

Resonant RF Circuit Enables Ion Containment and m/z -Dependent Axial Ejection for Corrected Time-of-Flight Discrimination

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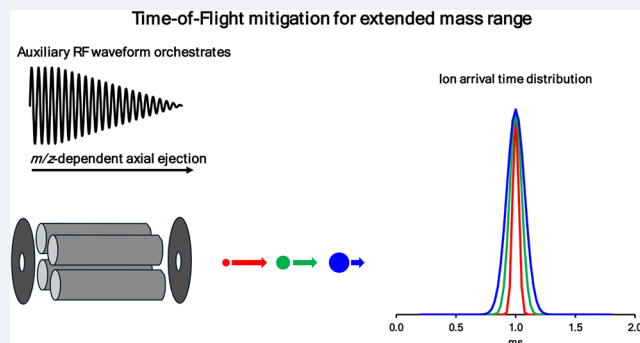
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ABSTRACT: Time-of-flight m/z discrimination limits the effective analytical m/z range for Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry because optimal ion arrival time at the ICR cell varies with $m/z^{1/2}$. Previously, an auxiliary RF waveform that allowed sequential m/z -dependent axial ejection from an external ion accumulation multipole resulted in mitigation of time-of-flight m/z discrimination, which improved ion transfer across a decade in the m/z range 200–2000. Here, a resonant RF axial ejection system based upon the same principle is implemented to further expand the m/z range that can be observed in a single mass spectrum. This new RF ejection system was installed without any change to the internal vacuum components. The RF ejection system has been significantly simplified over the initial implementation and installed and verified on several FT-ICR mass spectrometers in a multilab collaboration.

KEYWORDS: fourier transform ion cyclotron resonance, ICR, FTMS, time-of-flight discrimination



INTRODUCTION

External ion accumulation facilitates rapid, sensitive, and versatile FT-ICR MS.¹ Typically, all ions stored in an external ion trap or multipole storage device (MSD) are ejected at approximately the same time with the same kinetic energy. Thus, the optimal arrival time at the ICR cell is proportional to $m/z^{1/2}$, so low m/z species arrive at the ICR cell first, followed sequentially by higher m/z species. Due to the nature of the experiment, low m/z species may enter the ICR cell, reflect back toward the ion source, and exit prior to closure of the cell before higher m/z species ever reach the ICR cell. Typically, the ion flight time is optimized for the middle of the mass range of interest, with discrimination against both high- and low- m/z species. These species may still be observed in the mass spectrum, but with substantial attenuation compared to what was initially present in the MSD. As a mitigation strategy, an auxiliary RF axial ejection (AuxRF) method was introduced on FT-ICR mass spectrometers to mitigate time-of-flight m/z discrimination.² The AuxRF ejection method has been used successfully for numerous applications.^{3–5} The initial implementation utilized broadband RF power amplifiers, programmable function generators, and capacitive balance matching, which complicated and limited the dissemination of the technology. Here, the initial AuxRF method is innovated with

custom-built electronics to simplify implementation and further expand the observable m/z range. In this implementation, the m/z -dependent pseudopotential barrier created by the AuxRF waveform is used to correct for time-of-flight effects; similarly, the inclusion of an m/z -dependent AuxRF waveform could be used in conjunction with ion–ion reactions to physically separate lower charged products from the reactants,⁶ as shown by McLuckey et al.

EXPERIMENTAL SECTION

The distance between the MSD and ICR cell varies based upon magnet design and the vacuum system required to maintain ultrahigh vacuum $<1 \times 10^{-10}$ Torr for high-field FT-ICR analysis. For the FT-ICR mass spectrometers located at the National High Magnetic Field Laboratory (NHMFL), the ion flight distances are 9.4 T (~ 1.4 m),⁷ 14.5 T (1.7 m), and 21 T (1.9 m),^{8,9} while the 21 T at Pacific Northwest National Laboratory (PNNL) is 2.4 m.¹⁰ Initial testing of

