



Effects of ESI Source Parameters on Charged Droplets Observed in API-MS Systems

Physical & Theoretical
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Introduction

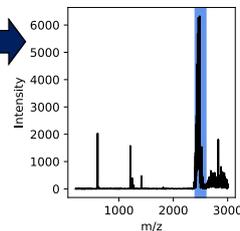
Electrospray ionization (ESI) is by far the most important atmospheric pressure ionization technique today. Recent experimental work [1,2] indicate that, contrary to a common assumption in the community, significant amounts of charged liquid droplets are aspirated into commercial MS systems, leading to potential instrument contamination and chemical interferences.

The generation of droplets in the ion source, and thus the characteristics of aspirated droplets, depends on the conditions in the ion source. Therefore, the operation parameters of the ion source also affect the charged liquid droplets observed in an ion trap mass analyzer.

Droplet Signature Measurements in Ion Trap



A Bruker amaZon Quadrupole Ion Trap (QIT) – MS with Electrospray Ionization (ESI) was used for the experiments. Ions from ESI are accumulated into the trap, and outside of a selected m/z range are ejected from the trap (ion isolation within the isolation range). The isolated ions can optionally be excited by collisions. The resulting ion population is mass analyzed leading to a result spectrum.



Mass Spectra

All used analytes have masses below 1000 Da. Intensive signals of isolated ions above that range clearly indicate the presence of large, multiply charged, aggregates in the ion trap. All signals outside the isolation range (marked blue) are generated after isolation and thus from the isolated particles.

Droplet Signatures – Fragmentation and Charge Loss

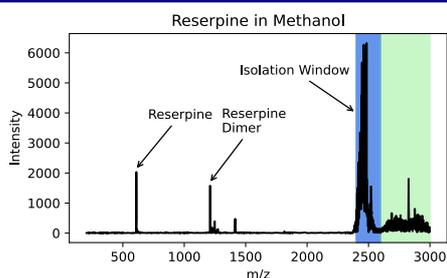


Fig. 1: Bare analyte and charge loss signals from isolated droplets / droplet fragments

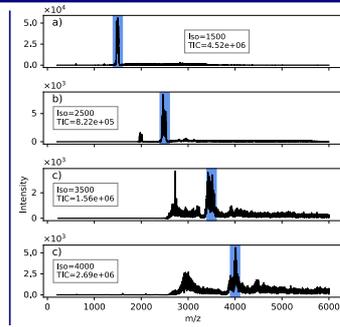
Large analyte carrying aggregates

left: Strong signals in the range $m/z > 1000$ are readily observed with ESI and Reserpine in Methanol as sprayed solution.

Bare Reserpine and Reserpine dimers, generated from the initially isolated droplet fragments, become visible with gentle collisional activation in the trap.

Charge loss

Intensive fragment signals are visible in the m/z range above the isolation range (marked green). Since cluster growth in the trap is unlikely, the signals are generated by charge loss processes.



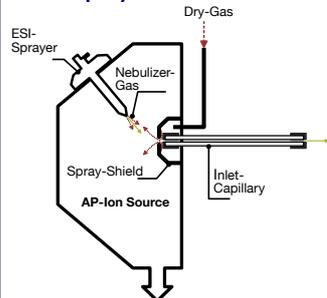
Isolation Range

left: Variation of the isolation range indicates that the initial particle distribution in the ion trap spans over a very wide m/z range with a high total amount of ions. This is attributed to the presence of large, highly charged droplets or droplet fragments as initial source. The remarkably different fragmentation patterns indicate a large chemical variety of the initially isolated particles.

Fig. 2: Isolation range variation for Reserpine in Isopropanol

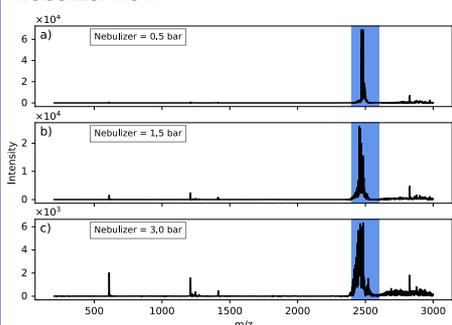
Effects of Ion Source Parameters

Electrospray Ion Source



left: ESI source: A liquid analyte solution is sprayed from an ESI-Sprayer into a strong electric field between the sprayer and the mass spectrometer (MS) entrance formed by the spray-shield and the inlet capillary entrance. A gas flow, the Nebulizer-Gas, injected at the sprayer tip, assists the spray process. An additional heated gas flow, the Dry-Gas, is introduced from the MS entrance towards the ion source. The Dry-Gas is intended to support the evaporation of liquid droplets within the source chamber.

