

Targeted and untargeted metabolic profiling by incorporating scanning FAIMS into LC-MS

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Introduction

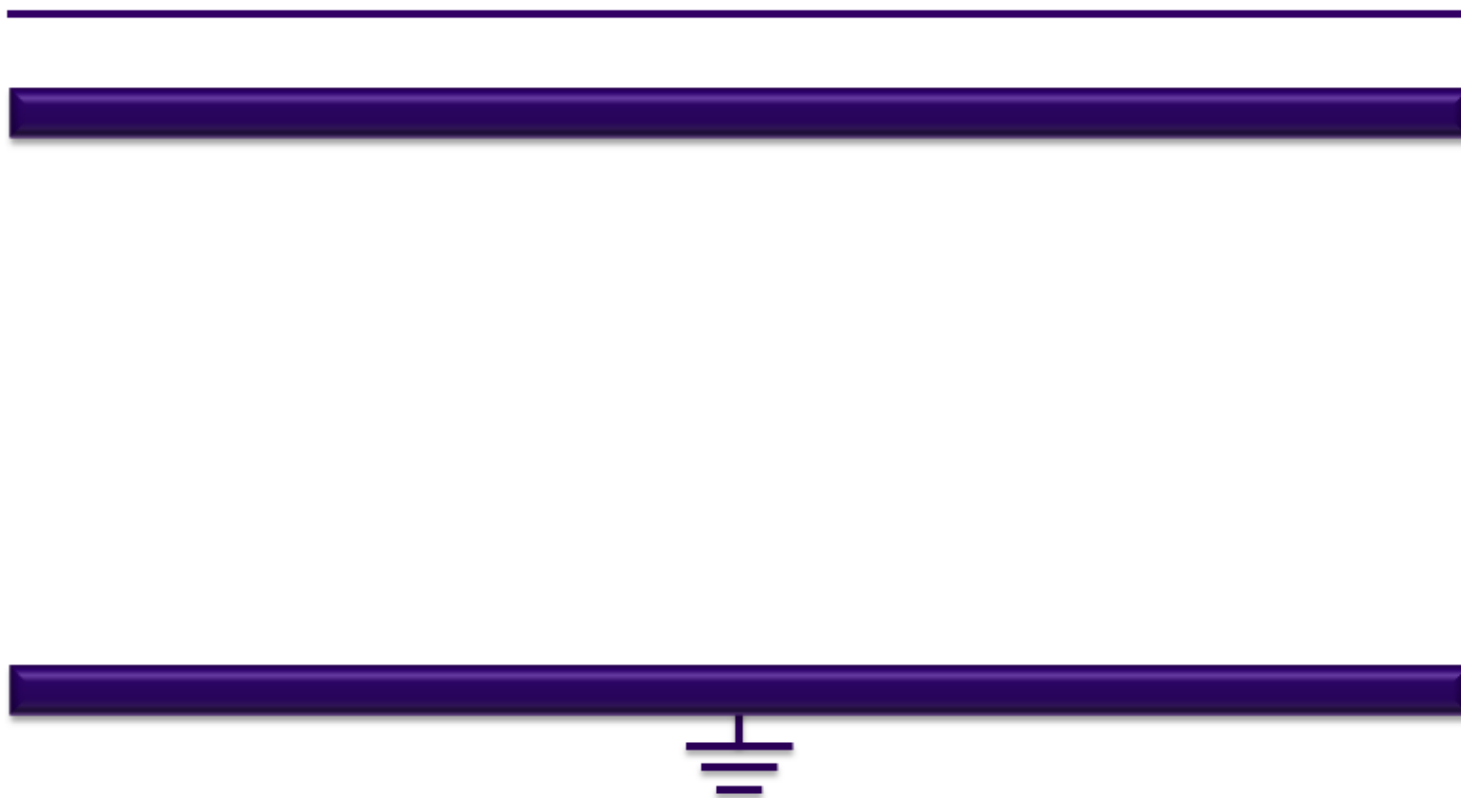
- LC-MS is a highly used technique for untargeted profiling analyses
- Incorporation of scanning ion mobility with LC-MS
- Why choose FAIMS over IMS (DT or TW)?
- Fast FAIMS scanning achievable with miniaturised FAIMS device
- Full scan FAIMS within time of a UHPLC peak
- Approach applicable to a range of mass spectrometers

FAIMS

High field

Low field

Dispersion
field (DF)

