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Improving the AC-ejection method for enhanced duty cycle and wide m/z range detection of ions in oTOF-MS

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Introduction

Orthogonal acceleration (OA) as a method for gating ions into a time-of-flight (TOF) analyzer can accommodate a greater flux of charges while achieving higher mass resolving power when compared to ejection of ions from a radio-frequency ion trap. The major drawback of the OA configuration is its low duty cycle, with the "Zeno pulsing" method being the most notable approach so far to address this limitation. Here we present a new implementation of such an AC-ejection method derived using simulations and experiments. The new design incorporates simplified electronics, can accommodate an even higher flux of charges (>10^7/s) and expands the detectable m/z range in a single TOF transient from <300Th to >10,000Th, without compromising TOF resolution and mass accuracy.

Results

Ion optics simulations were initially conducted to evaluate the standard method of gating ions from the collision cell into the TOF. Fig. 1 (a) shows a cross-sectional view of the collision cell, the focusing lenses and the pulsed extraction section of the orthogonal acceleration (OA) region. Fig. 1 (b) shows simulated results compared with experimental data to validate the ion optics model.

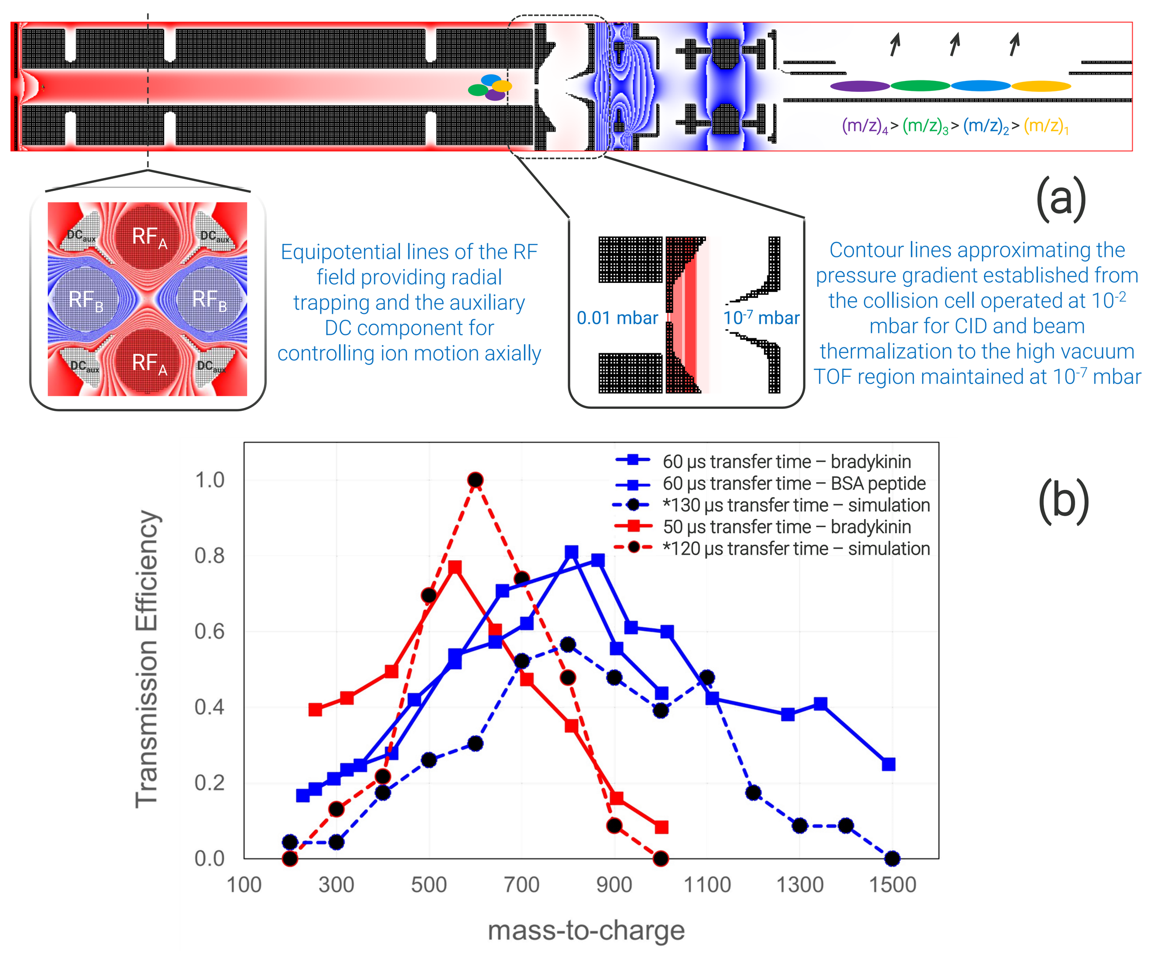

Fig. 1 (a) Ion optics simulation model and (b) simulated *vs* experimental data highlighting the mass discrimination effects for the standard DC gating method.

Simulations with the original design presented in Fig. 1 (a) were extended to include the application of a ramped AC-signal applied to the gate lens of the collision cell. Penetration of the AC field into the focusing lens system employed for collimating ions in the OA was shown to negatively affect TOF resolution and the m/z range detected. Complete loss of ion transmission was also observed over narrow m/z windows where ion transit times matched the frequency of the applied AC signal. Fig. 2 (a) shows the optimized design evaluated using simulations and experiments.

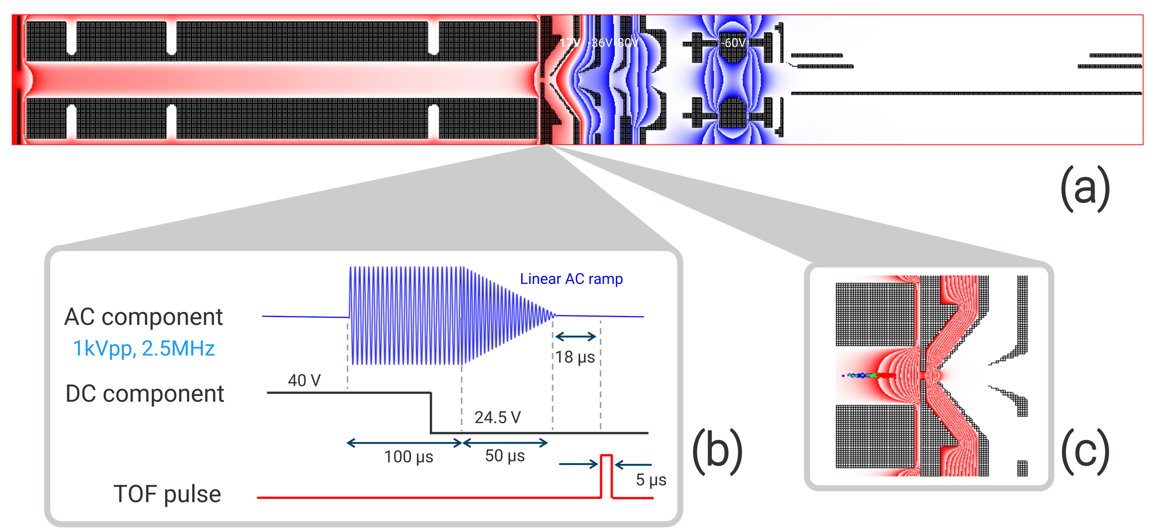

Fig. 2 (a) Ion optics simulation model of the new design (b) detail of the AC and DC components applied to the gate lens and (c) zoom view of the AC field confined by the AC-screen lens.

Figure 3 (a) shows the simulated beam parameters in the effective region of the OA for the original geometry and the new design configured with the AC-screen electrode and a modified focusing lens system for accommodating larger aperture sizes on the gate lens and reducing the gas load to the OA-TOF. Fig. 3 (b) compares the experimental TOF resolution and mass accuracy obtained in the original and new designs.

