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Single Quadrupole Mass Spectrometry: A Must-Have in the Chromatography Lab

Agenda

- Mass Spectrometry: Another Dimension in Separation
- Ion Chromatography with the new Thermo Scientific™ ISQ™ EC single quadrupole mass spectrometer
- The ISQ EC mass spectrometer as an LC-MS

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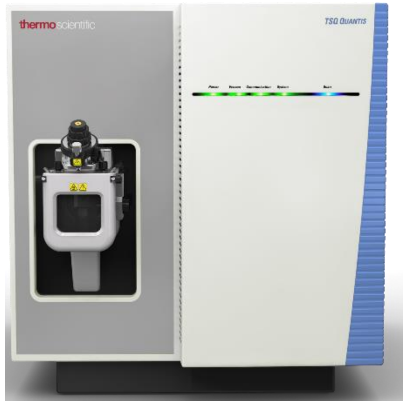
Mass Spectrometry: Another Dimension in Separation

- **Near-universal** detector
- **More selective** detector — at the same time
  - TIC Full Scan → SIM → SRM → HRAM (for all ionization techniques)
- Identification and structural information for each analyte
- Orthogonal dimension of species separation
- Alternative to 2D (IC × IC, LC × LC) techniques
- Opens up the door to ion mobility separation dimension (e.g. FAIMS) etc.

Increasing Selectivity from Single Quad to HRAM Mass Spectrometry

Thermo Scientific™
Q Exactive™ MS Family

Thermo Scientific™
TSQ Altis™ Triple Quadrupole MS



Thermo Scientific™
Quantis™ Triple Quadrupole MS

ISQ EC Single Quad MS

Benefits of Ion Chromatography-Mass Spectrometry

- IC compared to LC
  - Greater specificity and selectivity for ionic compounds
  - Metal-free flow path reduces fouling of ion-exchange columns
- MS vs. Conductivity Detection (CD)
  - Increased sensitivity and selectivity
  - Identification and quantification of small polar analytes that have the same retention times using single ion monitoring (SIM) or selective reaction monitoring (SRM) for MS/MS
- On-Line desalting for high ionic strength matrices
  - Reduces MS signal suppression and possible detector damage
- Analyte Confirmation
  - Combines the confirmation of analyte identification into one method
- Total Integrated Solution: IC, MS and Data Management

Ion Chromatography is Ideal for Mass Spectrometry (MS)

- Analytes are provided already in the **ionic form** needed for MS detection
- Thermo Scientific Dionex **suppressors** allow the use of standard IC eluents and methods and improve MS sensitivity, signal stability and salt/matrix tolerance
- IC-MS may use existing methods from **stand-alone IC**
- **Eluent generators** allow fast, clean switching between anions and cations in IC-MS
- Only need a stainless steel grounding union to couple the IC to the MS source while maintaining a totally **metal-free flow path** otherwise

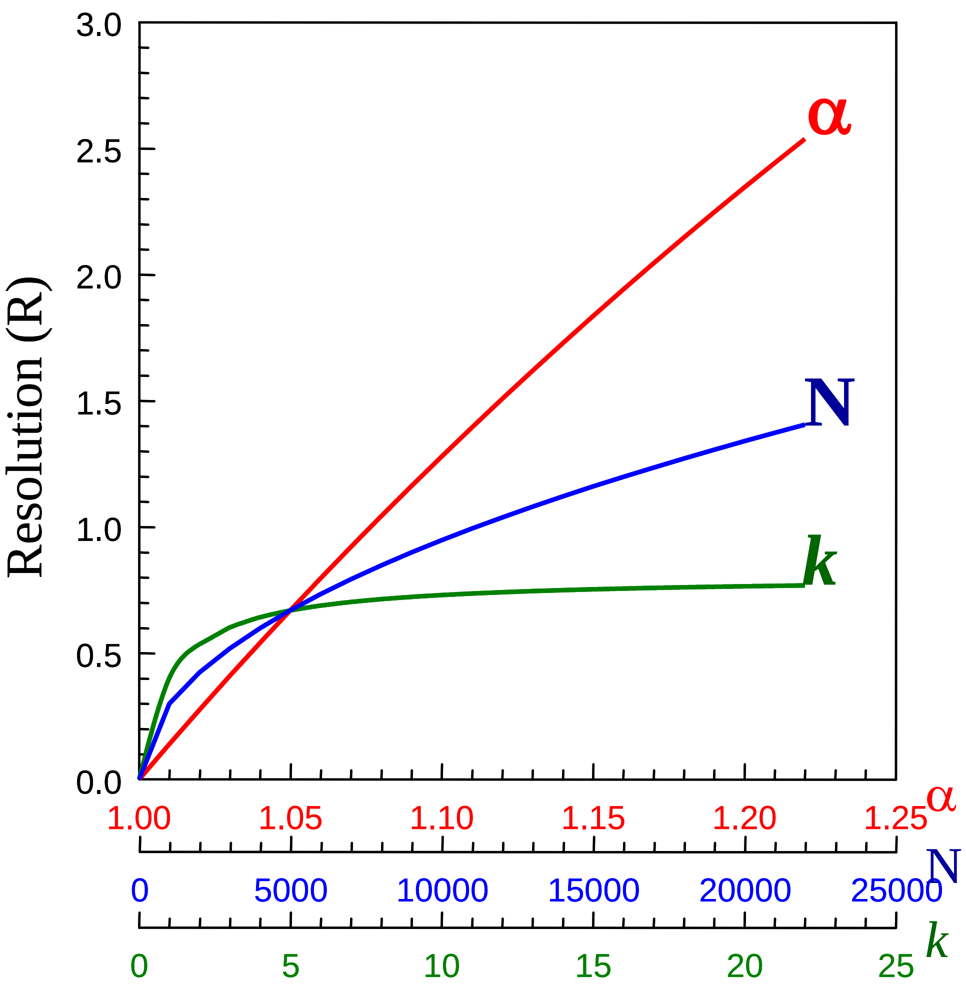
Selectivity Has the Most «depth» in the Parametric Space

Efficiency → Retention → Selectivity

$$R = \frac{\sqrt{N}}{4} \cdot \frac{k'}{k'+1} \cdot \frac{\alpha - 1}{\alpha}$$

$$\alpha = \frac{k_2}{k_1}$$

- **Selectivity (α) has the greatest impact on improving resolution.**



Electrospray Ionization (ESI)

Advantages

- Soft ionization = Preserves analyte's molecular ion
- Sensitive, rugged, well-established
- Compatible with a broad range of analytes and eluents

Disadvantages

- High-aqueous mobile phase lower volatility requires Heated ESI (HESI)
  - Requires elevated ESI Probe temperature and post-column solvent*
- Non-volatile buffers may precipitate inside ESI capillary
- Works best at low flow rates (2 mm i.d. columns)
- Ionization is inhibited by high salt/matrix concentrations

* not required on the new ISQ EC mass spectrometer, but some methods may still benefit from it

Components of the “IC” in IC-MS

- Standard suppressed IC chemistries
  - Does not require special unit or extensive modification
- Eluent Generator
  - Cleaner backgrounds, easy switch-over between anions and cations
- Electrical grounding union
- External water for suppressors

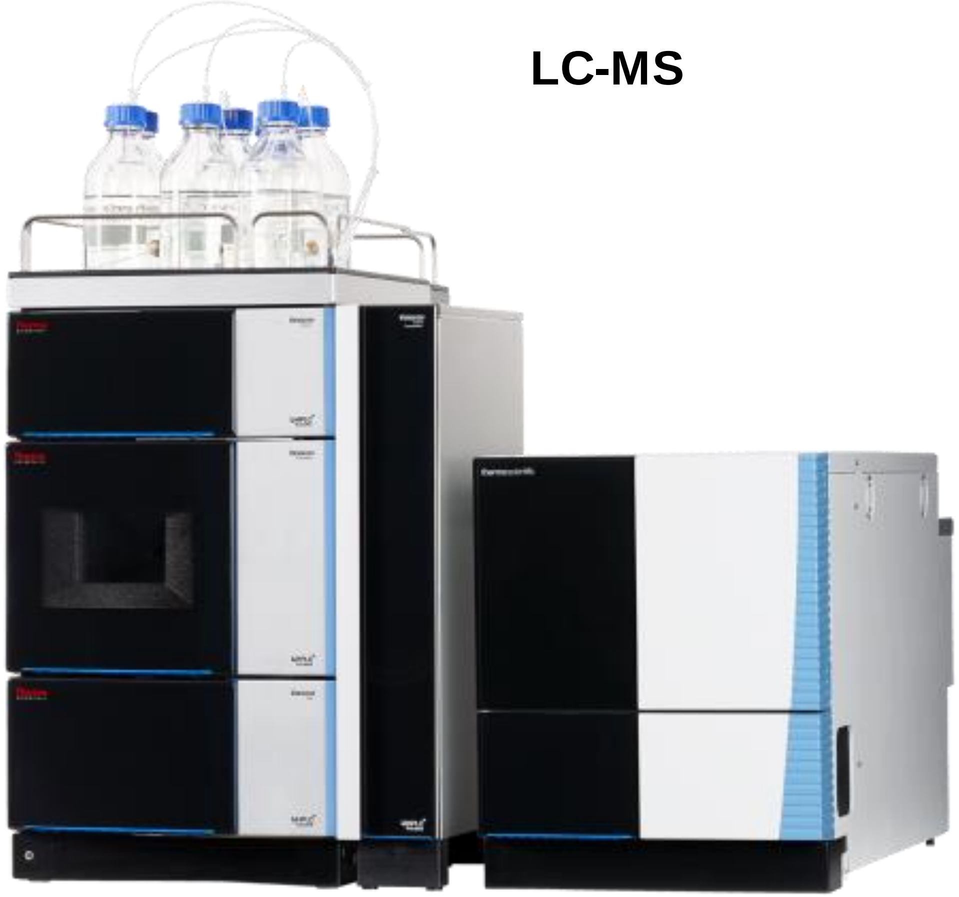
Thermo Scientific ISQ EC Single Quadrupole Mass Spectrometer

Coupled to Thermo Scientific™ Dionex™ Integrion™ HPIC™

IC-MS

Coupled to Thermo Scientific™ Vanquish™ HPLC system

LC-MS



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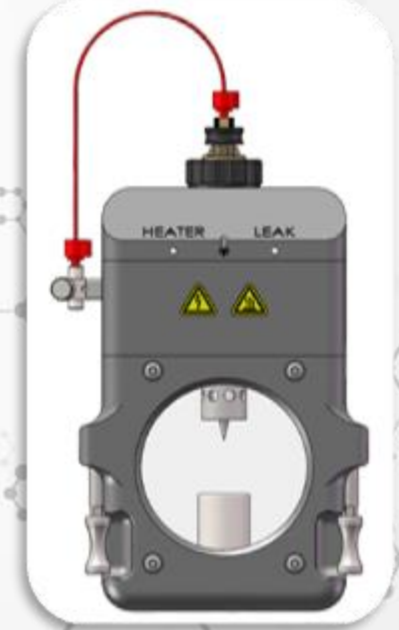
Combining the Best of Our Triple Quad MS Technologies

Thermo Scientific™
TSQ™ 8000 Evo Triple
Quadrupole GC-MS/MS

Thermo Scientific™
Chromeleon™ CDS Software

TSQ Altis Triple Quad MS



Thermo Scientific ISQ EC MS – Single Quadrupole MS for IC and LC

NEW!

