Combining ion mobility spectrometry with mass spectrometry for the analysis of complex samples: the potential for environmental analysis

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Mobility of an ion in a drift tube in the presence of an electric field gradient and a buffer gas (e.g. He, N\textsubscript{2} or air; 1-5 mbar or 1 bar)

\[ v_d = K \cdot E \]

[\( v_d \) = ion velocity, \( E \) = electric field gradient, \( K \) = ion mobility]
Under low field conditions, ion mobility (K) is determined by:

\[ K = \frac{3q}{16N} \left( \frac{2\pi}{\mu k_B T} \right)^{1/2} \left( \frac{1}{\Omega} \right) \]

[N = buffer gas number density, T = temperature, q = ionic charge, \( \mu = \) reduced mass and \( \Omega = \) collision cross section]

⇒ Separation depends on ion charge and shape/size
Ion mobility drift cell (Smiths Detection)

4.2 cm drift tube

Resolution in ion mobility spectrometry

Figure 2: Nano-ESI/IMS spectrum of L-arginine at 100°C using nitrogen drift gas.

\[ [\text{L-Arg}+\text{H}]^+ \]

\[ [\text{(L-Arg)}_2+\text{H}]^+ \]

\[ \text{[Solvent]}^+ \]

RP (FWHM) 32
Efficiency (N) 5800

[nano-ESI/IMS of L-arginine; 4.2 cm drift tube; N\(_2\) at atmospheric pressure]

Ion mobility in high and low electric fields

- Mobility is dependent on electric field strength

\[ K \left( \frac{E}{N} \right) = K(0) \left[ 1 + \alpha \left( \frac{E}{N} \right) \right] \]

- Alpha coefficient – compound (ion) dependent

Factors affecting differential mobility in the gas phase

- Ion/buffer gas interactions (clustering/declustering)
- Frictional heating
- Structural/conformational change
- Dipole alignment
Field Asymmetric Waveform Ion Mobility Spectrometry (FAIMS)/Differential mobility spectrometry (DMS)

- Compensation field (CF) set to transmit ions of selected differential mobility
- Continuous ion beam (equivalent to quadrupole mass filter)

FAIMS DF vs CF heat plot for 3-methylxanthine complexes

Dispersion field (DF, Td)

Compensation field (CF; Td)

[(3-MX)_4+Na]^+

DF 320 Td

[(3-MX)_4+Na]^+

Intensity vs CF (Td)

ESI-FAIMS-MS of 2,4,6-trimethylaniline and N,N-dimethyl-m-toluidine (Dispersion field = 230 Td; electrode gap = 100 μm; 50 ng/ml)

Selected ion response for m/z 136

[Smith R et al., Anal. Methods, 2013, 5, 3799]
Applications of ion mobility spectrometry: Stand-alone detection of explosives and chemical agents
Applications of ion mobility spectrometry: International space station cabin air
Environmental applications of ion mobility spectrometry:

Review: Marquez-Sillero et al, Ion-mobility spectrometry for environmental analysis, TRAC, 2011, 30, 677-690]
Ion mobility spectrometry configurations:

Sample extraction/inlet systems: membrane inlet, thermal desorption, SPE, SPME, GC, LC etc
Environmental applications of ion mobility spectrometry: detection of BTEX by multicapillary GC/DTIMS

Environmental applications of ion mobility spectrometry: detection of BTEX by multicapillary GC/DTIMS

[UV photoionization (positive ion), drift tube 6 or 12 x 1.5 cm (375 V/cm), drift gas N$_2$ at 200 ml/min, MCC SE-30 (70 cm)]

Environmental applications of ion mobility spectrometry: detection of BTEX by multicapillary GC/DTIMS

[UV photoionization (positive ion), drift tube 6 or 12 x 1.5 cm (375 V/cm), drift gas N\textsubscript{2} at 200 ml/min, MCC SE-30 (70 cm)]


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Stand-alone ion mobility: environmental applications

- Transportability/field-based application of DTIMS/FAIMS
- Ease of use
- High sensitivity (<ppm)
- Rapid response (seconds – minutes)
- Limited dynamic range (1-2 orders of magnitude for drift tube IMS)
  - Threshold monitoring
- Low resolution (not suitable for complex mixtures)

⇒ Combined ion mobility-mass spectrometry
Combining ion mobility spectrometry with mass spectrometry

MS: quadrupole, triple quadrupole, Q-trap, time-of-flight, Q-TOF, Orbitrap
Drift tube ion mobility spectrometry (DTIMS)

Static field

- Agilent 6560
- Excellims HRIMS
- Tofwerk IMS-MS

Travelling wave (TWIMS)

- Waters Synapt G2
ESI-IM(TWIMS)-MS analysis of protonated active pharmaceutical ingredients

A. Lamivudine
B. Lamotrigine
C. Rosiglitazone
D. Desfluro Paroxetine
E. Paroxetine
F. Lamotrigine impurity

ESI-IM(TWIMS)-MS drift time vs m/z plot for protonated active pharmaceutical ingredients

A. Lamivudine
B. Lamotrigine
C. Rosiglitazone
D. Desfluoro Paroxetine
E. Paroxetine
F. Lamotrigine impurity

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Environmental applications of ion mobility-mass spectrometry: targeted analysis
Environmental applications of ion mobility-mass spectrometry: detection of sulfonylurea herbicides in river water by ESI-DTIMS-quadrupole MS

