

Articles

Ion Isolation in a Continuous Zero Angle Reflecting Time-of-Flight Mass Spectrometer

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A continuous zero angle reflecting time-of-flight mass spectrometer capable of tandem mass spectrometry measurements with high resolution and high sensitivity has been developed. The instrument design features two pulsed-ion mirrors in a coaxial geometry. Ions can be reflected back and forth with the mirrors, which increases the net flight length and permits kinetic energy focusing for enhanced resolution. The instrument also contains an electrostatic particle guide which increases ion transmission efficiency and can be used in a bipolar pulsed mode to isolate ions of interest for structural study.

The increasing interest in elucidating biochemical pathways and identification of biomolecules that exist in only trace amounts has made time-of-flight mass spectrometry (TOF-MS) more popular in industrial, academic, and analytical laboratories.¹ Sensitivity in the attomole range has been demonstrated, and the mass range is limited only by the ionization method.^{2–4} The introduction of ²⁵²Cf plasma desorption techniques and matrix-assisted laser desorption ionization (MALDI) extended the mass range, which made TOF-MS useful for biomolecular studies.^{4,5}

Early instruments built for time-of-flight mass spectrometry improved the resolution of the instrument by increasing the length of the flight tube. Increasing the distance between the source and the detector allowed ions having small differences in velocity to become separated in space. Typical flight distances for commercial instruments were often 2–3 m long to provide adequate resolution. In addition to flight tube length, small variations in the kinetic energy imparted to the ions limit the ability to separate ions. Wiley and McLaren addressed this problem in 1955, by focusing the kinetic energy differences to a point in space using a pulsed-ion-source design.⁶ This approach provided a significant resolution improvement, but only a narrow mass region could be focused for any given delay. The approach was modified by Kinsel and

co-workers, who achieved kinetic energy and spatial focusing by applying a voltage pulse to a short field region located after the source.⁷ A major advance in kinetic energy focusing was the introduction of the ion mirror or ion reflector first described by Mamyrin.⁸ This approach works as a velocity-focusing device where isobaric ions having a higher velocity due to a small increase in kinetic energy penetrate deeper into the retarding field and thus spend more time being reflected than ions having the same mass but lower kinetic energy. To simplify focusing characteristics and minimize ion loss, initial designs minimized the angle of incidence relative to the ion reflector. This led to the development of the coaxial reflectron in which the ions were directed into the mass spectrometer through a small orifice in the center of the detector and then reflected back toward the detector at near-zero angles. This approach resulted in high ion transmission and improved sensitivity.

Increasing the flight length of a time-of-flight mass spectrometer using multiple reflection fields was first accomplished using parallel-plate electrostatic fields to reflect the ions back and forth between a 20 cm drift region.⁹ Although this design showed a marked enhancement of the mass resolution, the ion transmission was reduced to 15%.¹⁰ A gridless multireflectron system was introduced by Wollnik, who used discrete reflectron systems to increase both the path length and the resolution of the time-of-flight measurement. In this system, the ultimate length of the flight region was determined by the number of reflectrons used. Recently, two coaxial reflectron systems were also reported that increase the flight length using pulsed reflecting fields.^{11,12} These systems permit an increase in the net flight length by trapping ions between two coaxial reflectrons for a variable period of time. Unfortunately, ion loss and overlap of the multiple trajectories complicate the resultant spectra. To reduce the ion loss during multiple reflections, systems have been built using a quadrupole as an ion guide, thus increasing the transmission efficiency of the system and enhancing the sensitivity of the

