A Novel High-Resolution CDMS Instrument Prototype

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OVERVIEW

PURPOSE:
Development and characterization of high m/z resolution (HR) charge detection mass spectrometry (CDMS) traps.

METHOD:
Trap simulations, construction of two prototype traps and analysis of protein standards to determine trap properties.

RESULTS:
Trap *m/z* resolution (FWHM) of >11,000 and >14,000 for novel 3- and 4-electrode traps respectively.

INTRODUCTION

CDMS has emerged as a powerful new tool for the characterisation of heterogeneous high molecular-weight analytes. Independent measurements of *m/z* and *z* allow mass to be determined without deconvolution. In general, mass resolution is determined by both *m/z* and *z* resolution, but the newly introduced Waters™ Xevo™ CDMS instrument is capable of exact charge measurement.

The trap in a previously described prototype instrument[1] is capable of an *m/z* resolution of up to 200. For certain analytes (e.g. intermediate mass glycoproteins), higher resolution can reveal important additional structure. HR traps can also have higher capacity at a given resolution, offering higher throughput. We summarize the trap design process that we have adopted and present experimental data from two prototype HR traps demonstrating >10,000 FWHM *m/z* resolution, similar to the resolution previously reported by Reitenbach et al.[2].

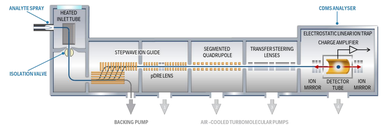

Figure 1 *The geometry of the Waters Xevo CDMS instrument.*

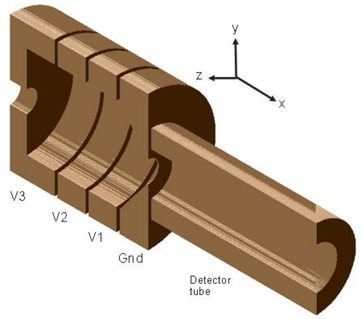

Figure 2 Section of *a 3-electrode trap geometry (showing one quarter of the full device which has axial symmetry). The traps described in this poster comprise a detector tube and shield electrode at ground potential and either 3 or 4 electrodes with tunable applied voltages V1, V2, V3…*

METHODS

In the instrument geometry used in this study (***Figure 1***), ions are cooled and accelerated to a nominal energy of 130 eV/z through a segmented quadrupole and a set of electrostatic focusing lenses. The front electrode set of the trap is pulsed, allowing a population of ions to enter. The ions then oscillate axially in the trap (typically 100-2000 ms), spending close to 50% of the trapping time in the centrally-situated detector tube (***Figure 2***). The charge induced on the detector is measured by a charge-sensitive amplifier and digitized.

The resulting transient is processed using a series of overlapping Fast Fourier Transforms to determine a range of ion properties including *m/z* (via oscillation frequency), charge state (via signal amplitude) and ion survival time.

Variations in axial ion energy lead directly to differences in axial oscillation frequency for otherwise identical ions, limiting the measured resolution.

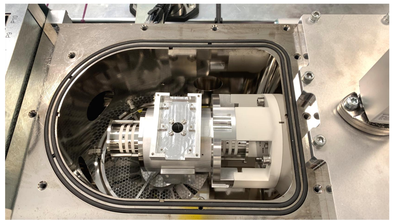

Figure 3 *Installation of a 3-electrode HR trap into a prototype version of the Xevo CDMS instrument using a specially constructed adaptor.*

These variations may be caused by

- the initial velocity and positional spread (phase space) of the incoming ions,
- collisions with gas molecules, reducing ion energy, and
- ion-ion interactions when several ions are trapped, leading to energy exchange.

It is therefore of interest to find trap geometries for which oscillation frequency is as nearly independent of ion energy (near the nominal ion energy) as possible. It is also important to ensure that the design is robust to inevitable imperfections in trap construction and applied voltages, and that a high percentage of ions are stable for the required trapping time.

The methods used to design of the traps evaluated in this poster has been described in detail elsewhere[3,4]. In short, a novel GPU-based solver was written, capable of calculating >15,000 100 ms trajectories in 8 mins on an NVIDIA® GV100 GPU. Electric fields were calculated using SIMION® 2020[5].