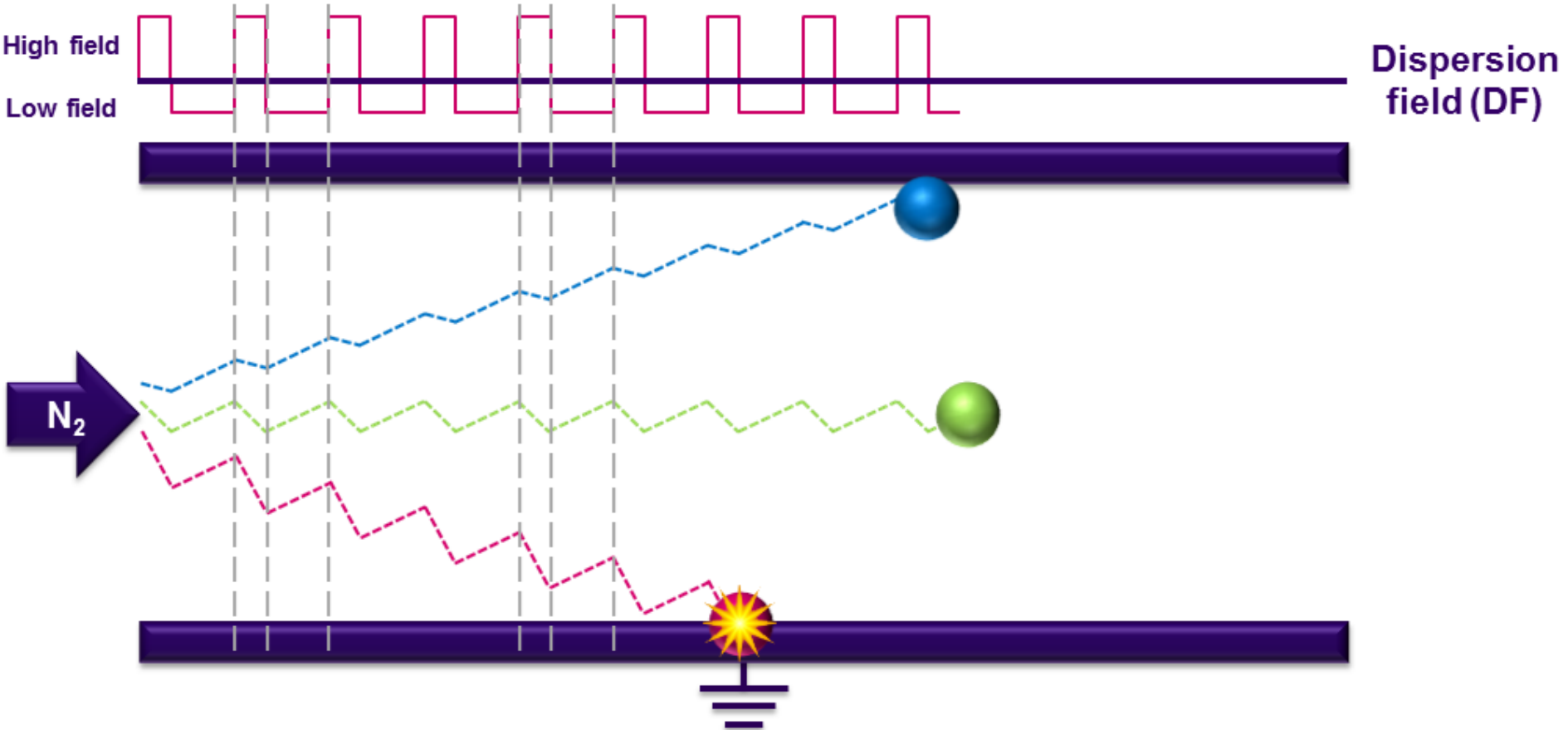


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University

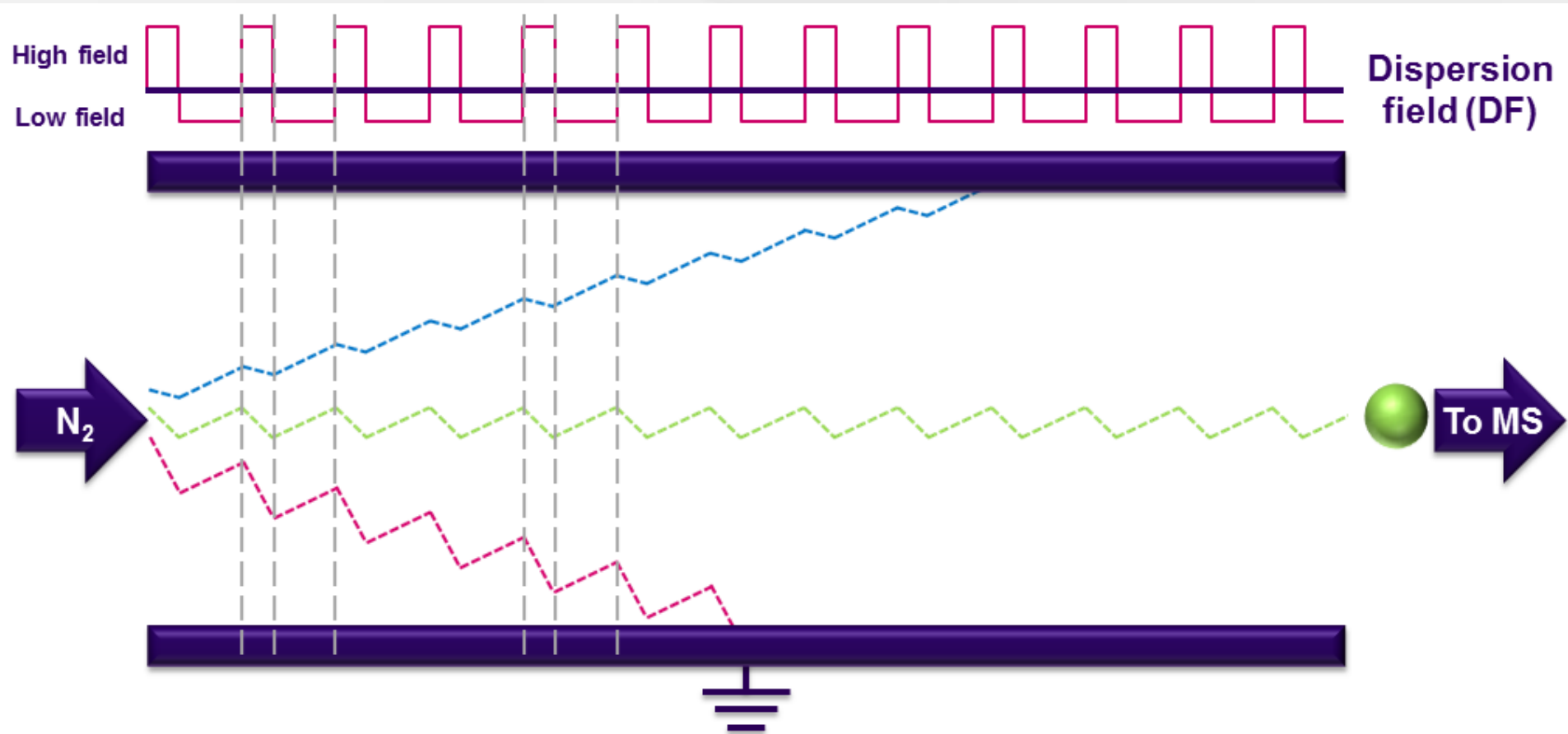


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Centre for Analytical Science

FAIMS



FAIMS



Untargeted profiling – IMS

Journal of Chromatography B, 871 (2008) 357–361

Contents lists available at ScienceDirect

Journal of Chromatography B

journal homepage: www.elsevier.com/locate/chromb



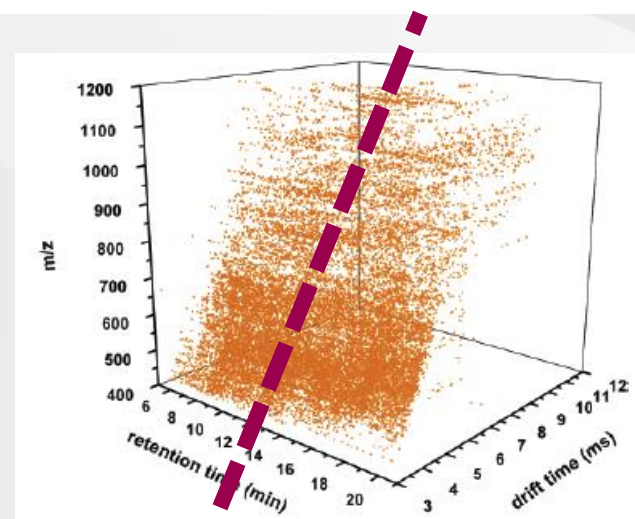
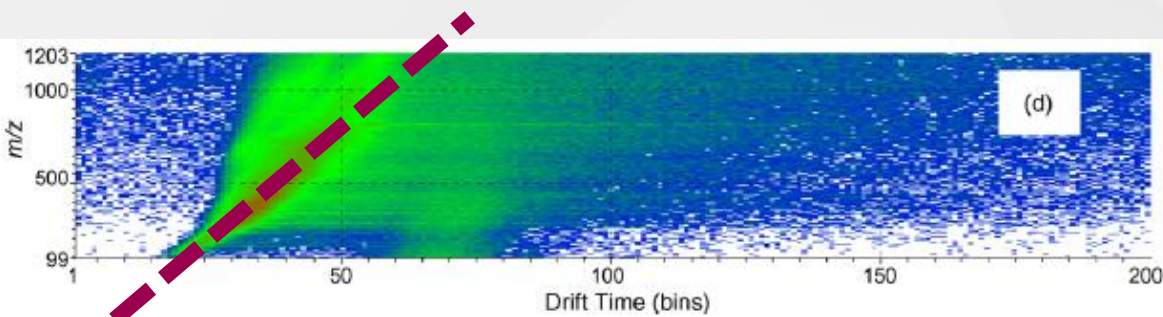
research articles **Journal of proteome research**

Toward Plasma Proteome Profiling with Ion Mobility-Mass Spectrometry

Stephen J. Valentine,[†] Manolo D. Plasencia,[‡] Xiaoyun Liu,[‡] Meera Krishnan,^{‡,§} Stephen Naylor,^{||} Harold R. Udseth,[⊥] Richard D. Smith,[⊥] and David E. Clemmer^{*‡}

An approach to enhancing coverage of the urinary metabonome using liquid chromatography–ion mobility–mass spectrometry[☆]

Emma L. Harry^a, Daniel J. Weston^b, Anthony W.T. Bristow^c, Ian D. Wilson^d, Colin S. Creaser^{a,*}



Harry et al, *J. Chromatogr. B*, 2008, 871, 357-361

Valentine et al, *J. Proteome. Res.*, 2006, 5, 2977-2984

Untargeted profiling – FAIMS

analytical
chemistry

No LC

ARTICLE

pubs.acs.org/ac

Nontarget Analysis of Urine by Electrospray Ionization-High Field Asymmetric Waveform Ion Mobility-Tandem Mass Spectrometry

Daniel G. Beach and Wojciech Gabryelski*

Assessing the Dynamic Range and Peak Capacity of Nanoflow LC-FAIMS-MS on an Ion Trap Mass Spectrometer for Proteomics

Jesse D. Canterbury, Xianhua Yi, Michael R. Hoopmann, and Michael J. MacCoss*

LC run time = 120 mins
FAIMS scan time = 2-3 s

Beach et al, *Anal. Chem.*, 2011, 83, 9107-9113

Canterbury et al, *Anal Chem*, 2008, 80, 6888-6897

Creese et al, *J Am Soc Mass Spectrom*, 2013, 24, 431-443



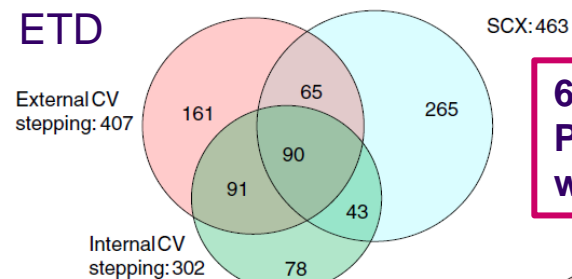
© The Author(s), 2013. This article is published with open access at Springerlink.com J. Am. Soc. Mass Spectrom. (2013) 24:431-443
DOI: 10.1007/s13361-012-0544-2

RESEARCH ARTICLE

Probing the Complementarity of FAIMS and Strong Cation Exchange Chromatography in Shotgun Proteomics

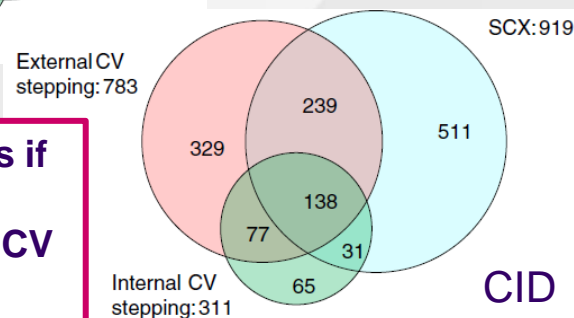
Andrew J. Creese,¹ Neil J. Shimwell,^{1,2} Katherine P. B. Larkins,¹ John K. Heath,¹ Helen J. Cooper¹