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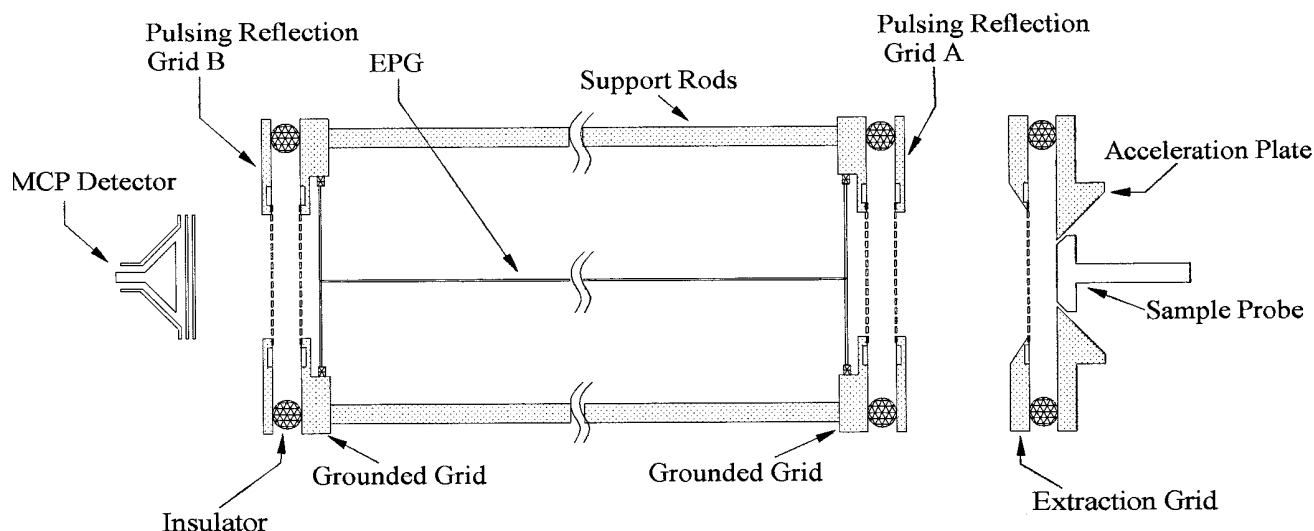


Figure 1. Schematic diagram of the multipass zero angle reflecting time-of-flight mass spectrometer. The voltages on grids A and B are controlled to permit multiple passes of ion packets through the drift region, resulting in extended flight lengths and kinetic energy focusing. High transmission of ions is maintained using an electrostatic particle guide (EPG).

measurements.¹³ An alternate approach for improving the transmission efficiency utilizes an electrostatic particle guide (EPG).^{14–16} Use of an EPG in conjunction with two coaxial reflectrons will capture ions that are accelerated slightly perpendicular to the ion optical axis and transport them to the detector for improved sensitivity.¹¹

Structural analysis in mass spectrometry is usually accomplished using MS/MS (or tandem MS) techniques. A typical MS/MS experiment couples two mass spectrometers in series. The first mass spectrometer isolates a particular ion to be studied. This ion packet is fragmented in the second mass spectrometer to obtain structural information.^{17–19} Use of multiple reflectrons to permit MS/MS studies was demonstrated by Cotter, who employed a tandem reflectron time-of-flight mass spectrometer to study collision-induced dissociation of ions formed by matrix-assisted laser desorption ionization.²⁰ Utilizing pulsed plates, Cotter was able to isolate an ion of interest between the two reflectron regions and use the second reflectron to study the dissociation product ions.

In addition to providing a method for increased ion transmission and therefore improved sensitivity, momentary reversals of the polarity of the potential on the EPG have been shown to be effective for selected ion elimination in time-of-flight mass spectrometry.²¹ Ion isolation using the radially homogeneous field lines produced by an EPG reduces the effects of positionally dependent ion acceleration often observed when ions are eliminated using pulsed plates. By combining pulsed repulsive and attractive potentials, the EPG eliminated low-mass background ions and

increased the transmission efficiency of higher mass ions.²² This technique also increased the signal-to-noise ratio by reducing detector saturation.

The instrument presented here utilizes two coaxial ion reflectors and a bipolar pulsed EPG to provide a method for high transmission and ion isolation in a multireflection system. The source, detector, and analyzers are on the same axis of ion motion, creating a continuous zero angle reflecting (CZAR) time-of-flight mass spectrometer. The incorporation of the EPG reduces ion loss during multiple reflections and permits a facile method of ion isolation and elimination of unwanted ions. This feature reduces the complexity of resultant spectra as well as a permitting a simple method for ion selection in tandem mass spectrometry experiments with both high resolution and high sensitivity.

