

Characterization of a detection system with high sensitivity and dynamic range for a novel HRAM mass spectrometer

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Introduction

Efficient ion detection is key to a mass spectrometer's sensitivity, and linearity of response typically dominates the dynamic range of the instrument. Detection systems in Q-ToF or QqQ mass spectrometers are usually based on ion-to-electron conversion and subsequent electron multiplication.

For the novel high-resolution and accurate-mass Thermo Scientific™ Orbitrap™ Astral™ analyzer¹, we have developed a detection system to maximize sensitivity, linear dynamic range, and detector lifetime which also allows for high resolution. The system is comprised of a post-acceleration electrode stack, EI-Mul's MTOF ion detector, and a preamplifier (see figure 1 b) and c). The electrode stack accelerates ions with an attractive potential of several kilovolts on the conversion dynode of the detector to increase the number of released secondary electrons and therefore the detection efficiency. The secondary electrons are accelerated on to the surface of a scintillator resulting in the release of photons which are further guided on a photomultiplier-tube with a gain of ca. 10⁵. The signal from the last dynode of the photomultiplier-tube is fed into the dual-channel preamplifier with a gain ratio of 1:10 to maximize the dynamic range. Both output signals are fed to an 14bit analog-to-digital converter for further processing.

Figure 1 a) shows a schematic drawing of the Astral analyzer and the primary ion trajectory through the analyzer. Trapped ions² are extracted into the Astral analyzer and travel along the drift direction back-and-forth between the two ion mirrors until they reach inflection point and return backwards. At the end of their return path, they traverse the post accelerator and arrive at the detector (shown in b). Panel c) shows a detailed view on the components of the ion-to-photon detector. The detector exhibits a time response of ca. 1.6ns to allow for high resolution measurements.