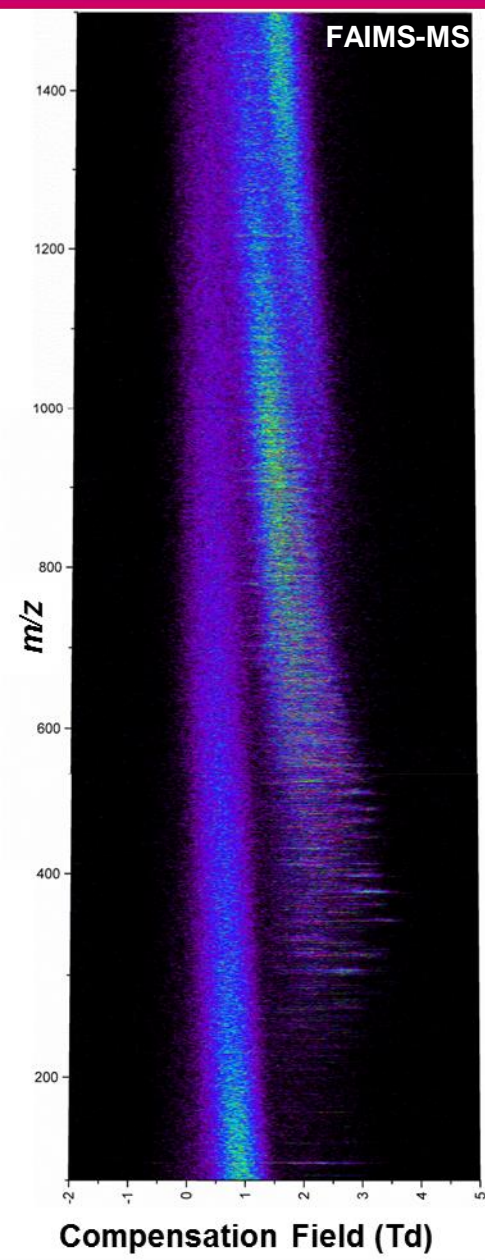
ETD



6 FAIMS conditions
Peptide IDs missed
with scanning mode

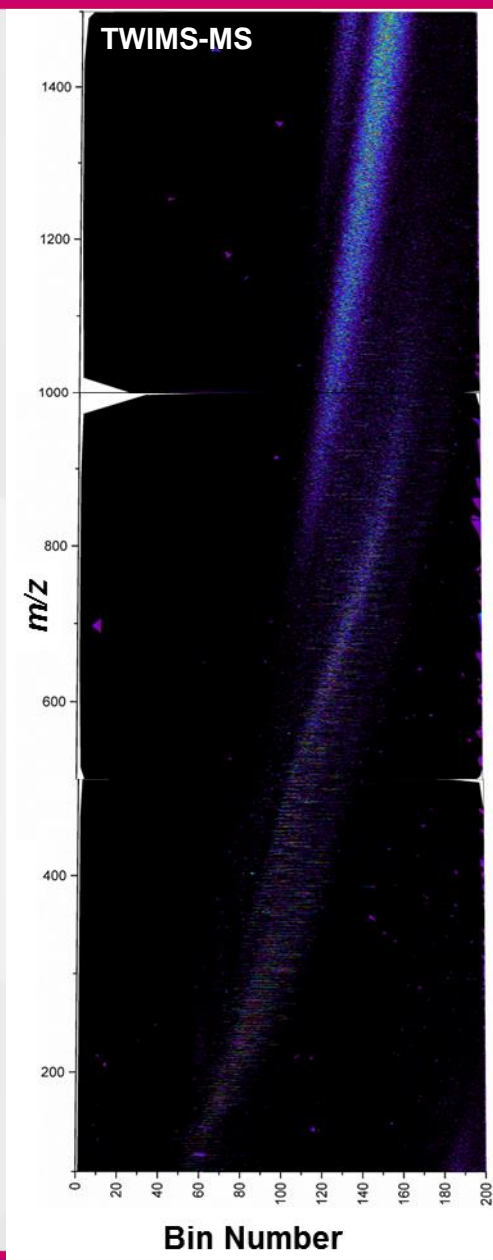
Scanning can miss ions if
the top of the LC peak
does not coincide with CV
for transmission





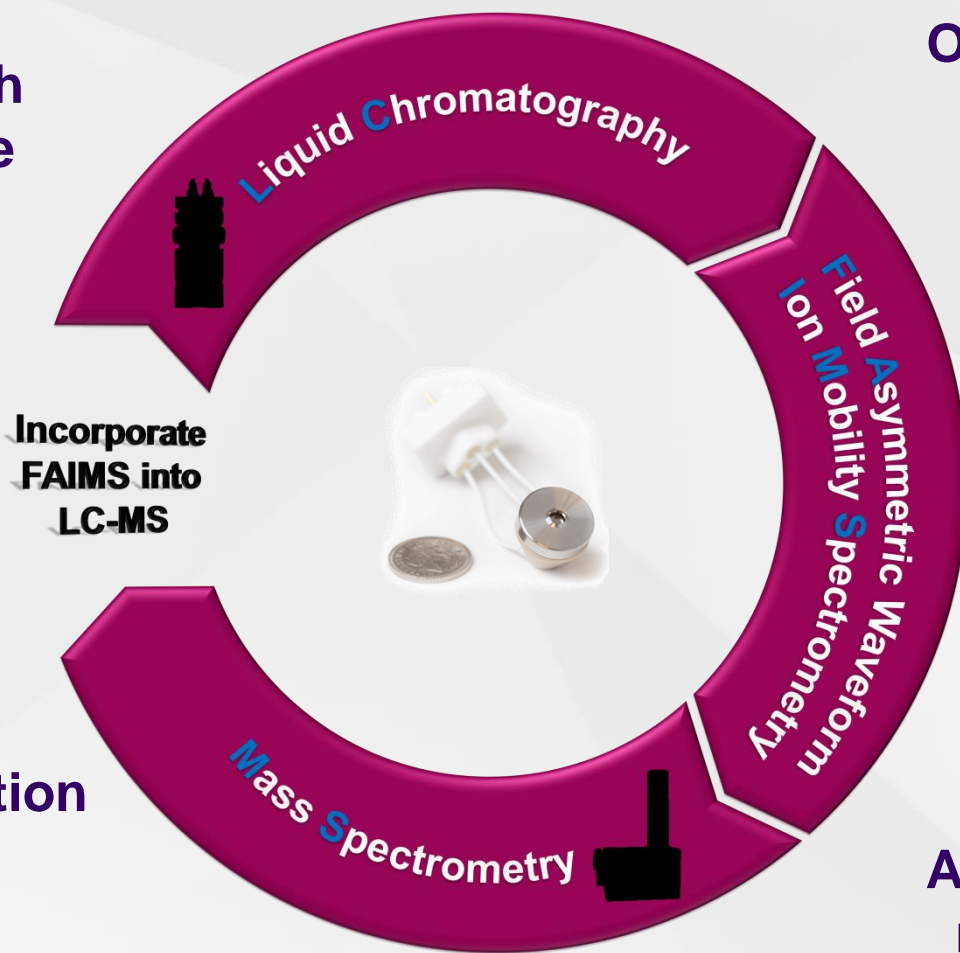
FAIMS vs TWIMS

- Direct comparison
- FAIMS covers a greater proportion of the analytical space
- FAIMS covers across the CF range at all m/z
- TWIMS shows a correlation between m/z and bin number
 - Bin number increases as m/z increases