EXPERIMENTAL SECTION

A schematic of the instrument is shown in Figure 1. Ions were produced by laser desorption from a stainless steel insertion probe which made contact with a floated acceleration plate. The ions were extracted by the potential difference between the acceleration plate and an extraction grid separated by a 6 mm insulator. Ions moved down the flight tube through an initially grounded grid (grid A) and a permanently grounded grid at the entrance of the drift region and interacted with the EPG located in the drift region. Upon exiting the drift region, the ions encountered a second isolated grid (grid B) prior to striking the detector.

The trajectory of the ions in a multipass flight is illustrated in Figure 2. If the voltage applied to grid B is higher than the source acceleration voltage, the potential barrier will reflect ions back toward the source optics (Figure 2A). If the voltage on the initially grounded grid A is switched to a higher positive voltage before the reflected ions arrive, the ions will be repelled again (Figure 2B). Finally, if grid B is switched to ground potential, the ions pass through for detection. The ions are reflected between

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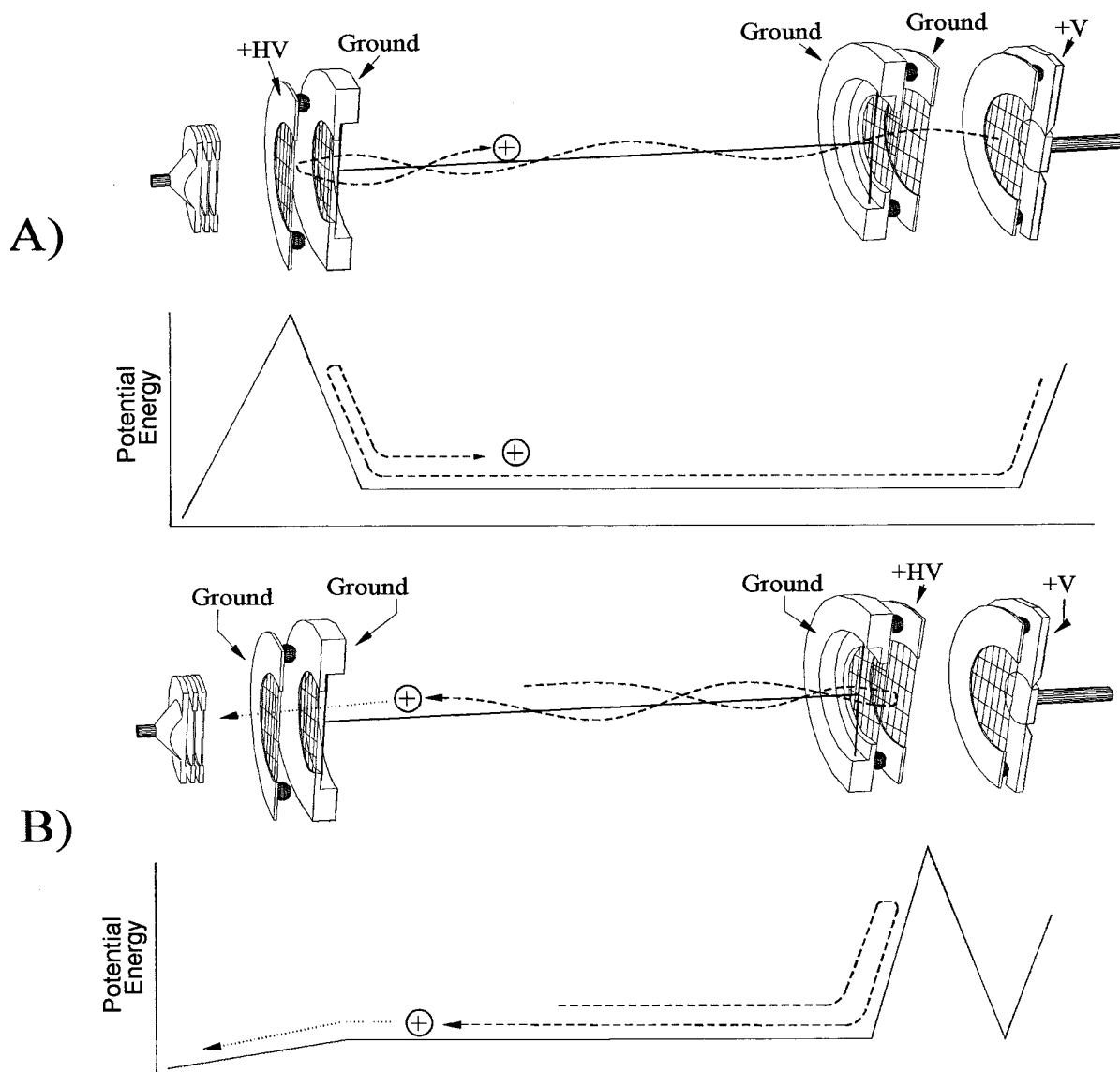