[ESI (positive ion), drift tube 375 V/cm, drift gas N\textsubscript{2} at 800 ml/min, river water sample spiked with 25 ppm sulfometuron-methyl]

Environmental applications of ion mobility-mass spectrometry: detection of sulfonylurea herbicides in river water by ESI-DTIMS-quadrupole MS

⇒ Rapid analyte detection/identification based on m/z and drift time

FAIMS-MS: cylindrical electrodes (Thermo Scientific)

(electrode gap ~ 1-3 mm)

Electrospray ion source → Mass spectrometer


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FAIMS-MS: planar electrodes

( electrode gap ~ 0.5 mm )

AB SCIEX SelexION


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Prototype Owlstone ultra-FAIMS chip mounted into chip cartridge located behind spray shield in Jet Stream ESI source in front of transfer capillary

(electrode gap 0.1 mm)
Environmental applications of ion mobility-mass spectrometry: detection of haloacetic acids in water by ESI-FAIMS-quadrupole MS

[ESI (-ve ion, PE Sciex API 300), DV -3400/-3600 V (0.75 MHz), drift gas N₂, 1 ppm]

[adapted from: B Ells et al., Anal. Chem. 2000, 72, 4555-4559]
Environmental applications of ion mobility-mass spectrometry: detection of haloacetic acids in water by ESI-FAIMS-quadrupole MS

Reducing chemical noise gives lower LOD and increased LDR

[adapted from: B Ells et al., Anal. Chem. 2000, 72, 4555-4559]
Environmental applications of ion mobility-mass spectrometry: non-targeted analysis
Heat plots for:

**FAIMS-TOFMS**
(Owlstone ultra-FAIMS; CF vs \( m/z \) at DF 240 Td)
and
**TWIMS-TOFMS**
(Waters Synapt G2; Bin No. (drift time) vs \( m/z \))

[Urine extract after SPE extraction; direct infusion; ESI]

⇒ Increased peak capacity in screening/’omics’ applications

Acquisition of nested LC-DTIMS (TWIMS)-MS datasets:
(Metabolite profiling of saliva for biomarkers of physiological stress)

⇒ 10 min LC run = 600 TWIMS spectra = 128,000 TOF mass spectra

[Malkar et al., Metabolomics, 2013, 9, 1192]
Acquisition of nested LC-DTIMS (TWIMS)-MS datasets: (Metabolite profiling of saliva for biomarkers of physiological stress)

\[ m/z \ 100.07 \pm 0.02; \ \delta-\text{valerolactam (2-piperidone)} \]

\[ m/z \ 100.0755 \text{ ‘up-regulated’ in saliva after exercise} \]
Acquisition of nested LC-DTIMS (TWIMS)-MS datasets for non-targeted analysis: analyte identification

- Retention time
- $m/z$ (accurate mass)/Tandem mass spectrometry (MS/MS)
- Ion mobility (drift time) $\rightarrow$ Collision cross section (CCS)
Ion mobility performance characteristics: structural analysis

Measurement of collision cross section ($\Omega$):
- Directly from the Mason-Schamp equation (static field drift tube IMS)
- Using calibrants (TWIMS and static field drift tube IMS)

$$K = \frac{(3q/16N)}{(2\pi/\mu k_B T)^{1/2}} \left(\frac{1}{\Omega}\right)$$
Correlating an experimental CCS with CCS derived from modelled/x-ray structures/library standards

- Modelled/x-ray structure
- Calculated CCS
- Compare CCSs
- Library of CCS values (e.g. metabolites)
- CCS value from analysis of standard
- Experimental CCS for unknown

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Acquisition of nested LC-IM-qTOF-MS data for non-targeted analysis: analyte identification in waste water sample by CCS measurement

**Graphical Data**

- **Counts** graph showing peaks at m/z values.
- **Drift time (ms)** graphs for m/z values.

**Textual Data**

- **LC retention time:** 10.72–10.75 min
Acquisition of nested LC-IM-qTOF-MS data for non-targeted analysis: analyte identification in waste water sample by CCS measurement

Ifosfamide (db CCS = 158.7 Å²)  
Cyclophosphamide (db CCS = 155.2 Å²)

EIC for the [M+Na]⁺ adducts (m/z = 283.0140) of ifosfamid and cyclophosphamide

Acquisition of nested UHPLC-FAIMS-TOF-MS data for non-targeted analysis of a urine extract

[Arthur K. et al., Anal. Chem. 2017 (DOI: 10.1021/acs.analchem.6b04315)]
Acquisition of nested UHPLC-FAIMS-TOF-MS data for non-targeted analysis of a urine extract

[Arthur K. et al., Anal. Chem. 2017 (DOI: 10.1021/acs.analchem.6b04315)]
Environmental analysis and ion mobility/mass spectrometry

• High level of orthogonality between ion mobility (differential mobility) and \( m/z \)
• High sensitivity
• Rapid response (seconds – minutes)
• Structural analysis/analyte identification
• Resolution of isobaric/isomeric ions (reduced chemical noise)

➤ Improved performance for targeted high throughput quantitative analysis

➤ Increased peak capacity for non-targeted (‘Omics’) applications
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