Apply approach to human urine

Incorporate into Omics workflow



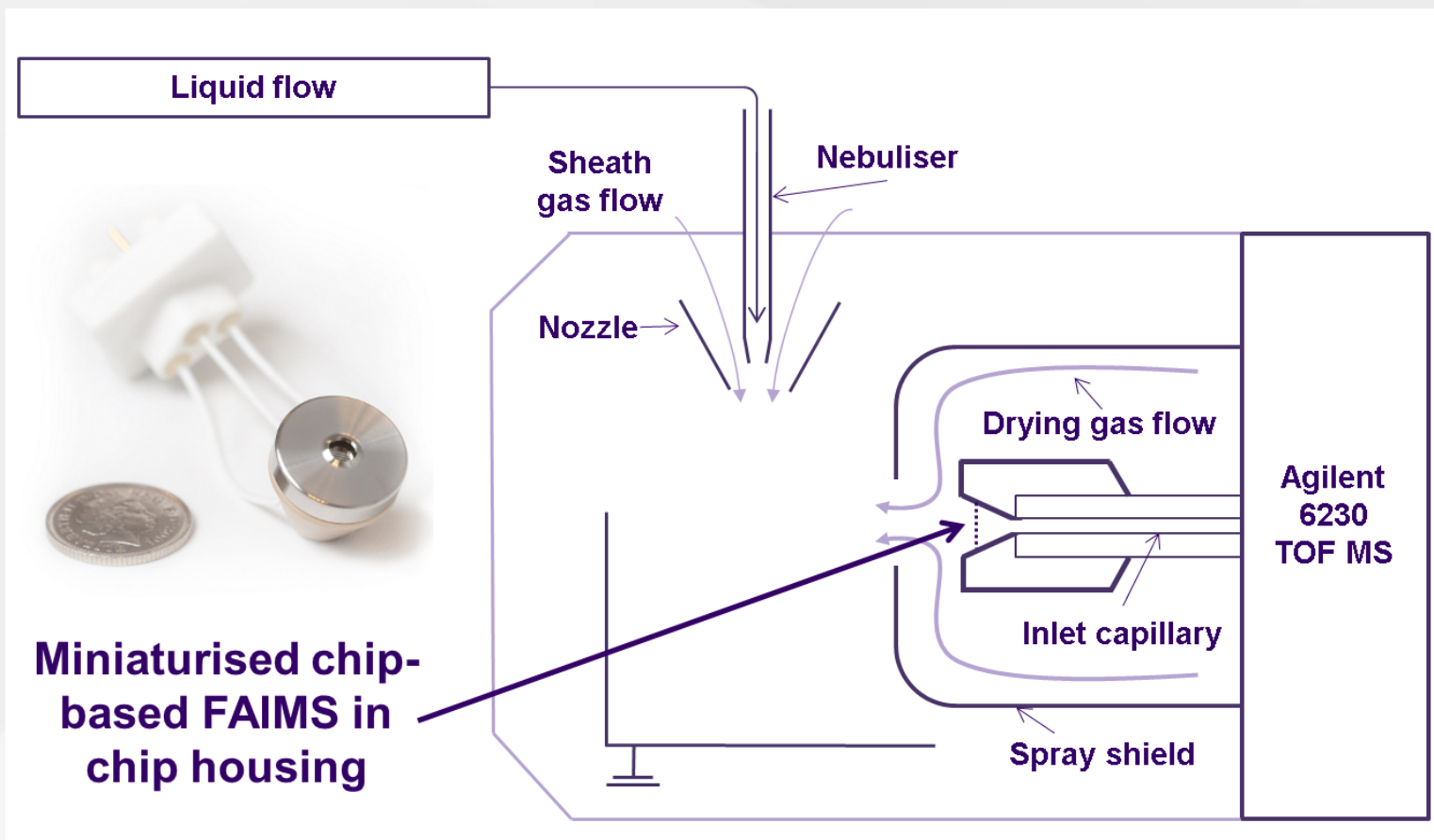
Incorporate FAIMS into LC-MS

Set-up

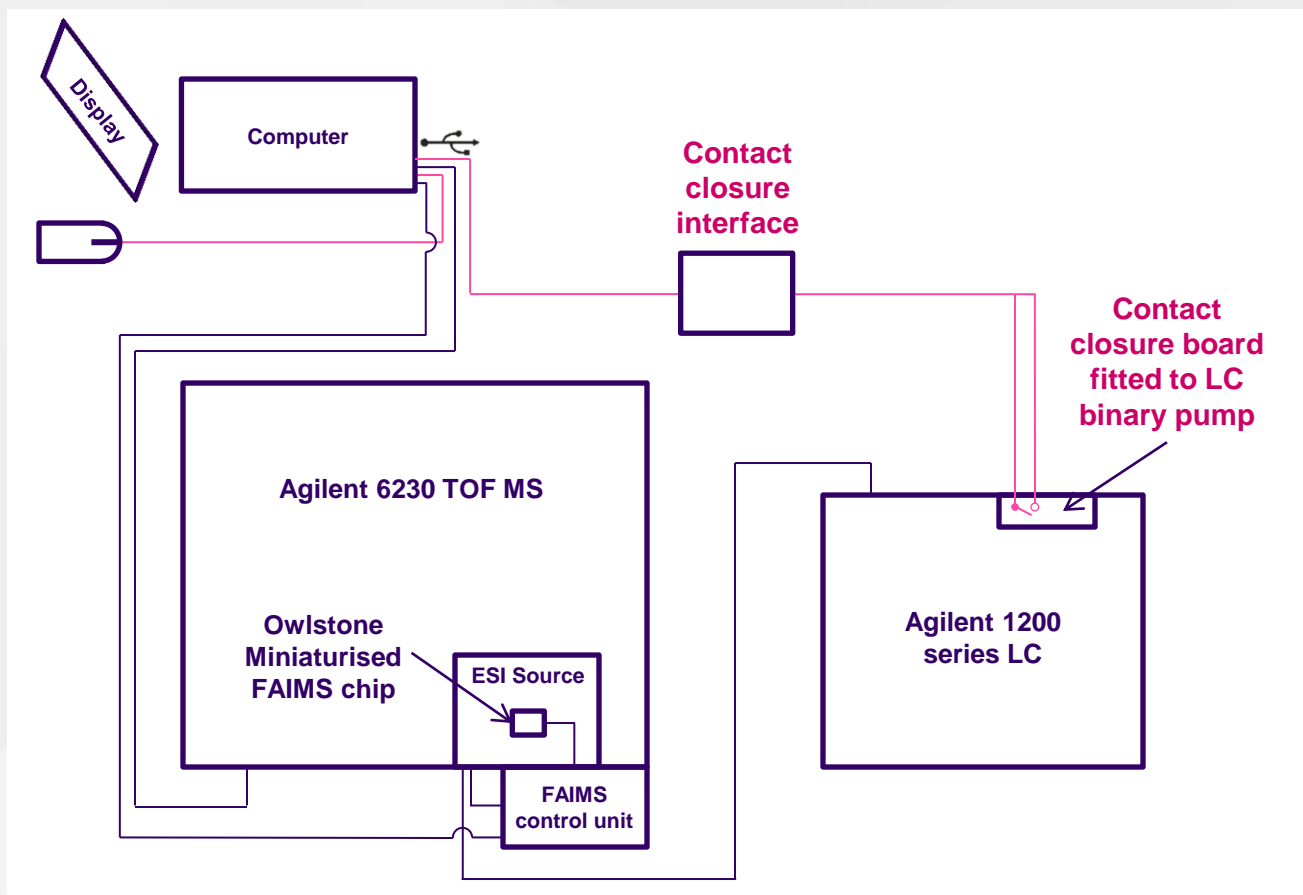
Modes of operation

Acquisition of nested data sets

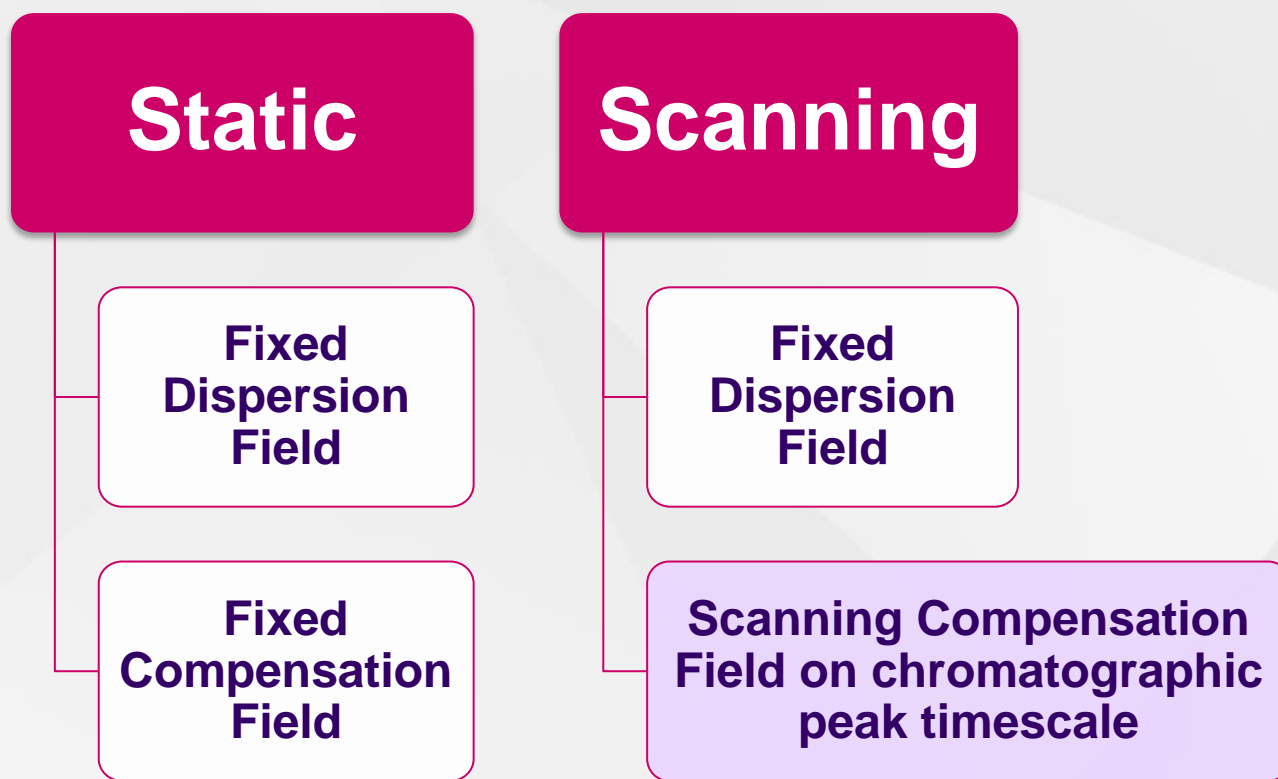
Miniaturised FAIMS with LC-MS



How? FAIMS/LC-MS Synchronisation