Figure 2. Schematic representation of the theory of operation. Ions are accelerated into the drift region through an initially grounded grid A (part A). The first reflectron region created by the potential on grid B initially reflects the sample ions back toward the source optics. Following acceleration into the drift region, the voltage on grid A is switched to a higher potential than that of the ion source (part B), causing ions to be reflected toward the detector. When the voltage on grid B is switched to ground potential, the ions exit the drift region for detection.

the ion mirrors for as long as the voltages are applied, so the net ion flight length can be manipulated by the instrument electronics.

The voltage was held at +5 kV on the source acceleration plate and at +1.5 kV on the extraction grid. Grid A, initially held at ground potential, provided secondary ion acceleration. Ions were generated by laser desorption using a Continuum MiniLite Nd: YAG laser that was frequency-tripled to 355 nm. The beam intensity was controlled using a translational shutter. The laser was focused using external optics into the vacuum chamber at a 45° angle with respect to the probe surface. The ion drift region, isolated on each end by a permanently grounded mesh, originated 11 cm from the ion source and was 66 cm long. Ions were detected using a Comstock CP625/M microchannel plate detector with chevron geometry located 11 cm from the exit of the ion drift region. The 50 Ω output of the detector was shunted to ground potential by a terminator, and the image current was digitized

using a LeCroy 9310 digital sampling oscilloscope (100 megasamples/s). Background pressure for the system was maintained at 2×10^{-9} Torr by a Pfeiffer/Balzers TPU 220 turbomolecular pump.

The electrostatic particle guide (EPG) consisted of a 0.25 mm diameter stainless steel wire suspended down the center of the ion drift region. The 60 cm wire was supported by isolated cross-hair wires. The voltage on the EPG could be externally controlled to permit two different modes of operation. In the electrostatic mode, the voltage placed on the EPG was adjusted to maximize ion transmission. Placing a static negative potential on the EPG permits the particle guide to increase transmission of the ions while in the drift region. Typical voltages used in the electrostatic mode were adjusted between -100 and -150 V. The electric field created by the negative potential on the EPG reduces the ion loss due to diverging trajectories following ion reflection in the two reflectron regions. In a bipolar pulsed mode, the EPG voltage

