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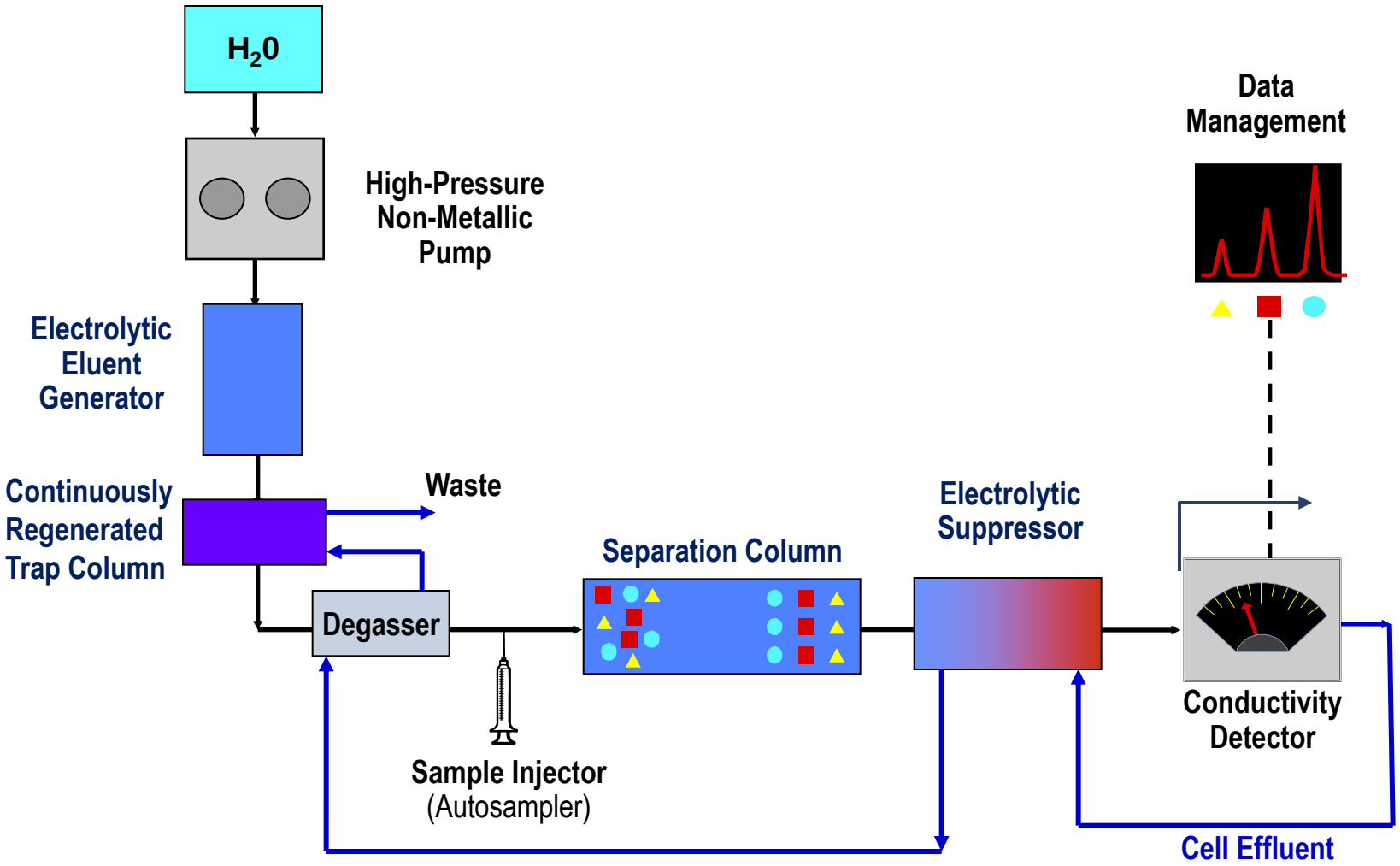
Coupling IC with Mass Spectrometry: Theory and Applications

Reagent-Free™ Ion Chromatography System



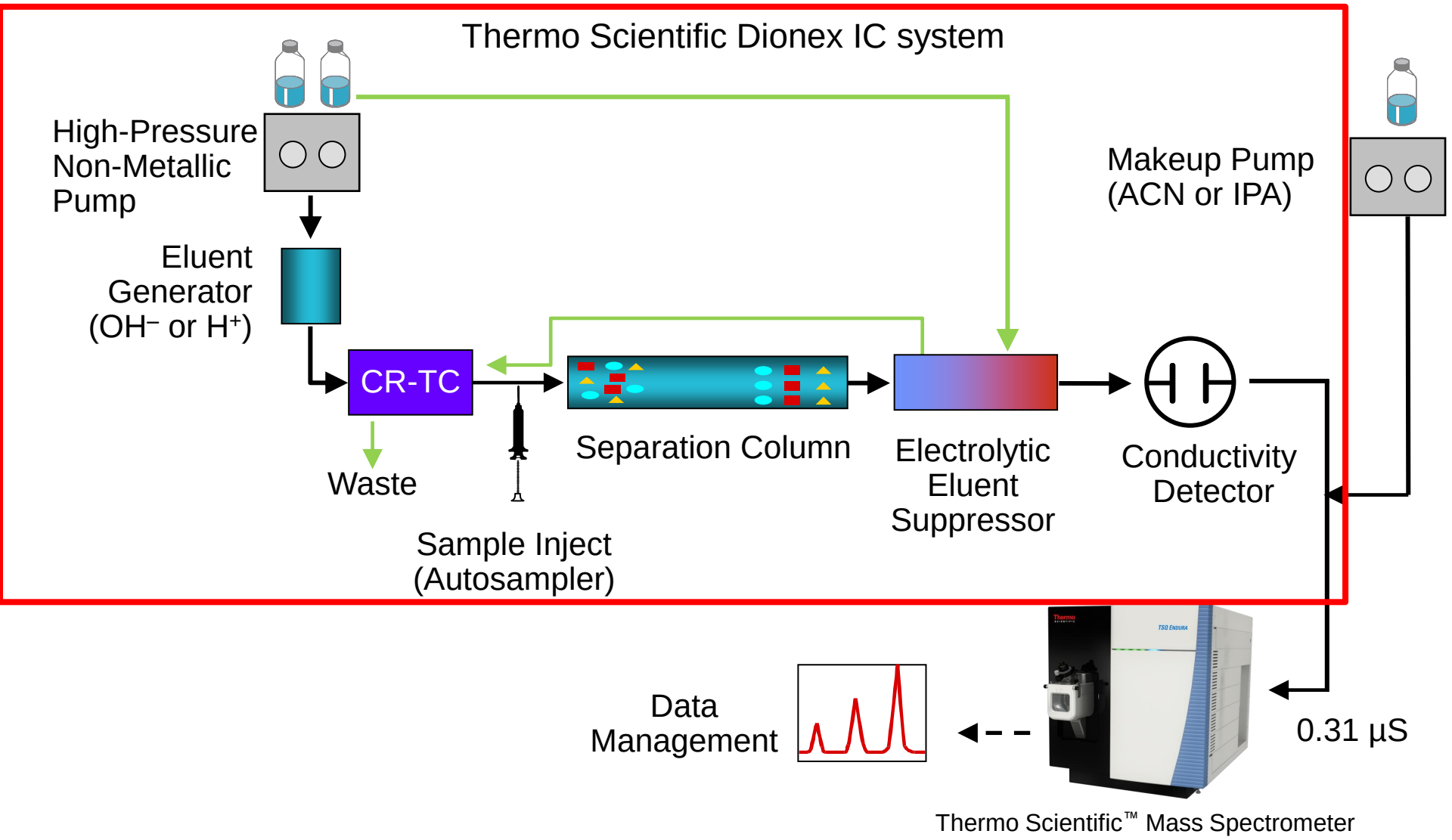
Mass Spectrometer

An atmospheric pressure region where ions are generated

A vacuum chamber where ions are separated

A detector (transducer) where ions are recorded

IC with MS-MS Flow Diagram



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Benefits of Ion Chromatography–Mass Spectrometry