LC-FAIMS-MS Modes of Operation



Application to Biological Matrices

FAIMS-MS

Optimisation of FAIMS
DF and CF

Targeted
LC-FAIMS-MS

Isobaric separation,
reduction in chemical
noise, in-source CID

Untargeted
LC-FAIMS-MS

Feature determination



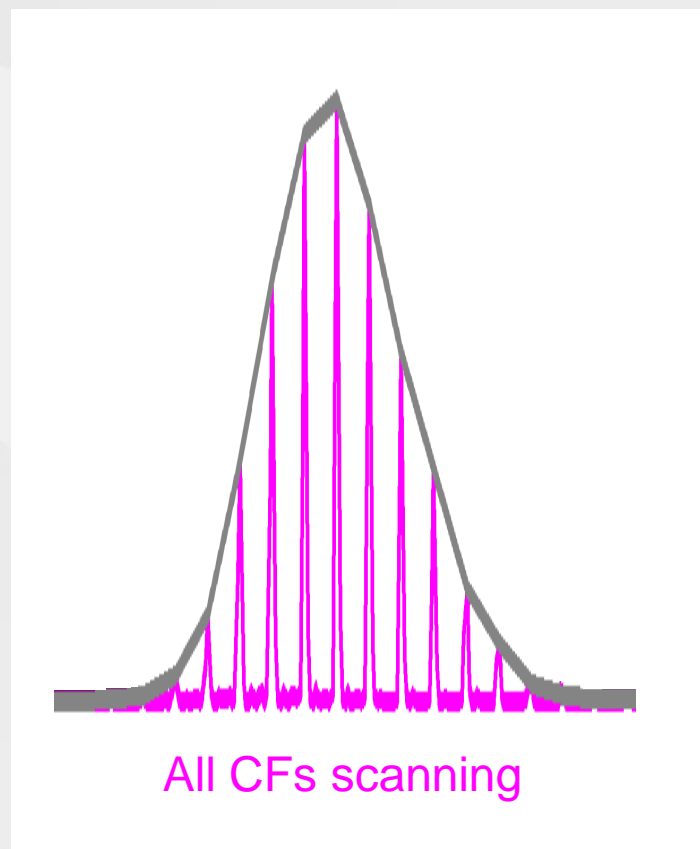
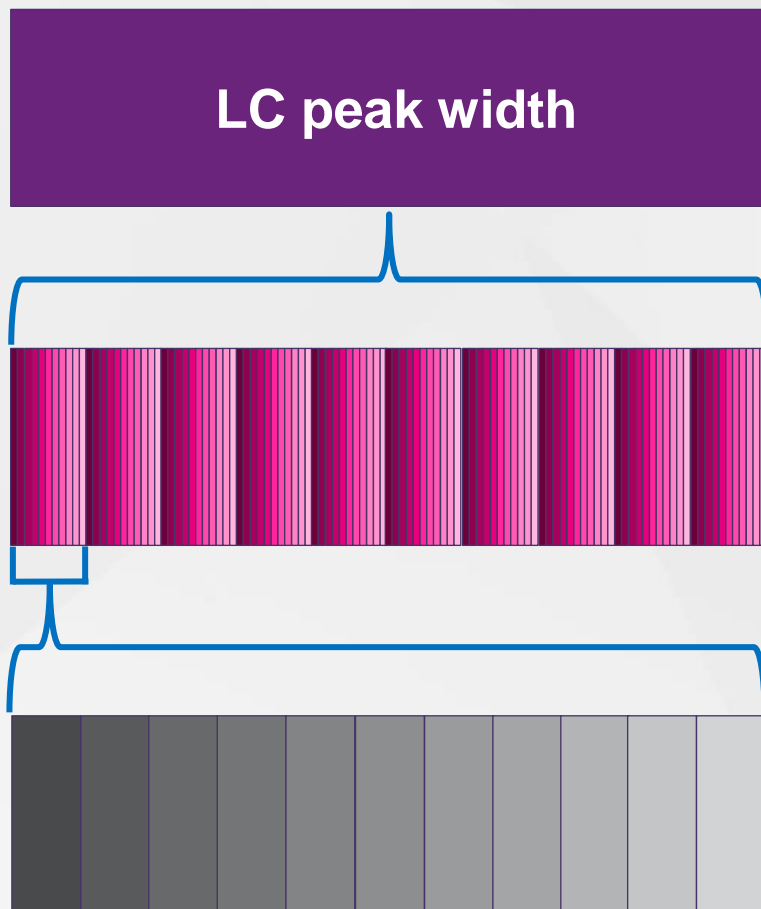
Scanning LC-FAIMS-MS – how?

