Improved Low Mass Transmission Efficiency in High Resolution Ion Mobility (HRIM) – Mass Spectrometry (MS) for Expanded Application Profiles

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Introduction

- Current MOBILion MOBIE™ hardware provides HRIM across a mass range of 300-3000 m/z.
- Improving Low Mass Transmission (LMT) would expand the breadth of applications MOBIE can be utilized for.
- We investigated modifications of a MOBIE platform to enhance LMT performance.
- Utility of improved LMT is demonstrated via Credentialed E. Coli metabolomics LC-HRIM-MS workflow.

Hardware Modifications

- The SLIM RF frequency was increased from the default of 800 kHz to 1.07 MHz using a MIPS Ultra High Q RF Head (GAA Custom Electronics)
- Simulations demonstrated improved low mass ion confinement with higher RF frequencies.
- Nitrogen drift gas was replaced with 5.0 grade Helium at 2.5 Torr.
- MS data was generated on an Agilent 6545B QTOF MS coupled to an Acquiris SA220 14-bit ADC.

Methodology

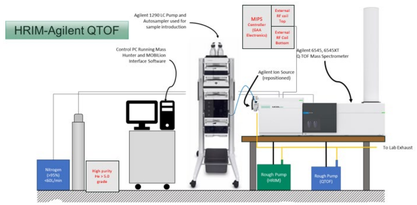


Figure 1. Diagram of hardware modifications to MOBIE system.

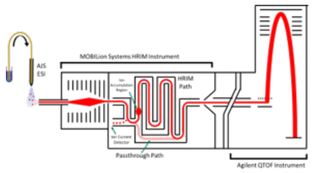


Figure 2. Diagram of SLIM ion path.

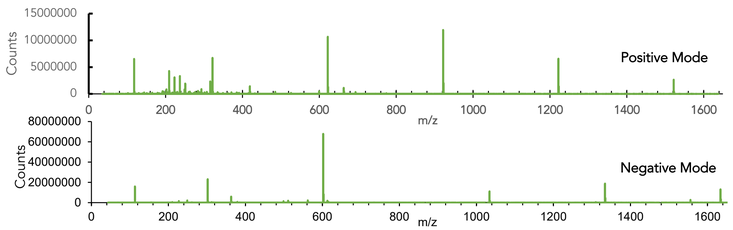
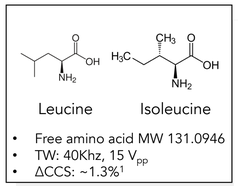


Figure 3. Positive and negative spectra of 20% Agilent tune solution showing low mass ion transmission in HRIM mode. The 6545B QTOF was operated in 1700 m/z mode.

Results



- Free amino acid MW 131.0946
- TW: 40Khz, 15 V_{pp}
- ΔCCS: ~1.3%[1]

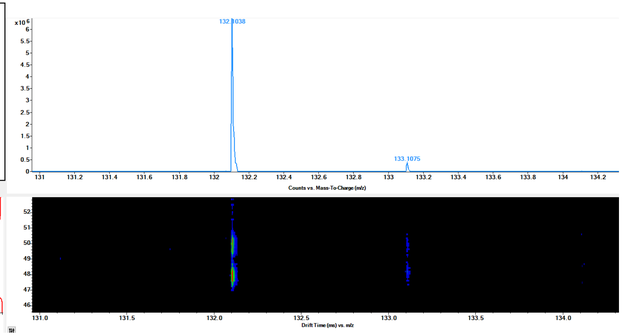


Figure 4. Separation of leucine and isoleucine at 132 m/z. 100pg each of leucine and isoleucine were infused at 5 µl/min in 50:50 Methanol:Water.

