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Simultaneous Isolation of Nonadjacent *m/z* Ions Using Mirror Switching in an Electrostatic Linear Ion Trap

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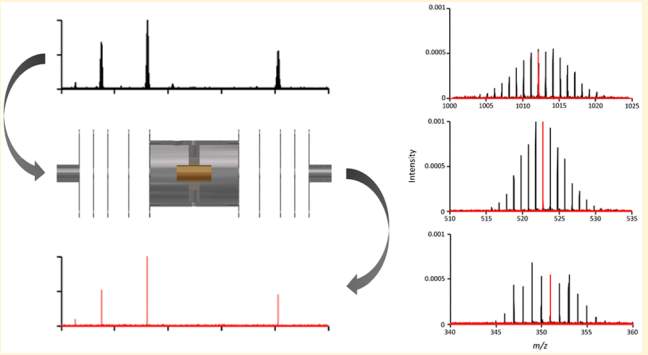
Supporting Information

ABSTRACT: Simultaneous isolation of ions of disparate mass-to-charge (*m/z*) ratios is demonstrated via appropriately timed pulsing of entrance and exit ion mirrors in an electrostatic linear ion trap (ELIT) mass spectrometer. Manipulation of the voltages of the entrance and exit mirrors, referred to as "mirror switching", has been demonstrated as a method in which ions can be both captured and isolated. High resolution isolation (>35 000) was previously demonstrated by selective gating of trapping electrodes to avoid ion lapping while closely spaced ions could continue to separate [Johnson et al. *Anal. Chem.* **2019**, *91*, 8789]. In this work, we demonstrate that advantage can be taken of the ion lapping phenomenon in an ELIT to enable the simultaneous isolation of ions of disparate *m/z* ratios using mirror switching. This process is demonstrated with minimal ion loss using isotopologues of three carborane compounds ranging in *m/z* from 320 to 1020. Simultaneous isolation is demonstrated with the isolation of two and three peaks in separate isotopic distributions as well as with the isolation of alternating isotopologues within the same distribution. Such simultaneous isolation experiments are particularly useful when conducting experiments in which a mass calibrant is needed or when multiplexing in a tandem MS workflow.



Applications for the simultaneous isolation of ions of nonadjacent *m/z* ratios include mass calibration[1,2] and multiplexing in tandem mass spectrometry.[3−5] Studies using simultaneous ion isolation have primarily used ion trapping instruments in conjunction with tailored waveforms such as correlated harmonic excitation fields (CHEF)[6,7] and stored waveform inverse Fourier transform (SWIFT),[8] broadband isolation techniques that operate by generating a tailored waveform that excites and ejects unwanted ions over time. Numerous techniques have been demonstrated for ion isolation within multiple reflection time-of-flight (MR-TOF) devices.[9−14] Of these methods, only one has demonstrated simultaneous isolation of multiple ion species of disparate *m/z*.[15] This isolation method uses selective modulation of an in-trap deflector consisting of two electrodes at the frequencies of the ions of interest. The deflector is at ground when the ions of interest are in the deflector region and at a low deflection voltage when the ions of interest are outside of the deflector region. This method, like SWIFT and CHEF, relies on an auxiliary signal to alter the trajectories of unwanted ions over time until they are ejected.

Mirror switching has been demonstrated as a method for high resolution and high efficiency ion isolation in an electrostatic linear ion trap (ELIT).[9] In addition, this method can be used to selectively retain multiple ions of disparate *m/z* ratios on the basis of their temporal/spatial overlap within the device. Unlike these other isolation methods, mirror switching relies solely on the instantaneous positions of ions in relation to the switching electrode. As a result, advantage can be taken of the high spatial and temporal separation achieved in relatively short time scales in MR-TOF experiments. In this work, a method based on mirror switching for simultaneous isolation of ions of nonadjacent *m/z* ratios is described and demonstrated. Efficient isolation of a single isotopologue each from two and three isotopic distributions of a mixture of three carborane ion populations is demonstrated. Furthermore, a method for simultaneous isolation of equally spaced ions in a narrow *m/z* range is also described and illustrated using a carborane ion isotopic distribution. Finally, an internal mass calibration is demonstrated by simultaneously isolating three calibrant ions from a tuning mixture and a single charge state of insulin.