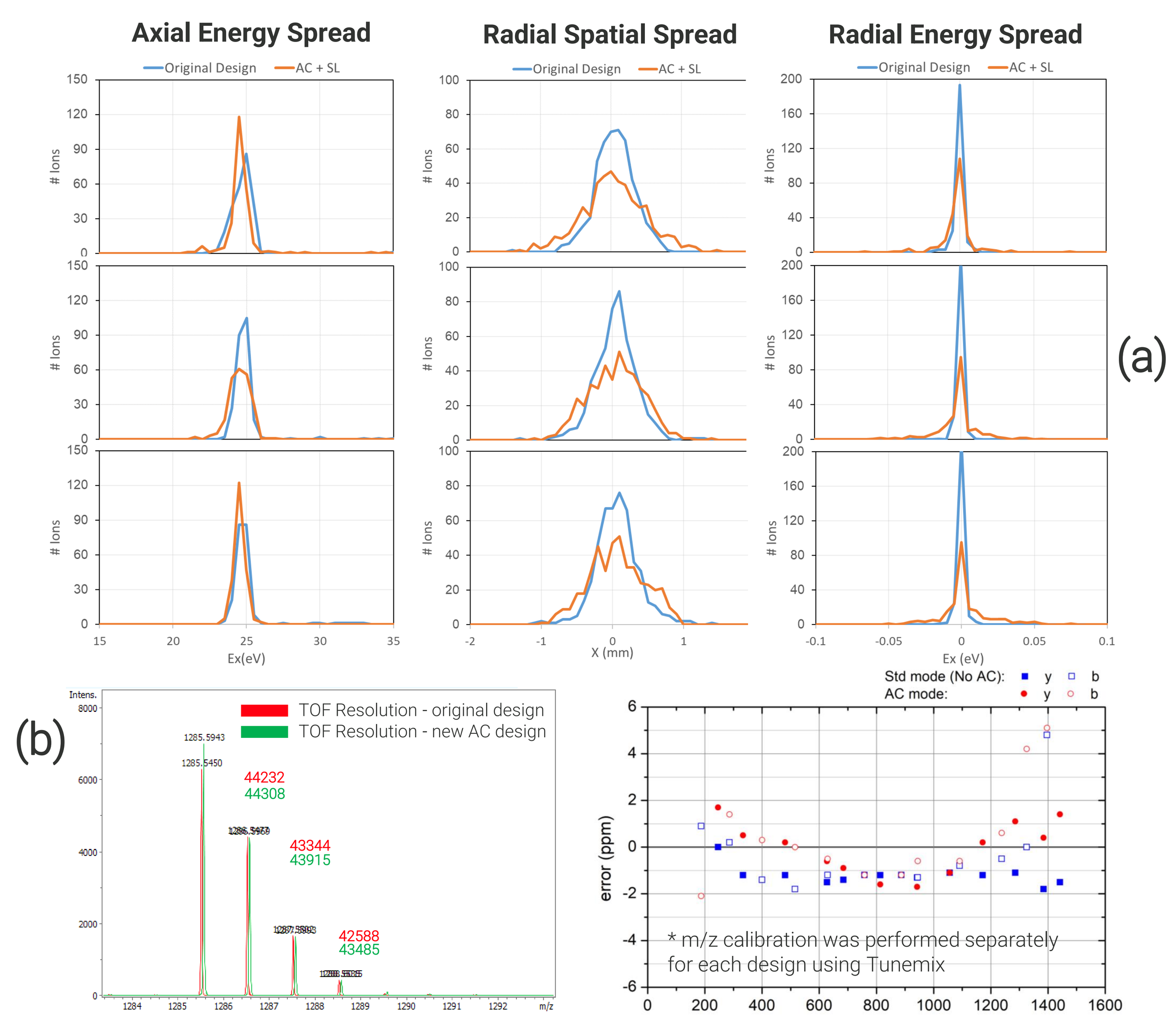

Fig. 3 (a) Simulated beam parameters in the OA region, (b) experimental TOF resolution for tunemix ions and mass accuracy for CID fragments of Glu 1 fibrinopeptide B.

The AC-ejection method parameters were optimized for detecting MS2 ECD and MS2 $_{c}$CID fragments of native carbonic anhydrase charge state 10+. Fig. 4 (a) shows the timing settings applied in the experiment using a 120 μs long AC ramp to bring ions over a wide m/z range into focus at the effective region of the OA. Settings for the standard gating mode are also shown. Fig. 4 (b) and (c) show the relative intensity of ECD fragments by scanning "transfer time" and the "time delay" employed in the standard DC gating and AC ejection methods, respectively.