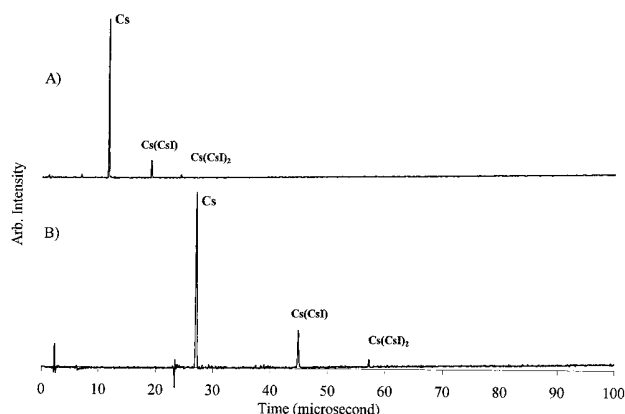


Figure 3. Time domain time-of-flight spectra for cesium iodide. (A) Time-of-flight spectrum for CsI accelerated straight through the flight tube with +5 kV of accelerating potential. The spectrum shows the arrival of the Cs^+ ion (m/z 133) at 11.5 μs , $\text{Cs}(\text{CsI})^+$ (m/z 393) at 18.5 μs , and $\text{Cs}(\text{CsI})_2^+$ (m/z 653) at 23.2 μs . (B) Zero angle reflecting time-of-flight spectrum using the pulsed reflecting grids A and B. The ions that were previously detected at 11.5, 18.5, and 23.2 μs are now seen at 27, 45, and 57 μs for Cs^+ , $\text{Cs}(\text{CsI})^+$, and $\text{Cs}(\text{CsI})_2^+$, respectively.

could be rapidly changed between +100 and -100 V. This momentary reversal of the polarity permits selective ion elimination by creating a deflection field during the ion flight. The voltage on the EPG during the bipolar pulsed mode was controlled using an R. M. Jordan 1040 remote pulsing circuit. Rise times for the pulsed circuit were less than 10 ns. The duration of the variable delay and the pulse width were controlled using a simple timing circuit triggered with the laser pulse.

The pulsed reflectron grid voltages were controlled using individual Behlke HTS 121 high-voltage transistor switches available from Eurotek, Inc. (Morganville, NJ). The switches were designed as both high-side and low-side configurations to provide both rapid fall times from 8 kV to ground potential on grid B and rapid rise times from ground potential to 8 kV on grid A in less than 500 ns. All events were timed using a Stanford Research DG535 programmable four-channel digital delay/pulse generator.

RESULTS AND DISCUSSION

The ability of the instrument to reflect ions using coaxial reflectrons with the EPG in the electrostatic mode is illustrated in Figure 3. Figure 3A is the spectrum for cesium iodide obtained without the use of the reflectrons. The spectrum shows the arrival of the Cs^+ ion (m/z 133) at 11.5 μs , $\text{Cs}(\text{CsI})^+$ (m/z 393) at 18.5 μs , and $\text{Cs}(\text{CsI})_2^+$ (m/z 653) at 23.2 μs . The ions traveled straight through the instrument corresponding to a flight length of 88 cm. Figure 3B shows the zero angle reflecting spectrum using the pulsed reflecting grids A and B. The voltage on grid B was initially +8 kV. The spike at 4 μs corresponds to inductive detection of the voltage change on grid A from an initial ground potential to +8 kV following ion extraction and acceleration into the drift region. The ions that were once detected at 11.5, 18.5, and 23.2 μs are now seen at 27, 45, and 57 μs for Cs^+ , $\text{Cs}(\text{CsI})^+$, and $\text{Cs}(\text{CsI})_2^+$, respectively. The increased peak separation resulted from increasing the net flight length from 88 to 220 cm. The increase of 132 cm corresponds to one additional flight back and forth in the 66 cm drift region. The negative voltage spike at 23 μs marks

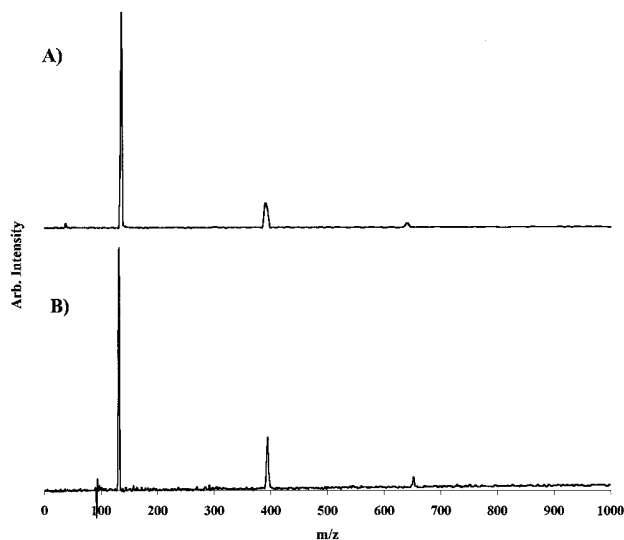


Figure 4. Mass-calibrated CsI spectra from the time domain spectra shown in Figure 3. The resolution obtained from a single pass through the drift region (A) is increased by a factor of 5 when the ions are reflected one time (B).