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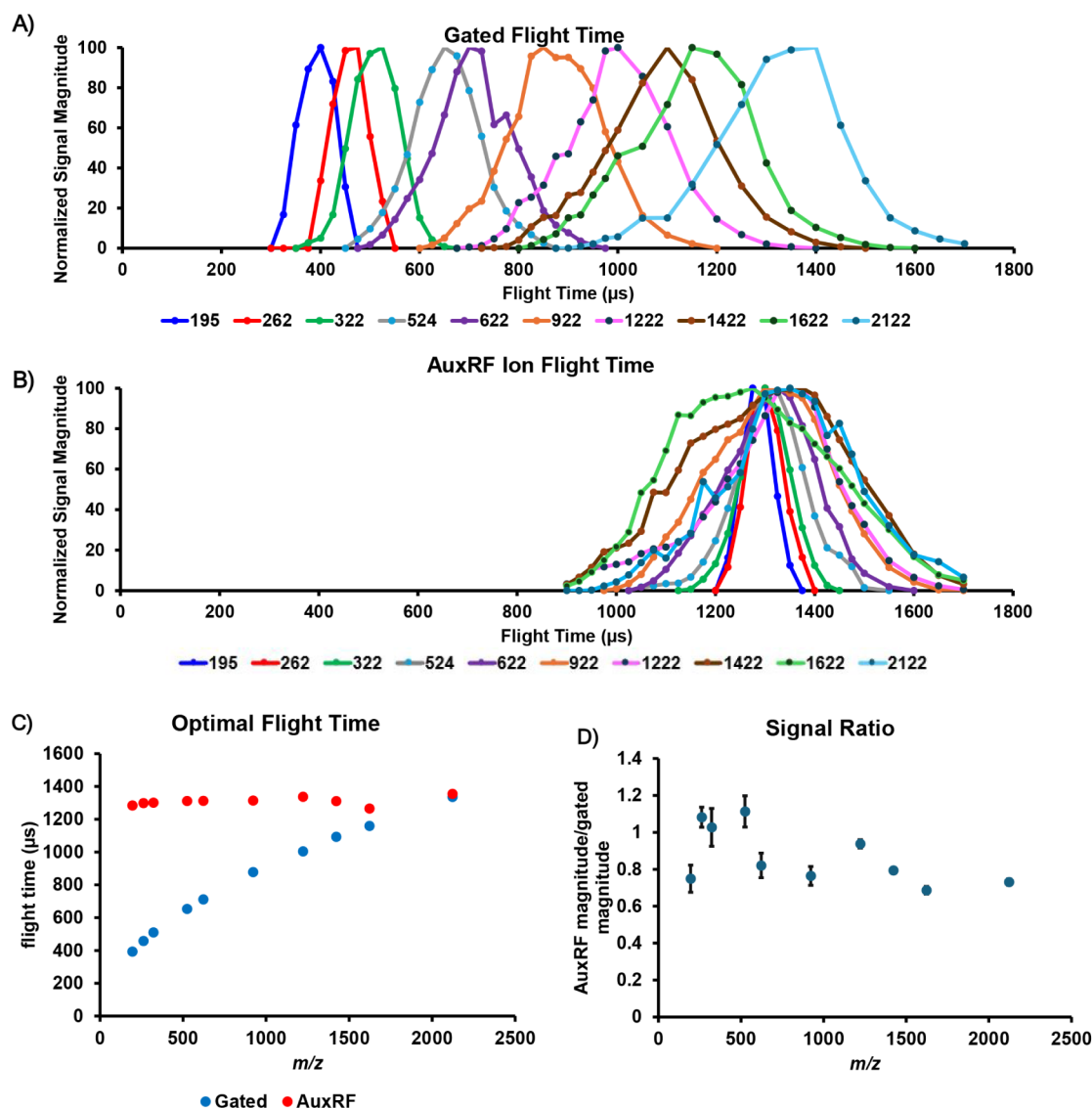


Figure 1. Time-of-flight profiles for different m/z species arriving at the ICR cell. (A) Time-of-flight profile with gated trapping. (B) Time-of-flight profile with AuxRF trapping enabled. (C) Optimal time-of-flight for arrival at the ICR cell. (D) Comparison of signal magnitude obtained in a single optimized AuxRF spectrum to the optimal flight time for each m/z species. Each spectrum consisted of 10 average scans; three separate time-of-flight profiles were recorded and averaged, alternating between gated and AuxRF transfer.