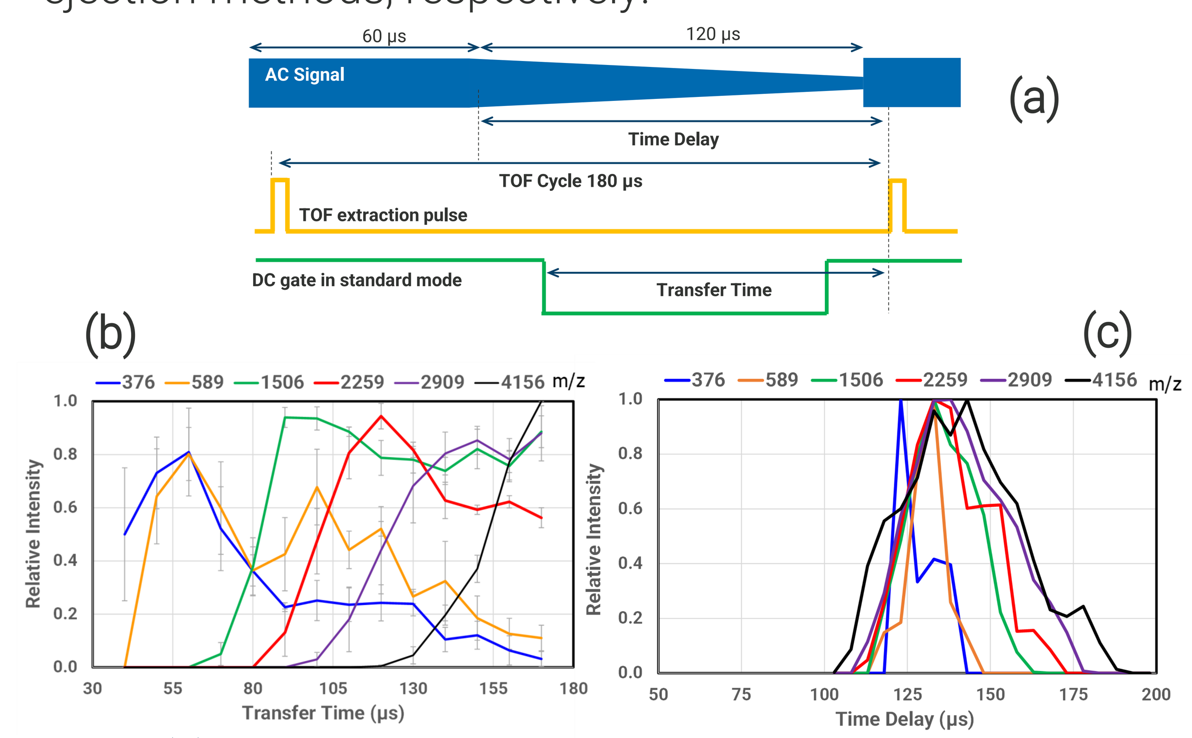

Fig. 4 (a) Timing settings applied in AC-ejection and standard DC gating modes, (b) transfer time scan in standard mode and (c) time delay scan in AC-ejection mode.

Fig. 5 (a) and (b) show the MS2 ECD and the MS2 $_{c}$CID mass spectra of carbonic anhydrase 10+ charge state generated with the new geometry of Fig. 2, and comparing AC-ejection with DC gating to highlight the gains across the entire m/z range detected in the TOF.