Proven, reliable and robust routine ISQ GC-MS platform

Robust, fixed source for maximum uptime and minimum cleaning

Best solution for routine IC-MS analysis, w/o solvent makeup; m/z 10–1250

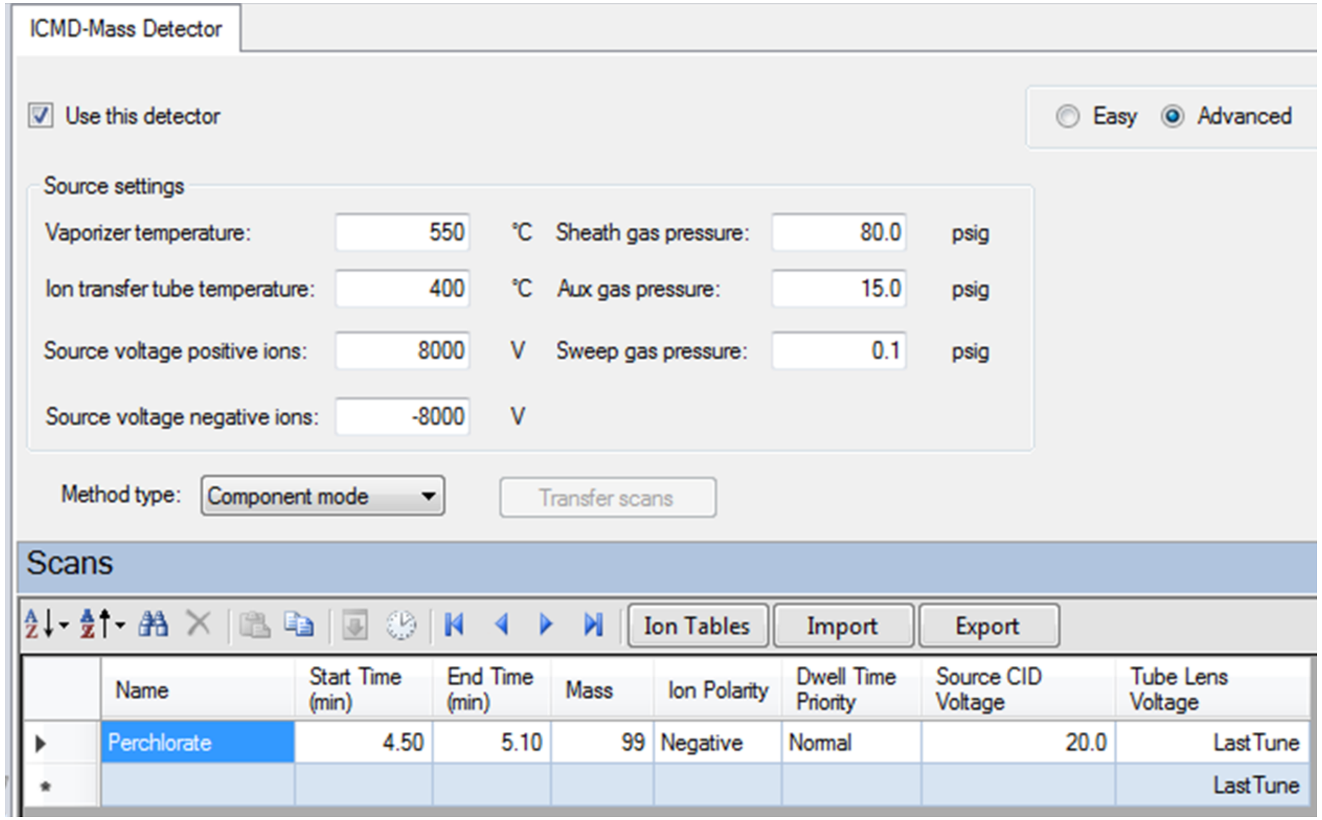
Fully integrated in Chromeleon 7 CDS and new Open Access UI

Best entry-level singleQ MS for small molecule pharmaceutical

Thermo Scientific ISQ EC MS Key Benefits

Gain Greater Insights From Your Sample	• Unmatched low mass sensitivity • Chromatographic peak confirmation
Resolve Complexity	• Analyze complex sample matrices • Hassle-free maintenance
Easily Mastered	• **Integrated tools to help master MS** • Hassle-free, seamless integration with IC or LC systems • Embedded control by Chromeleon CDS software

ESI Method Creation & Optimization Challenges



- ESI IC/LC-MS is inherently NOT like EI GC-MS
- What method parameters' set does a newbie start from?
- How do you optimize the whole multi-parametric method?
- Are method parameters inter-dependent?

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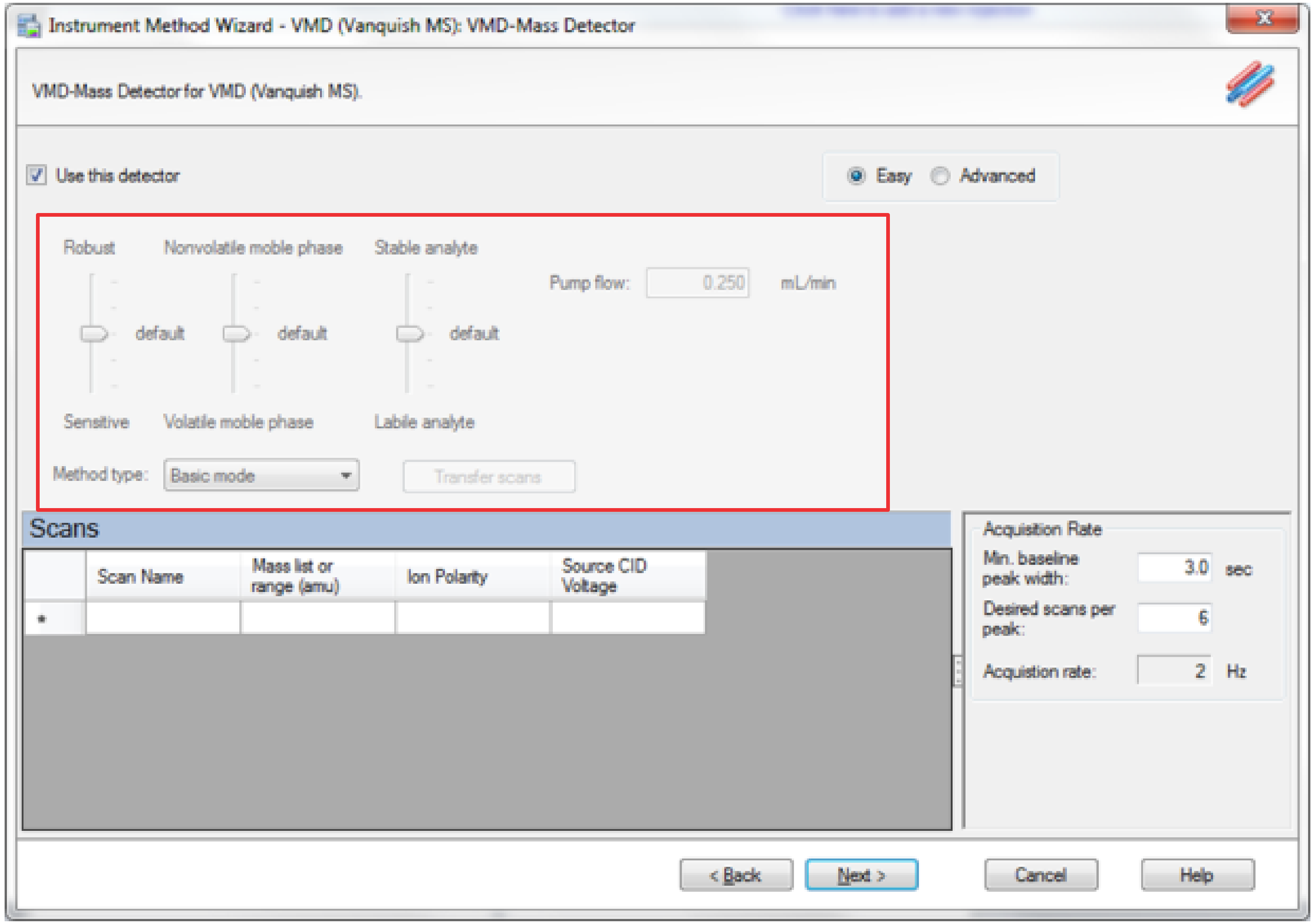
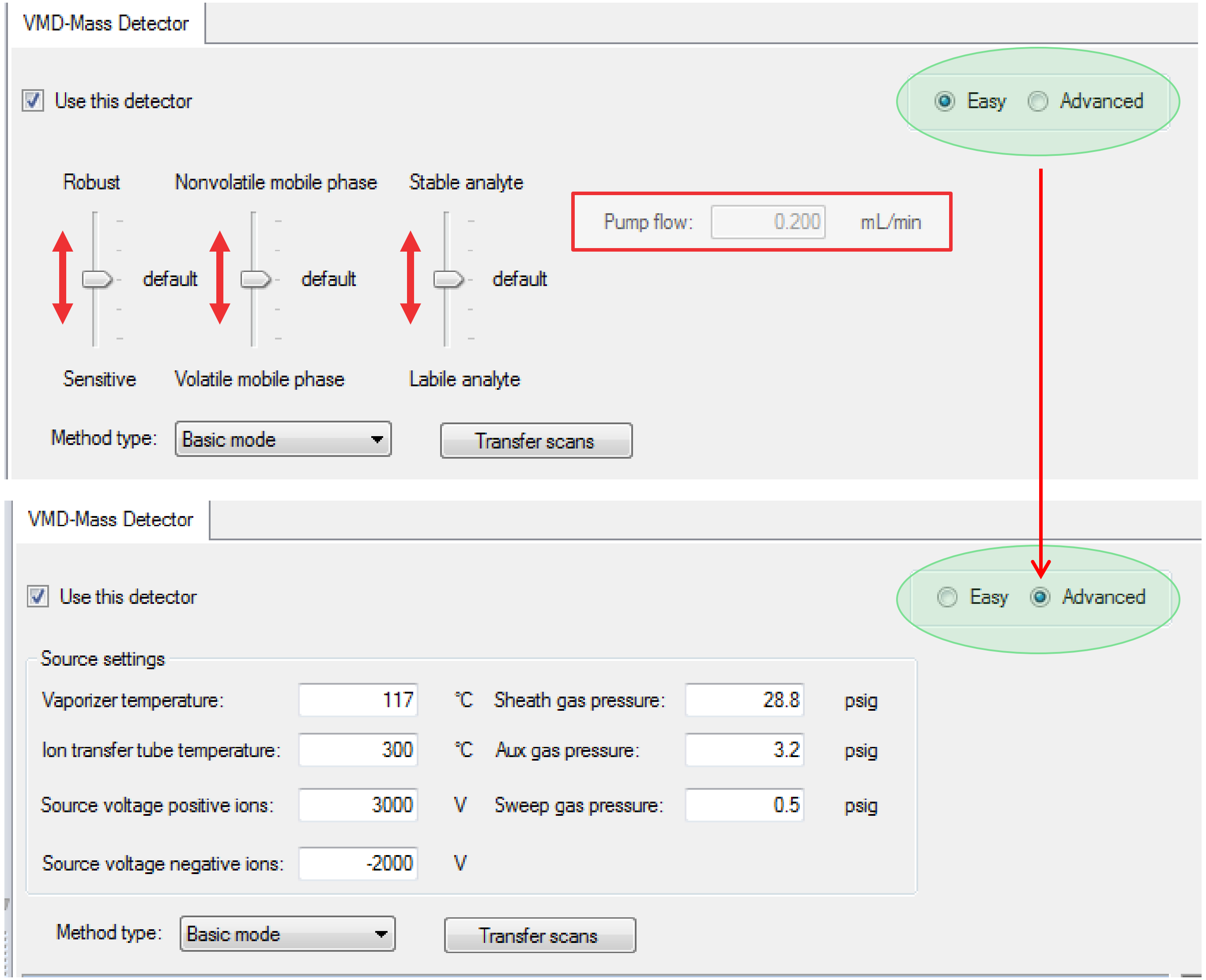
Thermo Scientific AutoSpray Technology – Patent Application Pending