EXPERIMENTAL SECTION

Materials. A mixture of carboranes consisting of $AgCH_{11}H_5Cl_6$, $CsCHB_{11}Cl_{11}$, and $AgCHB_{11}Br_{11}$ (100 μM each) was prepared in a solution using 50/50 (v/v) MeOH/H_2O. The carboranes were synthesized and provided by Professor C. A. Reed's group at the University of California, Riverside, Department of Chemistry. Methanol was purchased from Sigma-Aldrich (St. Louis, MO). Water was purchased

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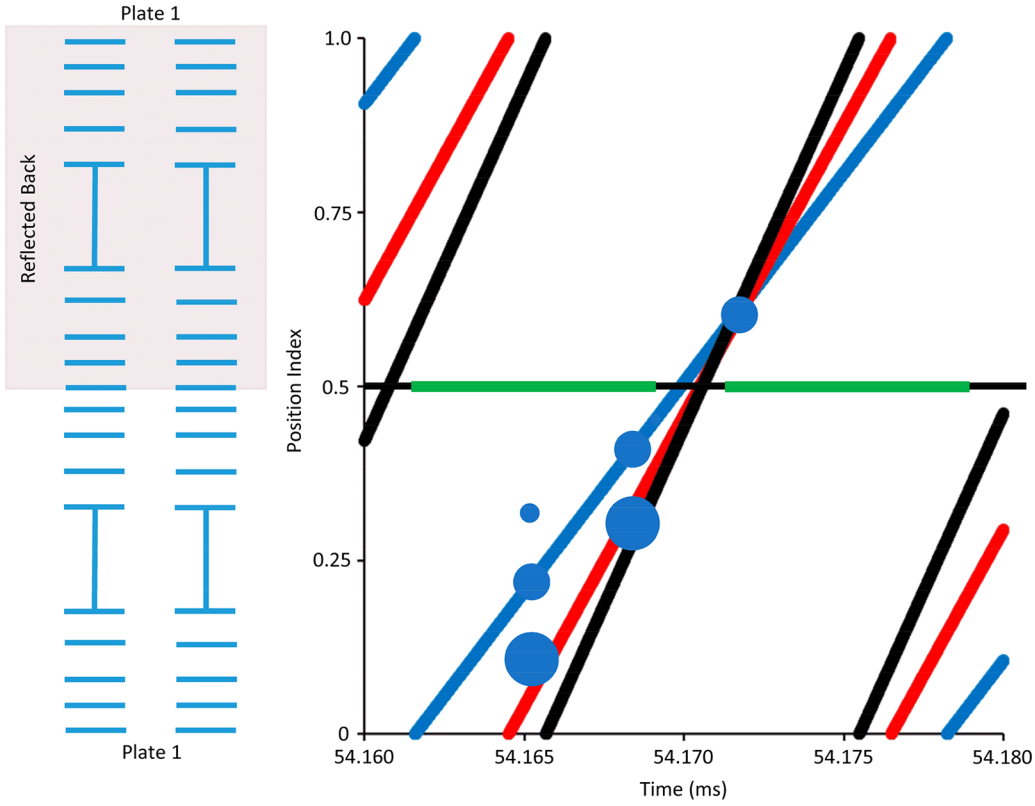

Figure 1. Trajectories of three ions, shown by lines (m/z 350.99 in black, m/z 522.76 in red, and m/z 1012.21 in blue). Neighboring isotopologues of the 1012.21 ion are depicted as circles, with the lighter isotopologue ahead in position of the 1012.21 ion, and the heavier isotopologue lagging behind. A position index of 0.5 corresponds to an ion located at plate 8, whereas between 0.5 and 1.0, the ion is traveling from 8 back to plate 1 (gray area). The cartoon depicting the device is mirrored about plate 8 such that a single period of ion motion is represented on the y-axis. A mirror switching pulse is depicted as a green window at plate 8, spanning the length of the isolation pulse. As long as plate 8 is pulsed back up to trapping voltage in time for the 1012.21 isotopologue to reach it (blue line), the light and heavy isotopologue of this distribution can be let out while the 1012.21, 522.76, and 350.99 m/z species are retained.

from Mallinckrodt (Phillipsburg, NJ). Insulin (from bovine pancreas) was purchased from Sigma-Aldrich (St. Louis, MO). Insulin was prepared to a final concentration of 20 μM in 49.5/49.5/1 (v/v/v) MeOH/H_2O/AcOH. LC/MS tuning mix for ESI (G2421A) was purchased from Agilent Technologies (Santa Clara, CA).

Mass Spectrometry. All experiments were carried out on a home-built 5.25″ ELIT that has been described previously.[16] The nanoelectrospray ionization (nESI) source and the method by which ions are concentrated and injected into the electrostatic linear ion trap (ELIT) have been described previously, and a brief description is provided in the Supporting Information.[17] Procedures for obtaining mass spectra via Fourier transformation (FT) have been described, and a short summary is provided in the Supporting Information.[16] On the basis of the gain of our detection circuitry, the number of charges associated with the experiments described herein is estimated to be on the order of 5000.

Ion Isolation. Ion isolation was performed by pulsing of the first plate of the ELIT (plate 1) or the last plate (plate 8) or both from their nominal trapping potentials (~2360 V) to ground at some specified time after ion injection. The time in which the electrodes were pulsed and the duration they were held at ground was set by a pulse/delay generator (model 575, Berkeley Nucleonics, San Rafael, CA). A home-built digital signal joiner was used to combine waveforms from multiple signal sources such that a single mirror could be pulsed multiple times by coupling up to three input TTL signals. Mirror switching was done using ORTEC 556 power supplies and solid-state switches (HTS 31-03-GSM, Behlke Electronics GMBH, Kronberg, Germany).

