Ultrasensitive SLIM Serpentine Ultra-long Path with Extended Routing (SUPER) high resolution ion mobility-MS using large ion populations and peak compression

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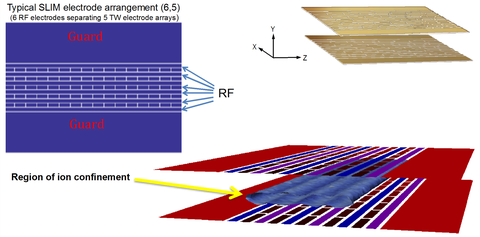
Introduction

The benefits of ion mobility (IM) separations generally increase as separation power increases. However, the highest resolution IM separations reported to date have been achieved in conjunction with significant ion losses or over a very limited mobility range, substantially limiting their practicality and applicability. Limitations are not only related to the long path lengths needed for much higher resolution, but also the limited size of injected ion populations, and the decrease in IM peak intensities due to diffusion and other factors.

In this work we are developing ultrahigh resolution IM with MS based upon use of traveling waves (TW) in long serpentine path and multi-pass Structures for Lossless Ion Manipulations (SLIM).

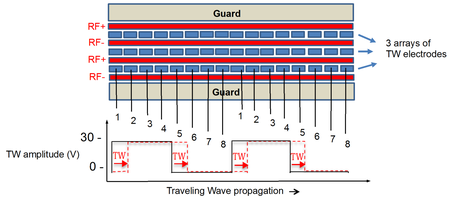
SLIM are constructed from electric fields

- SLIM ion conduits, switches, traps, etc. constructed from electric fields in a gas at low pressure (e.g. 4 torr N_2) in the gap between two surfaces
- Electric fields generated by applying appropriate potentials to mirror-image arrays of electrodes on the two surfaces



Creating traveling waves in SLIM

One of two SLIM surfaces with 4 RF electrodes separating 3 TW electrode arrays



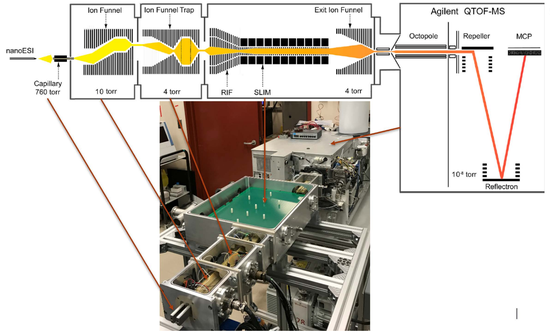
~ 1 bin/cm; TW speed typically 50 to 100 m/s

Hamid et al., Anal. Chem., *87*, 11301 (2015)

SLIM SUPER IM-MS implementation

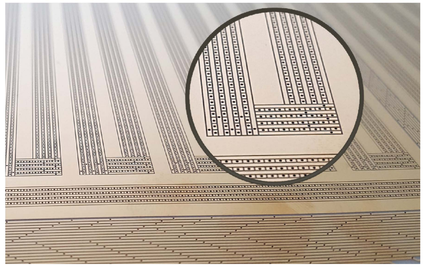
Long serpentine path and multi-pass SLIM designs were developed and appropriate potentials created pseudopotentials that confine ions between the surfaces in 2 to 4 torr N_2 and effectively eliminate ion losses. SLIM ion switches were used to select ions for either multi-passes through the same long serpentine path (~13 m), or to shunt ions to the MS. Some SLIM designs incorporated compression ratio ion mobility programming (CRIMP) capabilities in which ion distributions could be temporally and spatially compressed. Separations were evaluated using standard samples and challenging mixtures.

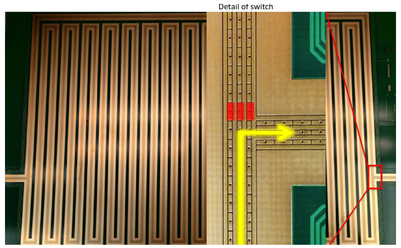
SLIM implementation with high resolution TOF MS



One surface of a long path (13 m) SLIM module

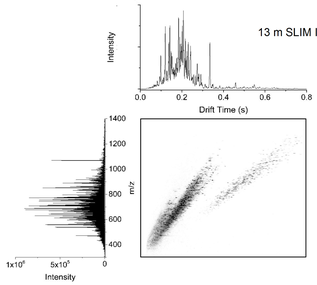
Long path IM module consists of two 14" x 18" surfaces with mirror image electrode arrays (5,4)
Each surface has 54,000 TW electrodes; two surfaces spaced by ~2.9 mm



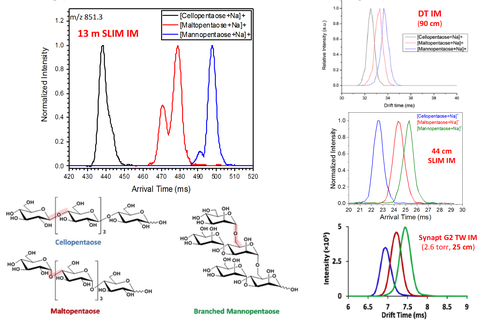


IM separations in 13 m SLIM IM-MS rival LC

SLIM IM-MS of same peptide and protein mixture tryptic digest provides IM peak capacities of ~250



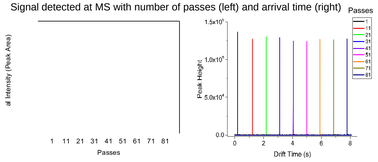
Comparison of IM separations for 3 pentasaccharides using long path SLIM, drift tube, short SLIM and Waters Synapt G2 IM-MS