- Unique Thermo Scientific™ **AutoSpray™** software technology **translates physical properties** of the analyte, mobile-phase and system-wide instrument settings into **optimal method parameters**
- **Easy Mode** for the **novice** user, advanced **tools** for the **MS expert**
- ***Auto-tune* as part of a sequence**
- **Real-time scanning** for online signal optimization



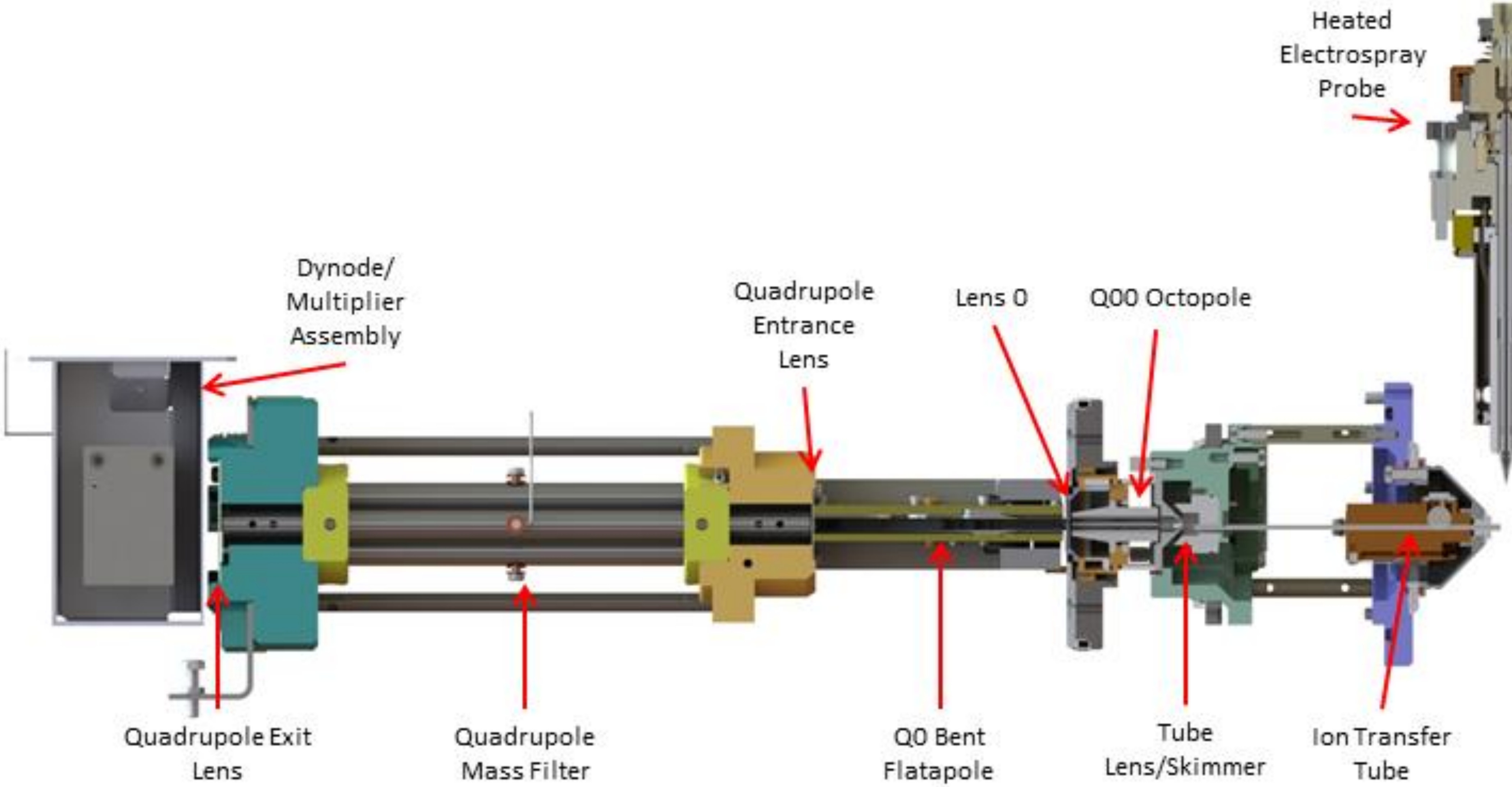
ISQ EC MS is easy to adopt and master

Thermo Scientific AutoSpray Technology Implementation in MS Method Editor GUI

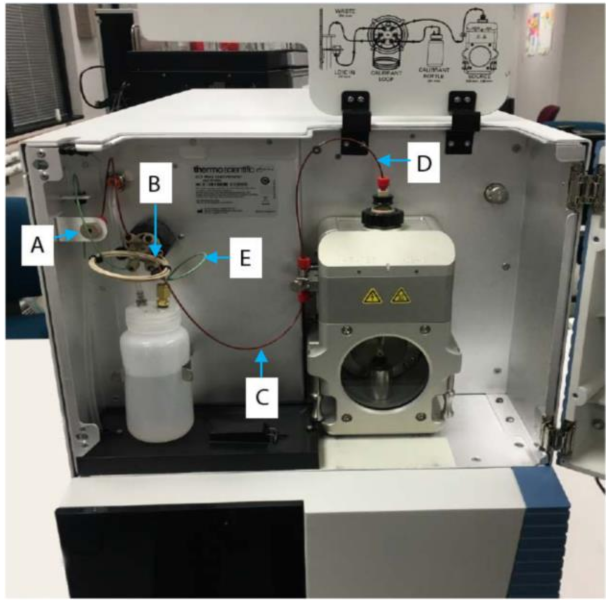


- Use the sliders as a teaching tool how settings impact analyte and background
- Use calculated values as a good starting point for method development
- Helpful to novice and expert

Hardware Benefits: Orthogonal Source, Two Offsets, Vacuum Interlock



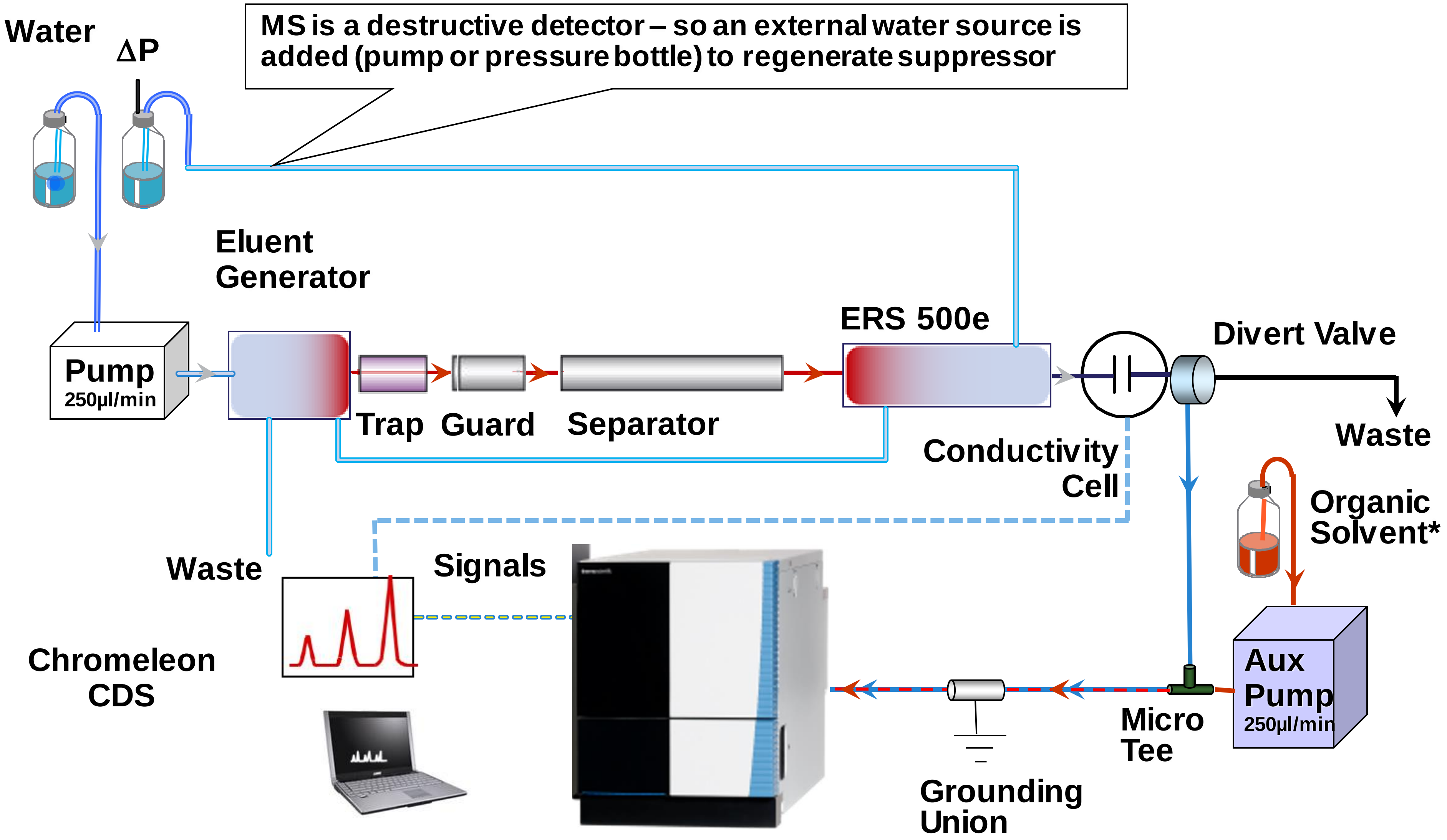
Robustness Design Features



A	Instrument inlet
B	Inlet to valve
C	Valve to grounding union
D	Grounding union to source (probe)
E	Reference calibrant to valve

