Development and Evaluation of Long Serpentine Path Traveling Wave SLIM Modules for High Resolution Ion Mobility Separations

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Overview

- A 13-m long serpentine Traveling Wave Structures for Lossless Manipulations (TW SLIM) module was designed for achieving high resolution ion mobility separations.
- Achieved 5-fold greater resolution than commercially available drift tube or traveling wave IM-MS platforms.
- Peak capacity and peak generation rates were estimated to be 246 and 369 s^{-1} at the optimum conditions.
- Previously unachievable separation for peptides, sugars and lipids were realized.

Introduction

- Ion Mobility Spectrometry (IMS) is a well established analytical method that separates ionic species based on differences in their mobilities in a buffer gas.[1-2]
- One limiting feature of contemporary IMS is its relatively low resolution compared to HPLC or CE.
- Conventional IMS instruments commonly have drift tubes of ≲1m providing resolving powers of ~50-120.[3-7]
- While this resolution is sufficient for differentiation of chemical classes and determination of cross sections,[8] many separations require much higher resolution.

Methods

Fig.1

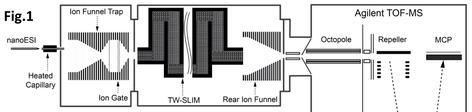


Fig.2

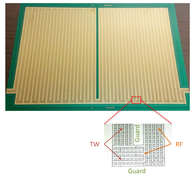


Fig.1 Schematic diagram of the TW SLIM IMS-MS developed for this work.

Fig.2 Photo of the TW SLIM bottom board showing the electrodes arrangement and details of a "U" turn region (inset) showing the RF, traveling wave, and guard electrodes.

Results

Ion Transmission and Robustness

Fig.3

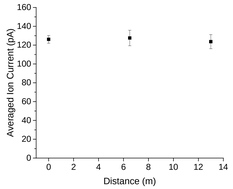


Fig.3 Ion current measurement demonstrates the lossless ion transmission through the entire TW SLIM module.

Fig.4

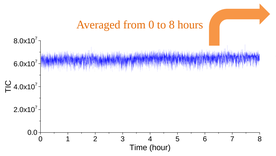


Fig.5

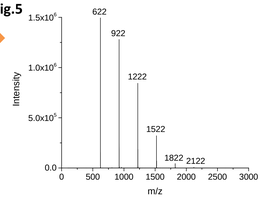


Fig.4 Robust performance of the 13-m TW SLIM IMS module was achieved (e.g., with no evidence of performance drift due to surface charging). Additionally, the mass spectrum (inset) shows a wide m/z range (**Fig.5**).

Characterization of Parameters

Fig.6

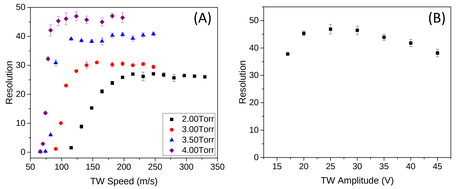
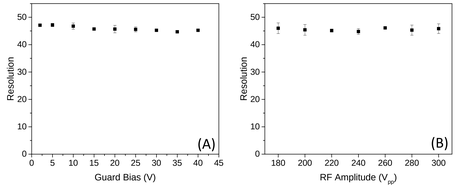


Fig.6A The maximum m/z 622-922 resolution of ~47 was achieved at 4.00 Torr, which is about ~5-fold greater than the resolution of a conventional drift tube IMS (~10).[9]
Fig.6B The optimum m/z 622-922 resolution of 47±2 was obtained with TW amplitudes between 20 V and 30 V.

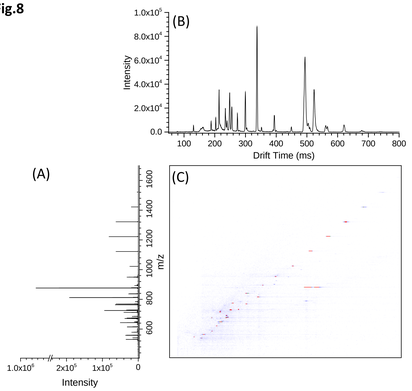
Fig.7



The guard bias (**Fig.7A**) and RF amplitude (**Fig.7B**) have no degrading effects on resolution.