the switch from +8 kV to ground potential on grid B. Ion transmission was maximized using a negatively charged EPG.

In addition to increasing the net flight path, the dual reflectron fields provide kinetic energy focusing. The enhancement in mass resolution is illustrated in Figure 4, showing the mass-calibrated spectra from the time domain spectra shown in Figure 3. The resolution obtained from a single pass through the drift region (Figure 4A) was increased by a factor of 5 when the ions were reflected one time (Figure 4B). Adjusting the depth of the reflecting fields and the acceleration potential could further enhance the resolution.

The effect of continuously reflecting the ions between grids A and B with the EPG in the electrostatic mode is illustrated in Figure 5. Figure 5A shows the spectrum for Cs^+ , $\text{Cs}(\text{CsI})^+$, and $\text{Cs}(\text{CsI})_2^+$ following a nonreflected flight through the drift region with arrival times of 12, 19, and 23 μs , respectively. When the voltage on grid B was switched from an initial +8 kV to ground potential 22 μs after ion formation (Figure 5B), the three ions arrived at 25, 43, and 55 μs following a 220 cm flight. When grid B was switched to ground potential 30 μs after ion formation (Figure 5C), the Cs^+ ion was reflected twice, traveling 352 cm in 40 μs . Since grid B was switched to ground potential prior to the arrival of $\text{Cs}(\text{CsI})^+$ and $\text{Cs}(\text{CsI})_2^+$, their arrival times remained unchanged at 43 and 55 μs , respectively. When the voltage on grid B was pulsed to ground potential 42 μs after ion formation (Figure 5D), the Cs^+ ions were reflected three times (484 cm flight) and arrived at 53 μs , $\text{Cs}(\text{CsI})^+$ was reflected two times (352 cm) and arrived at 68 μs , and $\text{Cs}(\text{CsI})_2^+$ arrived following a single reflection (220 cm) in 55 μs .

Continuous reflection between the ion mirrors is possible, but potential ion scrambling can make spectral interpretation difficult. In addition to ion arrival times becoming scrambled in their relative flight paths, peak broadening occurs during multiple reflections. Although there was a clear improvement in the resolution for multiple passes relative to a nonreflected path, the gain in resolution decreased for multiple passes through the drift

