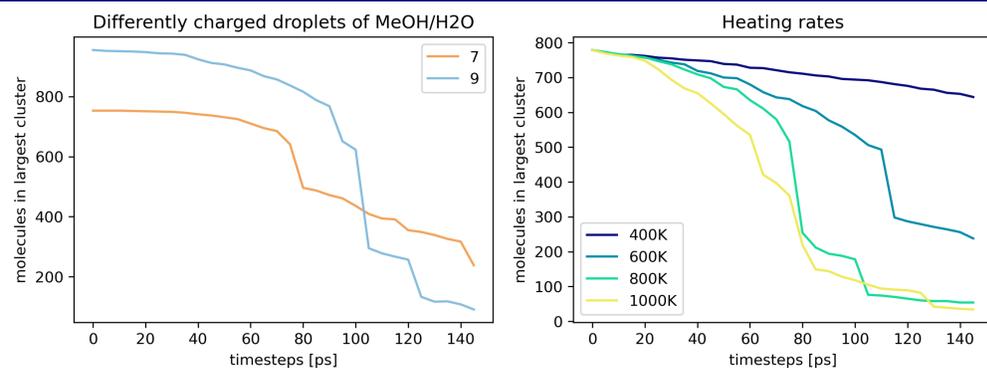


Fig. 1: Fragmentation of droplets in dependency of charge (left) and final temperature (right)

## Solvent Dependency

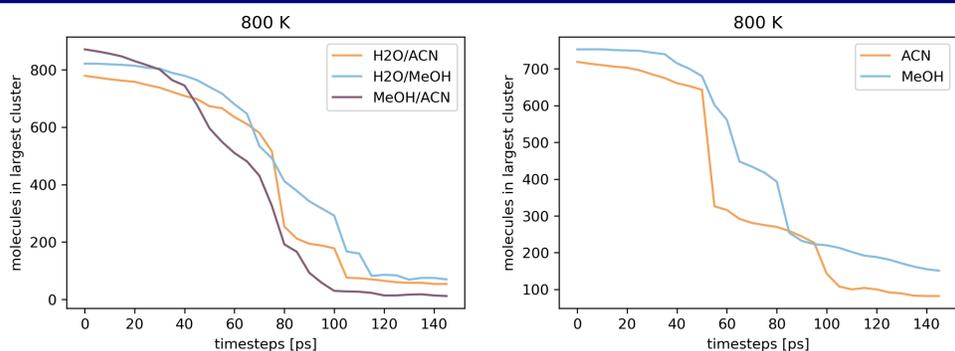


Fig. 2: Simulations of idealized solvent droplets with 800 K final temperature

Idealized droplets originating from ESI-MS are simulated to estimate their behavior at elevated effective ion temperatures. The stability of the droplets depends on the composition of the system.

The left panel shows different systems with a charge of 7. Polar molecules like water can stabilize the droplets by arranging around the ions. This is shown particularly in the simulation of a droplet without water, as it evaporates faster than droplets containing water. The right panel shows the evaporation process of droplets with a charge of 9. The droplets are made up of one part water and two parts of the indicated solvent (acetonitrile or methanol). The results indicate that droplets with methanol evaporate at a slower rate, which could be explained by the ability of methanol to build hydrogen bonds.

## Analyte Dependency

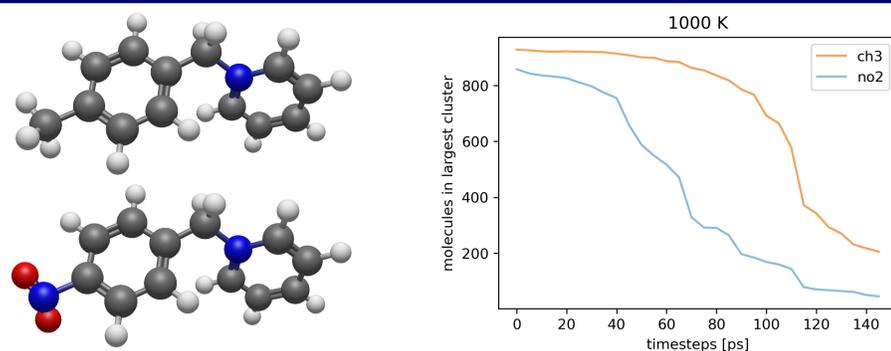


Fig. 3 Benzyl-Pyridinium thermometer-ions with CH<sub>3</sub> or NO<sub>2</sub> as variable substituent in solvent droplets consisting of acetonitrile and water at 1000 K

In mass spectra the signals of different thermometer-ions can be separated, even though the species are structurally and chemically similar.

To simulate systems closer to reality, ionized thermometer-ions were designed for this simulation instead of using small cations, like lithium.

Simulations suggest different droplet stabilities depending on the solvated analyte ions, as visible in Fig. 3. This phenomenon is observed even with high temperatures which lead to the eventual total fragmentation of the droplets.

Droplets with more polar NO<sub>2</sub>-groups evaporate faster than droplets with a CH<sub>3</sub>-group.

## Conclusion and Outlook

The presented simulations demonstrate that the chosen approach appears to be feasible. The simulations show a clear dependency of the observed fragmentation patterns on droplet temperature and composition. High temperatures lead to higher fragmentation rates and smaller resulting fragments. Simulations with different droplet compositions show significantly different droplet stabilities and internal structure. Simplified systems suffice to make preliminary qualitative comparisons of the various chemical systems in droplets.

However, modeling of larger and more complex droplets is also possible with LAMMPS and proves to be an interesting approach for comparison with experimental mass spectra of droplets. By heating up the same droplet several times with a different random seed, a sufficient statistical set of fragmentation events and thus resulting fragments can be obtained, for example to derive simulated mass spectra. An example for this process is shown in Fig. 4.

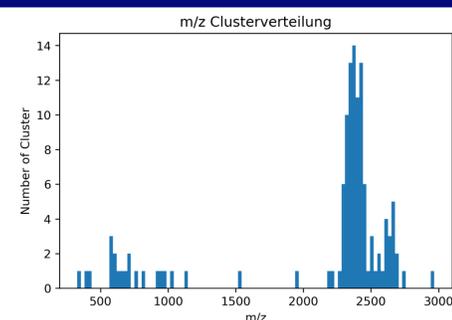


Fig. 4: simulated mass spectrum

## Literature

[1] C. Markert, M. Thinius, L. Lehmann, C. Heintz, F. Stappert, W. Wissdorf, H. Kersten, T. Benter, B. B. Schneider, T. R. Covey, *Analytical and Bioanalytical Chemistry*, **2021**, *413*, 5587–5600.