- ✓ Robust source **maintains ionization stability** over a wide range of flow rates
- ✓ Convenient built-in **spray needle calibration** adjustment tool further aids robustness
- ✓ **Enhanced spray stability** in wider flow rate range with redesigned needle tip
- ✓ Orthogonal spray geometry and automated gas flow streams for **solid performance** with dirty samples
- ✓ **Worry-free operation** with intelligent, experiment-based method editor and built-in leak sensor

IC-MS Schematics



* not required on the new ISQ EC MS but most methods would benefit from it

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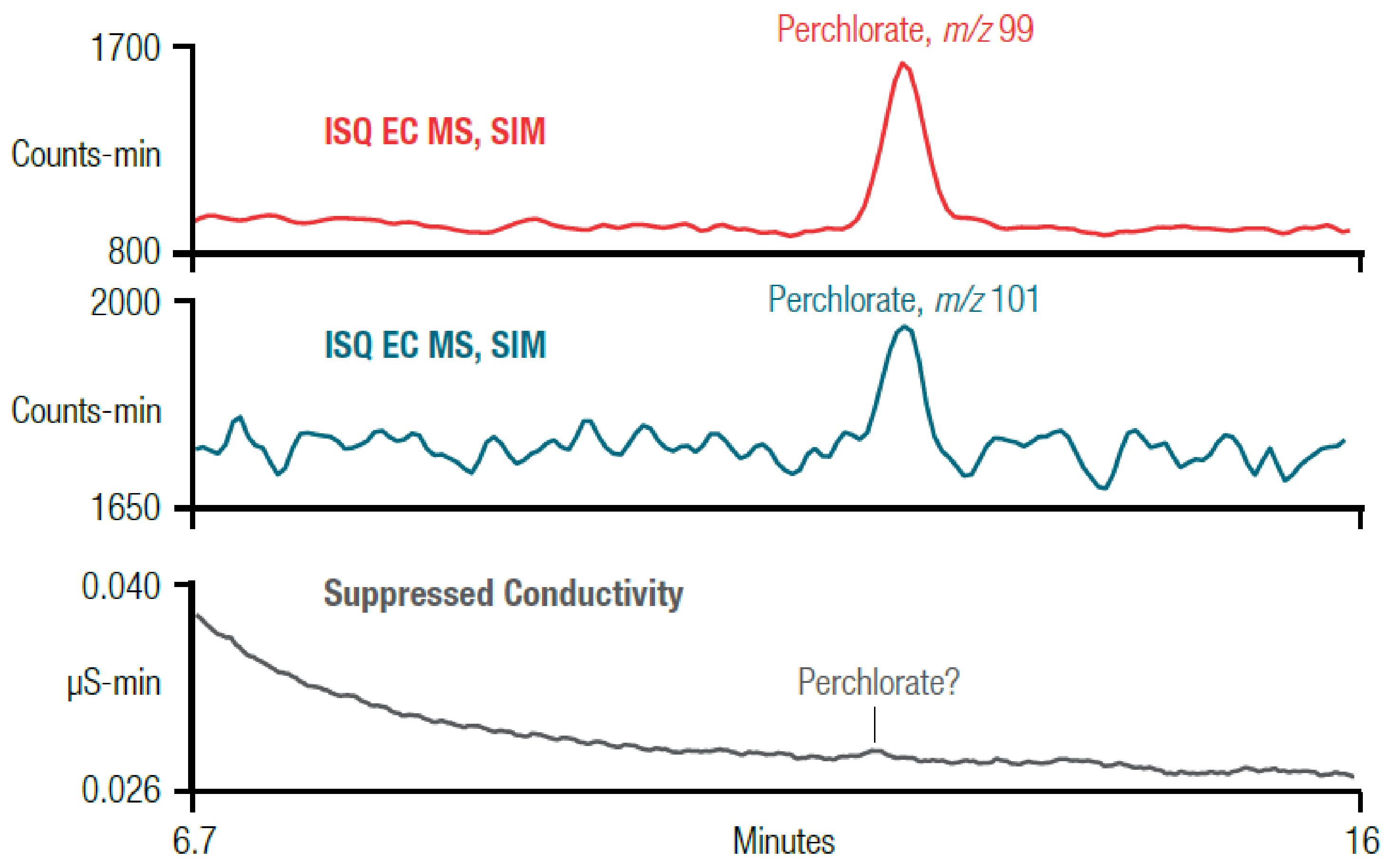
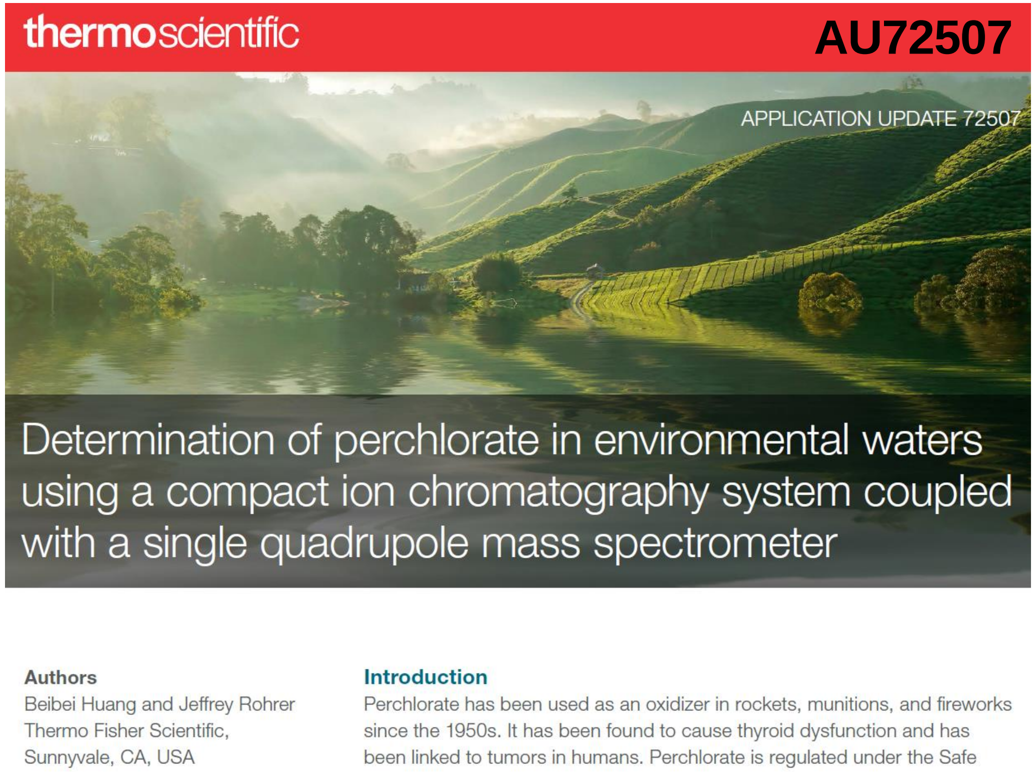
IC-MS: Improved Low-Mass Sensitivity in Drinking Water





pH = 7

$[H^+] = [OH^-] = 10^{-7}$ mol/L

Mass conc. (OH^-) ≈ 200 ppt

Required LODs are not achievable by Conductivity Detector, as CD is not SELECTIVE enough