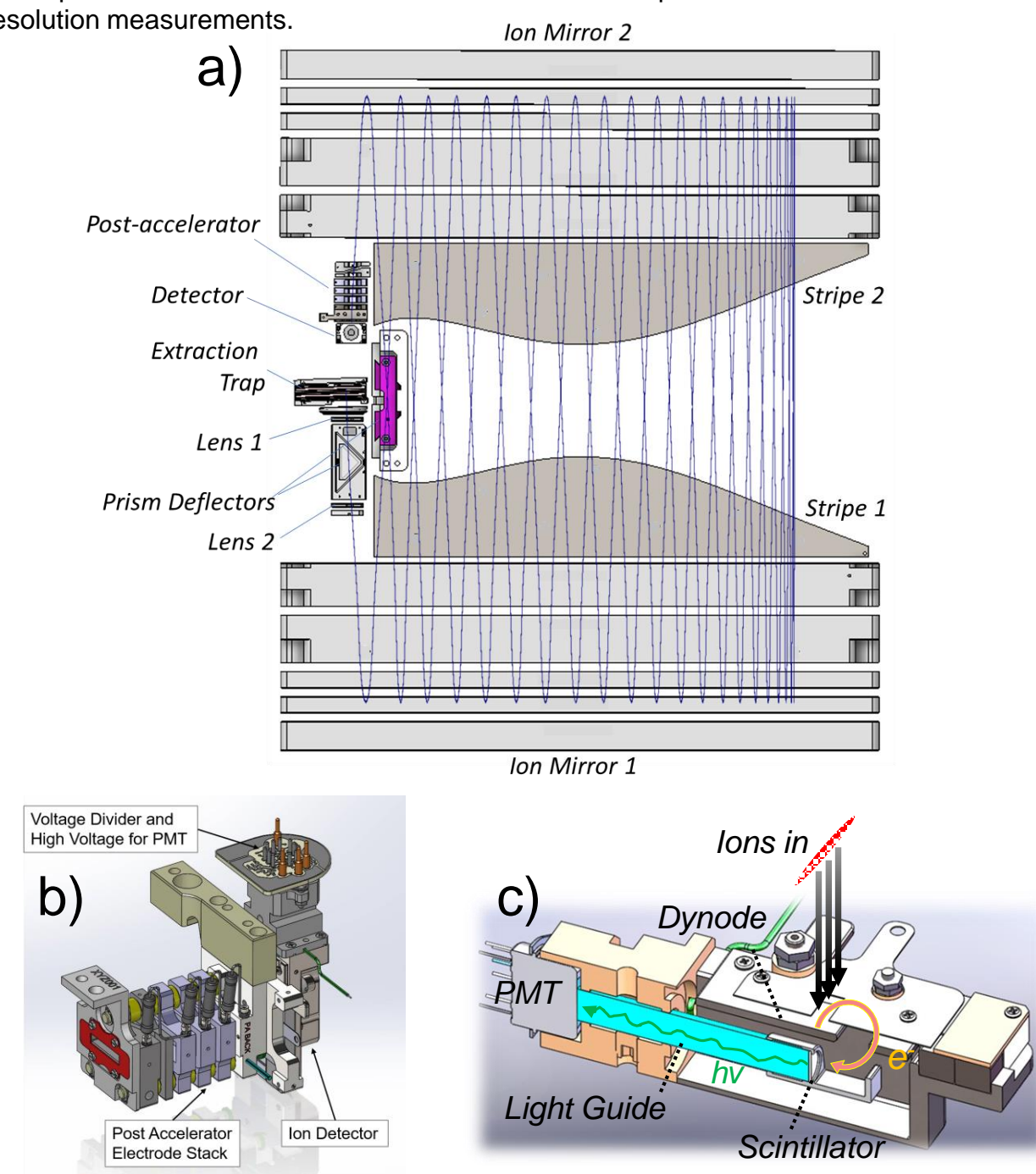


Figure 1. a) Schematic drawing of the Astral analyzer and the primary ion trajectory. b) 3D-model of the post acceleration electrode stack and the MTOF ion detector of the Astral analyzer. c) Detailed drawing of the ion detector.

Experimental

Experimental data was obtained on a prototype system comprising an Astral analyzer coupled to a Thermo Scientific™ Orbitrap™ Exploris™ 480 mass spectrometer. Electro sprayed ions from Thermo Scientific™ Pierce™ FlexMix™ calibration solution and ammonium hexafluorophosphate (AHFP) were used to characterize the detection system over a wide m/z-range.

To exclude effects from multi-ion peaks and variations of the signal intensities coming from the electrospray source, single ion measurements were performed to investigate most of the characteristics of the detection system. The mirror system of the Astral analyzer was hereby utilized by setting the high voltages at the mirror electrodes in a defocusing mode to effectively defocus the ions of a given mass-to-charge ratio. The separation between single ion events and electrical noise peaks was guaranteed by high detection thresholds at the ADC and sufficiently high gain on the detector level.

Results

Sensitivity Figure 2 shows the single ion detection efficiency as function of the PMT voltage (top panel) and the mass-to-charge ratio (bottom panel). Single ions intensities of m/z 524 were measured by defocusing the mirror system of the Astral analyzer under varying PMT voltages. Around 550V is needed to reach a detection efficiency of 80% without compromising the linear dynamic range of the detection system, the correct setting of the PMT voltage is therefore a trade-off between high detection efficiency and achievable dynamic range. The mass-to-charge ratio dependency was determined using FlexMix and AHFP and shows a high detection efficiency over the mass range, dropping down to 80% at m/z 5000 as electron yield at the conversion dynode has a higher probability for zero electrons being released.