RESULTS AND DISCUSSION

In a closed-loop MR-TOF device, such as an ELIT, all ions of a given m/z ratio either lap or are lapped by ions of other m/z ratios (i.e., the racetrack effect) given a sufficiently long storage time. To avoid ambiguities due to ion lapping in single ion isolation experiments using mirror switching, care must be taken to release potentially lapped or lapping ions while ions of very similar m/z ratio can continue to separate. This can be done via the judicious timing of ion release events to manage the trapped mass range inside the device. The racetrack effect can be exploited, however, if more than one ion species of disparate m/z ratios is to be isolated simultaneously as in, for example, a tandem MS workflow. In the following, we describe and illustrate multiple ion isolation in the general case, which makes no constraint on the difference in m/z ratios of the selected ions, and in a special case, in which multiple ions of a small relative Δm are to be selected simultaneously.

Timing of Ion Release Events for Multiple Ions of Arbitrary Δm. Prediction of ion position and direction in the ELIT is necessary in establishing the timing for ion release in a multiple ion isolation experiment. The instantaneous ion position and direction in the ELIT is related to the number of

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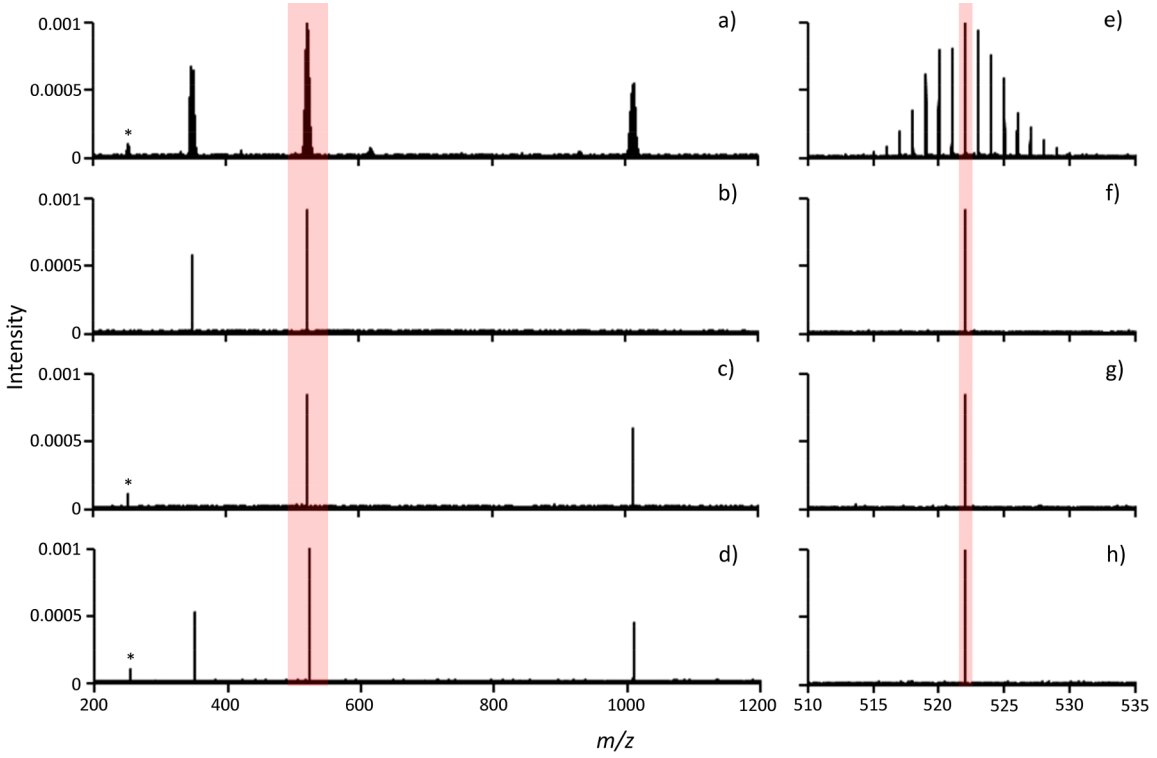

Figure 2. (a) eFT mass spectrum of $CHB_{11}H_5Cl_6^-$ (349.70 average m/z), $CHB_{11}Cl_{11}^-$ (523.51 average m/z), and $CHB_{11}Br_{11}^-$ (1012.56 average m/z). (b) Simultaneous isolation of m/z 350.99 and 522.76. (c) Simultaneous isolation of m/z 522.76 and 1012.21. (d) Simultaneous isolation of a single isotopologue from each of the three carborane distributions (m/z 350.99, 522.76, and 1012.21). (e–h) Zoom-ins of the $CHB_{11}Cl_{11}^-$ distribution for each adjacent mass spectrum. All isolations were done after a separation time of 54.25 ms. All eFT spectra are averages of 100 transients of 500 ms. The asterisks (*) denote the second harmonic of $CHB_{11}Br_{11}^-$.