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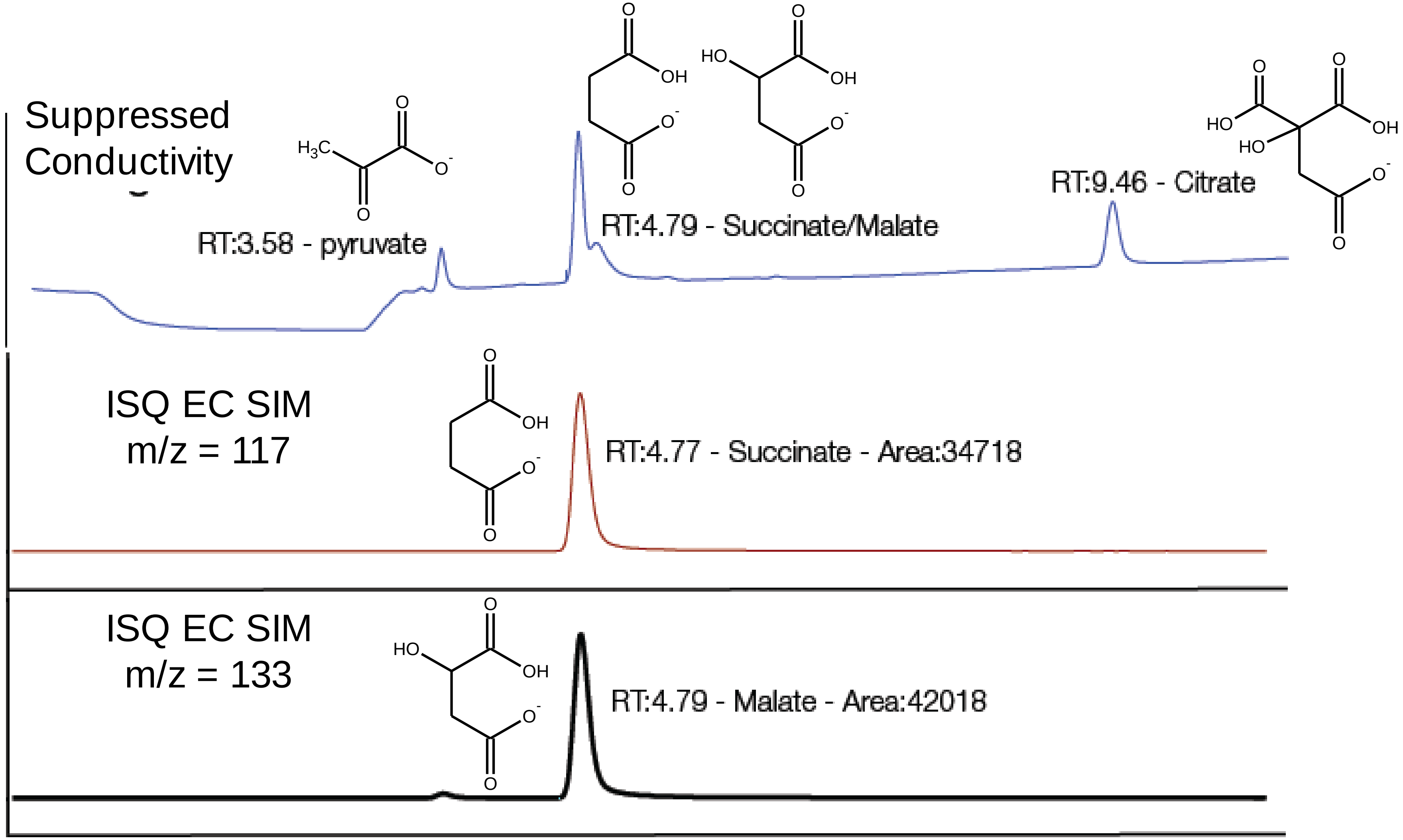
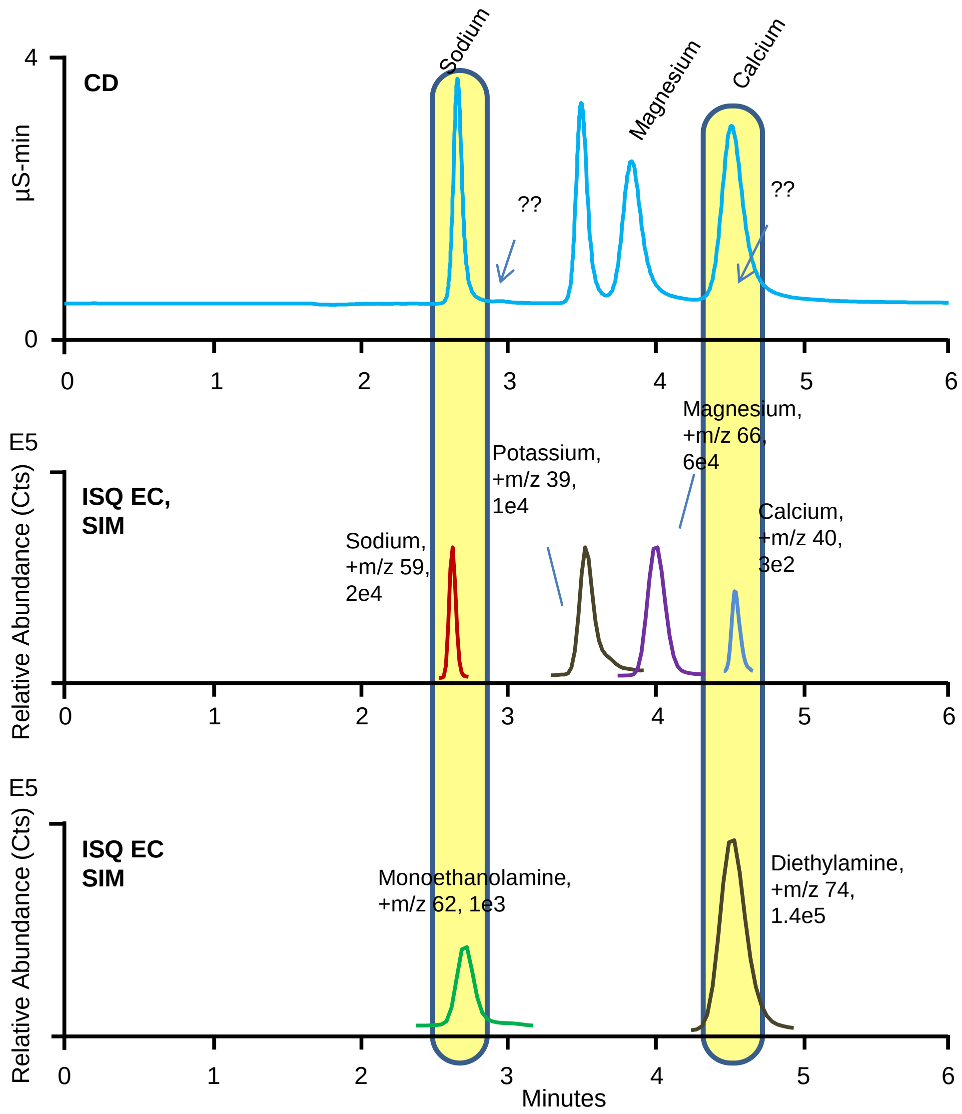
If **Coelution** Causes **False Positive** Quantitation... Use IC-MS



Why IC-MS? Because separation by IC may not be enough.

IC-MS: Resolving Coelution and Quantitation in Spoiled Grape Juice



Resolve monoethanolamine and diethylamine in MS dimension

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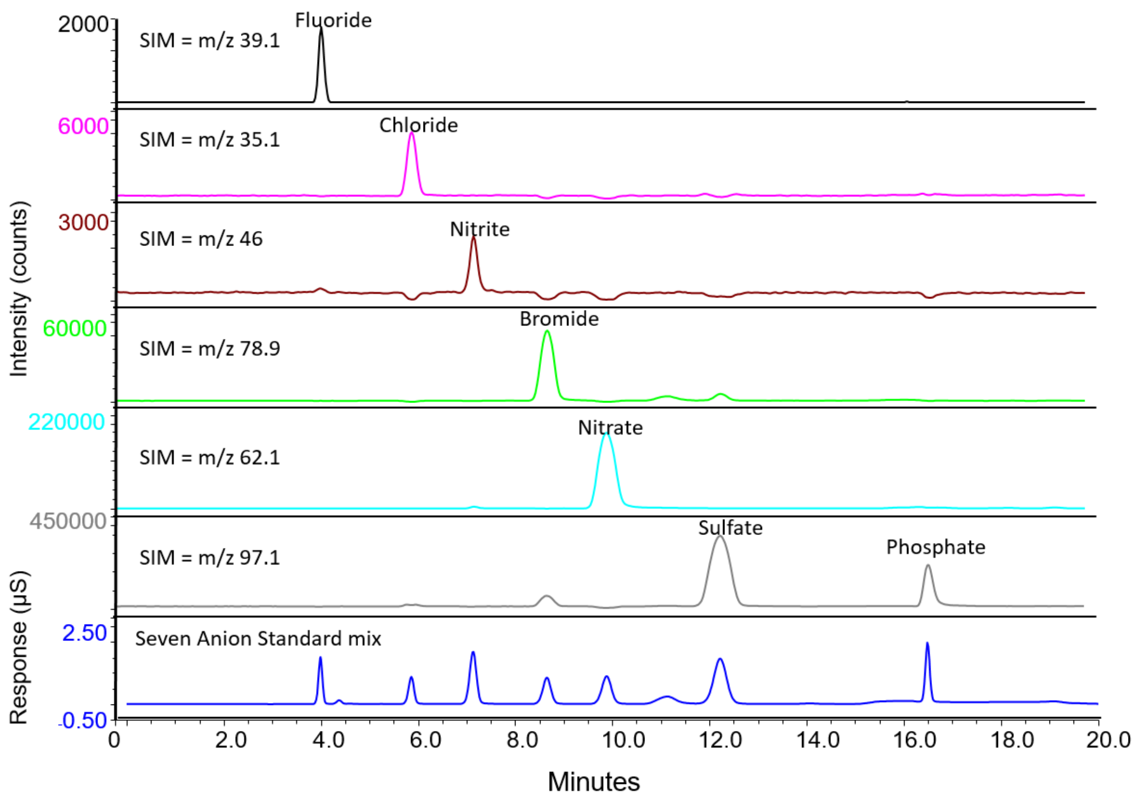
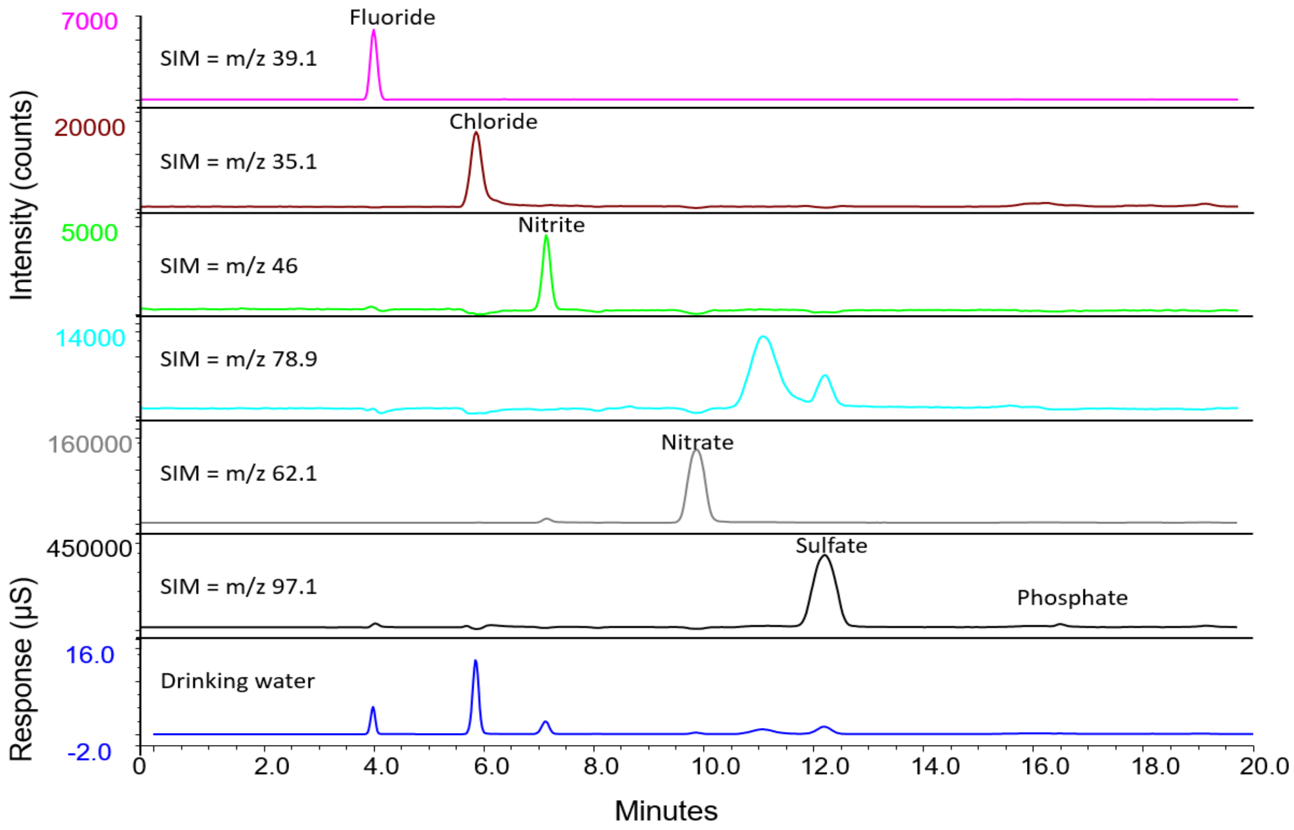
IC-MS of Anions