Nebulizer Flow



left: Dependency of the droplet stability on the nebulizer pressure with Reserpine in Methanol:

The relative amount of bare analyte, analyte dimer and charge loss signals increase with increasing nebulizer pressure, indicating decreasing internal stability of the initially isolated particles.

Fig. 3: Nebulizer Gas variation with Reserpine in Methanol

Dry Gas Flow

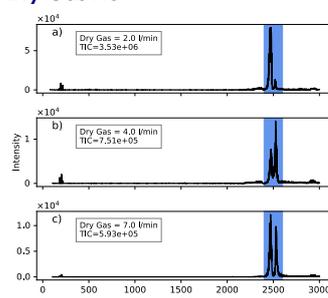
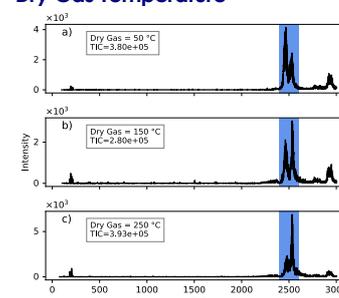


Fig. 4: Dry Gas flow and temperature variation with Benzylpyridinium thermometer Ions in 1:1 Acetonitrile / Water

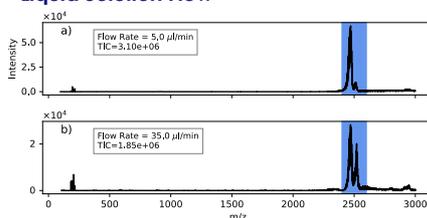
above: Measurements with dry gas parameter variations reveal significant effects of the dry gas flow and temperature on the observed signal structure within the isolation range with Benzyl-

Dry Gas Temperature



pyridinium Thermometer Ions. Additionally, the relative amount of charge-loss signals differs significantly, indicating effects of the dry gas parameters on the internal structure of the isolated droplet species.

Liquid Solution Flow



left: The variation of the liquid flow rate has a notable, but surprisingly subtle effect on the observed mass spectra. The liquid flow rate does not stand out as dominant relatively to other ion source parameters.

Fig. 5: Variation of the liquid flow rate with Benzylpyridinium thermometer Ions

Conclusions

- Strong signatures of aspirated droplets are observed in the Amazon Ion Trap with Reserpine and Benzyl-Pyridinium thermometer ions
- Variations of ion source parameters affect the observed mass signals originating from aspirated droplets or droplet fragments significantly
- The shape of mass signals within the isolation range as well as the relative intensities of charge-loss signals and bare analyte signals depend on the ion source parameters
- The nebulizer gas flow has a pronounced effect on the observed stability of droplet species

Outlook

- Replication of the presented findings on other commercial ESI-MS systems
- Characterization of other ion source and MS entrance stage designs regarding the coupling of ion source parameters to the aspirated droplet ensemble
- Assessment of long-term stability and drift
- Coupling to LC systems for high flow measurements and assessment of effects of transient changes of spray conditions
- Numerical modelling of droplet trajectories and droplet fragmentation within ion source and MS entrance stage

Literature

- [1] Kang, Y., Schneider, B.B., Covey, T.R.: On the Nature of Mass Spectrometer Analyzer Contamination. *J. Am. Soc. Mass Spectrom.* 28, 2384–2392 (2017). <https://doi.org/10.1007/s13361-017-1747-3>
- [2] Markert, C., Thinius, M., Lehmann, L., Heintz, C., Stappert, F., Wißdorf, W., Kersten, H., Benter, T., Schneider, B.B., Covey, T.R.: Observation of charged droplets from electrospray ionization (ESI) plumes in API mass spectrometers. *Anal. Bioanal. Chem.* (2021). <https://doi.org/10.1007/s00216-021-03452-y>