- IC vs. 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
- 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)

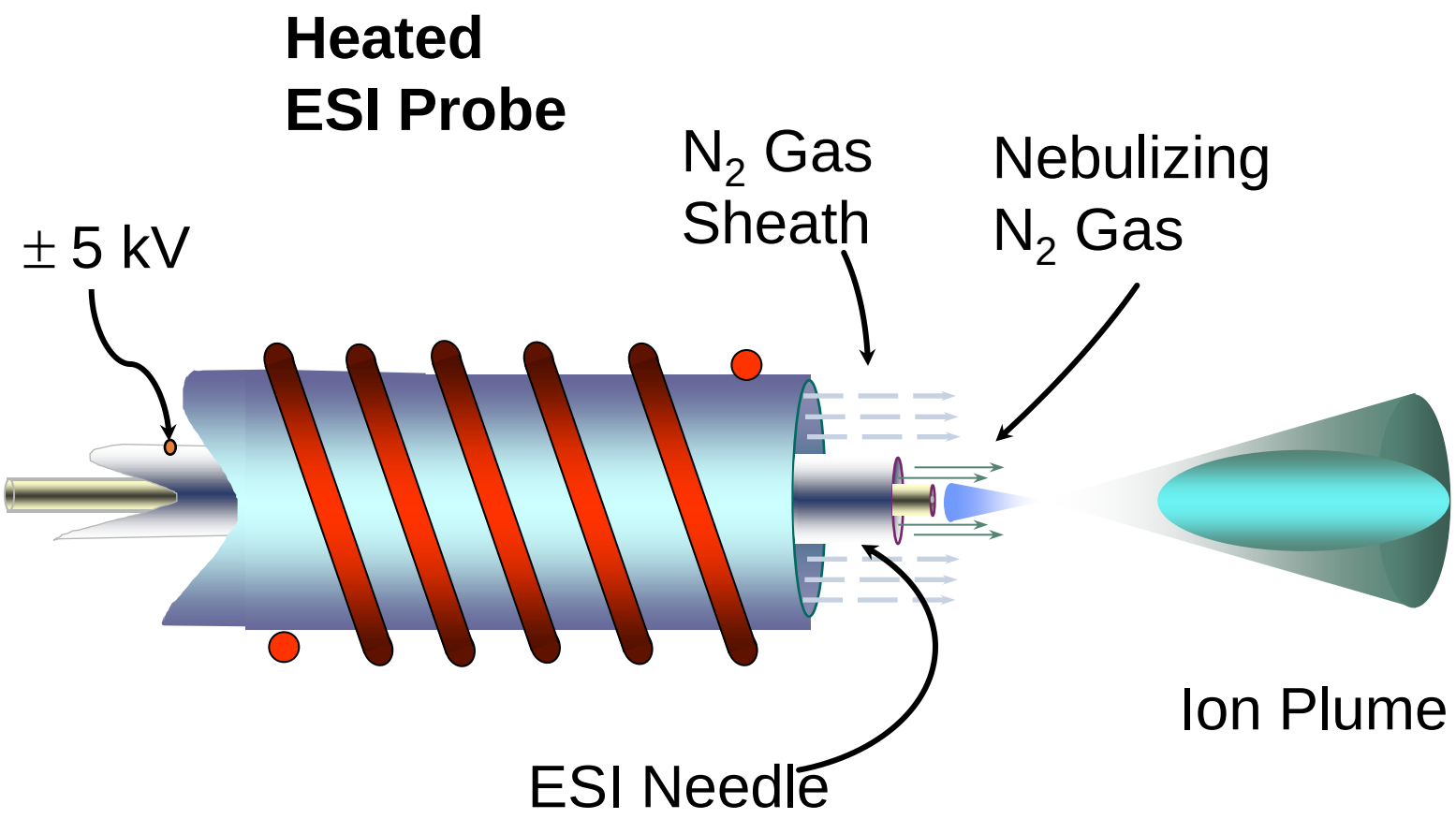
- Analytes are provided in the ionic form needed for MS detection
- Thermo Scientific Dionex suppressors allow the use of standard IC elements and methods
- Eluent generators with deionized water feed allows for fast, clean switching between anions and cations in IC-MS.
- Moreover, background is pure water after suppressor thus allows easy and advantageous switching between anion IC and cation IC into MS.

IC to MS Interface

Atmospheric Pressure Ionization (API)

- INTERFACE for the mass spectrometer
  - Changes liquid from the IC or LC to a gas
  - Introduces gas into the mass spectrometer
- It is an IONIZATION SOURCE
  - Ionizes the liquid/gas and the analytes
  - Operates in either positive or negative ion modes
- Two principal API techniques are:
  - Electrospray Ionization (ESI) used for ion chromatography because the analytes are already ionized
  - Atmospheric Pressure Chemical Ionization (APCI) used primarily for normal phase chromatography where analytes are not ionized

Electrospray Nozzle Detail



Thermally Assisted Pneumatic Nebulization

Electrospray Ionization

Advantages

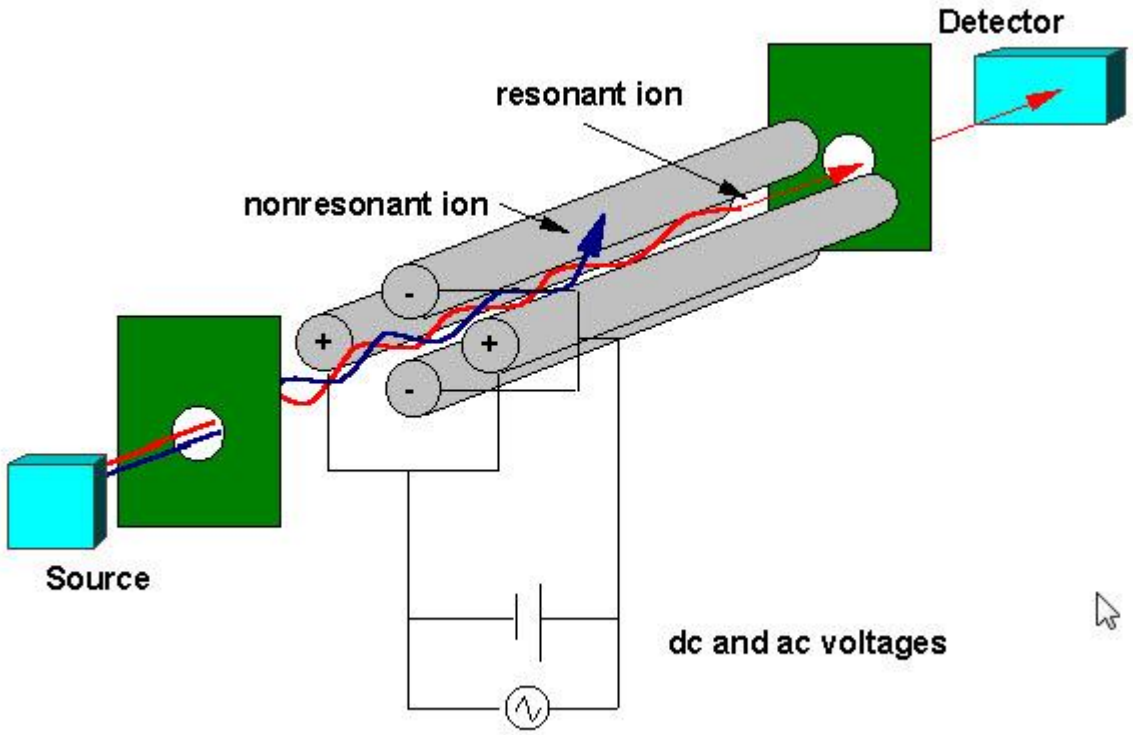
- Preserves analyte molecular ion
- Sensitive and rugged
- Compatible with a broad range of compounds