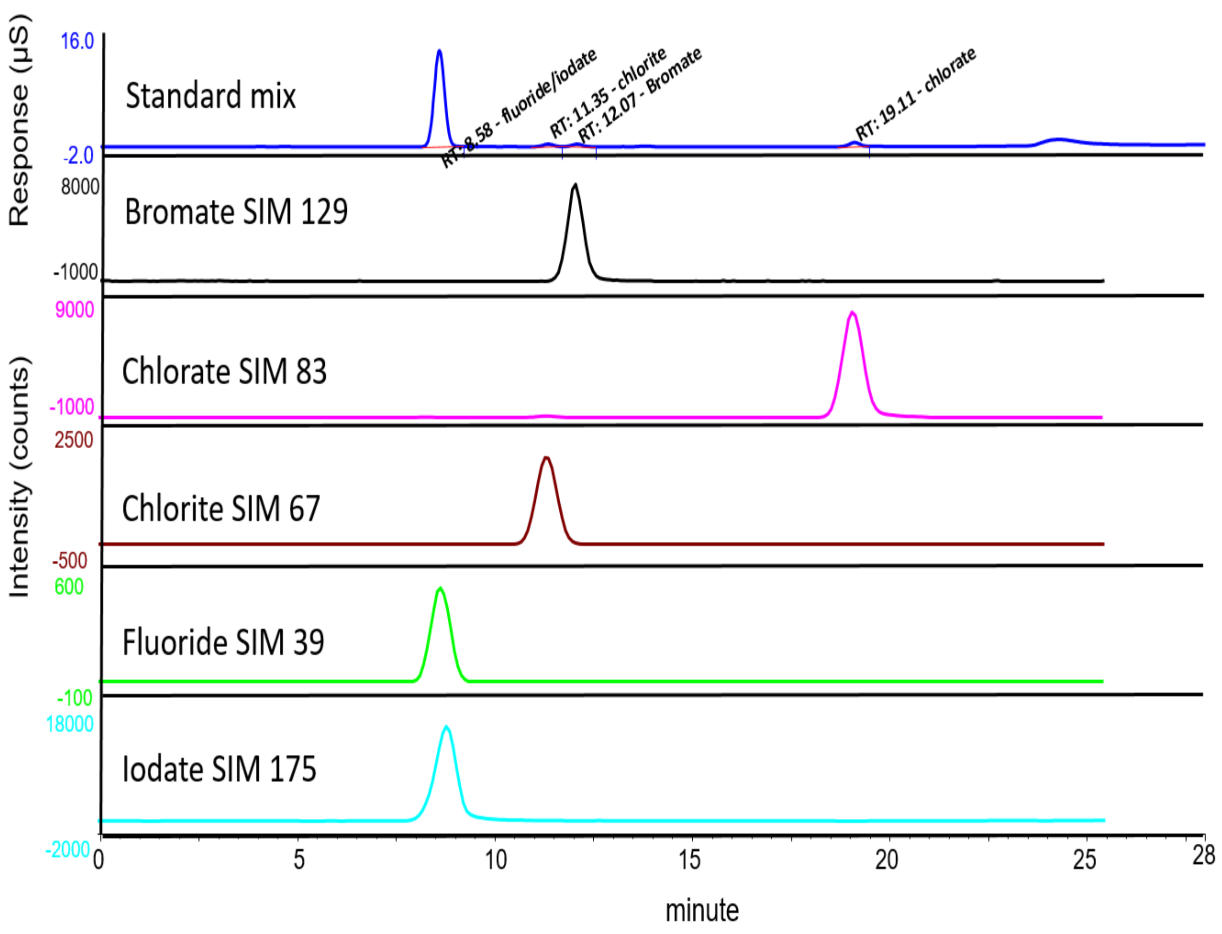
7 Anion Standard



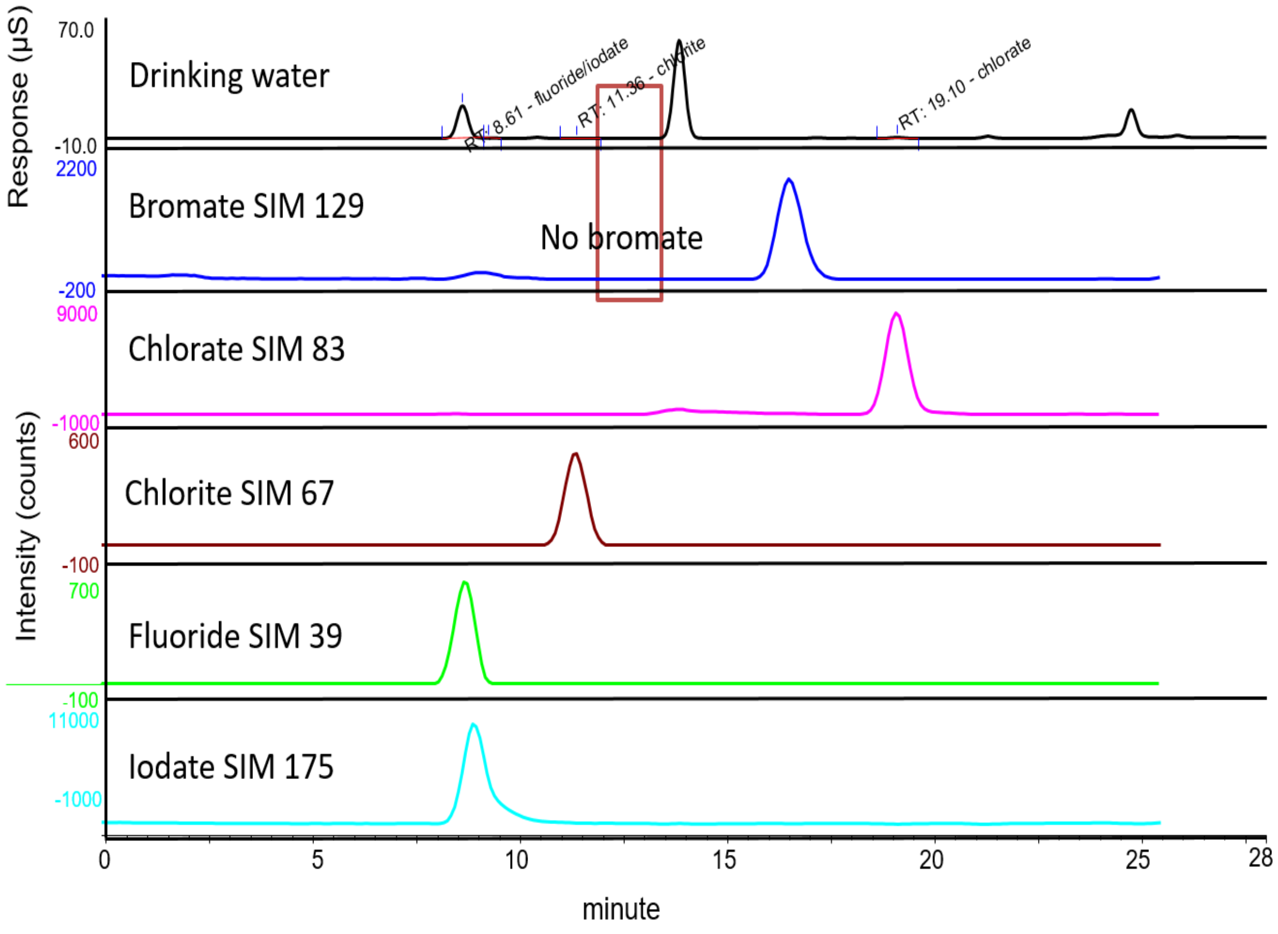
Municipal Drinking Water

Fluoride detected as $[F(HF)]^-$ at m/z = 39.1

Oxyhalides

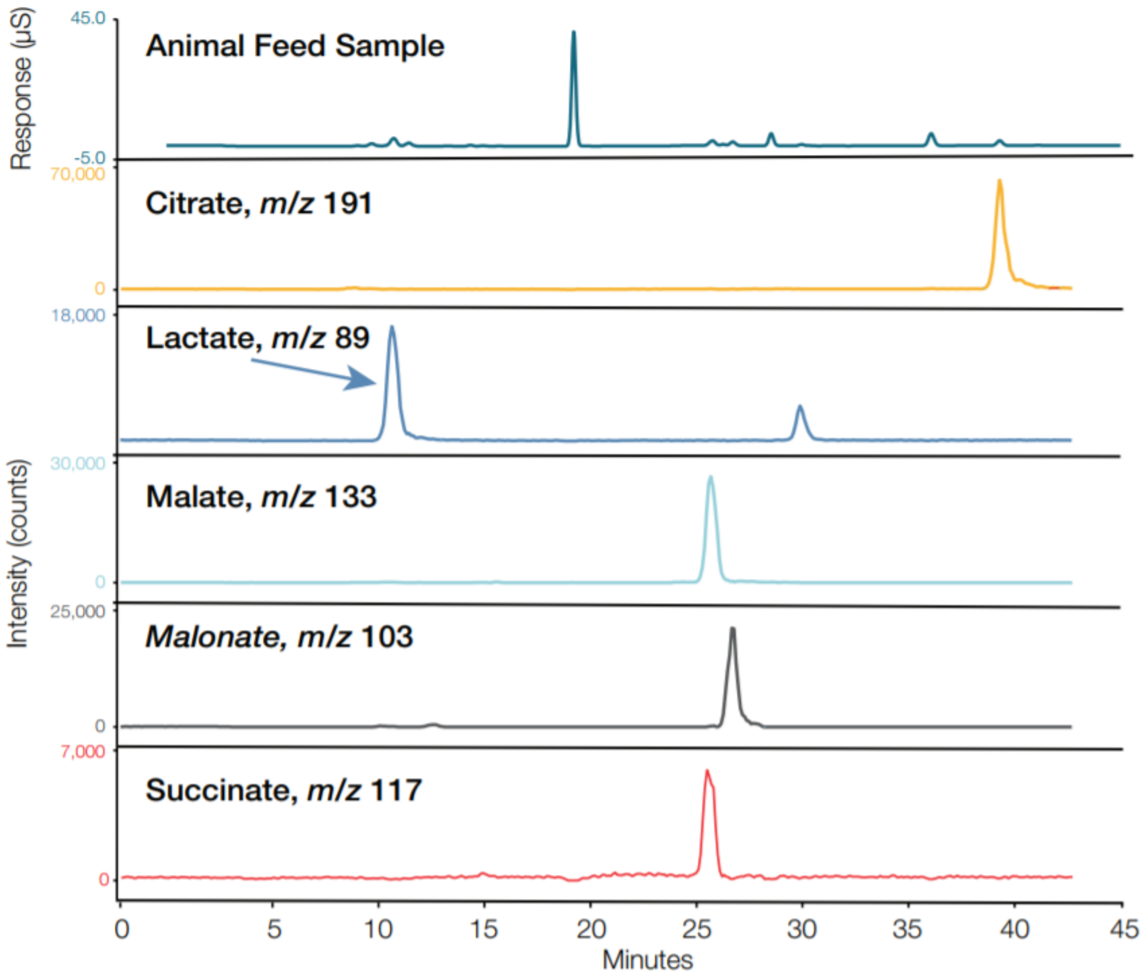


Oxyhalide Standard



Oxyhalides in Drinking Water

IC-MS of Animal Feed

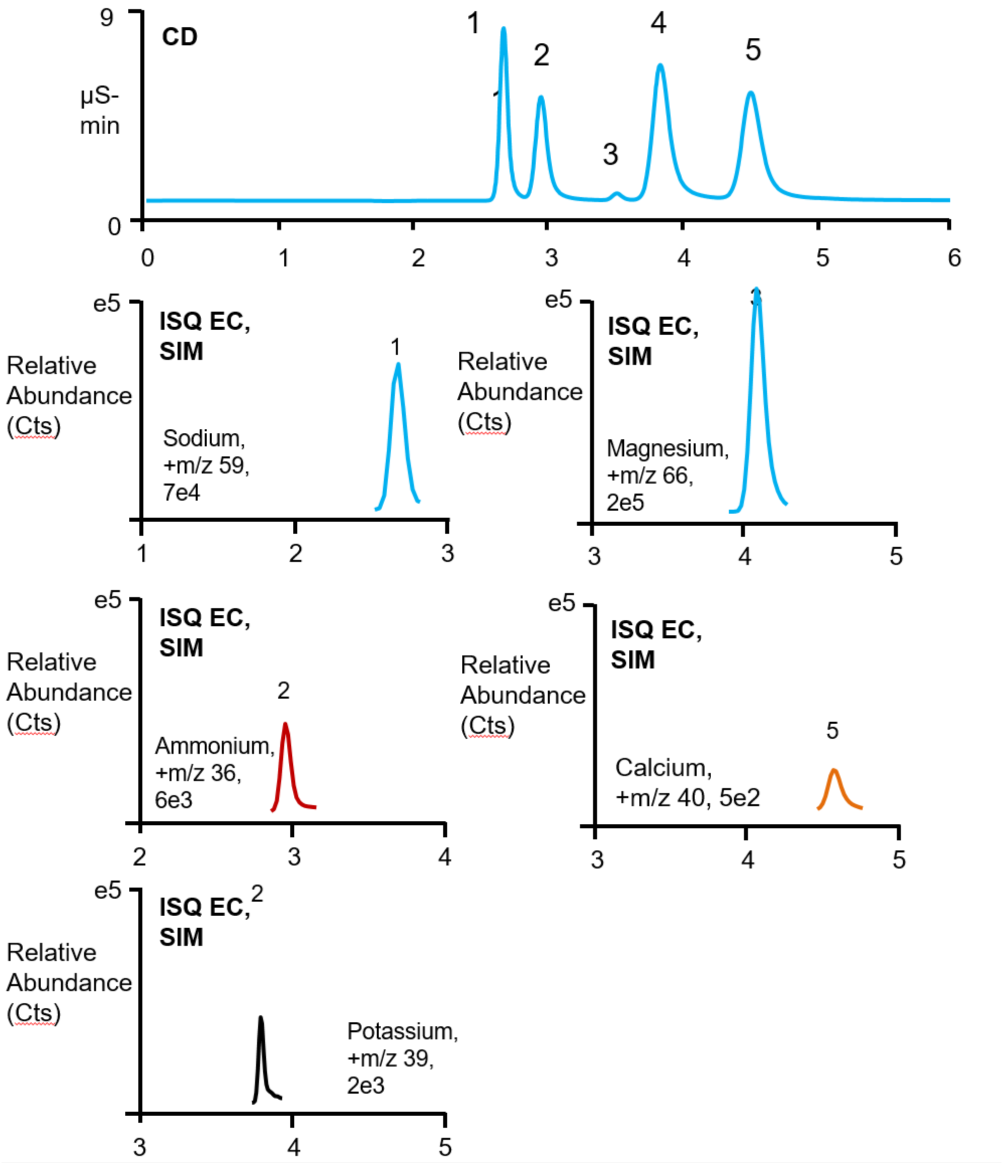


System: Thermo Scientific™ Dionex™ Integrion HPIC System, ISQ EC MS
Columns: Thermo Scientific™ Dionex™ IonPac™ AS11-HC-4µm Guard, 2x50mm, Dionex IonPac AS11-HC-4µm Analytical, 2x250mm
Eluent Source: Thermo Scientific™ Dionex™ EGC 500 KOH cartridge, Thermo Scientific™ Dionex™ CR-ATC™ 600 trap column
Gradient: 1mM KOH (0-8min), 1-30mM (8-30min), 30-60 mM (30-44min), 60mM (44-45min)
Column Temp.: 40ºC
Flow Rate: 0.35 mL/min
Inj. Vol.: 2.5 µL
Oven Temp.: 30 ºC
Detection: Suppressed conductivity, ThermoScientfic™ Dionex™ AERS™ 500e suppressor, 2mm, Autosuppresion, 52 mA, external water mode (0.7 mL/min) via ASP pump