laps an ion has undergone after its initial entrance into the ELIT. This includes the number of laps after the plate 1 ion mirror is pulsed high to trap injected ions plus the fractional lap that each injected ion undergoes once it enters the ELIT and before plate 1 is pulsed high. Because of the m/z dependent flight time differences of the ions injected from the accumulation quadrupole, trapped ions of each m/z ratio undergo a unique fraction of one lap prior to the initial plate 1 mirror switch. When ions have experienced half a lap, they are positioned at the turning point near plate 8, and when ions have experienced an integer lap number, they are located at the turning point near plate 1. The fractional lap value can be denoted as a position index in which ions at plate 8 have a position index of 0.5 and ions at plate 1 have a position index of 0 or 1, depending on whether they are traveling to or from plate 8. Position indices of 0.0−0.5 denote ions moving in the direction of plate 8, whereas position indices of 0.5−1.0 indicate ions moving in the direction of plate 1. Hence, determination of the fractional lap number from the instant an ion enters the ELIT as a function of time indicates the position and direction of the ion. A Matlab script (MATLAB 2019a) was written to calculate position indices as a function of time for multiple ions at the same time.

Figure 1 is provided to illustrate a pulse sequence that could be used to isolate simultaneously three ions from three distinct isotopic distributions using a plot of position index versus storage time (corrected for the fractional lap number for each m/z value of interest). The position index versus time plots for m/z 350.99 (black line), m/z 522.76 (red line), and m/z 1012.21 (blue line) over a 20 μs time period is provided in the figure along with a diagram that relates the position index to plate locations in the ELIT. The schematic diagram of the ELIT plates on the left indicates that position indices of 0.0−0.5 relate to ions moving in the direction from plate 1 to plate 8 and that position indices of 0.5−1.0 relate to ions moving in the direction from plate 8 to plate 1. Three blue dots of small, medium, and large size represent the next smaller isotopologue (smallest dot) and next larger isotopologue (large dot) of the m/z 1012.21 ion (medium dot) at three distinct storage times. The solid horizontal line indicated at position index 0.5 represents the voltage applied to the plate 8 mirror. Black represents the full voltage of the mirror, which is effective at reflecting (storing) ions, whereas green represents a potential that releases ions from the trap. This diagram shows that the plate 8 voltage can be dropped anywhere between the first intersection of the m/z 350.99 line with the 0.5 position index and the corresponding intersection of the m/z 1012.21 line to release any ions that approach plate 8 during that period, including the lighter isotopologue of the m/z 1012.21 ion. To retain the three ions of interest, it is necessary to restore the plate 8 voltage to the trapping level prior to the first intersection of the blue line with position index 0.5 until just after the second intersection of the black line with 0.5 position index. Plate 8 can then be pulsed down to release ions until such time that the m/z 350.99 ion returns to plate 8. An analogous process can be repeated, as necessary, to remove any residual untargeted ions whenever the three ions of interest are in close proximity.

Simultaneous isolation is demonstrated in Figure 2 using centrally located isotopologues of three carborane ion distributions: $CHB_{11}H_5Cl_6^-$ (349.70 average m/z), $CHB_{11}Cl_{11}^-$ (521.92 average m/z), and $CHB_{11}Br_{11}^-$

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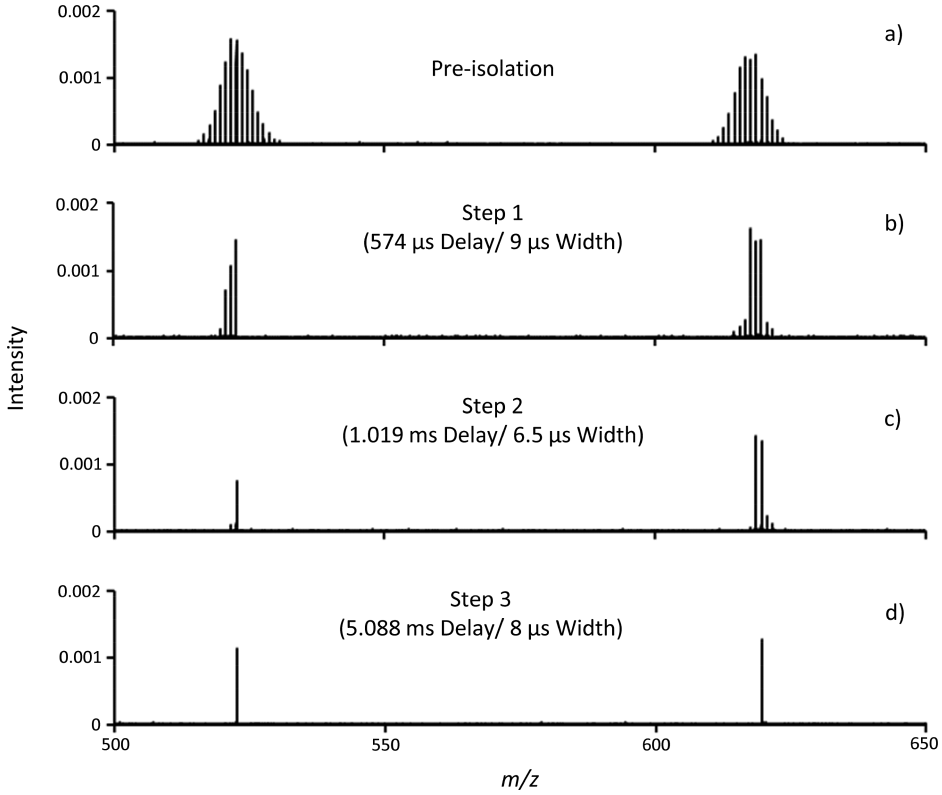