A representative initial phase space distribution was used for all ions, and trap geometry and voltages were optimized. Factors considered during optimization included *m/z* resolution, duty cycle (with a target of 50%), and tolerance of resolution and stability to reasonable mechanical offsets and tilts.

Two candidate trap geometries having detector tubes of length ~75 mm (50% longer than the prototype CDMS trap) were selected for further investigation: a 3-electrode trap having a theoretical m/z resolution of ~30,000 and a 4-electrode trap with a theoretical resolution of ~190,000.

These traps were constructed and installed into prototype instruments for evaluation. ***Figure 3*** shows the 3-electrode trap being installed into a prototype instrument using a specially designed adaptor.

A variety of protein standards (Sigma Aldrich) were buffer exchanged into 200 mM ammonium acetate solution using Bio-Spin® P-6 size-exclusion columns (Bio-Rad Laboratories). Ions were generated in positive ion mode using nanoelectrospray ionization using pulled glass emitters (5um tip diameter).

Trap voltages were tuned using the melittin and ubiquitin protein standards.

RESULTS

Figure 4 shows the *m/z* histogram of myoglobin ions obtained using the 4-electrode trap. The inset shows the resulting mass histogram from combining charge states $z=14^+$ to 21^+. The width of this peak is consistent with an m/z resolution of at least 14,000.

Figure 5 shows mass histograms of detected ubiquitin ions measured using the 3- and 4-electrode traps together with simulated data at FWHM *m/z* resolution of 11,000 and 14,000 respectively.

Figure 6 shows the proportion (relative to 100ms) of β-Galactosidase ions that were stable in the trap for survival times up to 5 seconds. This shows excellent stability with 80% of ions surviving to 2 seconds, and >70% surviving for the full 5 seconds.

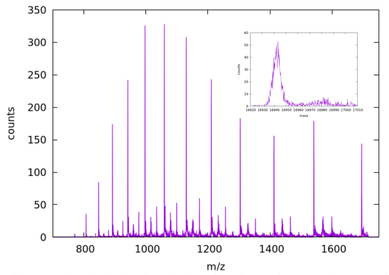

Figure 4 *4-electrode data showing charge states of myoglobin and the resultant mass histogram (inset).*

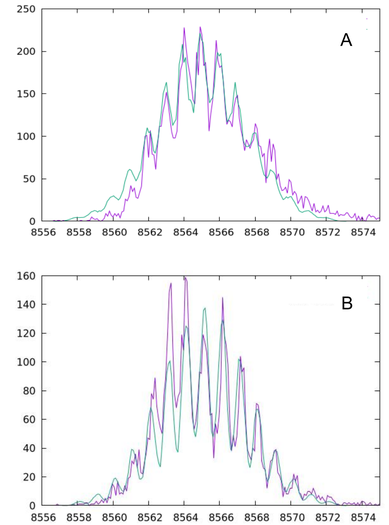

Figure 5 ***A)*** *3-electrode data showing partial resolution of ubiquitin isotopes.(resolution ~ 11,000)* **B)** *4-electrode data showing improved isotope definition (resolution ~14,000). The green traces show simulated data at the measured resolution.*

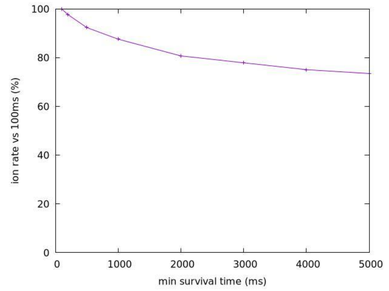

Figure 6 *Proportion of β–Galactosidase ions that survive for a given trapping time (relative to 100ms), obtained on the 4-electrode trap.*

CONCLUSION

- An *m/z* resolution of >10,000 (FWHM) has been measured for both the 3- and 4- electrode HR traps.
- Stability for 5 second trapping of >70% has been observed for the 4-electrode HR trap.
- Future work will look at more complex analytes including glycoproteins.
- Factors that limit the observed resolution (when compared with the simulated values), will also be explored, and the ion capacity of the traps will be measured for a variety of analyte classes.

REFERENCES

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