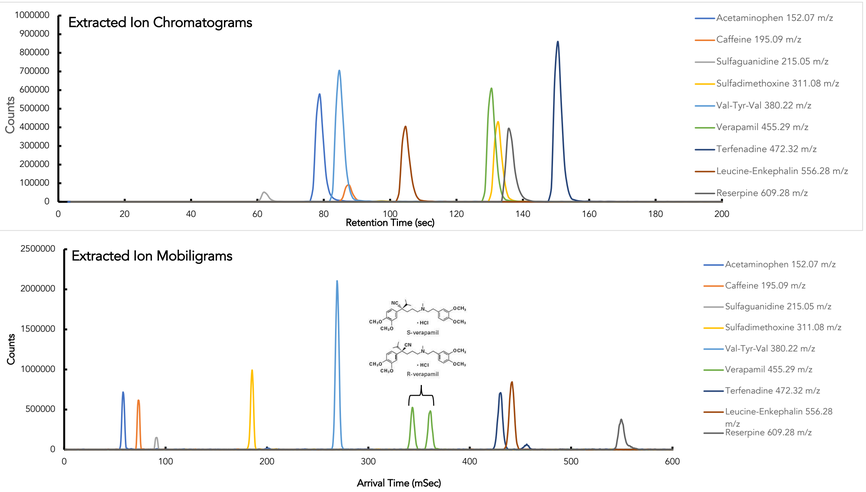
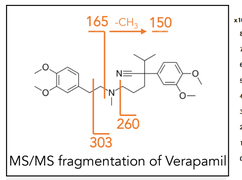


Figure 5. HRIM achieves baseline separation of QC reference compounds. TOP: EIC of Waters LCMS QCRM (part num: 186006963-1) of all 9 compounds relative to HPLC Retention Time. BOTTOM: Mobiligram showing all 9 compounds (149 m/z – 608 m/z) sorted by mass in HRIM. Verapamil is commercially available as a racemic pair and are baseline separated possibly through a proton-induced chirality mechanism[2].

References:
1. Zheng *et al.* Chem. Sci. 8(11), 2017 pp7724-7736.
2. Leritano C. *et al.* Angew. Chem. Int. Ed. Engl. 61(9), 2022.
3. Chytil L. *et al.* J. Chromatography B 878(30), 2010.
4. Mahieu NG *et al.* Anal. Chem. 86, 2014, pp 9583-9589.
5. Di Poto C. *et al.* J. Am. Soc. Mass Spectrom. 32(8) 2021, pp 2072-2080.

Results



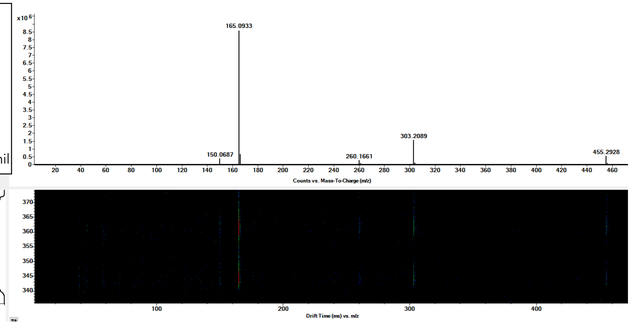
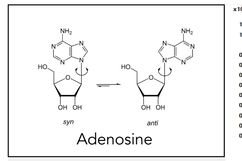


Figure 6. Mobility Aligned Fragmentation (MAF) of Verapamil at 30 eV showing identical fragmentation patterns of both mobility peaks. The MS/MS spectra match well with previously published Verapamil spectra[3].



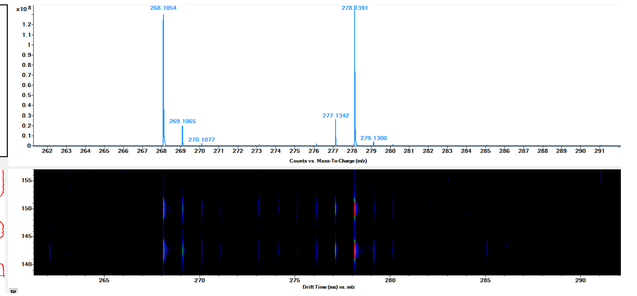


Figure 7. Baseline separation of *Syn-* and *Anti-* Adenosine conformers. Identification of Adenosine from HILIC-Z chromatography of credentialed *E. Coli* kit (Cambridge Isotope Labs, part # MSK-CRED-KIT). Standard was mixed in a 1:1 C^{12}/C^{13} ratio and analyzed via HILIC-Z HPLC chromatography[4]. Mobility alignment of the two peaks confirms isotopologues with 10 carbons each. Identification of Adenosine was confirmed by MAF. The two peaks in the mobiligram represent the *Syn-* and *Anti-* conformers of Adenosine. These conformers have been previously observed but are baseline separated for the first time here[5].

Conclusions

- The use of Helium and higher frequency RF on the SLIM boards dramatically improves low mass range down to ~100 m/z.
- We demonstrate separation of isomers, conformers and racemic pairs in the mobility domain.
- This improved mass range extends the range of applications for the MOBIE platform.