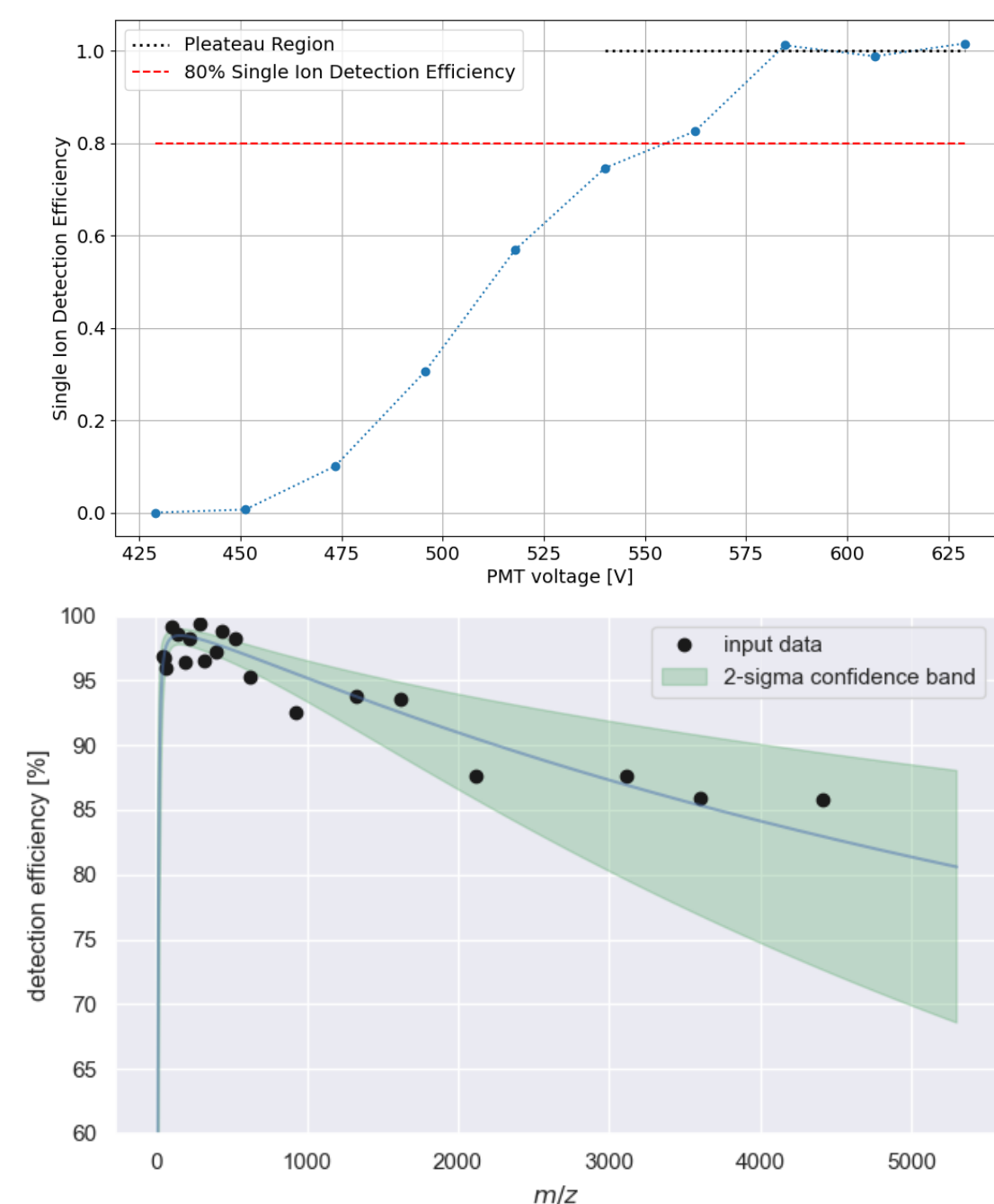


Figure 2. Top: Single ion detection efficiency as function of the PMT voltage using a single ion distribution of m/z 524. Bottom: Single ion detection efficiency as function of mass-to-charge ratio determined with data obtained with FlexMix and AHFP.

Linear Dynamic Range Figure 3 shows a FlexMix mass spectrum acquired in a single shot for a m/z range of 150-1500 with typical resolution values of 80-100k. The most intense peak, doubly charged MRFA at m/z 262, contains several thousand charges while the detection system is still able to detect single ions like m/z 448.235 with an intensity of 0.04% showing a linear dynamic range much higher than 1:1000.

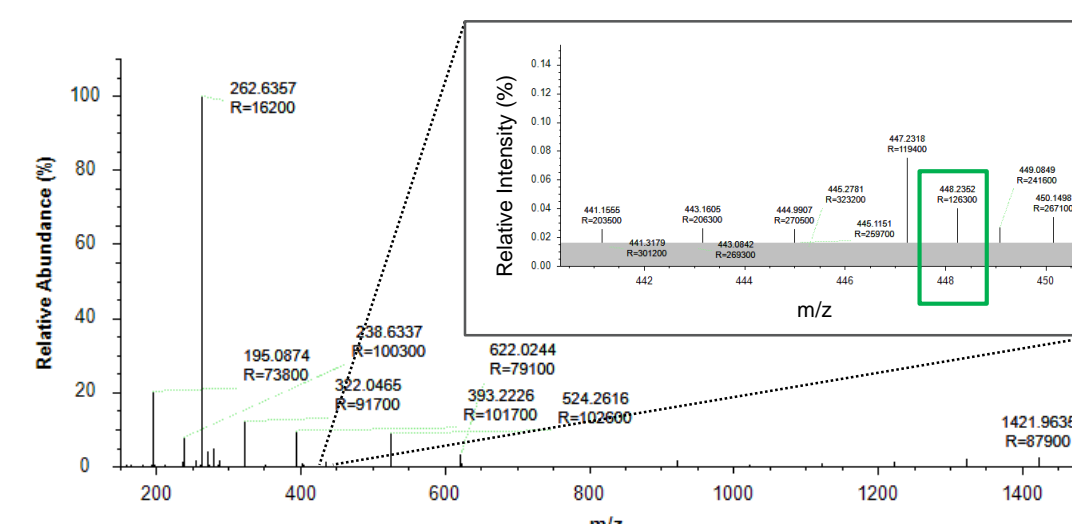


Figure 3. Mass spectrum of FlexMix for around 10000 charges. Single-ion peaks like m/z 448.235 (green box) can still be detected at a relative intensity of ca. 0.04% showing a dynamic range of higher than 1:1000.