the AuxRF system (GAA Custom Electronics, LLC) was performed on the NHMFL 9.4 T FT-ICR mass spectrometer (Supplementary Figure 1) with FlexMix (Thermo Fisher Scientific). The AuxRF waveform is applied to all rods in the MSD, which creates a symmetrical m/z -dependent pseudopotential barrier between the multipole rods and the MSD lenses.¹¹ The m/z confinement will depend on the AuxRF frequency and amplitude, as well as the offset between the bias to the MSD rods and the exit lens. As the AuxRF voltage is progressively decreased, ions are sequentially ejected from the MSD from high to low m/z .¹² Typical parameters (positive ion mode) used are MSD bias 1 V, exit lens -3 V, main RF drive 2.0 MHz, 450 V_{pp}, and AuxRF drive 1.0 MHz, 500 V_{pp}, with a ramp time of ~ 1 ms. Exact extraction parameters depend on instrument configurations.

Circuit Description

The RF ejection system uses two interconnected resonant RF generators to produce one pair of RF outputs with both phase and antiphase main RF and in-phase AuxRF. The oscillatory frequencies of the two resonant RF generators operate independently. The frequency of the main RF applied for radial ion confinement depends on the capacitive load of the multipoles and the inductance of the

resonant coil. Programmable relays provide termination of the resonant coil across several different lengths (inductive loads), which allows for application-dependent switching of the main RF frequency between 800 kHz and 2.5 MHz with an RF voltage >800 V_{pp}. The auxiliary RF frequency is adjusted to $\sim 1/2$ the main RF frequency with an output of >800 V_{pp}. At 1.0 MHz auxiliary RF frequency and >800 V_{pp}, the highest expected m/z for confinement is >4000 , determined empirically. The auxiliary waveform can be adjusted for multistage linear voltage ramps. The multistage voltage ramp definition is extremely flexible for fine-tuning the time-of-flight profiles as the m/z range of interest increases. Example AuxRF ramp profiles are shown in Supplementary Figure 2.

RESULTS

AuxRF voltage is applied to the MSD rods after ion accumulation has occurred, and ions in the MSD await transfer to the ICR cell for analysis. Ions are actively bunched at the exit of the MSD with an axial voltage gradient.¹³ Once the DC potential applied to the exit lens of the MSD is lowered, high m/z ions that exceed the pseudopotential barrier

created by the AuxRF voltage exit the MSD. The AuxRF voltage is then decreased to sequentially release ions in order of heaviest to lightest m/z from the MSD. The duration of the AuxRF voltage ramp is adjusted to temporally focus the arrival time of the broadest possible m/z range within the ICR cell. Figure 1 shows the normalized signal magnitude at different time-of-flight trapping periods for the typical gated trapping method (Figure 1A) versus the AuxRF ejection method for various m/z species in FlexMix (Figure 1B). The conventional gated trapping method revealed expected time-of-flight profiles, with lower m/z species having shorter optimal flight periods, while with the AuxRF method all ions arrive at the ICR cell at approximately the same time. Also, for both transfer methods, the time-of-flight arrival profile widens with increasing m/z ; therefore, the low m/z species spend the least amount of time in the ICR cell during the transfer event, have the narrowest arrival distribution, and precise ion transfer timing is required for optimal trapping. Tracking the signal magnitude as a function of individual flight time allows reconstruction of the m/z distribution that originated in the MSD compared to the distribution that reaches the ICR cell for detection. Comparison of signal magnitude at the ICR cell eliminates additional biases that may be associated with the transfer process; e.g., the bias would be present in both the gated and AuxRF transfer methods. For hybrid instruments with a detector that allows m/z analysis before the MSD, the transfer parameters are tuned to reduce transmission bias between detectors. Here, the optimal AuxRF flight time was 1.39 ms, with a standard deviation of 25 μ s across all trapped m/z species. With the correct ramp parameters for the AuxRF ejection, the optimal trapping period is independent of m/z (to a first approximation with a linear ramp), while the standard gated trapping is dependent on $m/z^{1/2}$, consistent with time-of-flight theory. Comparison of signal magnitude between trapping methods is shown in Figure 1D. The signal magnitude for optimized AuxRF transfer conditions is compared to the signal magnitude at the optimal flight time with the gated trapping method for each m/z . AuxRF ejection results in >80% of the maximum signal across the m/z range in a single trapping event. With gated trapping, a large voltage gradient is applied along the z -axis of the MSD that extracts the ions from the device in a very narrow period. This exacerbates the time-of-flight dispersion but results in larger signal magnitude over a narrower m/z range. A wider m/z range can be obtained by lowering the axial voltage gradient; therefore, the ions exit the MSD over a longer period. However, this also reduces the maximum observed signal for each m/z species for a single gated-trapping experiment.