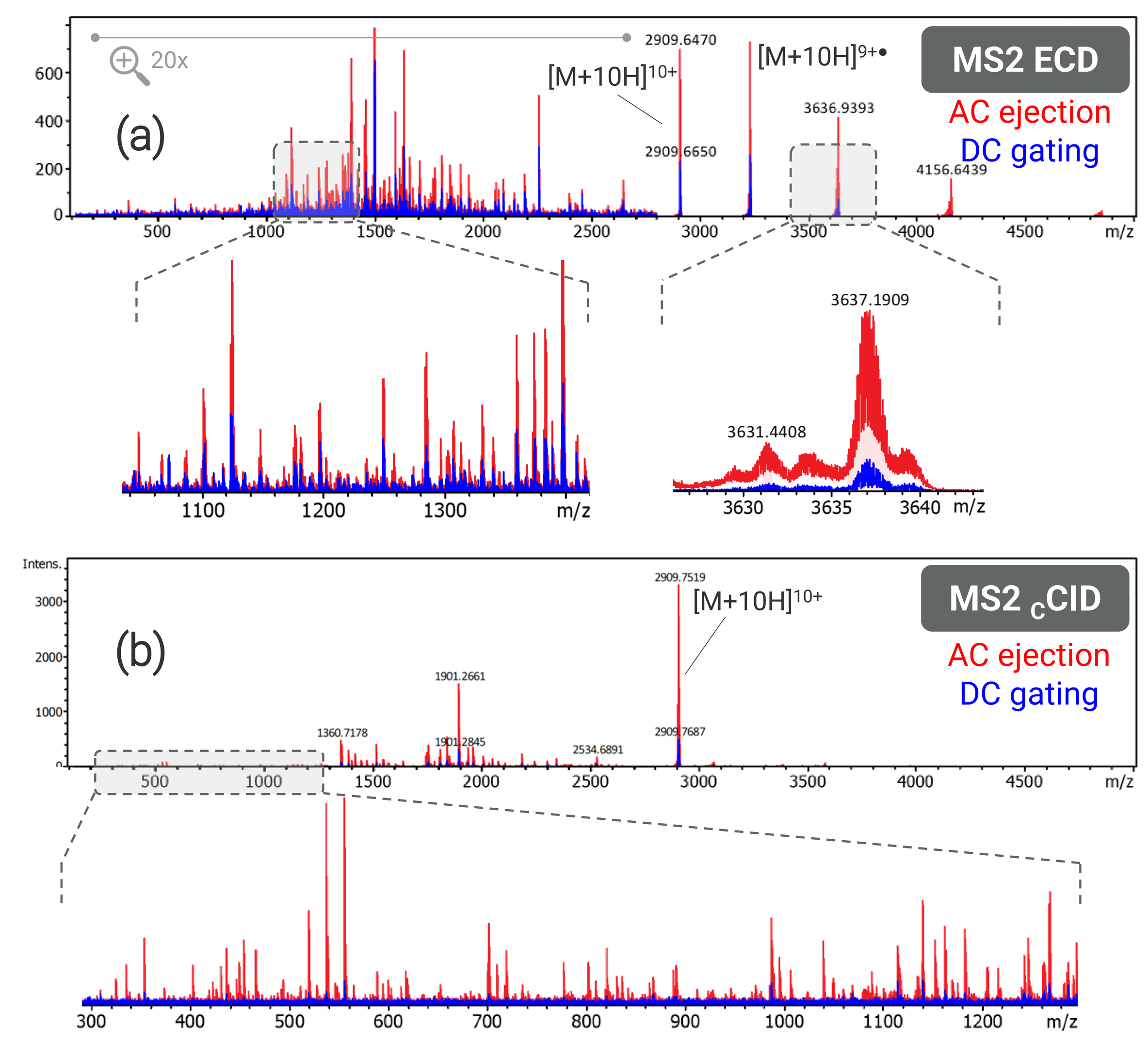

Fig. 5 (a) MS2 ECD and (b) MS2 $_{c}$CID spectra of native carbonic anhydrase charge state 10+ with AC-ejection and the standard gating methods.

Fig. 6 shows the ion intensity gains obtained with the AC-ejection method, normalized to the maximum intensity of ECD and $_{c}$CID fragments measured across all transfer times covering the m/z range of interest in the standard DC gating method.

