High Performance Ion Mobility Spectrometry – An Ideal Field Analytical Instrument

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Ion Mobility Spectrometry

Interaction based separation rely on analyte and drift media properties

Ion mobility based separation relates to gas phase size, shape, and stereostructure

High speed m/z correlated separation at low instrument cost with portability

\[ v = KE \Rightarrow \frac{L}{t_d} = K \frac{V}{L} \Rightarrow K = \frac{L^2}{Vt_d} \]

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

\[ \mu = \frac{mM}{(m + M)} \]

\[ t_d = \frac{16N}{3} \left( \frac{\mu kT}{2\pi} \right)^{\frac{1}{2}} \frac{L^2}{Vq} \left( \frac{\Omega}{q} \right) \Rightarrow t_d \propto \frac{\Omega \mu^{\frac{1}{2}}}{q} \]
In Instrumentation Field
IMS Adoption is Accelerating

“Ion Mobility…A prevailing theme at ASMS this year”  
JP Morgan, “ASMS 2013 Final Thoughts”

Number of Topics about Ion Mobility Spectrometry by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Papers Published</th>
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<tbody>
<tr>
<td>1952</td>
<td>0</td>
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<tr>
<td>1962</td>
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<td>1972</td>
<td>0</td>
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<td>1982</td>
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<td>1992</td>
<td>0</td>
</tr>
<tr>
<td>2002</td>
<td>0</td>
</tr>
<tr>
<td>2012</td>
<td>350</td>
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</table>

Waters Synapt G2
Excellims MA3100 with Thermo Orbitrap
Agilent 6560
AB Sciex Seletion
Hyphenated IMS-MS

(A)  

(B)  

(C)  

Selected Mobility Analyzer (example of trapped solar mass)  

Operating Modes  
1. Open  
2. Closed  
3. Open & close to generate 2D IMS-MS Dots  
4. Closed  
5. Pass only a selected mobility window  
6. Narrow grid  
    Simultaneous pass multiple selected mobility windows

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July 13, 2015
NEMC 2015, Chicago
Hyphenated HPLC-IMS

Resolve coeluting isomers
Shorten LC methods
Separate complex mixtures
Eliminate specialty columns

LC Separation:
- Column: Thermo Scientific Acquity C18, 2.1 x 250mm, 5.0μm
- Mobile Phase: H₂O (A), ACN (B)
- Flow Rate: 0.200 mL/min
- Injection Volume: 5.0 μL
- Gradient: Hold 0% B for 8 min, hold 15% B for 7 min, hold 40% B for 10 min
- UV Detection: 190 nm (blue), 210 nm (red)

Intensity Scaling: 5.8x
Bring Spectrometers toward the Analytical Targets

For targeted field analysis, IMS has superior advantages because of its robustness and no vacuum required.

- Resolution 450,000
- Resolution 1000
- Resolution 250
- Resolution 70-120
- Resolution 35
- Resolution 15

m/z measurement
Vacuum measurement
Reduced performance in field-use

Size measurement
Ambient pressure
Easiest field-use
Improved performance
Standalone High Performance Ion Mobility Spectrometry

Resolving Power $R = \frac{t_d}{t_{w1/2}}$

$R = 98 \quad N = 53000$

Resolving Power (R)
(U)HPLC 65 145
Analysis Time 3 min 20 min 10 sec

CoQ10
**HPIMS For Field Analysis**

- **Car-mount HPLC-UV**
- **ESI-HPIMS**
- **GC-MS**
- **Thermal Desorption IMS**

**One Step Liquid Sample Analysis - Directspray Ionization**

**Electrospray Source**

- Sample: 1-8 μL/min
- Sheath Liquid (ACN or MeOH): 0.5-4 μL/min
- 1.5 - 5 kV

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NEMC 2015, Chicago
**HPIMS for Explosive Detection**

**Explosives Detection**

**HPIMS with Thermal Desorber and Neg Mode Corona Discharge Ionization**

![Graph showing detection of TNT and C4 using HPIMS](image)

- 1 ng TNT
- 5 ng C4

1 ng TNT and 5 ng C4 using CDI-TD and HPIMS

**ESI-HPIMS: C. Wu and co-workers, *IJMS, 2010, 298, 64.*
ESI-HPIIMS Enables Detection of HME and Inorganic Explosives

(a) ESI-IMS-MS at Faraday detector 0.1 mg/mL AN with 1:1 D-fructose

(F+NH₄)⁺

(b) ESI-IMS-MS at Faraday detector 0.1 mg/mL AN with 1:1 D-fructose

[NH₄NO₃]⁻

(NO₂)⁻

(F+NO₃)⁺

Inorganic Anions with Directspray GA2100 HPIMS

Intensity (arb. units)

<table>
<thead>
<tr>
<th>Anion</th>
<th>6</th>
<th>6.5</th>
<th>7</th>
<th>7.5</th>
<th>8</th>
<th>8.5</th>
<th>9</th>
<th>9.5</th>
<th>10</th>
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</thead>
<tbody>
<tr>
<td>NO₃⁻</td>
<td>5</td>
<td></td>
<td>7</td>
<td></td>
<td>8</td>
<td></td>
<td>9</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>ClO₃⁻</td>
<td></td>
<td>8</td>
<td>9</td>
<td></td>
<td>10</td>
<td></td>
<td>11</td>
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<tr>
<td>ClO₄⁻</td>
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<td>8</td>
<td></td>
<td>9</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>MnO₄⁻</td>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td>7</td>
<td></td>
<td>8</td>
<td></td>
<td>9</td>
</tr>
</tbody>
</table>