Chromatographic Peak

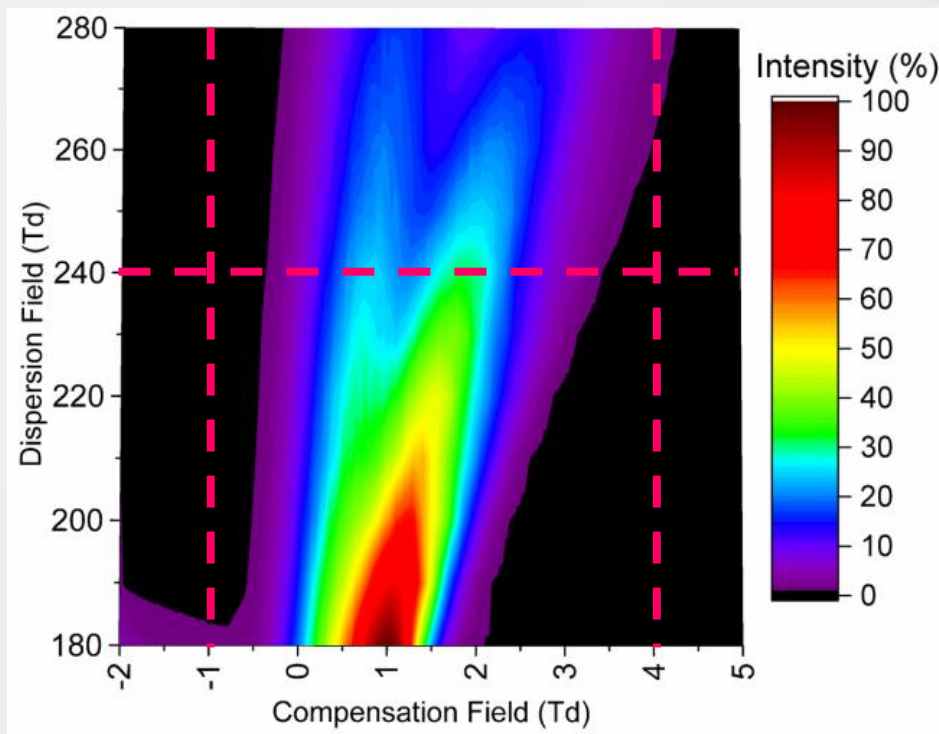
LC peak width

Compensation Field Scan
11 CFs per s

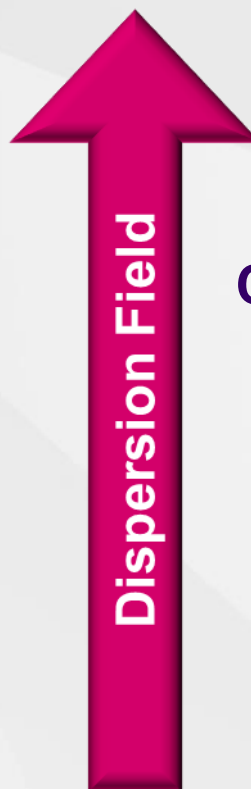
Mass Spectra
1 per CF



DF and CF Selection for Untargeted Analysis of Human Urine



FAIMS-MS



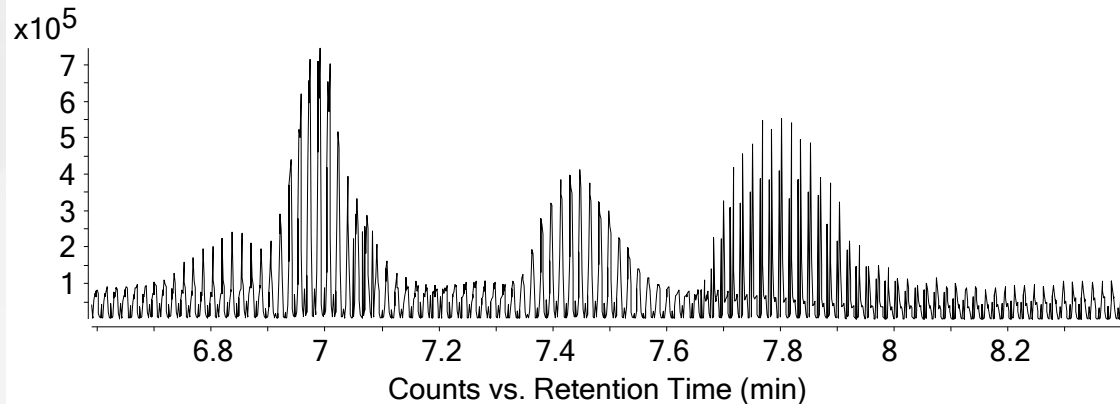
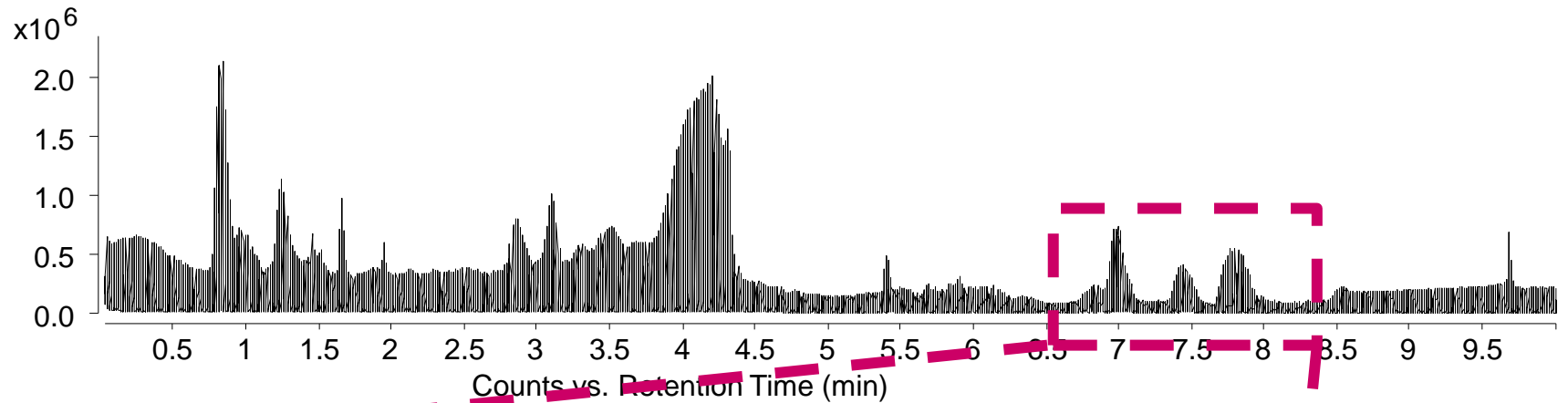
CF resolution



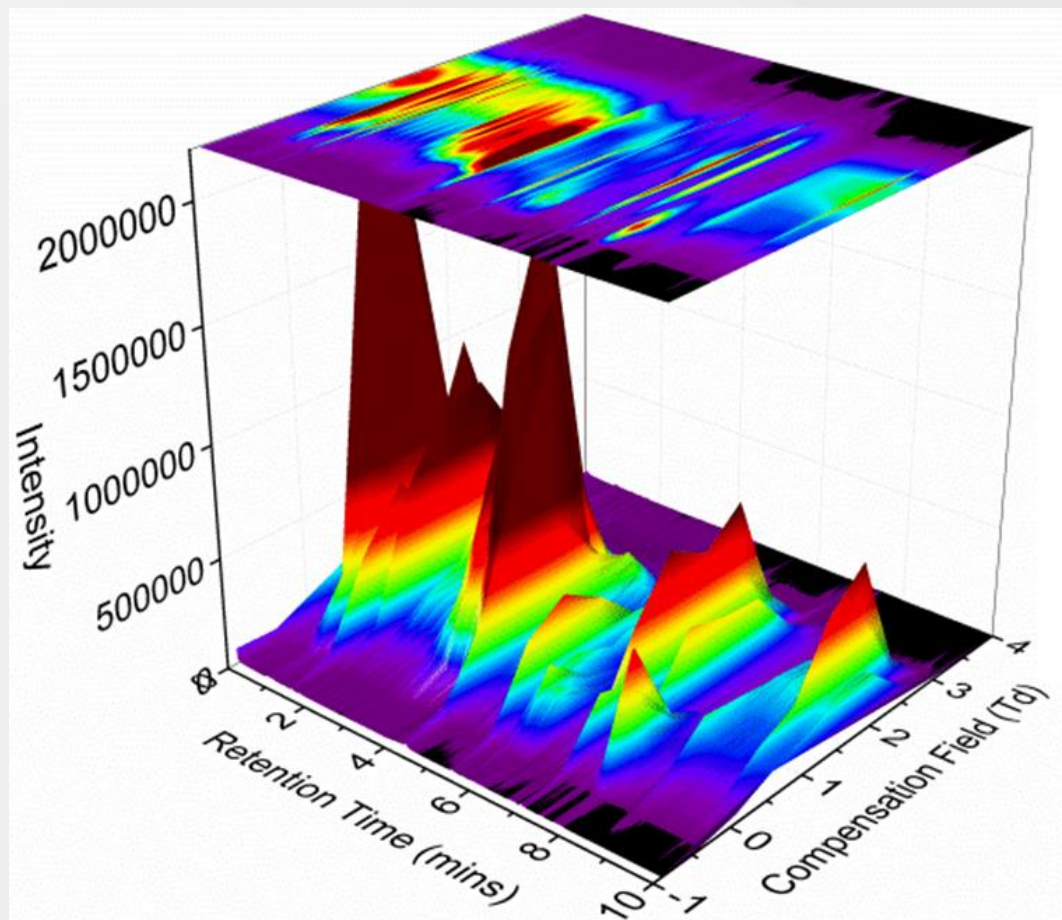
Intensity



Human Urine TIC – Scanning approach



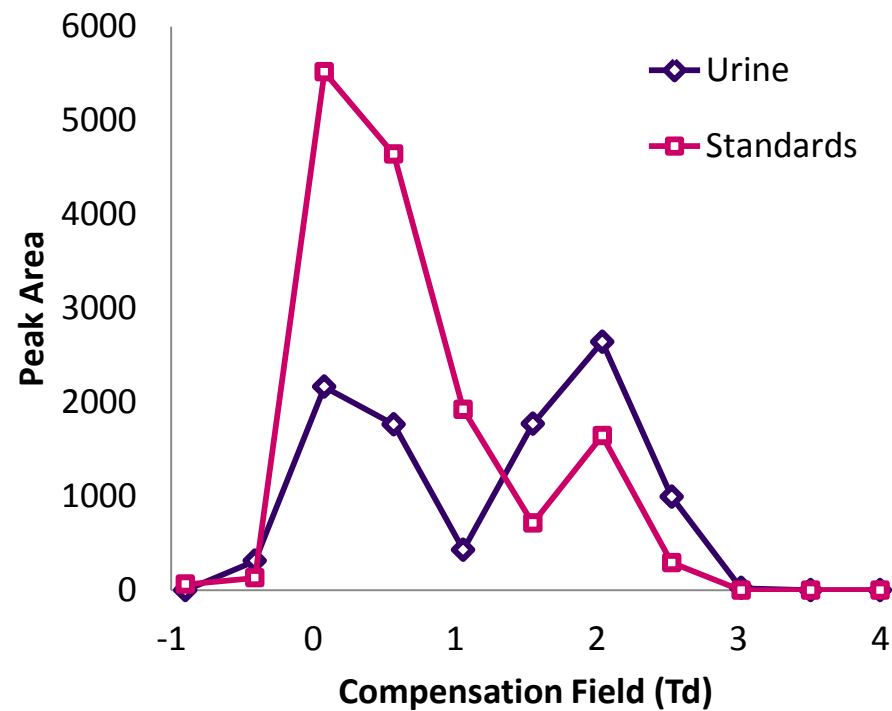
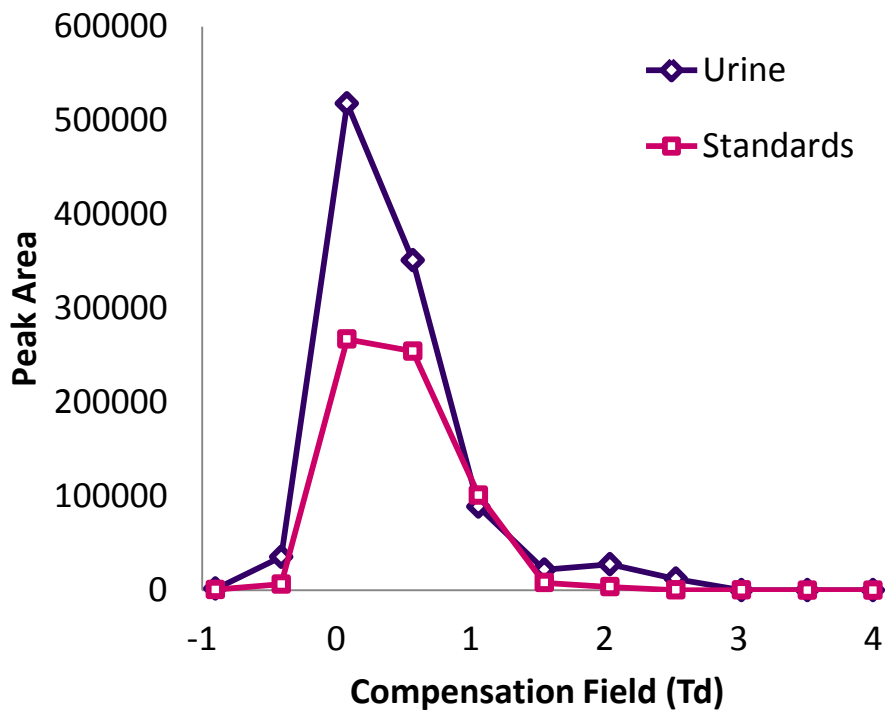
Human Urine TIC – Scanning approach