MS conditions are the same as shown in method except for as below:
SIM mode: 89, 103, 117, 133, 191

Identification of common organic acids in an animal feed sample by the comparison of t_R and *m/z*

Determination of Cations in a Ground Water Sample

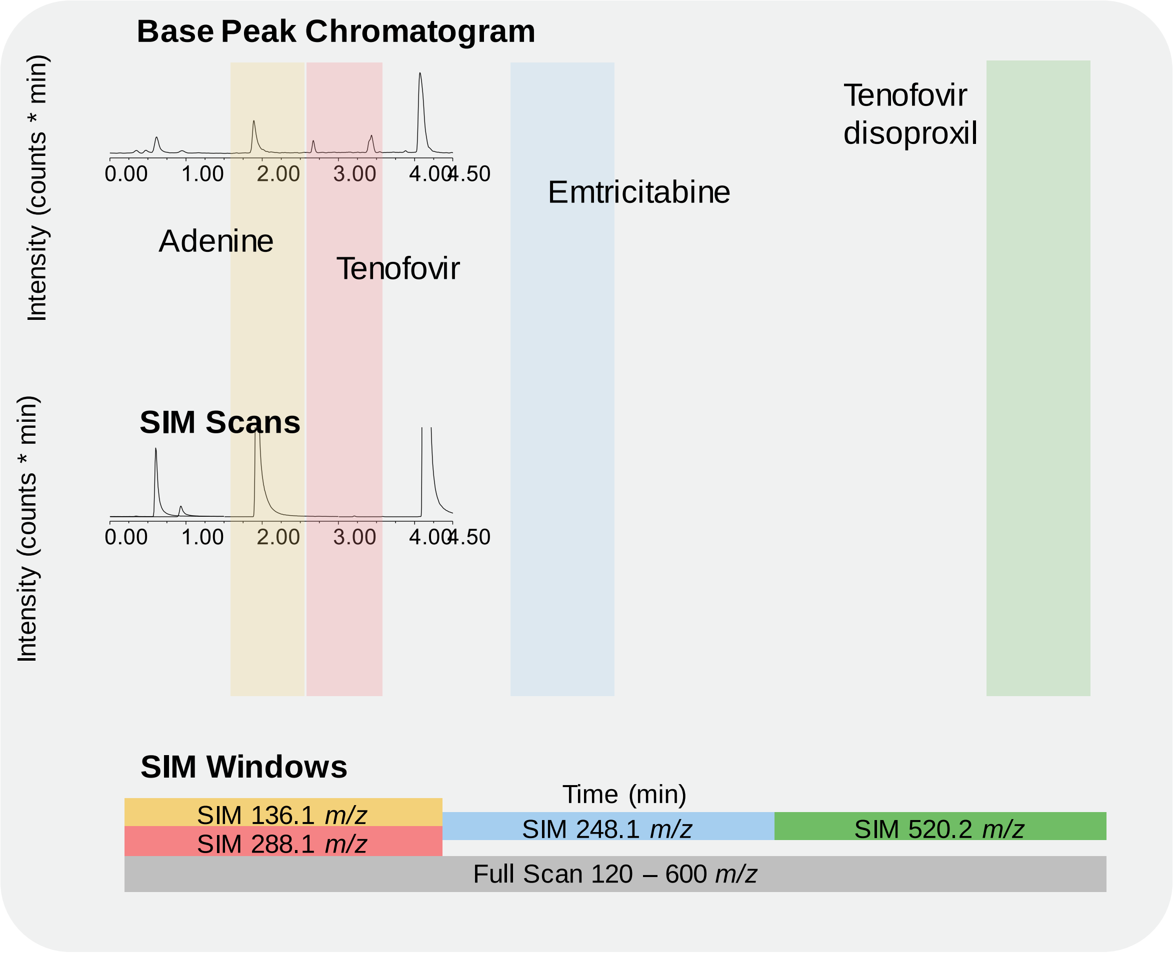


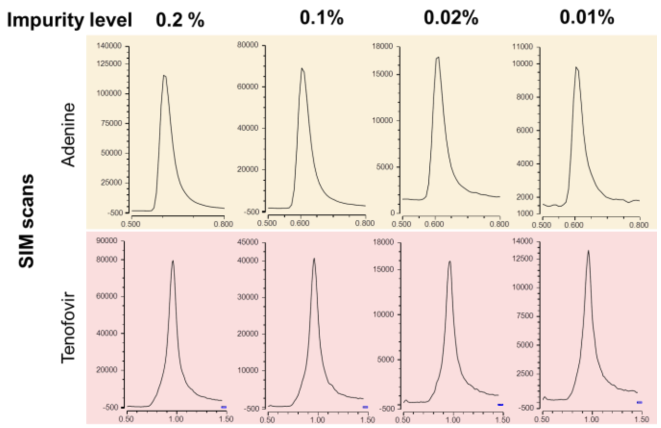
Columns: Dionex IonPac CG12A, CS12A, 2 mm
Eluent: 22 mM Methanesulfonic Acid (MSA)
Eluent Source: Thermo Scientific™ Dionex EGC™ 500 MSA cartridge, Thermo Scientific™ Dionex™ CR-CTC™ 600 trap column
Flow Rate: 0.5 mL/min
Inj. Vol.: 100 µL
Oven Temp.:30 ºC
Detector 2: ISQ EC MS, +ESI, +3000 V source, HESI II
Scan mode: Full scan: 18-250 m/z, and SIM
Make-up solvent: none
Source Temp.: Vaporizer 250 ºC , Ion Transfer 300 ºC
N_2 Gas flow (psi): Sheath 60, Aux 26, Sweep 0.5
Sample Prep.: 100-fold dilution with DI