Detector Gain Stability Figure 4 shows the signal intensity of single ions of m/z 524 measured over 30 hours with an automatic detector calibration routine³ while continuously delivering FlexMix onto the detection unit. The single ion area and therefore the detector response is highly stable allowing a more accurate quantification of the number of ions on a peak. The detector gain is also stable after venting and baking the system due to the capsulated PMT.

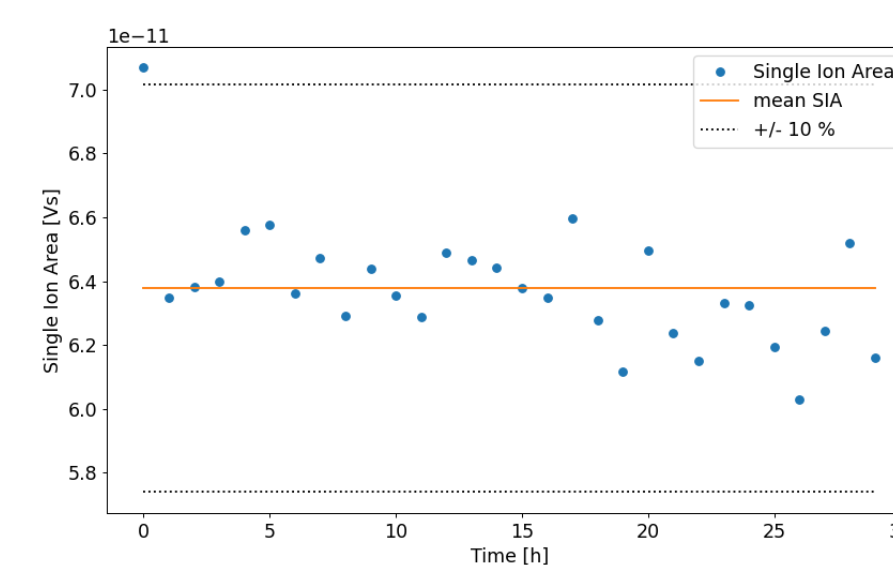


Figure 4. Single ion area measured over 30 hours while delivering FlexMix onto the detection system.

Detector Lifetime Figure 5 shows the detector lifetime measurements in a dedicated test stand delivering ions up to m/z 614 from PFTBA vapor. The single ion pulse height distribution was continuously monitored throughout the experiment with a total delivered charge of 5.6µC corresponding to more than one year of typical instrument usage. The average pulse height dropped by only 7%. This highlights the potentially long detector lifetime of several years of the ion-to-photon detector due to its capsulated PMT.

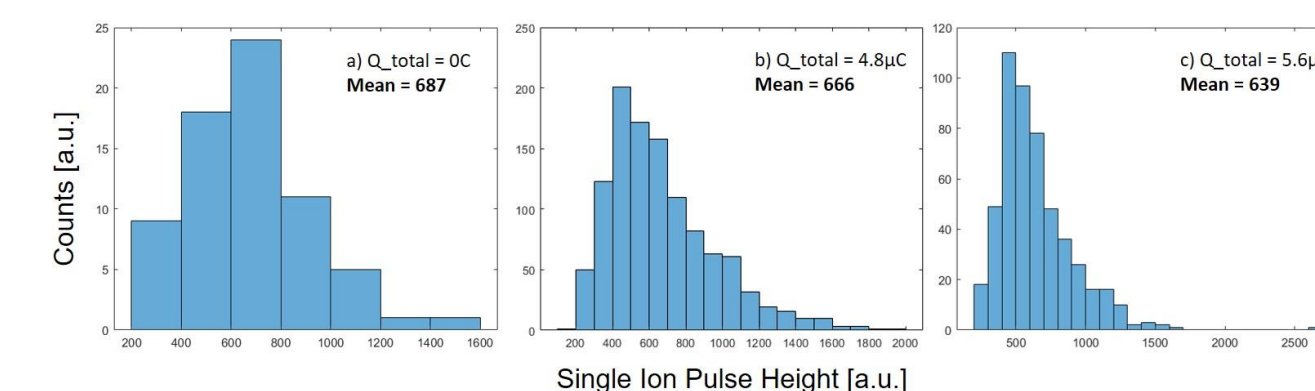


Figure 5. Pulse height distributions of single ions after delivery of a total charge of a) zero, b) 4.8µC, and c) 5.6µC with a decrease in gain of around 7%. For typical usage, a total delivered charge of 5µC is expected in one year.