Disadvantages

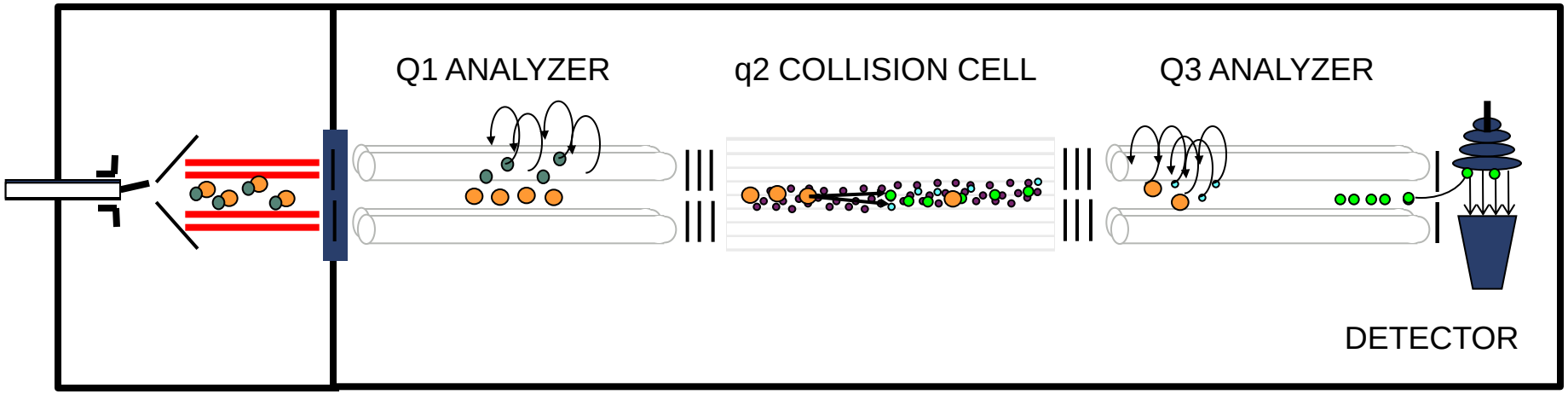
- High-aqueous mobile phase volatility
  - Requires elevated ESI Probe temperature and post-column solvent
- Non-volatile buffers may precipitate inside ESI capillary
- Works best at low flow rates (2 mm i.d. columns)
- Ionization is inhibited by high salt concentrations

Single Quadrupole MS

- Ions source, Mass analyzer (Quadtrupole) and Detector
  - Scanning mode
  - Filtering mode, Single ion monitoring (SIM)

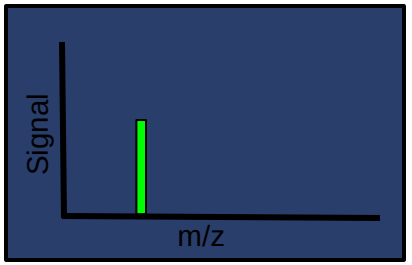


Triple Stage Quadrupole (TSQ)



- Two quadrupole mass analyzers, one collision cell
- MS or MS/MS with linked scans