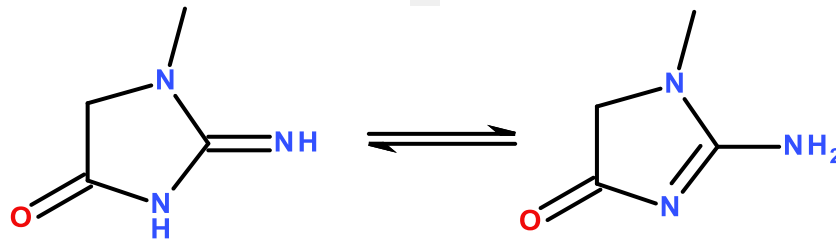
- CF deconvolution into individual channels
- CF adds another dimension of separation



Urinary Creatinine

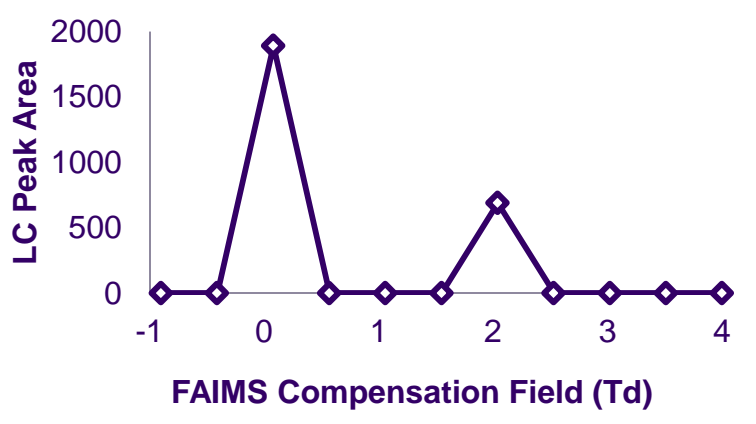


$[M+H]^+$
 m/z 114.066

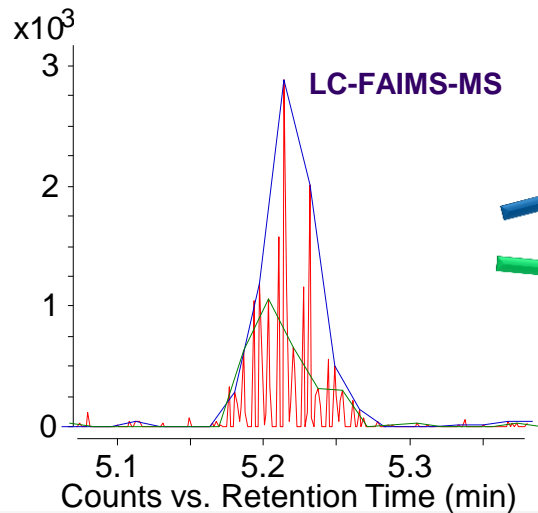
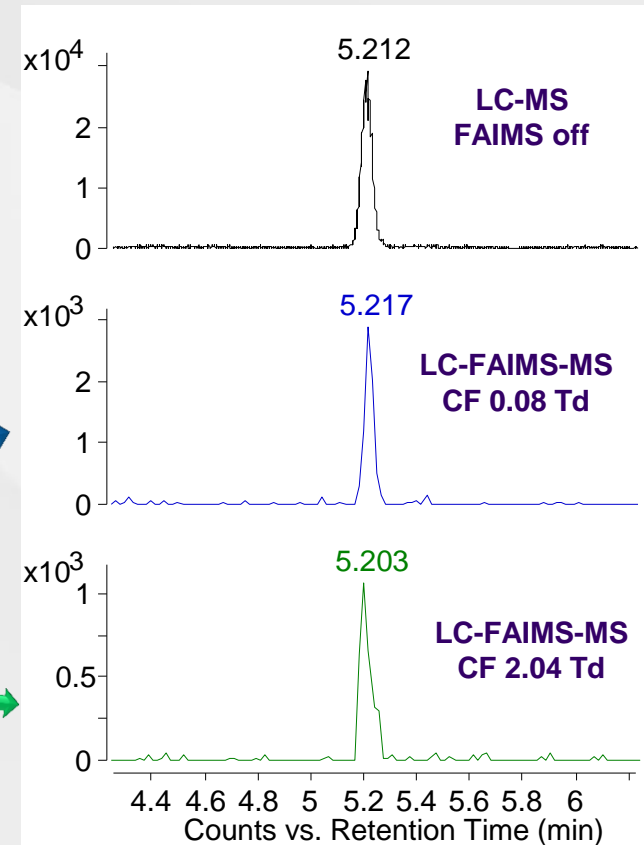


$[M+Na]^+$
 m/z 136.048

Isobaric Separation



m/z 207.11
RT 5.21 min



FAIMS off = 1 feature
FAIMS on = 2 features

Reduction in Chemical Noise and Interferences

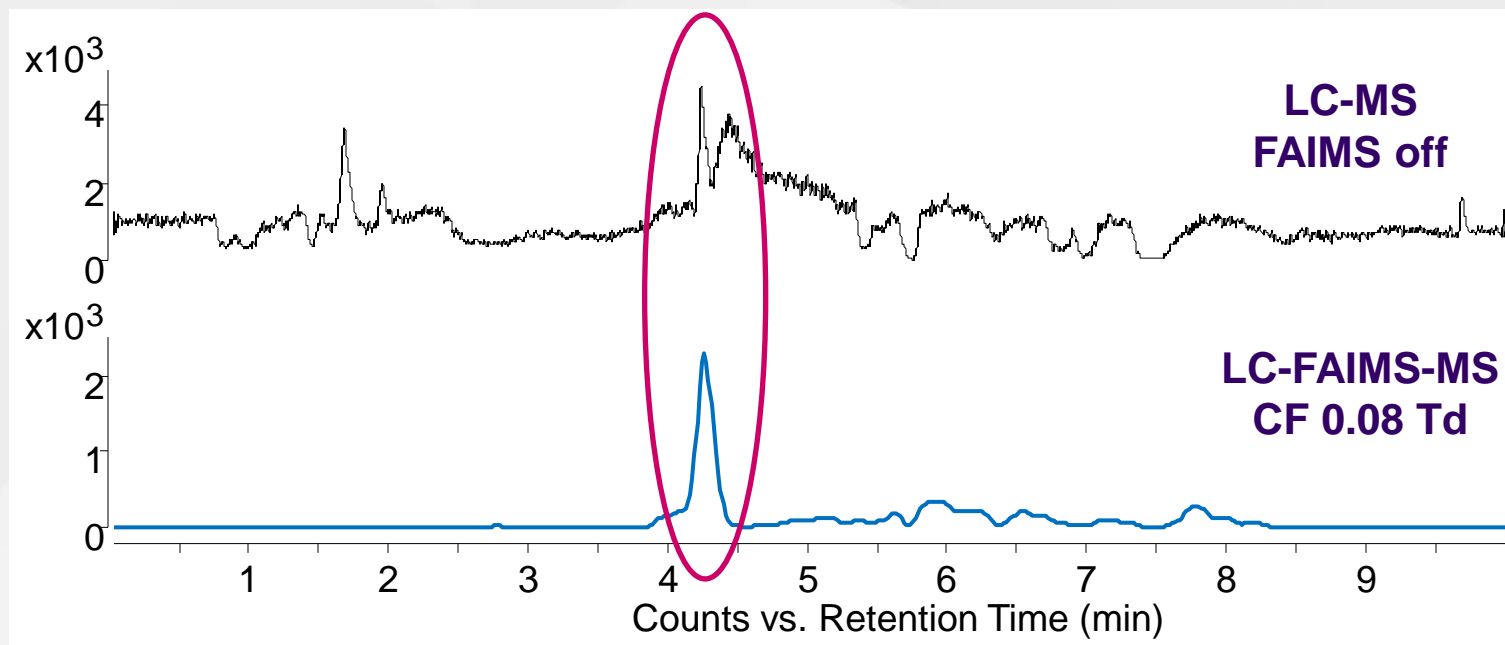
m/z 331.21, RT 4.24 min

FAIMS off

S:N = 2.7

FAIMS on

S:N = 124.1



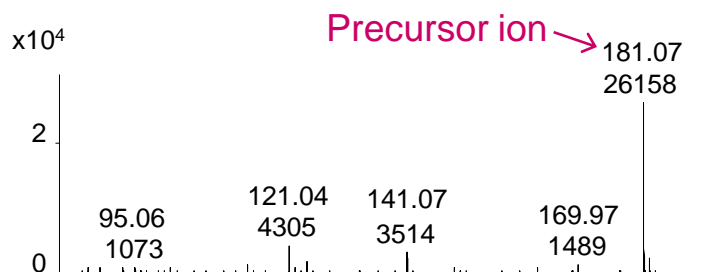
FAIMS off = 0 features, FAIMS on = 1 features