Figure 3. eFT mass spectra demonstrating stepwise simultaneous isolation of m/z 520.76 and 619.68 from a mixture containing $CHB_{11}Cl_{11}^-$ (521.92 average m/z) and $CHB_{11}H_5Br_6^-$ (616.40 average m/z). (a) Mass spectrum prior to any isolation steps. (b) Mass spectrum after a single mirror switching isolation pulse after 574 μs of storage. (c) Mass spectrum after the addition of a second mirror switching isolation pulse after 1.019 ms of storage. (d) Mass spectrum after the addition of a third mirror switching isolation pulse after 5.088 ms of storage. These spectra are averages of 100 transients of 500 ms.

(1012.56 average m/z). The three distributions prior to ion isolation are shown in Figure 2a. Figure 2b shows the isolation of the m/z 350.99 and 522.76 ions from the $CHB_{11}H_5Cl_6^-$ and $CHB_{11}Cl_{11}^-$ distributions, respectively, whereas Figure 2c shows the isolation of the m/z 522.76 and 1012.21 ions from the $CHB_{11}Cl_{11}^-$ and $CHB_{11}Br_{11}^-$ distributions, respectively. These two spectra illustrate that ions of any two arbitrary m/z ratios can be isolated simultaneously. Simultaneous isolation of three ions of interest (m/z 350.99, 522.76, and 1012.21) is shown in Figure 2d. The isolation efficiency for each case is illustrated in Figure 2e–h, which compares the preisolation $CHB_{11}Cl_{11}^-$ distribution (Figure 2e) with the isolated m/z 522.76 ion following the three isolation experiments (Figure 2f–h). In all three cases, the pre- and postisolation abundances of the m/z 522.76 ion are observed to be within the experimental variation of the carborane distribution signal. (The pre- and postisolation results for all three carborane distributions associated with the experiment of Figure 2d are provided in Figure S-1, again showing ion isolation efficiency to be within the reproducibility of the abundance measurement.) A total storage time of 54.25 ms was used for all three isolation examples. In the case of the simultaneous isolation of three ions (Figure 2d,h), four ion overlap events were chosen and used for successive release (via plate 8) of unwanted isotopologues (see Table S-1 for pulse times and widths).

Figure 3 illustrates the stepwise release of ions resulting in simultaneous isolation of the m/z 520.76 and 619.68 ions from a mixture containing $CHB_{11}Cl_{11}^-$ (521.92 average m/z) and $CHB_{11}H_5Br_6^-$ (616.40 average m/z). In this example, the m/z range is small enough to clearly see the individual isotopologues of each distribution during the stepwise ion release process. Figure 3a shows the preisolation mass spectrum of the two isotopic distributions. Figure 3b–d shows the remaining ions after each ion release event (plate 8) with the timing of the steps shown in the figure. In this case, the isolation could be affected in slightly over 5 ms.

One of the applications for the simultaneous isolation of multiple ions of disparate m/z ratios is the inclusion of ions of known m/z for mass calibration associated with the measurement of the m/z of an analyte of interest. A simple example is provided in Figure 4, which shows the results for the simultaneous isolation of three calibrant ions (m/z 622.029, 922.010, and 1521.971) generated from a tuning mix supplied by Agilent for LC/MS calibration along with the $[M + 4H]^{4+}$ ions generated by nano-ESI of bovine insulin (Figure 4a). Figure 4b shows a blow-up of the experimental insulin $[M + 4H]^{4+}$ isotopologue distribution (black) with the theoretical isotopologue distribution in red. The mass calibration derived from the three tuning mix ions yielded mass measurements for the insulin isotopologues with an average mass measurement error of 10 ppm.