Peak Capacity and Peak Generation Rate

Fig.8



- The peak capacity of the present long path TW SLIM module was estimated at about 300 for a TW speed of 148 m/s under optimum conditions.
- At a traveling wave speed of 148 m/s, the estimated peak generation rate was 483 s^{-1}.

Ion Mobility Separations

Fig.9

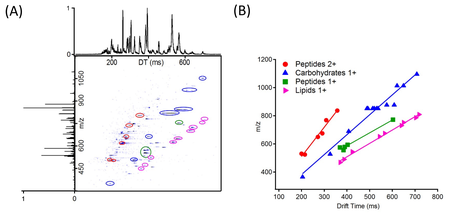


Fig.9 Different molecular classes typically separate by different "trend lines", with 2+ peptides arriving first (red), then 1+ carbohydrates (blue), 1+ peptides (green), and finally the 1+ lipids (pink) arriving last due to the distinct backbone structures of each molecule type.

Fig.10

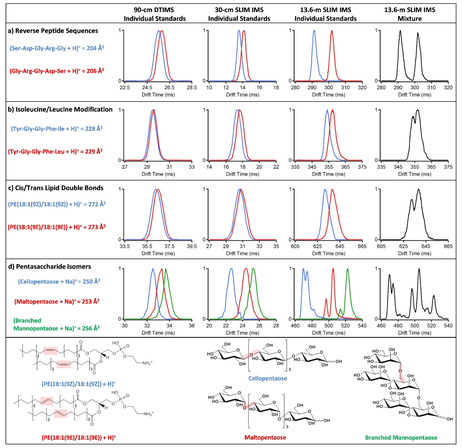


Fig.10 Initial examples of separations achieved included: reverse peptides; two peptides that differ only by a leucine residue being replaced by isoleucine; the cis- and trans-double bond orientations for complex glycerophosphoethanolamine (PE) lipid isomers; and pentasaccharide ion conformations not distinguishable from the other IMS platforms (in addition to revealing new conformer peaks).

Conclusions

- Lossless ion transmission for the 13-m TW SLIM IMS.
- Robust performance achieved over long periods.
- The maximum resolution for the separation of *m/z* 622 and 922 of 47 was achieved at 2.75-mm gap and 4.00 Torr N_2.
- The resolution was shown to be independent of guard electrode potential and RF amplitude.
- Peak capacity and peak generation rate were estimated to be 246 and 369 s^{-1}.
- Separations were achieved for a set of challenging peptides/lipids/carbohydrates mixtures.
- Unachievable separations for different isomers were realized by the 13-m long serpentine TW SLIM IMS.

Acknowledgements

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References

1. Mason, E. A.; McDaniel, E. W. Transport Properties of Ions in Gases; Wiley: New York, 1988.
2. Revercomb, H. E.; Mason, E. A. Anal. Chem. 1975, 47, 970.
3. Wyttenbach, T.; von Helden, G.; Bowers, M. T. *J. Am. Chem. Soc.* **1996**, *118*, 8355.
4. Liu, Y. S.; Valentine, S. J.; Counterman, A. E.; Hoaglund, C. S.; Clemmer, D. E. *Anal. Chem.* **1997**, *69*, A728.
5. Fernandez-Lima, F. A.; Becker, C.; McKenna, A. M.; Rodgers, R. P.; Marshall, A. G.; Russell, D. H. *Anal. Chem.* **2009**, *81*, 9941.
6. Kwasnik, M.; Fuhrer, K.; Gonin, M.; Barbeau, K.; Fernandez, F. M. *Anal Chem* **2007**, *79*, 7782.
7. Kanu, A. B.; Gribb, M. M.; Hill, H. H. *Anal. Chem.* **2008**, *80*, 6610.
8. May, J. C.; Goodwin, C. R.; Lareau, N. M.; Leaptrot, K. L.; Morris, C. B.; Kurulugama, R. T.; Mordehai, A.; Klein, C.; Barry, W.; Darland, E.; Overney, G.; Imatani, K.; Stafford, G. C.; Fjeldsted, J. C.; McLean, J. A. *Anal. Chem.* **2014**, *86*, 2107
9. Hamid, A. M.; Ibrahim, Y. M.; Garimella, S. V. B.; Webb, I. K.; Deng, L.; Chen, T.-C.; Anderson, G. A.; Prost, S. A.; Norheim, R. V.; Tolmachev, A. V.; Smith, R. D. *Anal. Chem.* **2015**, *87*, 11301.

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