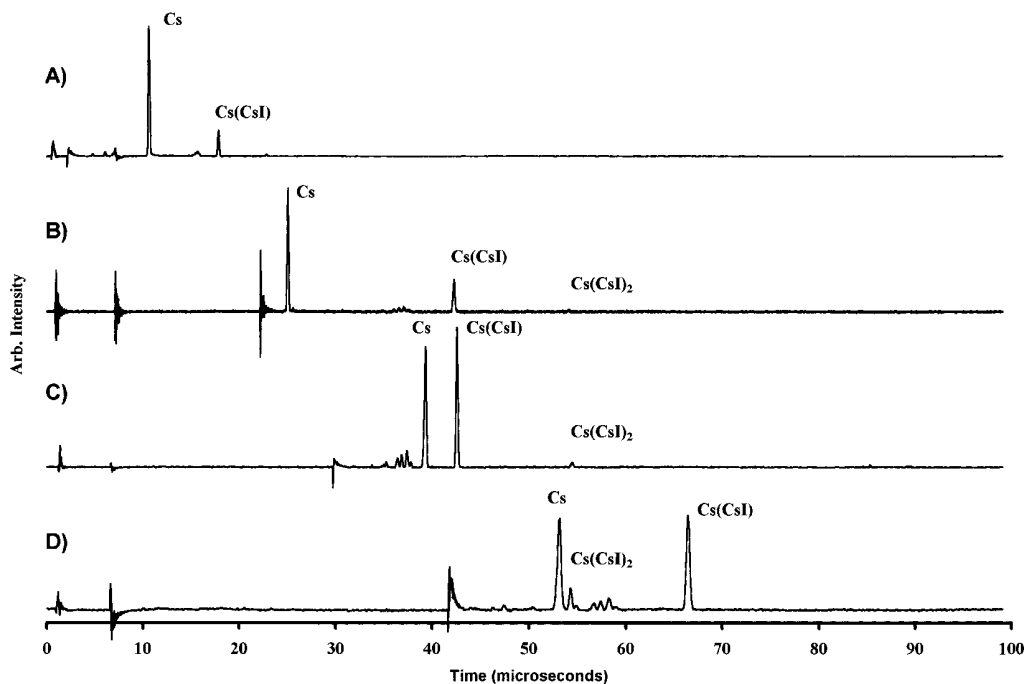


Figure 5. Spectra showing the effect of extended reflection of Cs ion packets using the coaxial reflectrons. The voltage on grid B is switched to potential at (A) 3 μ s after ionization, permitting a straight path through the instrument and an 88 cm flight length, (B) 22 μ s after ionization, creating an effective 220 cm flight region, (C) 30 μ s after ionization, creating a 352 cm flight length for the Cs⁺ ions, and (D) 42 μ s after ionization, creating a 484 cm flight length for the Cs⁺ ions.

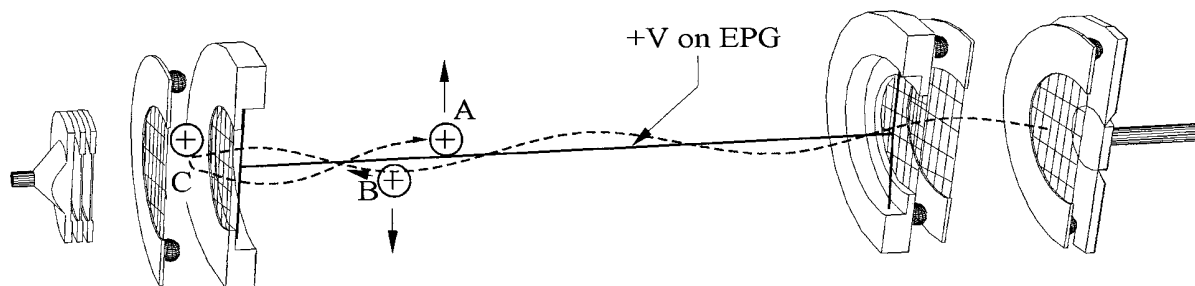


Figure 6. Conceptual diagram showing how a bipolar pulsed EPG can selectively eliminate or isolate ions. When the bipolar EPG is pulsed to a positive voltage, ions in the drift region (positions A and B) are repelled from the ion optical axis and are eliminated. If the ions of interest are in a reflectron region (position C) when the EPG is pulsed, the ions will be shielded from the repulsive potential and will not be eliminated.

region. For example, in Figure 5B, the peak width for the Cs⁺ ion packet detected following a single reflection through the drift region ion path was 160 ns, corresponding to a ΔM of 1.7 amu. When the Cs⁺ ion packet was reflected three times through the drift region (Figure 5D), the peak width was increased to 400 ns, corresponding to a ΔM of 2.0 amu. The loss of resolution observed results from the difficulty in accurately focusing the kinetic energy of the ion packets following multiple reflections and field imperfections in the ion optics used. The inability to focus the kinetic energy differences of ion packets by accurately matching the focal plane of the reflectrons with the detector position following multiple passes results in the loss of resolution in Figure 5D.