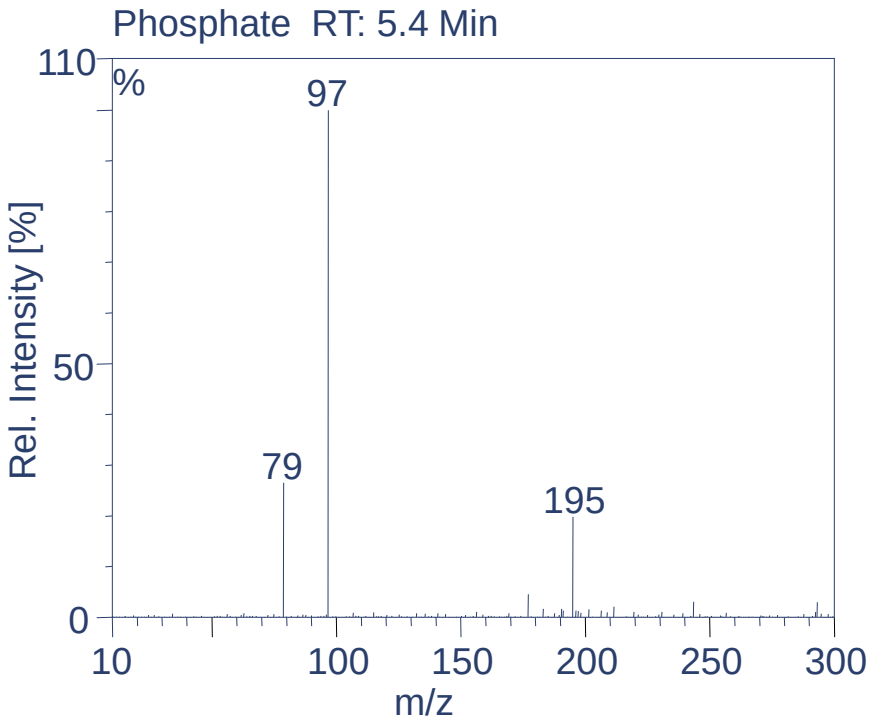
Single Reaction Monitoring

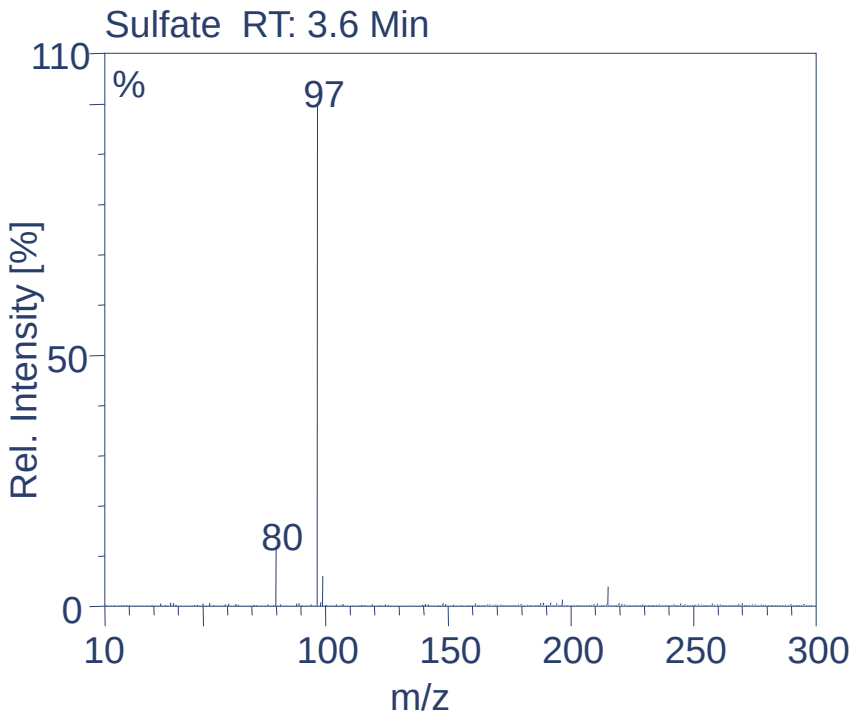


Single and Triple Quadrupole MS Analyzers

- MS single quadrupole analyzer
  - Molecular ion
  - Some fragmentation
- Triple Quadrupole MS-MS (Thermo Scientific TSQ or QqQ)
  - Composed of a quadrupole (Q1), followed by a collision cell (q2), another quadrupole (Q3), and detector
  - Provides high specificity and focus of molecular ion by eliminating all background ions
  - Fragmentation to ensure improved signal to noise and specificity

Phosphate and Sulfate have the Same Nominal Mass/Charge (m/z = 97)





IC coupled with Single Quadrupole MS (Thermo Scientific™ MSQ Plus™)

MSQ Plus MS is designed for IC

- Compact design
- Single quadrupole, low mass detector, 17–2000 m/z range
- Enhanced low-mass response for analytes below 60 m/z
- High-sensitivity, self-cleaning ESI ionization source
- Controlled and software:
  - Thermo Scientific™ Dionex™ Chromeleon™ Chromatography Data System (CDS) software or
  - Thermo Scientific™ Xcalibur™ software

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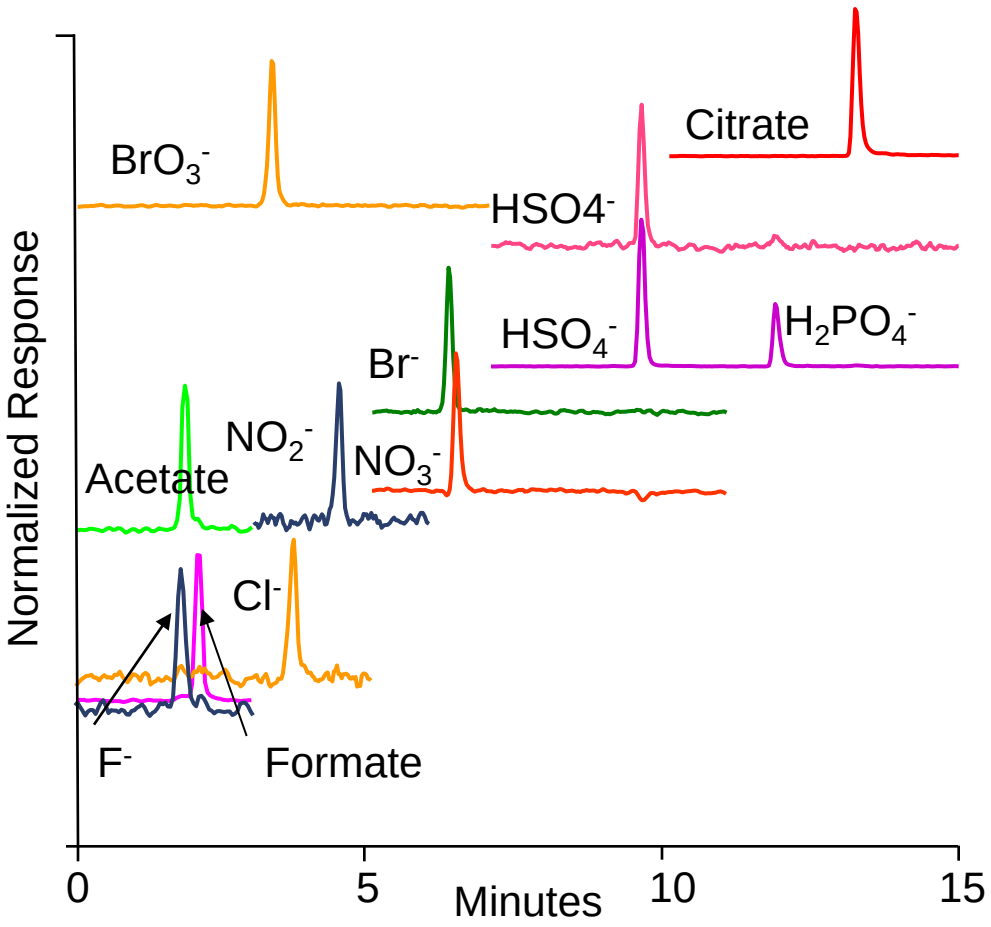
Optimized for Detection of Very Low Mass Ions



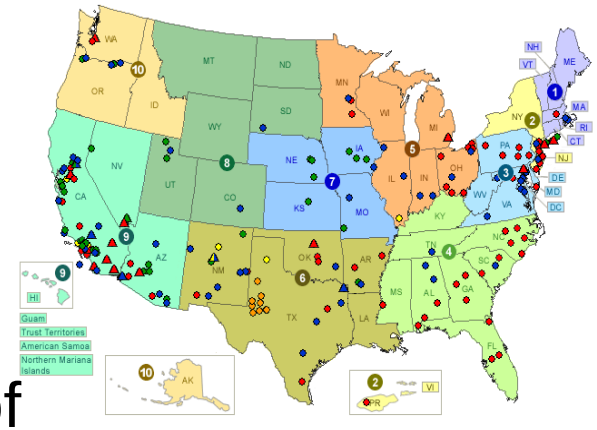
AN243

Column:	Thermo Scientific™ Dionex™ IonPac™ AS11, 2 × 250 mm
Eluent (EG):	KOH
Gradient:	0.5–38 mM KOH (0 –18 min)
Flow Rate:	0.5 mL/min
Temp:	30 °C
Suppressor:	Thermo Scientific™ Dionex™ ASRS™ Anion Self Regenerating Suppressor, external water mode
MS Conditions:	MSQ Plus MS, -ESI 50 V, 400 °C, SIM
Inj. Vol.:	25 µL

SIM Peaks:	µg/L	SIM
1. Fluoride	130	19
2. Acetate	300	59
3. Formate	300	45
4. Bromate	100	127
5. Chloride	30	35
6. Nitrite	100	46
7. Bromide	100	81
8. Nitrate	100	62
9. Sulfate	150	97/99
10. Phosphate	15097	
11. Citrate	300	191