Timing of Ion Release Events for Multiple Ions of Fixed and Small Relative Δm. A special case for simultaneous ion isolation arises when there are multiple peaks with a small fixed mass spacing within a distribution of a much larger average mass (e.g., the isotopologue distribution of a relatively large molecule). In this scenario, closely and regularly spaced ions can be released in a selective manner using a single ion release gate. We illustrate this capability in

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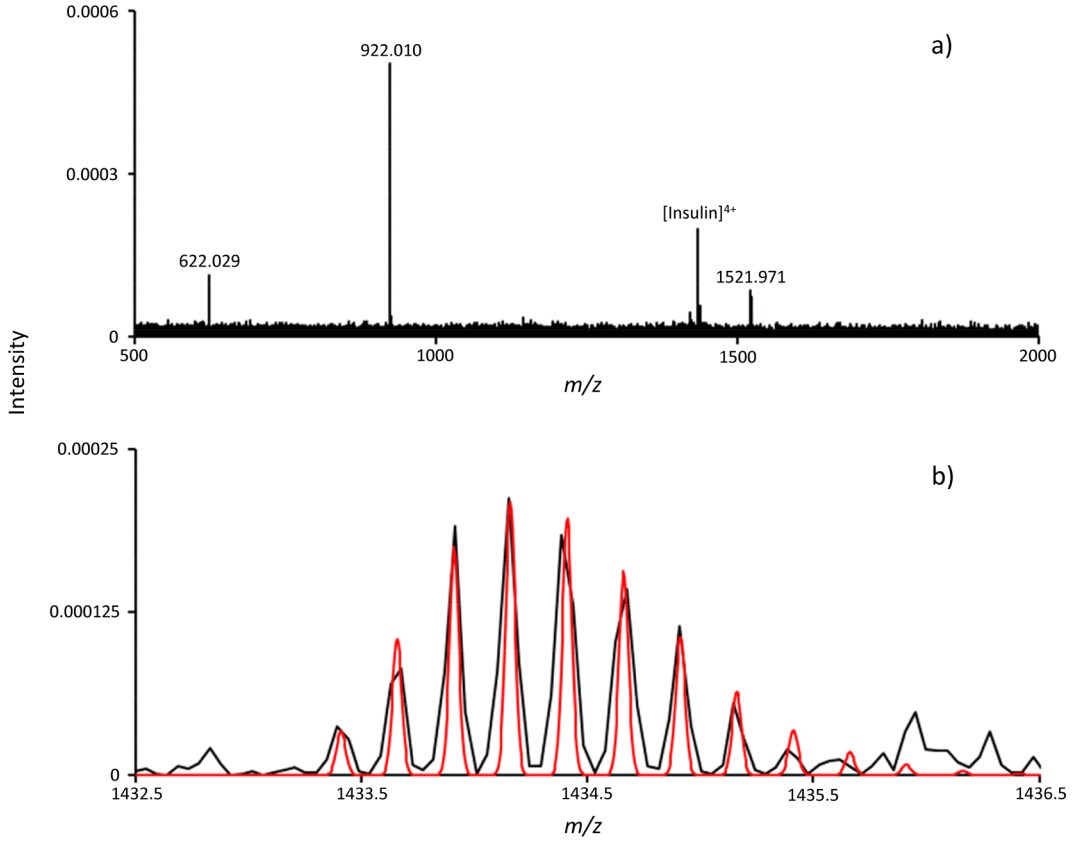

Figure 4. (a) eFT mass spectrum of three calibrant ions and the $[M + 4H]^{4+}$ ion of bovine insulin, simultaneously isolated from a mixture of ESI tuning mix and bovine insulin. (b) Expanded region for the $[M + 4H]^{4+}$ of bovine insulin (black) with a simulated isotopologue distribution for the theoretical mass (red). All eFT spectra are averages of 100 transients of 400 ms.

Figure 5 with the isotopologues of a carborane anion distribution. Figure 5a shows the preisolation mass spectrum of the isotopologue distribution of $CHB_{11}Br_{11}^-$ (average m/z of 1012.56), whereas Figure 5b,c shows the postisolation spectra of the even (Figure 5b) and odd (Figure 5c) isotopologues following single plate 8 release pulses of 5 μs at 16.779 and 16.7765 ms, respectively. These multiple simultaneous isolation events are possible because of the periodicity that arises from regularly and closely spaced peaks within a distribution of relatively high m/z ions.

The phenomena underlying the isolation data of Figure 5 are described below for an isotopic distribution. Consider an ion of mass m, with isotopologue spacing of 1 Da. The frequency with which adjacent isotopologues will overlap in the ELIT (i.e., the beat frequency of the pair of ions) is given by the difference in the fundamental oscillation frequencies of the two ions, as indicated in eq 1, where c is the frequency-to-mass calibration for the ELIT.[18]

$$\Delta\nu_{1\mathrm{Da}} = \frac{c}{\sqrt{m}} - \frac{c}{\sqrt{m+1}} = \frac{c(\sqrt{m+1} - \sqrt{m})}{\sqrt{m(m+1)}} \quad (1)$$