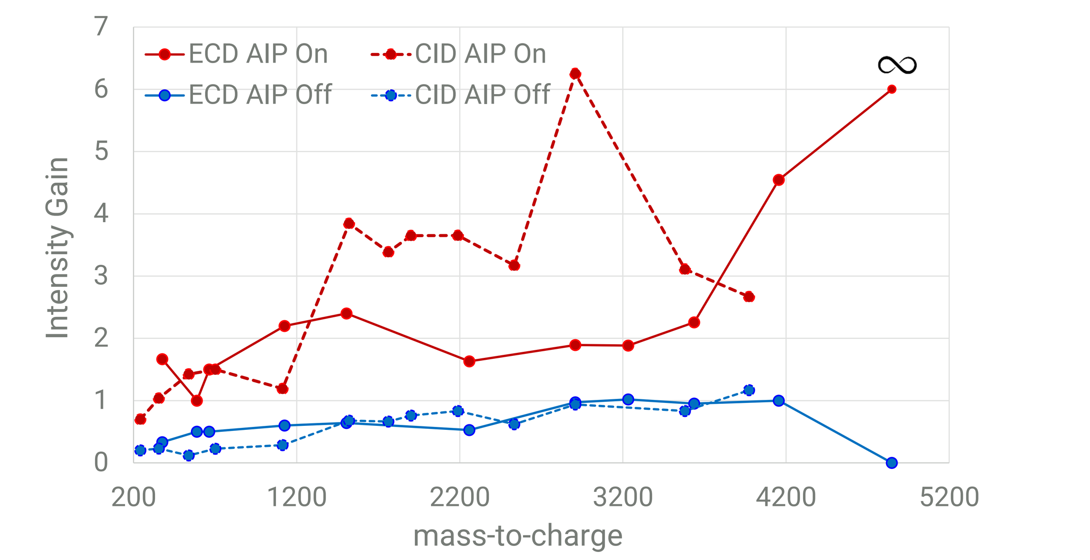

Fig. 6 Intensity gains in MS2 ECD and MS2 $_{c}$CID experiments with native carbonic anhydrase obtained with AC-ejection normalized to the optimum transfer time settings for every m/z value in the standard DC gating method.

Fig. 7 shows an MS2 ECD spectrum of intact native NIST antibody charge state 21+ where with appropriate tuning of the AC-ejection method parameters, the m/z range recorded in a single TOF transient can be extended from <250 Th to >10,000 Th.

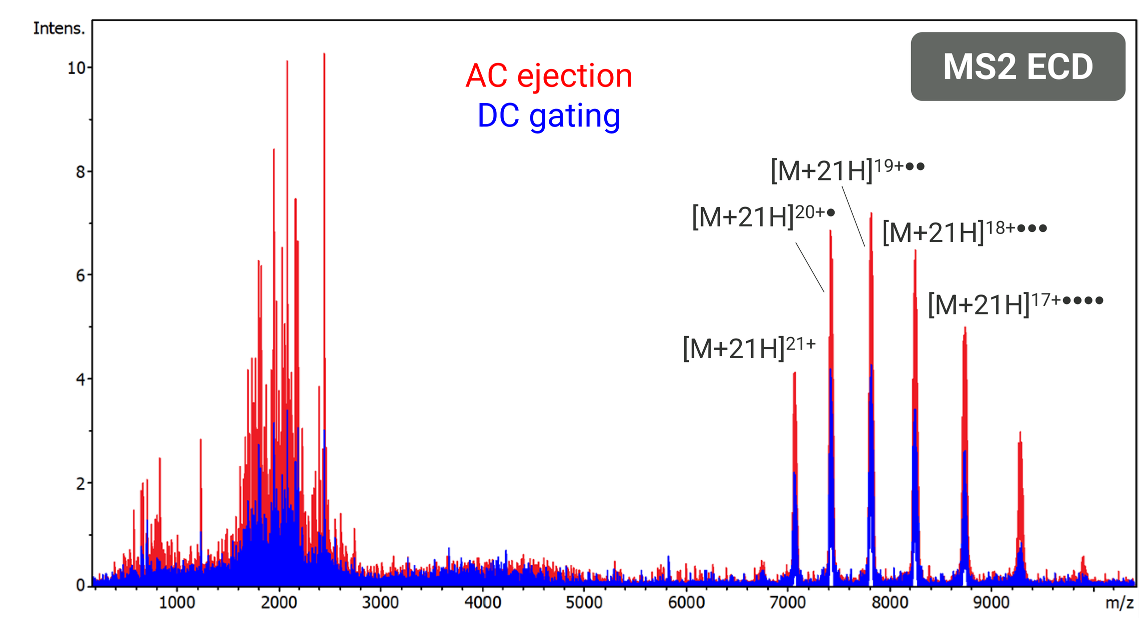

Fig. 7 MS2 ECD spectra of intact NIST mAb charge state 21+ obtained with AC-ejection and the standard DC gating methods.

Conclusions

► A simplified implementation of the AC-ejection method is successfully introduced in the timsOmni platform, addressing mass discrimination effects typically observed in OA-TOF analyzers

► Ion optics simulations were used to evaluate the standard DC gating method and investigate alternative designs based on the AC-ejection concept.

► Enhanced ion transmission and extended m/z range detection is accomplished with this new design, suitable for bottom-up and top-down MS.

Technology