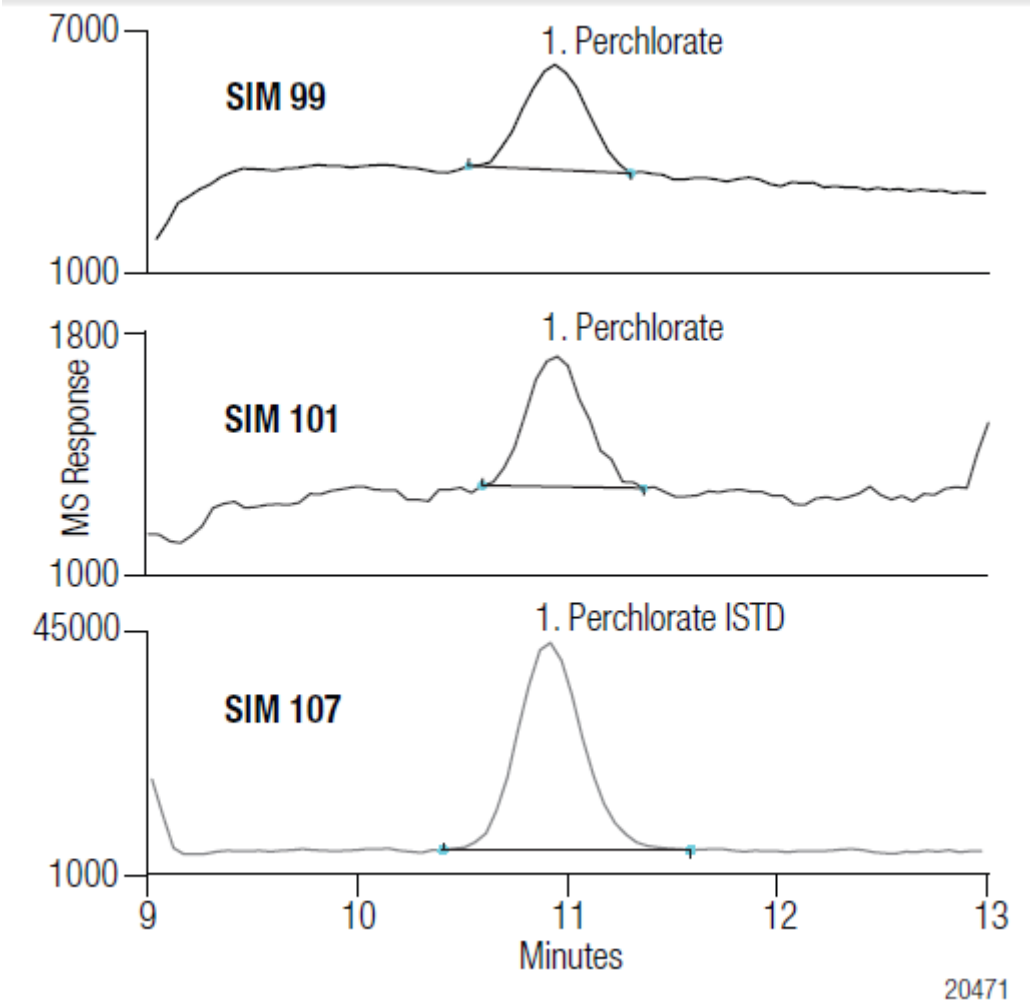
Perchlorate Health Issues

- Interferes with thyroid hormone production and metabolism regulation
- May cause tumors
- Interferes with neurological development of fetus and infants
- Regulated under Safe Drinking Water Act (2011)
  - Maximum Contamination Level of 6 µg/L (ppb) by 2013
  - Promulgated to the states
  - MA (2 µg/L); CA (6 to 1 µg/L)
  - Other states: health screening limits of 4 to 51 µg/L



U.S. EPA website (www.epa.gov)

High Ionic Matrix Spiked with 125 ppt Perchlorate and Internal Standard

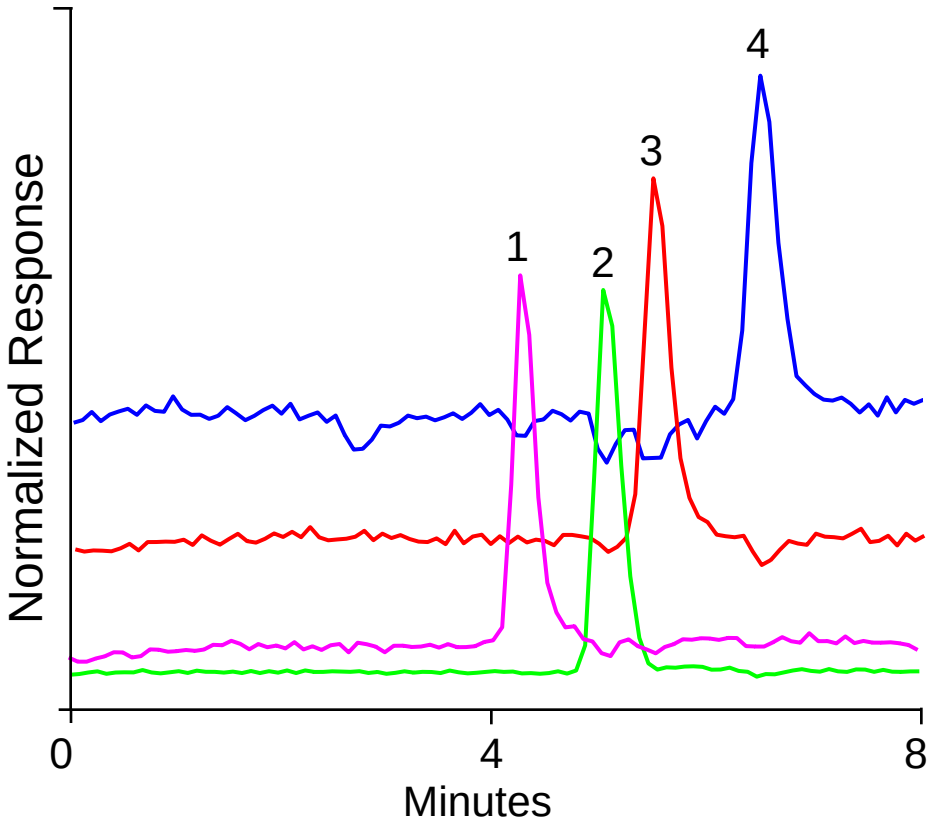


Column:	Dionex IonPac AS16, 2 × 250 mm
Eluent (EG):	45 mM KOH
Flow Rate:	0.30 mL/min
Temp:	30 °C
Suppressor:	Dionex suppressor, external water mode
Inj. Vol.:	100 µL
MS Conditions:	MSQ Plus MS, -ESI, Cone: 70 V, Probe: -3kV, 450 °C, Dwell: 1 s, Span: 0.3 amu SIM as indicated

SIM Peaks:		(ppt)
1.	Perchlorate	125
1.	Perchlorate Internal Std	1000
2.	MCL (CA, MA)	1000–6000