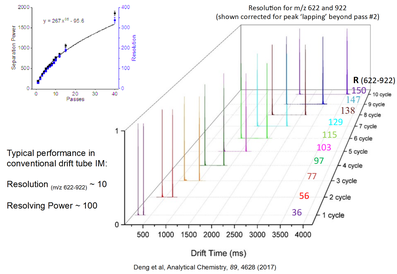
Ions can be stored or manipulated losslessly for long times

- Efficient transmission for ion populations undergoing up to 81 passes in 'traveling traps' (surfing) covering **more than 1 km**
- Much longer distances should be feasible as ions can be trapped and losslessly stored for >5 hr in SLIM

Signal detected as MS with number of passes (left) and arrival time (right)



Resolution increases with (path length)$^{0.5}$ in SLIM SUPER IM



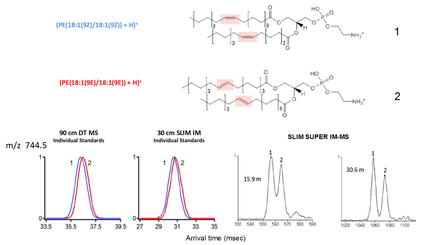
Typical performance in conventional drift tube IM:

Resolution $_{(m/z\ 622\text{-}922)}$ ~ 10

Resolving Power ~ 100

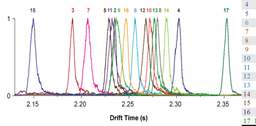
Deng et al, Analytical Chemistry, *89*, 4628 (2017)

IM resolution of cis/trans double bonded lipid isomers



SLIM SUPER IM-MS of Aβ(17-28) isomers

135 m (10 passes); $[M + 2H]^{2+}$

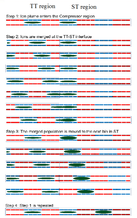


	Sequence	Feature	DT (s)
2	LVFFAEDVGSDK	L-Asp, L-Asp	2.234
3	LVFFAEDVGS(dD)K	L-Asp, D-Asp	2.190
4	LVFFAEDVGS(bD)K	L-Asp, L-isoAsp	2.301
5	LVFFAEDVGS(dbD)K	L-Asp, D-isoAsp	2.229
6	LVFFAE(dD)VGSDK	D-Asp, L-Asp	2.256
7	LVFFAE(dD)VGS(dD)K	D-Asp, D-Asp	2.207
8	LVFFAE(dD)VGS(bD)K	D-Asp, L-isoAsp	2.280
9	LVFFAE(dD)VGS(dbD)K	D-Asp, D-isoAsp	2.238
10	LVFFAE(bD)VGSDK	L-isoAsp, L-Asp	2.272
11	LVFFAE(bD)VGS(dD)K	L-isoAsp, D-Asp	2.232
12	LVFFAE(bD)VGS(bD)K	L-isoAsp, L-isoAsp	2.268
13	LVFFAE(bD)VGS(dbD)K	L-isoAsp, D-isoAsp	2.277
14	LVFFAE(dbD)VGSDK	D-isoAsp, L-Asp	2.289
15	LVFFAE(dbD)VGS(dD)K	D-isoAsp, D-Asp	2.149
16	LVFFAE(dbD)VGS(bD)K	D-isoAsp, L-isoAsp	2.246
17	LVFFAE(dbD)VGS(dbD)K	D-isoAsp, D-isoAsp	2.352

Compression Ratio Ion Mobility Programming (CRIMP)

CRIMP in SLIM allows:

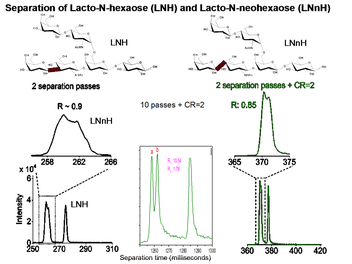
- Application of ***any*** integer value compression ratio
- Can be applied to any ion distribution
- No loss of resolution
- Also provides basis for using much larger ion populations



- Compression occurs at interface of traveling trap (TT) and 'stuttering trap' (ST) regions
- TT region runs continuously; ST region stops moving periodically
- ST region is halted half the time for CR = 2

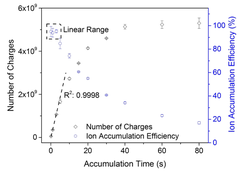
Garimella et al., Analytical Chemistry, *88*, 11877 (2016)

Separation of Lacto-N-hexaose (LNH) and Lacto-N-neohexaose (LNnH)

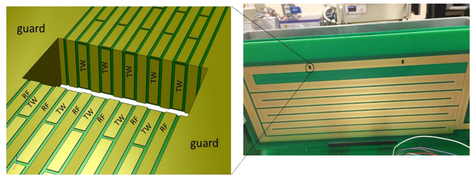


CRIMP enables use of ~1000-fold larger ion populations

- Accumulation and trapping in a large portion of the separation path prior to compression
- Basis for greatly increased measurement dynamic range (and coverage)

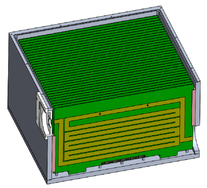


An ion elevator enabling multi-level SLIM



In progress

- Much longer path (~500 m) multi-level SLIM SUPER IM under construction aiming to provide separation peak capacities of >5000
- Projected ability to trap and accumulate ion populations >10^{10} in <10 s, for high dynamic range SLIM SUPER IM-MS analyses taking <1 min



Acknowledgements

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