The initial AuxRF ejection implementation was limited by the maximum RF V_{pp} amplitude available to create the m/z -dependent pseudopotential barrier and thus limited the highest m/z species that could be contained. Figure 2 shows the optimal flight time that can be obtained with the original AuxRF maximum voltage amplitude (~ 350 V_{pp}), which limits convergence of optimal time-of-flight

to approximately m/z 950, after which the optimal time-of-flight matches the gated trapping results because the pseudopotential is not high enough to contain species $m/z > 950$. With the new AuxRF ejection system, much higher AuxRF voltage is demonstrated, Figure 2 also shows the optimal time-of-flight at higher AuxRF voltage that extends the mass discrimination correction beyond m/z 2000. A ramp time of 1.45 ms with an initial AuxRF amplitude of 600 V_{pp} resulted

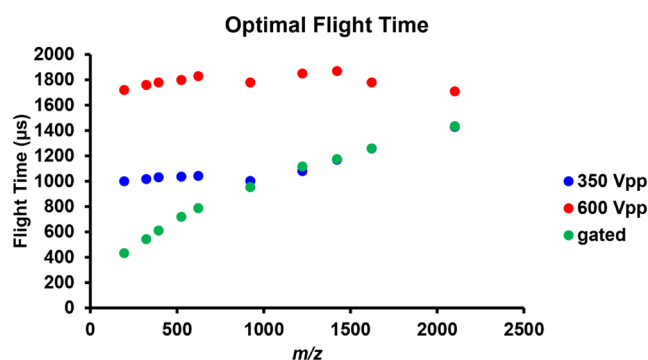


Figure 2. Optimal time-of-flight for arrival at the ICR cell with different initial RF voltages applied for the AuxRF (350 V_{pp} or 600 V_{pp}). The time-of-flight for the gated trapping is included for reference. The AuxRF voltage ramp time profile requires recalibration upon AuxRF voltage change.

in an optimized average time-of-flight of $1.78 \text{ ms} \pm 50 \mu\text{s}$. As ions exit the MSD, they must traverse the m/z -dependent pseudopotential barrier generated by the AuxRF, as the barrier is reduced during the ramp and the m/z cutoff approaches a fraction of that particular m/z species, ions begin to exit the MSD. Therefore, ramp rate reduction allows more time for ions of the appropriate m/z to interact with the pseudopotential barrier. This leads to ions exiting the MSD over a protracted period, which broadens the ions' arrival distribution and reduces maximum observed signal magnitude.

The new AuxRF ejection system has been implemented on several FT-ICR mass spectrometers across two laboratories and features a low barrier for installation and ease of use. Figure 3 shows the mass distribution for FlexMix on the 21 T FT-ICR mass spectrometer, located at PNNL, with and without the AuxRF enabled. Here, the utility of the AuxRF transfer method is demonstrated by increased signal magnitude and a substantial broadening of the effective m/z transmission window. Under standard conditions, efficient transmission is largely confined to a central region ($m/z \sim 900\text{--}1600$), whereas AuxRF enables robust signal across a much wider range ($m/z \sim 200\text{--}2100$), corresponding to an approximate 3-fold expansion in effective transmission bandwidth. Features near the edges of the distribution show the largest gains in signal-to-noise ratio, and several are only observed with AuxRF, consistent with mitigation of time-of-flight discrimination (Supplementary Figure 3). This illustrates that this device is hardware-agnostic, as the instrument configuration on this instrument differs significantly from NIMFL instrument designs. In addition, the hybrid modality of modern instruments incorporates multiple mass analyzers; this provides insight into where mass biases may exist during ion transfer or detection efficiency between analyzers. Ideally, the same m/z distribution and relative signal abundance would be identical across each mass analyzer housed in the same instrument. Supplementary Figure 4 shows the comparison of the m/z distribution for different mass analyzers (ion trap, Orbitrap, FT-ICR) obtained on a custom Eclipse-FT-ICR quaternary hybrid mass spectrometer. The overall m/z distribution is very similar between the different mass analyzers.