Selective ion elimination using the coaxial reflectrons can reduce spectral complexity and provide a method of ion selection for potential chemical studies. Fast moving (low mass) ions can be eliminated if grid A is kept at ground potential while these ions pass through. The potential can then be raised to reflect slower moving (high mass) ions to the detector. The bipolar pulsed EPG can also be used for ion selection. When the bipolar

EPG is pulsed to a positive voltage, ions in the drift region (Figure 6, positions A and B) are repelled from the ion optical axis and are eliminated. If the ions of interest are in a reflectron region (Figure 6, position C) when the EPG is pulsed, the ions will be shielded from the repulsive potential and will not be eliminated. Figure 7 shows the spectra for Cs⁺ (Figure 7A) and Cs(CsI)⁺ (Figure 7B) isolated using the EPG in the bipolar pulsed mode. This isolation eliminates the problems associated with ion scrambling. Furthermore, because the ions are isolated while still in the flight region, tandem experiments using the second reflectron as a kinetic energy analyzer are possible without the addition of a second flight region.

CONCLUSIONS

A continuous zero angle reflecting time-of-flight mass spectrometer allowed multiple passes of ions through a single drift region. The effective flight length was increased without increasing overall instrument size, and the electrostatic particle guide was useful for maintaining high ion transport efficiency. The dual

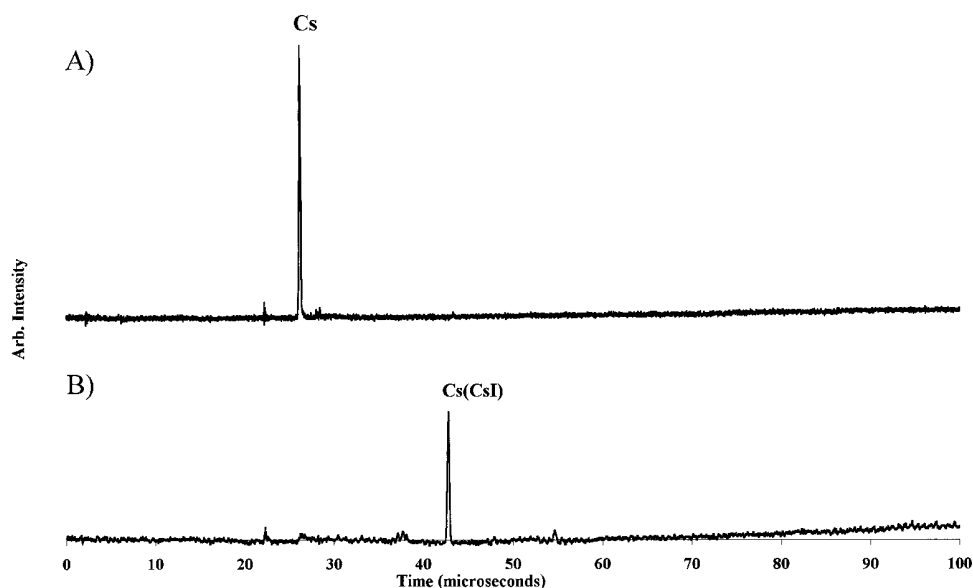


Figure 7. Spectra showing selective isolation of Cs^+ ions (A) and $\text{Cs}(\text{CsI})^+$ ions (B) using bipolar pulsing of the EPG.

coaxial reflectrons improved the mass resolution by focusing kinetic energy differences of isomass ions.

Ion scrambling can occur if the potentials on the reflectrons are not controlled carefully. Ions of low mass were shown to arrive later than higher mass ions when the voltage on grid B was switched to ground potential following the reflection of high-velocity ions. The bipolar pulsing EPG permitted ion selection and eliminated unwanted background signals. Since the selected ions were in the reflectron region during ion ejection, there were no calibration problems caused by misdirected acceleration. Ion selection can eliminate ion-scrambling problems. The ability to select specific ions expanded the potential of the multipass system to perform tandem mass spectrometry experiments without the addition of a second mass analyzer. The system simplicity and

increased functionality combined with the ability to perform MS/MS experiments illustrate how instruments with this design can compete with more costly dual-analyzer systems.

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