Matrix: 1000 mg/L chloride, carbonate, and sulfate

IC-MS of Sodium and Small Amines

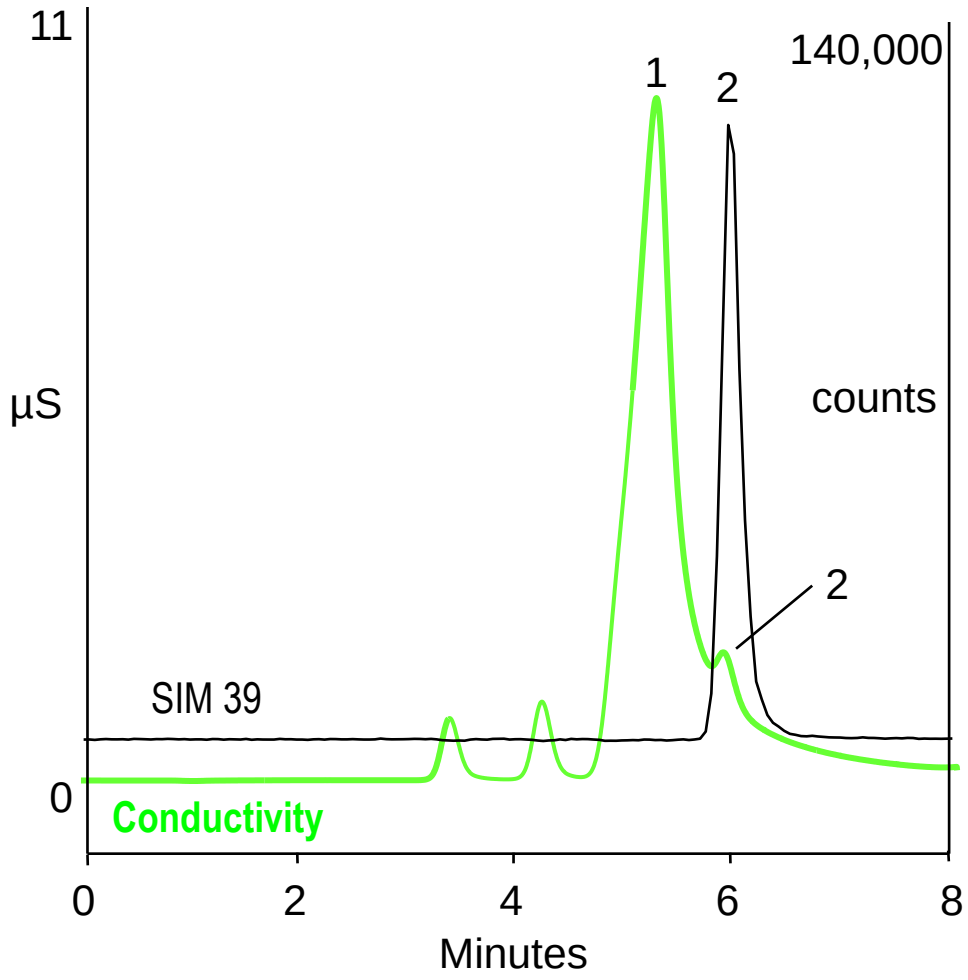


Column:	Dionex IonPac CS12A-MS, 2 × 100 mm
Eluent (EG):	MSA
Gradient:	4–10 mM MSA (0–6 min), 10 mM (6–8 min)
Flow Rate:	0.25 mL/min
Temperature:	30 ºC
Suppressor:	Dionex CSRS Suppressor, external water mode
Inj. Vol.:	25 µl
MS Conditions:	MSQ Plus MS, +ESI, 50 V, 350 ºC, SIM as indicated

SIM Peaks:

1. Sodium, *m/z* 23	(contaminant)
2. Methylamine, *m/z* 32	50 µg/L (ppb)
3. Dimethylamine, *m/z* 46	40
4. Trimethylamine, *m/z* 60	150

Low Level Potassium in Diethanolamine by IC-MS

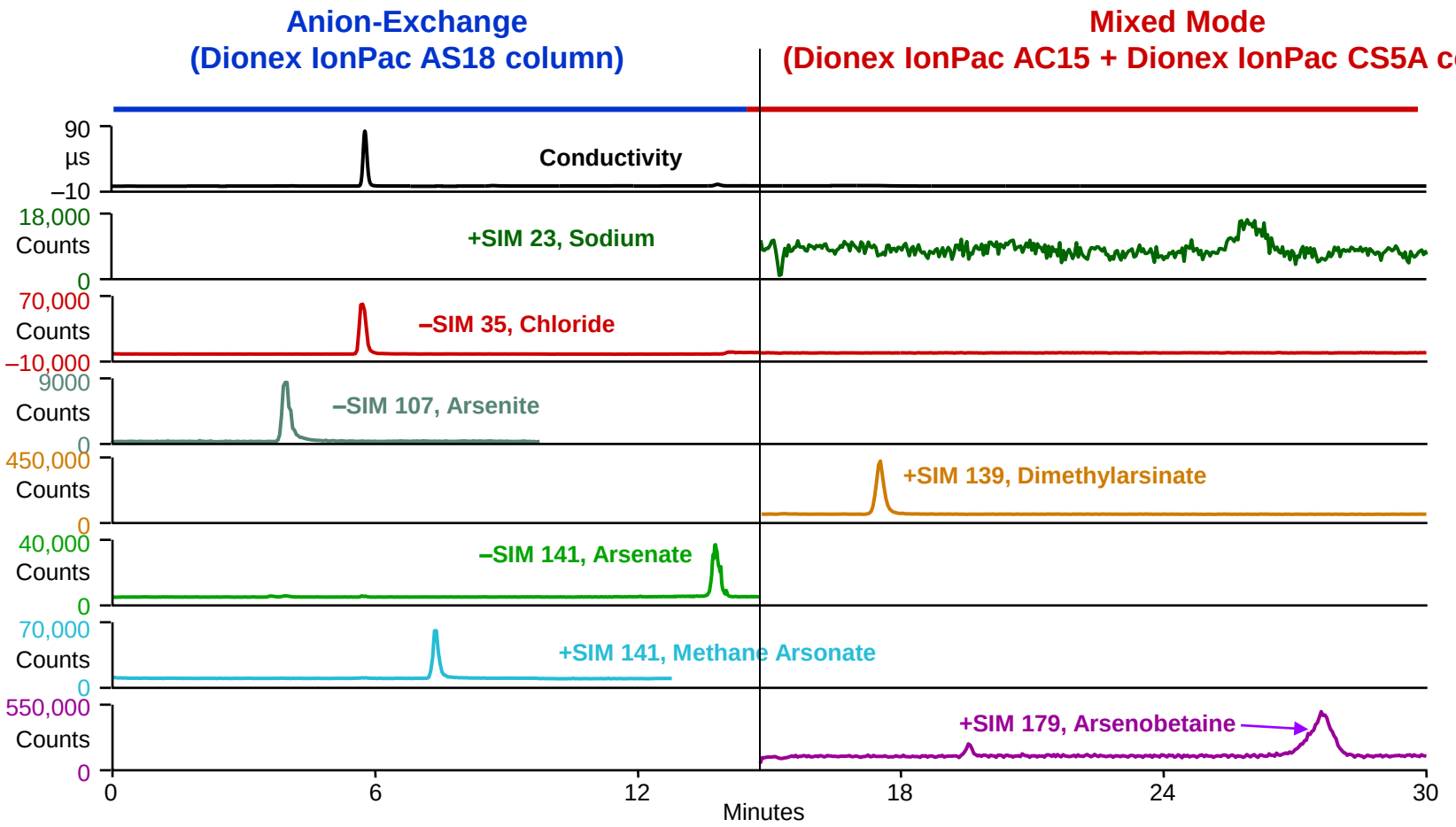


Column:	Dionex IonPac CS12A-MS, 2 × 100 mm
Eluent (EG):	MSA
Gradient:	4–10 mM MSA 0–6 min, 10 mM 6–8 min
Flow Rate:	0.25 mL/min
Temp:	30 °C
Suppressor:	Dionex CSRS suppressor, external water mode
Inj. Vol.:	25 µL
MS Conditions:	MSQ Plus, +ESI, 50 V, 350 °C, SIM as indicated