CONCLUSION

We describe a dual-resonant RF circuit for ion axial confinement and ejection to eliminate time-of-flight dispersion

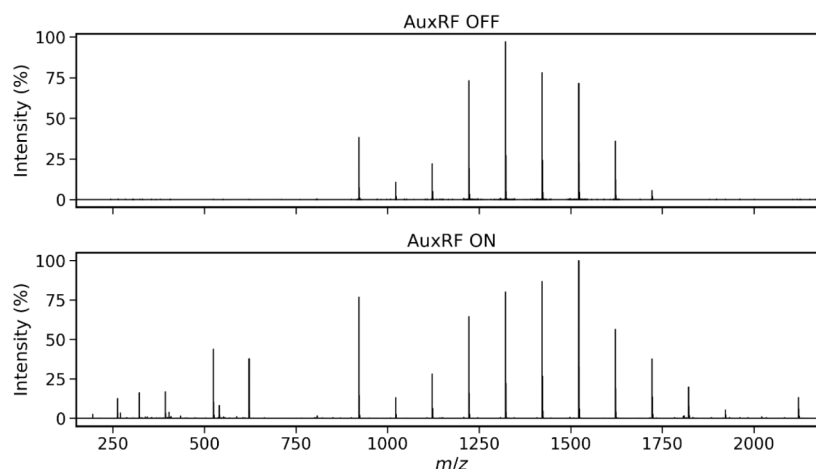


Figure 3. Spectra for FlexMix acquired with AuxRF Off (top) and AuxRF On (bottom) with the 21 T FTICR located at PNNL. Spectral intensities are normalized to the maximum across both data sets. Data were acquired with a 1.5 ms TOF (AuxRF OFF) or 1.8 ms TOF (AuxRF ON). AuxRF settings were a 1.8 ms ramp down from 400 V_{pp} at 855 kHz. Main RF was 1.96 MHz at 800 V_{pp} in both cases. Spectra are a single spectrum with 4 microscan (transient) averages.

in FT-ICR MS. The system is entirely external to the vacuum system, so no modification to in-vacuum hardware is required. The system has been installed on several FT-ICR instruments across multiple laboratories to demonstrate utility and ease of implementation. The new RF axial ejection system provides access to significantly higher RF voltages for confinement of higher m/z species than the initial implementation. An optimized auxiliary RF voltage ramp facilitates efficient ion transmission and trapping across the entire mass range m/z (200–2000) to the ICR cell with a single ion transfer event. The AuxRF ejection system expands the mass range for ion axial confinement beyond m/z of 2000. Under these constraints, a linear voltage ramp no longer satisfied the timing requirements to focus the entire m/z range with a single ion transfer period. Therefore, a multistage AuxRF ramp function is implemented to approximate this nonlinear process and facilitate fine-tuning of the ion arrival time as the m/z range of interest increases. The ion arrival time distribution is slightly increased for AuxRF compared to the normal gated-trapping method. Though the axial ejection method here is demonstrated for FT-ICR MS, it could be implemented on other instrumentation that might suffer from time-of-flight dispersion (i.e., ELIT).

■ ASSOCIATED CONTENT

SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jasms.6c00246>.

- (1) Auxiliary RF waveform for controlled ion extraction,
- (2) detection and sensitivity gain vs m/z with and without AuxRF, and
- (3) broadband spectral comparison between FT-ICR, Orbitrap, and ion trap on the same instrument (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