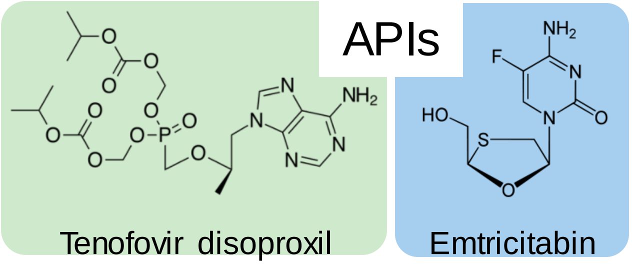
Peaks:	m/z	CID (V):
1. Sodium*$2H_2O^+$	59	10
2. Ammonium*H_2O^+	36	2
3. Potassium	39	45
4. 2Magnesium*H_2O^+	66	5
5. Calcium	40	45

LC-MS: To simultaneously quantitate targets and screen for unknowns

ISQ EC MS







Why MS? Because it is both more universal and more selective detector.

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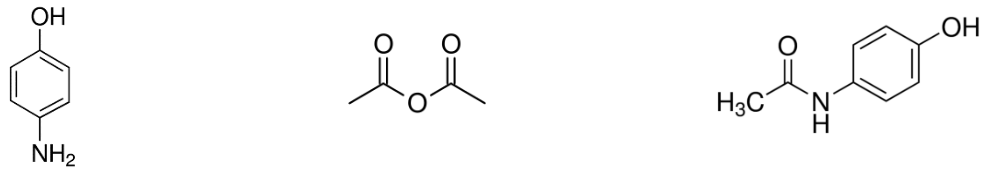
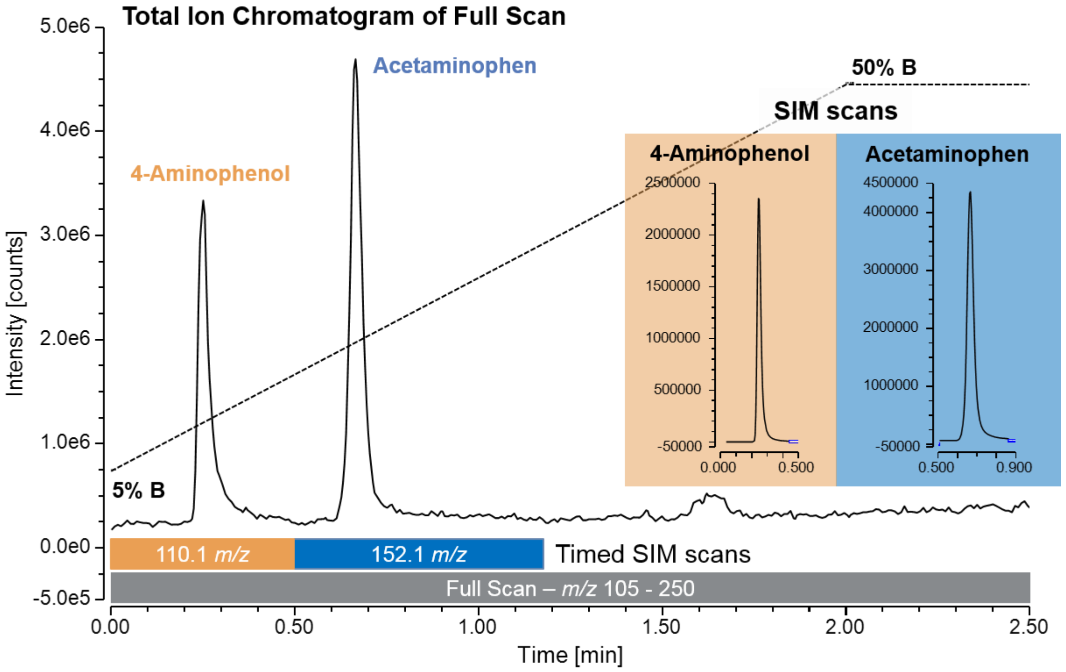
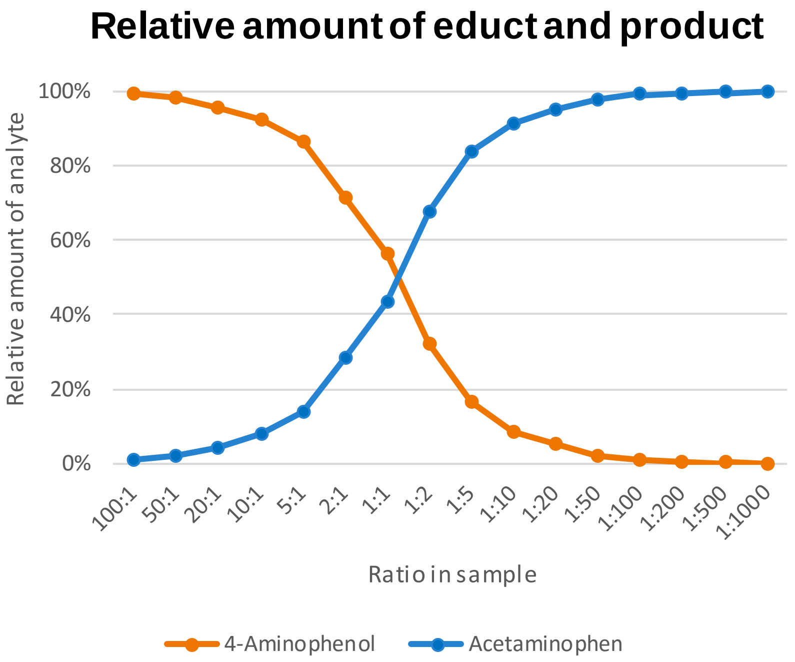
Thermo Scientific ISQ EC MS as LC-MS: Synthesis Monitoring & Reaction Confirmation

4-Aminophenol + Acetic Anhydride → Acetaminophen + Acetic Acid



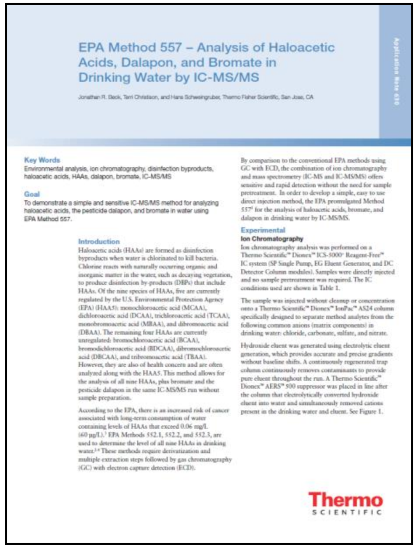


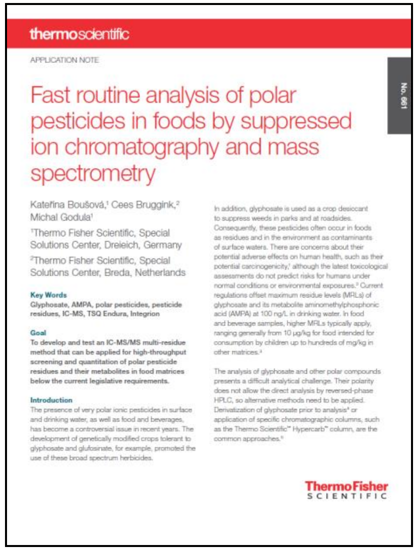


More robust, off-the-shelf solution with reduced support needs

IC-MS Published Applications

- Published Thermo Scientific™ Dionex™ IC-MS applications:
  - Perchlorate in Environmental Waters (AN151 & APN 203)
  - Determination of Low Molecular Mass Organic Acids in Biomass (AB104)
  - Determination of Acrylamide in Water (AN409)
  - Determination of Fluoroacetic Acid in Water (AN276)
  - Determination of Common Anions and Organic Acids (AN243)
  - Determination of Common Cations and Amines (AN269)
  - Determination of Haloacetic Acids in Drinking Water (AN454 & AN630)
  - Determination of Polar Pesticides and their Breakdown Products in Environmental Water (AN491)
  - Determination of Polar Pesticides and their Breakdown Products in Food Samples (AN661)
  - Determination of Nitrogen Mustard Hydrolysis Products as Ethanolamines in Water Samples
  - Determination of Endothall in Water (AN263)
  - Determination of Ultratrace Level Perchlorate in Liquid and Powdered Baby Formula
  - Determination of Small Organic Acids in Sea Water by IC-MS (AN1000)
  - Pathway-Targeted Metabolomic Analysis in Oral/Head and Neck Cancer Cells using IC-MS (AN622)
  - Using ion chromatography with electrospray ionization mass spectrometry for the determination of cations and amines in alkanolamine scrubbing solutions soon to be published (AN72609)


EPA Method 557 – Analysis of Haloacetic Acids, Dalapon, and Bromate in Drinking Water by IC-MS/MS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APPLICATION NOTE

Fast routine analysis of polar pesticides in foods by suppressed ion chromatography and mass spectrometry

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Summary

- IC-MS is the method of choice for sensitive and selective determinations of ions
- Aqueous samples can be directly injected into the IC system, eliminating the need for derivitization with minimal sample preparation
- IC-MS can be used to confirm the identity of small polar molecules

Join the Fun! *Cache a Chromeleon* Game

- Use your mobile device to complete challenges and earn a Charlie Chromeleon plush toy!
- If you are playing, you have earned points for attending this seminar. Be sure to scan the barcode on the desk outside the door.
- Ask booth staff for more details on how to play.

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Thank You

Please join me in the

Ion and Liquid Chromatography

sections of our booth where I’ll

address additional comments and questions.