SIM Peaks:

1. Diethanolamine
2. Potassium, *m/z* 39 200 µg/L (ppb)

Separation and Detection of Arsenic Species Using A Dual RFIC System with MS (-SIM and +SIM)



Slingsby et al., *Am. Lab.*, 2007

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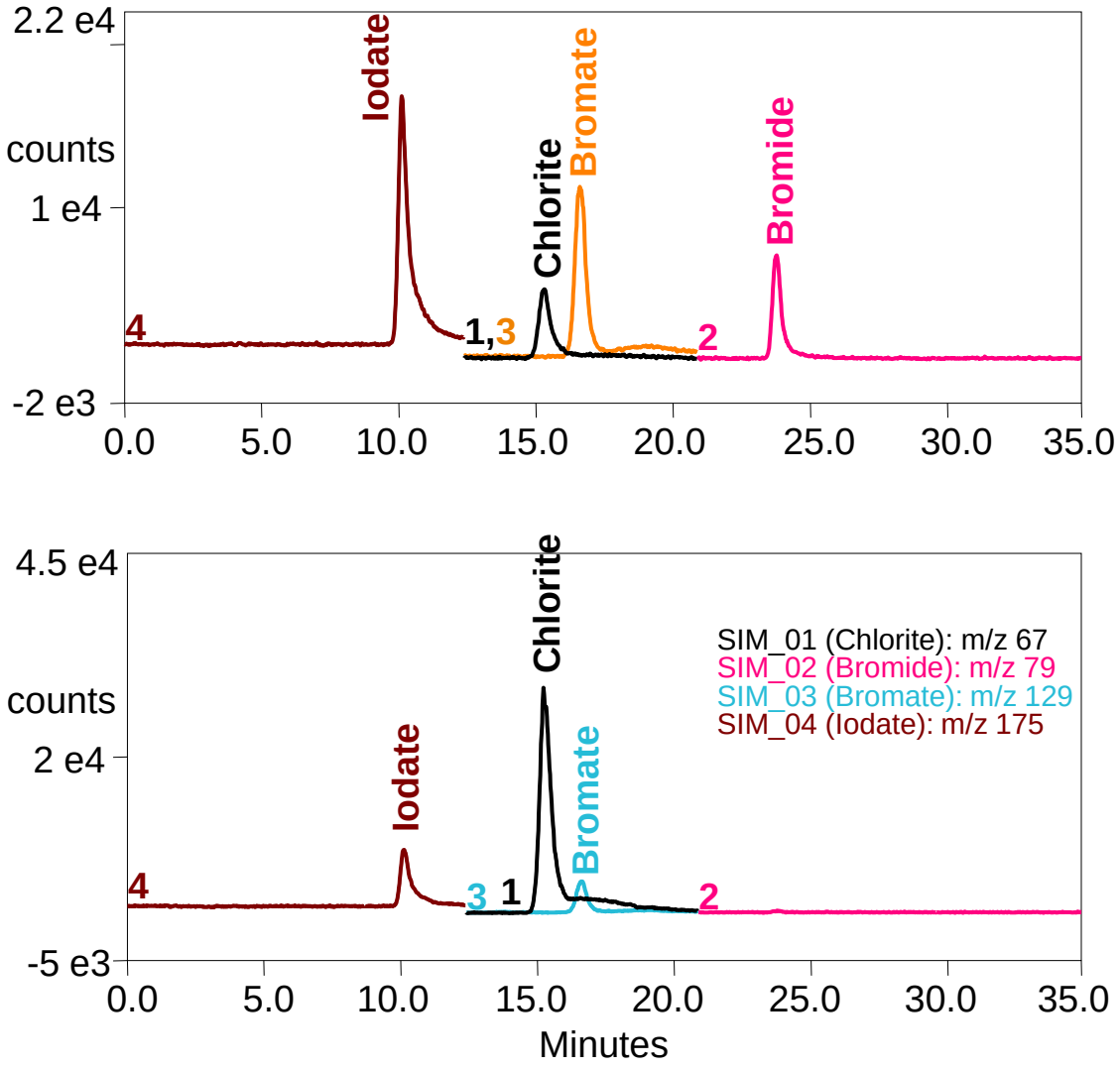
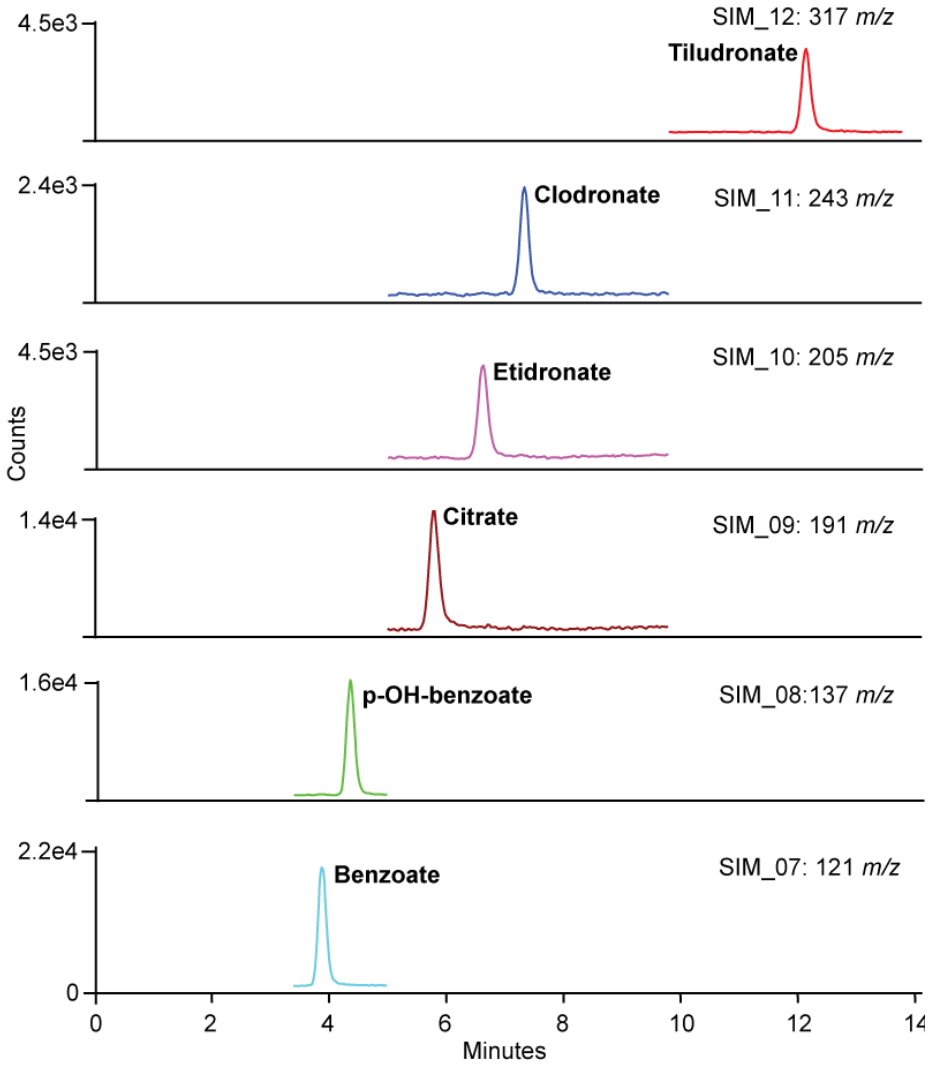
Oxyhalides and Bromide in Drinking Water by IC-MS