- (1) Senko, M. W.; Hendrickson, C. L.; Emmett, M. R.; Shi, S. D. H.; Marshall, A. G. External Accumulation of Ions for Enhanced Electrospray Ionization Fourier Transform Ion Cyclotron Resonance Mass Spectrometry. *J. Am. Soc. Mass Spectrom* **1997**, *8* (9), 970–976.
- (2) Kaiser, N. K.; Savory, J. J.; Hendrickson, C. L. Controlled Ion Ejection from an External Trap for Extended m/z Range in FT-ICR Mass Spectrometry. *J. Am. Soc. Mass Spectrom* **2014**, *25* (6), 943–949.
- (3) Smith, D. F.; Podgorski, D. C.; Rodgers, R. P.; Blakney, G. T.; Hendrickson, C. L. 21 T FT-ICR Mass Spectrometer for Ultrahigh-Resolution Analysis of Complex Organic Mixtures. *Anal. Chem* **2018**, *90* (3), 2041–2047.
- (4) Weisbrod, C. R.; Anderson, L. C.; Hendrickson, C. L.; Schaffer, L. V.; Shortreed, M. R.; Smith, L. M.; Shabanowitz, J.; Hunt, D. F. Advanced Strategies for Proton-Transfer Reactions Coupled with Parallel Ion Parking on a 21 T FT-ICR MS for Intact Protein Analysis. *Anal. Chem* **2021**, *93* (26), 9119–9128.
- (5) Bahureksa, W.; Borch, T.; Young, R. B.; Weisbrod, C.; Blakney, G. T.; McKenna, A. M. Improved Dynamic Range, Resolving Power, and Sensitivity Achievable with FT-ICR Mass Spectrometry at 21 T Reveals the Hidden Complexity of Natural Organic Matter. *Anal. Chem* **2022**, *94* (32), 11382–11389.
- (6) Horn, S. A.; Pizzala, N. J.; McLuckey, S. A. Parallel Valet Parking: Selective Ion Escape over an AC Barrier during Ion/Ion Reactions in a Quadrupole Linear Ion Trap. *Can. J. Chem* **2026**.
- (7) Kaiser, N. K.; Quinn, J. P.; Blakney, G. T.; Hendrickson, C. L.; Marshall, A. G. A Novel 9.4 T FTICR Mass Spectrometer with Improved Sensitivity, Mass Resolution, and Mass Range. *J. Am. Soc. Mass Spectrom* **2011**, *22* (8), 1343–1351.
- (8) Hendrickson, C. L.; Quinn, J. P.; Kaiser, N. K.; Smith, D. F.; Blakney, G. T.; Chen, T.; Marshall, A. G.; Weisbrod, C. R.; Beu, S. C. 21 T Fourier Transform Ion Cyclotron Resonance Mass Spectrometer: A National Resource for Ultrahigh Resolution Mass Analysis. *J. Am. Soc. Mass Spectrom* **2015**, *26* (9), 1626–1632.
- (9) Weisbrod, C. R.; Canterbury, J. D.; Senko, M. W.; Babcock-Adamss, L.; Polak, M.; Kaiser, N. K.; Anderson, L. C.; Hakansson, K.; Hendrickson, C. L. Fully Parallelized Tandem MS on a 21 T FT-ICR/Orbitrap/Quadrupole/Ion Trap Hybrid Mass Spectrometer, In *73rd ASMS Conference on Mass Spectrometry and Allied Topics*, Baltimore, MD, ASMS 2025.
- (10) Shaw, J. B.; Lin, T.-Y.; Leach, F. E. I.; Tolmachev, A. V.; Tolić, N.; Robinson, E. W.; Koppenaal, D. W.; Paša-Tolić, L. 21 T Fourier Transform Ion Cyclotron Resonance Mass Spectrometer Greatly Expands Mass Spectrometry Toolbox. *J. Am. Soc. Mass Spectrom* **2016**, *27* (12), 1929–1936.
- (11) Londry, F. A.; Hager, J. W. Mass Selective Axial Ion Ejection from a Linear Quadrupole Ion Trap. *J. Am. Soc. Mass Spectrom* **2003**, *14* (10), 1130–1147.
- (12) Loboda, A. V.; Chernushevich, I. V. A Novel Ion Trap That Enables High Duty Cycle and Wide m/z Range on an Orthogonal Injection TOF Mass Spectrometer. *J. Am. Soc. Mass Spectrom* **2009**, *20* (7), 1342–1348.
- (13) Wilcox, B. E.; Hendrickson, C. L.; Marshall, A. G. Improved Ion Extraction from a Linear Octopole Ion Trap: SIMION Analysis and Experimental Demonstration. *J. Am. Soc. Mass Spectrom* **2002**, *13* (11), 1304–1312.