Nitrate  Permanganate  Chlorate  Perchlorate

TATP

[NO₃]⁻
Reaction Monitoring – Radiopharmacy

- Constrained versus straight geometry identified in the gas phase
- 2 amu difference in OH-compound compared to a F-compound shows baseline separation due to hydrogen bonding interaction
Process Monitoring – Surfactants

Journal of Chromatography A
Volume 852, Issue 2, 13 August 1999, Pages 475–485
Cleaning Validation

- Speed is critical
- At line analysis is desirable

### Swab Recovery

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HPLC</th>
<th>ESI-HPIMS</th>
<th>Commercial IMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovery (%)</td>
<td>84.5</td>
<td>83.4</td>
<td>Not detectable</td>
</tr>
<tr>
<td>Precision RSD (%)</td>
<td>2.1</td>
<td>8.0</td>
<td>Not detectable</td>
</tr>
<tr>
<td>Total analysis time per run</td>
<td>~12 min</td>
<td>&lt; 1 min</td>
<td>NA</td>
</tr>
</tbody>
</table>

- Spike level: 1.66 μg/cm²
- Results from HPLC and ESI-HPIMS analysis are comparable
Food Safety Inspection
Banned Sweetener

Signal Intensity (Arb. Units)

Sodium Cyclamate Directspray ESI-HPIIMS

- 500 ppb
- 50 ppb
- 9 ppb

Drift Time (s)

- 500 ppb Cyclamate
- 50 ppb Cyclamate
- 9 ppb Cyclamate
Directspray Milk Sample Melamine Detection

**ESI-HPIMS of Melamine**

- Melamine standard in ESI solvent
- 1 ppm

**ESI-IMS of Melamine in 1% Milk**

- Melamine standard (ESI solvent)
- Melamine in milk matrix

**Simplified sample prep:**
- Denatured 1 mL of 1% milk with 5 mL of 1M acetic acid (aq)
- Filtered with 0.45 m nylon syringe filter
- Add 1 mL methanol and analyzed both spiked and unspiked

36 ppm of melamine detected with good signal-to-noise in milk
- Lower concentrations should be detectable
Food Safety Inspection
Food Dye

Allura Red AC

- Negative ion mode with air drift gas
- Detect anion of salt
- 170°C IMS temperature
- Can detect 50 ppb
Food Safety Inspection

Coca-Cola – spiked with DCHP

Use a simplified sample preparation and detect phthalate spiked into an actual beverage sample

Black: Blank – MeOH/water(90:10)
Red: Coke/MeOH (90:10)
Green: Coke/MeOH/DCHP(5 ppm)

• Diluted Coca-cola 9:1 with methanol both spiked and unspiked
• Can detect 5 ppm in the cola
• Factor of 30 lower than the current accepted method can detect
Rhodamine B – Illegal Food Dye

- Lowest conc. detected with GA2100 (ESI solvent) = 50 ppb
- Sciex published method <100 ppb with LC-MS
Malachite Green – Aquaculture By-product

- Lowest conc. detected (ESI solvent) with GA2100 ~ 100 ppb
- Two-order of magnitude linear response range
Drug Safety Inspection
Herb Medicine Additives – Prescription Drugs

Rosiglitazone 357.428
Pioglitazone 356.44
Ciprofloxacin – Antibiotic Residue

- Lowest concentration detected (in ESI solvent) = 75 ppb
- Two order of magnitude linear response

Ciprofloxacin Calibration curve

$R^2 = 0.9927$
ESI-HPIMS for Online Water Analysis

**Thiodiglycol (TDG) Response Curve ESI-HPIMS**

![Thiodiglycol (TDG) Response Curve ESI-HPIMS](chart)

**Calibration:**
- Slope: 1.0072
- Interception: 0.0000
- Averaging C: 1

**TDG ESI-IMS Calibration Curve**

- $y = 1631x + 24.96$
- $R^2 = 0.998$

**DIMP in Tap Water with ESI-IMS**

- **Intensity (Arb. Units)**:
  - Drift Time (ms): 1, 2, 3, 4, 5, 6, 7, 8, 9

- **Concentration (mg/ml)**:
  - TDG ESI-IMS Calibration Curve

- **Thiodiglycol (TDG)** Response Curve ESI-HPIMS

**Data Points:**
- Blank 0 ppm DIMP, Tap Water
- 5 ppm DIMP, Tap Water
- 50 ppm DIMP, Tap Water
- Blank HPLC Water

**Graphs:**
- Total Intensity vs. Concentration (mg/ml)
- Drift Time (ms) vs. Intensity (Arb. Units)
Controlled Substances – Improve Throughput of Forensics Labs

Hallucinogens/Dissociative Drugs
ESI-HPIMS at 180 C

ESI-HPIMS Response Curve for PCP

ESI-IMS of Morphine and Codeine in Urine

Methamphetamine

Cocaine

Δ-9-THC
Controlled Substances – Bath Salts

MW = 221  Butyl1
MW = 275  MDPV

Naph  MW = 281
Future Developments

- Reduce Car-mount system to handheld size without compromising performance
- New sample introduction enable direct analysis
- Rapid sample preparation method development

HPIMS can be used for the analysis of solid, liquid, and gas samples

HPIMS from Car-mount to Handheld

DART Ionization for direct sample introduction
Acknowledgement:

DHS: HSHQDC-09-C-00110
EPA: EP-D-10-025
FDA: 1R43FD003502

Thank you.

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