In-source CID vs FAIMS-selected CID

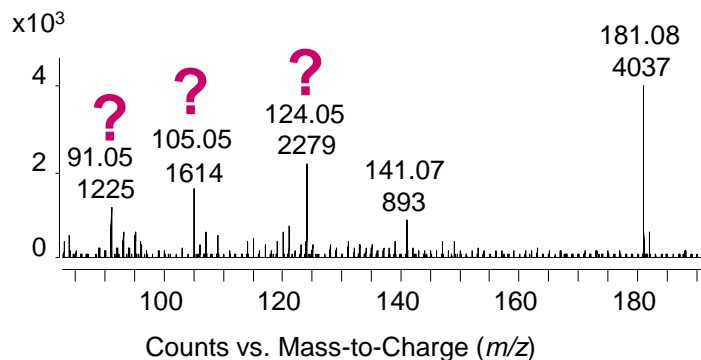
LC-MS

LC-FAIMS-MS

Frag 200 V



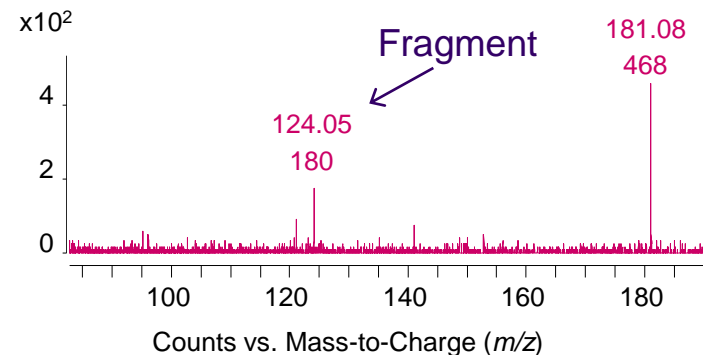
Frag 350 V



Frag 200 V

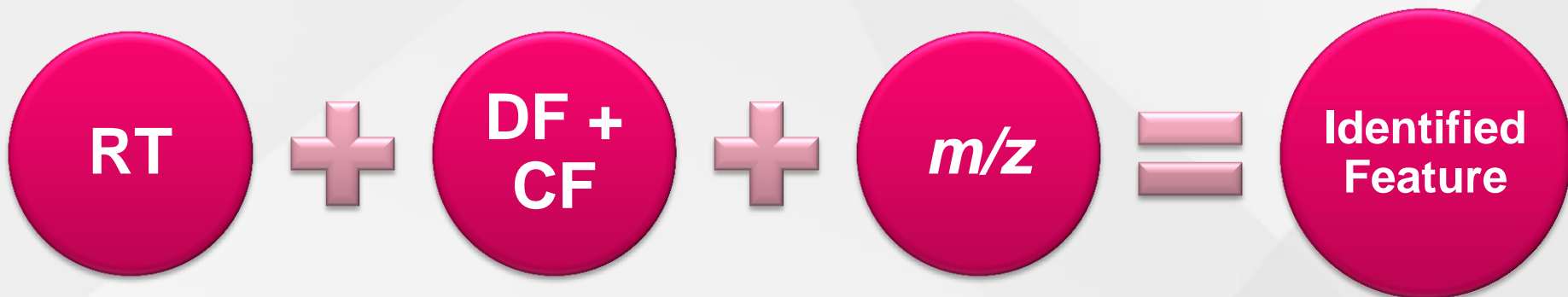


Frag 350 V

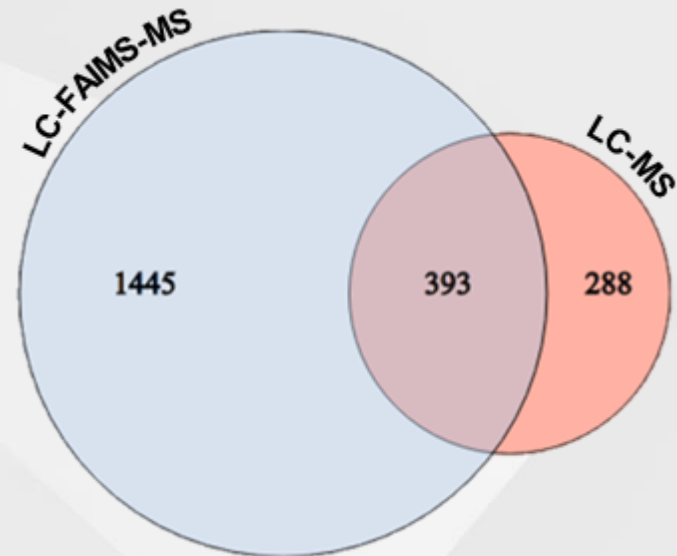
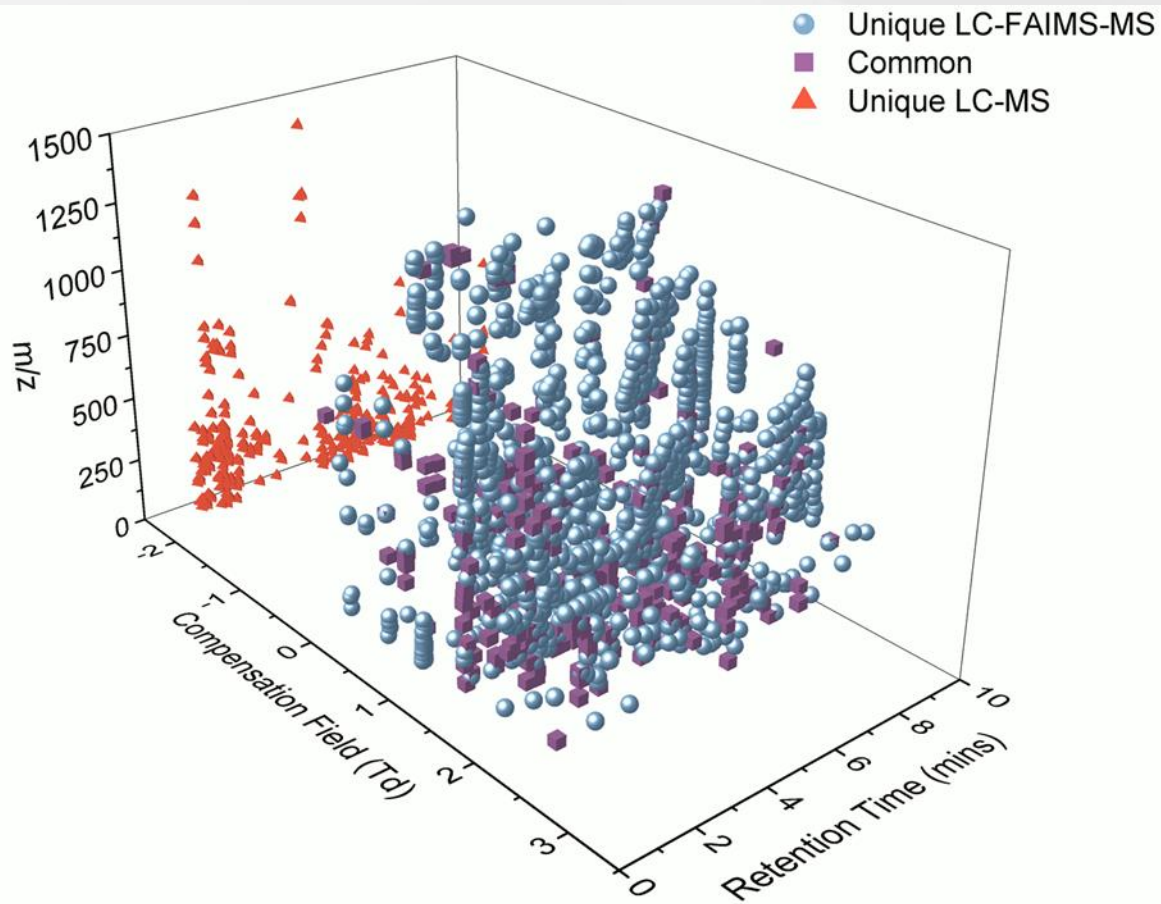


FAIMS-IN-SOURCE COLLISION INDUCED DISSOCIATION FISCID

Untargeted Feature Determination



Acquisition of Nested Data Sets



Identified features based upon RT, m/z and CF

Conclusions

- Acquisition of LC-FAIMS-MS nested data sets on timescale of UHPLC peak for the first time
- Increase in peak capacity using LC-FAIMS-MS in comparison to LC-MS
- Higher level of orthogonality with m/z / RT than IMS
- Separation of isobaric and co-eluting analytes
- DF + CF as additional identifiers
- Can be integrated into non-targeted omics workflows
- Applicable to a range of mass spectrometers

Acknowledgments

- **Loughborough University:**

- Colin Creaser
- James Reynolds
- Matthew Turner



- **Owlstone:**

- Lauren Brown

- **Staff and researchers at the Centre for Analytical Science**



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