Similarly, the beat frequency between m and its isotopologue 2 Da away is given by

$$\Delta\nu_{2\mathrm{Da}} = \frac{c}{\sqrt{m}} - \frac{c}{\sqrt{m+2}} = \frac{c(\sqrt{m+2} - \sqrt{m})}{\sqrt{m(m+2)}} \quad (2)$$

The ratio of beat periods, given by the inverse of the ratio of beat frequencies, is shown by eq 3:

$$\frac{\text{beat period 1 Da}}{\text{beat period 2 Da}} = \frac{\Delta\nu_{2\mathrm{Da}}}{\Delta\nu_{1\mathrm{Da}}} = \frac{\sqrt{m(m+1)}}{\sqrt{m(m+2)}} \times \frac{\sqrt{m+2} - \sqrt{m}}{\sqrt{m+1} - \sqrt{m}} \quad (3)$$

If m is large compared with the Δm (2 or 1 in this case), the term $\frac{\sqrt{m(m+1)}}{\sqrt{m(m+2)}}$ approaches 1, whereas $\frac{\sqrt{m+2} - \sqrt{m}}{\sqrt{m+1} - \sqrt{m}}$ approaches 2. Thus, to a first approximation, the beat period between an ion of mass m and an ion 1 Da away will be twice the beat period of the ion m and an isotopologue 2 Da away. Likewise, the beat period for the 1 Da spacing will be three times that for a spacing of 3 Da and so forth. Defining the beat period between m and $m + 2$ as T, the beat period between m and $m + 4$ will be $T/2$, and between m and $m + 6$, it will be $T/3$, and so on. Therefore, after time T has passed, and if ion m is of even nominal mass, all even isotopologues will be overlapping with the ion m ($m + 4$ will have overlapped with m once already, $m + 6$ will have overlapped twice, etc.). In contrast, the beat period between ion m and $m + 1$ will be $2T$; between m and $m + 3$, it will be $2T/3$; and between m and $m + 5$, it will be $2T/5$. Therefore, after time T has passed, these odd isotopologues will have undergone $N + 1/2$ beat periods (for example $T/(2T/3) = 1 + 1/2$) with ion m and its corresponding set of even isotopologues, which will all be overlapping. This means they will be almost perfectly separated by half the lap time of m from ion m and the set of even isotopologues containing m. Thus, a single appropriately timed gate can allow for the

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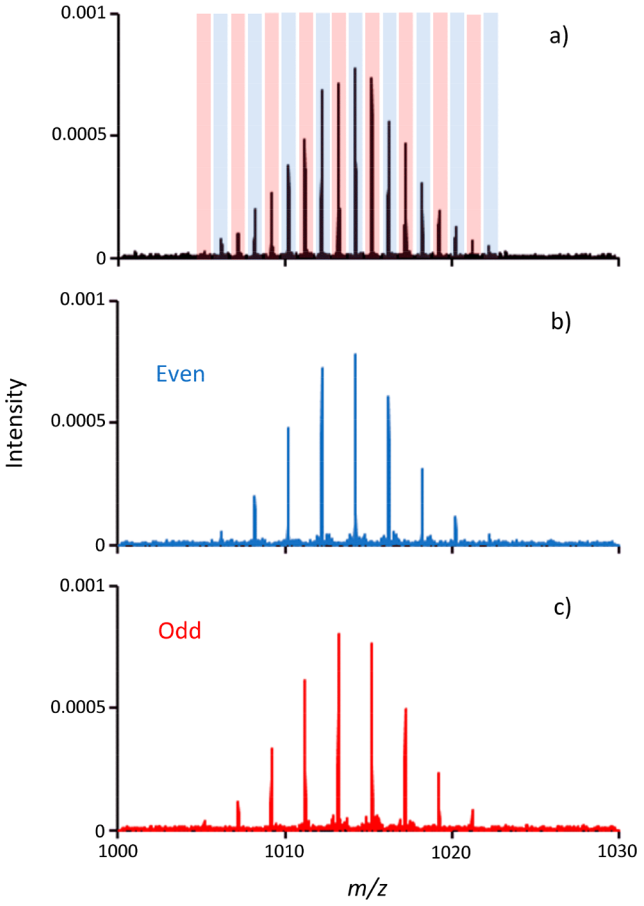

Figure 5. (a) eFT mass spectrum of $CHB_{11}Br_{11}^-$ (1012.56 average m/z). (b) Isolation of isotopologues with an even nominal m/z using a 5 μs isolation window after 16.779 ms of separation. (c) Isolation of isotopologues with a nominal odd m/z using a 5 μs pulse after 16.7765 ms of separation. All eFT spectra are averages of 100 transients of 500 ms.

simultaneous release of either all odd or all even isotopologues. This can be extended to separate ions with a spacing of 3 Da as well, although in this case, at the beat period between m and m + 3, the distribution will form three sets of ions, now separated by one-third the lap time of m. We further note that this technique is not necessarily limited for use with isotopic mass differences of 1 Da. For example, the mass of a protein may be large enough compared with the masses associated with sodium and other adductions for this technique to be performed to isolate alternating degrees of adduction.

