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
Untargeted profiling – IMS


Untargeted profiling – FAIMS

No LC

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


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
External CV stepping: 407
Internal CV stepping: 302

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

CID
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
Set-up

Modes of operation

Acquisition of nested data sets

Incorporate into Omics workflow

Apply approach to human urine

Incorporate FAIMS into LC-MS

Liquid Chromatography

Field Asymmetric Waveform Ion Mobility Spectrometry

Mass Spectrometry
Miniaturised FAIMS with LC-MS

Liquid flow

Sheath gas flow

Nebuliser

Nozzle

Drying gas flow

Agilent 6230 TOF MS

Inlet capillary

Spray shield

Miniaturised chip-based FAIMS in chip housing
How? FAIMS/LC-MS Synchronisation

Diagram:

- Computer
- Contact closure interface
- Contact closure board fitted to LC binary pump
- Agilent 6230 TOF MS
- Owlstone Miniaturised FAIMS chip
- ESI Source
- FAIMS control unit
- Agilent 1200 series LC
LC-FAIMS-MS Modes of Operation

Static
- Fixed Dispersion Field
- Fixed Compensation Field

Scanning
- Fixed Dispersion Field
- Scanning Compensation Field on chromatographic peak timescale
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
  - All CFs scanning
DF and CF Selection for Untargeted Analysis of Human Urine

FAIMS-MS

Dispersion Field

Intensity

CF resolution
Human Urine TIC – Scanning approach
Human Urine TIC – Scanning approach

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

\[[\text{M+H}]^+] \quad m/z \ 114.066\]

\[[\text{M+Na}]^+] \quad m/z \ 136.048\]
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

FAIMS-IN-SOURCE COLLISION INDUCED DISSOCIATION

FISCID

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Untargeted Feature Determination

RT + m/z = Identified Feature

RT + DF + CF + m/z = Identified Feature
Acquisition of Nested Data Sets

Identified features based upon RT, \textit{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
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