Mass-to-Charge and Charge Dependency The left panel in figure 6 shows the single ion area measured as function of mass-to-charge ratio in the m/z range from 42-7000 using FlexMix and AHFP. The measured data is corrected for the ion-to-electron conversion efficiency (red circles) using simulated electron yield estimates. The detector response reaches its maximum at around m/z 140 and decreases to around 80% for m/z 42. Towards higher m/z, the response curve decreases down to 20% at m/z 7000 due to the lower velocity of the ions when impinging on the conversion dynode. The mass-to-charge dependency is applied in the Astral analyzer data processing for higher accuracy when determining the number of charges in the peak. Note that electro sprayed ions above m/z 3000 are usually multiply charged. The right panel shows the charge state dependency of the single ion area using Ubiquitin and Angiotensin. The detector response is very linear up to at least charge state 12 allowing a direct determination of the number of charges together with the mass-to-charge dependent correction function (left panel).

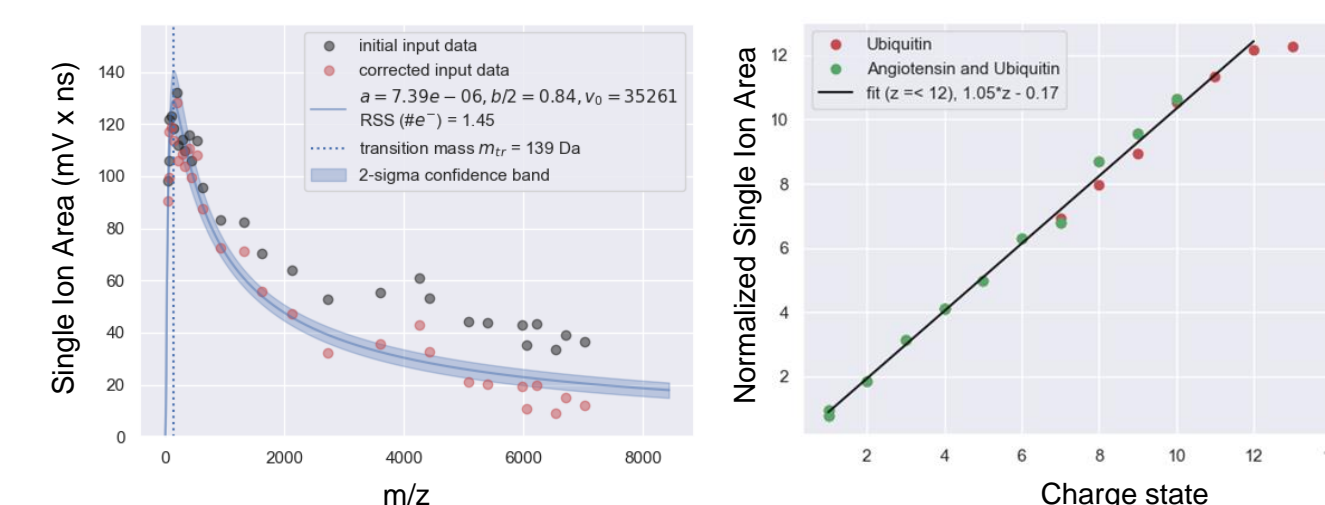


Figure 6. Left: Single ion area as function of mass-to-charge ratio determined in a m/z range 42-7000 using FlexMix and AHFP. The raw data (black circles) are corrected by the m/z-dependent ion-to-electron conversion. The mass-to-charge dependency is modelled using the corrected data (red circles). Right: Normalized single ion area as function of the charge state measured for Angiotensin and Ubiquitin. The response is linear up to at least charge state 12.

CONCLUSION

The detection system of the new Astral mass analyzer has been fully characterized concerning its sensitivity, dynamic range, detector gain stability, detector lifetime and the mass-to-charge dependent response. The high sensitivity and linear dynamic range of the detection system allow the detection of single ions and multi-ion peaks with several thousand charges in a single shot. The high gain stability means less frequent calibration runs and longer usage of the detector compared to conventional MCPs and electron multipliers.

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