CONCLUSIONS

An approach for simultaneous isolation of multiple ions of disparate m/z ratios is demonstrated in an electrostatic linear ion trap. Simultaneous isolation takes advantage of both the rapid spatial separation of ions and the periodic nature of ion overlap in a closed path MR-TOF device. Mirror switching isolation pulses can be timed to coincide with overlapping events and because the ions of interest are spatially overlapped during the isolation event, they can be isolated from contaminant ions simultaneously. The time in which the overlap event occurs can be determined on the basis of ion frequencies and beat periods within the device. Furthermore, the position and direction of ion motion can be predicted and used to optimize the timing of mirror switching isolation. To demonstrate simultaneous isolation, isotopologues were selected from three carborane distributions and isolated in a combination of ways. In all cases, at least 75% of the preisolation signal was observed after ion isolation. This capability is useful for multiplexed MS/MS experiments and for inclusion of calibrant ions for high mass measurement accuracy applications. In addition, equally spaced ions with a small mass range can be simultaneously isolated if the m/z spacing is small compared with the nominal m/z of the isolated ions.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.analchem.9b03560.

Additional description of our mass analysis procedures, table with the times used for isolation of all three carborane species found in Figure 2d, and expanded view of the pre- and postisolation for the mass spectra presented in Figure 2a,d (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) McDonald, L. A.; Barbieri, L. R.; Carter, G. T.; Kruppa, G.; Feng, X.; Lotvin, J. A.; Siegel, M. M. *Anal. Chem.* **2003**, *75*, 2730−2739.
(2) Wootton, C. A.; Sanchez-Cano, C.; Lopez-Clavijo, A. F.; Shaili, E.; Barrow, M. P.; Sadler, P. J.; O'Connor, P. B. *Chem. Sci.* **2018**, *9*, 2733−2739.
(3) Kruppa, G.; Schnier, P. D.; Tabei, K.; Van Orden, S.; Siegel, M. M. *Anal. Chem.* **2002**, *74*, 3877−3886.
(4) Wilson, J.; Vachet, R. W. *Anal. Chem.* **2004**, *76*, 7346−7353.
(5) Ledvina, A.; Savitski, M.; Zubarev, A.; Good, D.; Coon, J.; Zubarev, R. *Anal. Chem.* **2011**, *83*, 7651−7656.
(6) O'Connor, P. B.; Little, D. P.; McLafferty, F. W. *Anal. Chem.* **1996**, *68*, 542−545.
(7) De Koning, L.; Nibbering, N. M. M.; Van Orden, S.; Laukien, F. *Int. J. Mass Spectrom. Ion Processes* **1997**, *165*, 209−219.
(8) Marshall, A. G.; Wang, T. C. L.; Ricca, T. L. *J. Am. Chem. Soc.* **1985**, *107*, 7893−7897.
(9) Johnson, J. T.; Carrick, I. J.; Eakins, G. S.; McLuckey, S. A. *Anal. Chem.* **2019**, *91*, 8789.

DOI: 10.1021/acs.analchem.9b03560
Anal. Chem. 2019, 91, 12574−12580

(10) Toker, Y.; Altstein, N.; Aviv, O.; Rappaport, M.; Heber, O.; Schwalm, D.; Strasser, D.; Zajfman, D. *J. Instrum.* **2009**, *4*, P09001.
(11) Hilger, R. T.; Santini, R. E.; McLuckey, S. A. *Int. J. Mass Spectrom.* **2014**, *362*, 1−8.
(12) Wienholtz, F.; Kreim, S.; Rosenbusch, M.; Schweikhard, L.; Wolf, R. *Int. J. Mass Spectrom.* **2017**, *421*, 285−293.
(13) Dickel, T.; Plaß, W. R.; Lippert, W.; Lang, J.; Yavor, M. I.; Geissel, H.; Scheidenberger, C. *J. Am. Soc. Mass Spectrom.* **2017**, *28*, 1079−1090.
(14) Fischer, P.; Knauer, S.; Marx, G.; Schweikhard, L. *Rev. Sci. Instrum.* **2018**, *89*, No. 015114.
(15) Fischer, P.; Marx, G.; Schweikhard, L. *Int. J. Mass Spectrom.* **2019**, *435*, 305−314.
(16) Dziekonski, E. T.; Johnson, J. T.; Lee, K. W.; McLuckey, S. A. *Anal. Chem.* **2017**, *89*, 10965−10972.
(17) Hilger, R. T.; Dziekonski, E. T.; Santini, R. E.; McLuckey, S. A. *Int. J. Mass Spectrom.* **2015**, *378*, 281−287.
(18) Johnson, J. T.; Lee, K. W.; Bhanot, J. S.; McLuckey, S. A. *J. Am. Soc. Mass Spectrom.* **2019**, *30*, 588−594.

DOI: 10.1021/acs.analchem.9b03560
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