Column:	Dionex IonPac AG19/AS19, 2 mm i.d.
Eluent:	KOH gradient
Flow:	0.25 mL/min
Detection:	Suppressed conductivity
Background Signal:	< 3 µS/cm
Suppressor:	Dionex ASRS suppressor, 2 mm, external water mode
Temperature:	30 °C
Inj. Vol.:	250 µL
MS Conditions:	MSQ Plus, negative ESI
Needle Volt.:	3 kV
Cone Volt:	50 V (chlorite) and 75 V (iodate, bromate and bromide)
Probe Temp.:	400 °C

Bisphosphonate Pharmaceuticals and Excipients by Cap IC-MS



IC Instrument:	Dionex ICS-5000^{+} Capillary IC
Column:	Dionex IonPac AG18-Fast/AS18-Fast, 0.4 mm i.d.
Column Temp:	40 °C
Eluent:	Thermo Scientific Dionex EGC-KOH (Capillary) Cartridge
Gradient:	40–50 mM KOH (0–5 min), 50–100 mM KOH (5–8 min), 100 mM KOH (8–14 min)
Flow Rate:	0.02 mL/min
Injection:	0.2 ng in 2 µL
MS Conditions:	MSQ Plus MS, -ESI, SIM
Probe Temp:	300 °C
Needle Volt:	3.5 kV
Solvent:	20 µL/min acetonitrile

AN 1001, Thermo Fisher Scientific, 2012

IC coupled with Triple Quadrupole MS (TSQ)

Thermo Scientific TSQ Quantiva and Thermo Scientific TSQ Endura Mass Spectrometer Overview

TSQ Endura

Extreme Quantitative Value

- Best-in-class performance
- Unprecedented usability
- Exceptional robustness

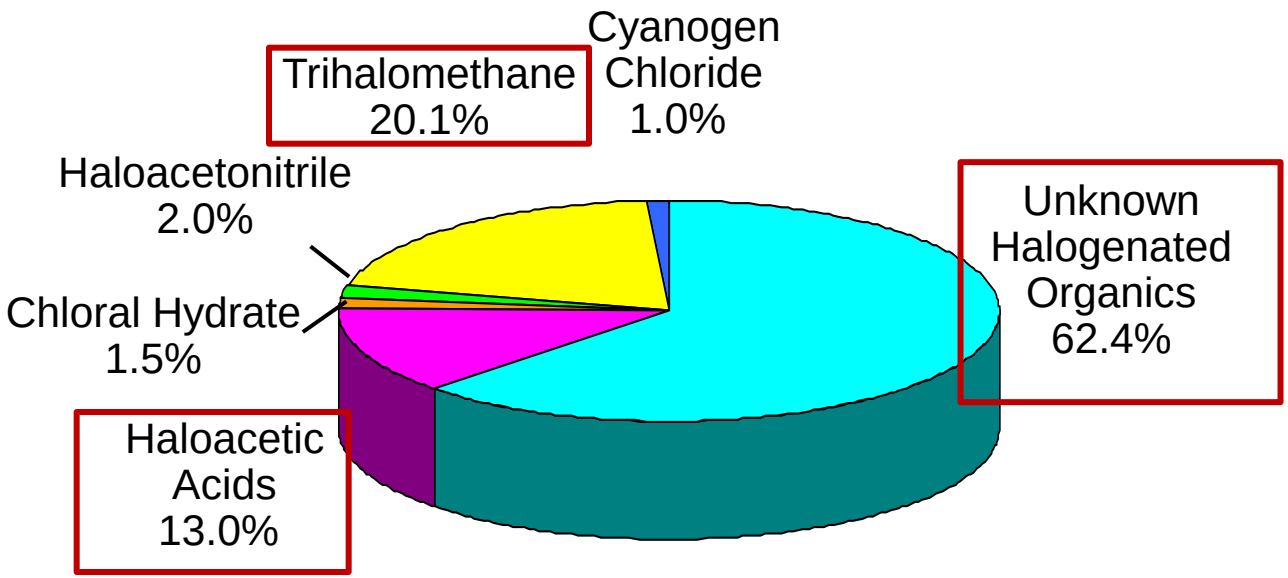
TSQ Quantiva

Extreme Quantitative Performance

- Attogram sensitivity
- Unprecedented usability
- Exceptional robustness

Occurrence of Disinfectant Treatment Byproducts

Haloacetic acids are formed when chlorine or other disinfectants react with naturally occurring organic and inorganic matter in water

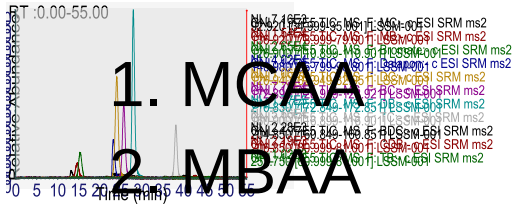


Haloacetic acids (HAA5 and HAA9)

Acid	HAA	Formula	pK_a
Monochloroacetic Acid	MCAA*	$ClCH_2CO_2H$	2.86
Dichloroacetic Acid	DCAA *	Cl_2CHCO_2H	1.25
Trichloroacetic Acid	TCAA *	Cl_3CCO_2H	0.63
Monobromoacetic Acid	MBAA *	$BrCH_2CO_2H$	2.87
Dibromoacetic Acid	DBAA *	Br_2CHCO_2H	1.47
Tribromoacetic Acid	TBAA**	Br_3CCO_2H	0.66
Bromochloroacetic Acid	BCAA**	$BrClCHCO_2H$	1.39
Chlorodibromoacetic Acid	CDBAA**	Br_2ClCCO_2H	1.09
Bromodichloroacetic Acid	BDCAA**	Cl_2ClCCO_2H	1.09
Bromate	--	BrO_3^-	
Chlorite	--	ClO_2^-	
Chlorate	--	$Cl0_3^-$	

*HAA5; **HAA9

Overlaid Chromatograms with Diversion Windows (Dionex ICS-5000+ System with TSQ Endura MS)



1. MCAA
2. MBAA
3. Bromate
4. Dalapon
5. DCAA
6. BCAA
7. DBAA
8. TCAA
9. DCBAA
10. DBCAA
11. TBAA

Conditions:
see AN 630

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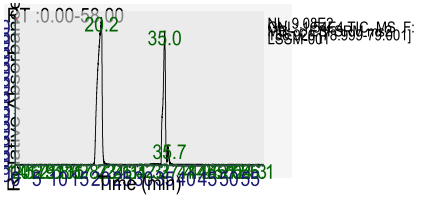
Diverts to Waste, Eliminates Salts from Matrix



Cl^-

CO_3^{2-}

SO_4^{2-}

NO_3^-

Conditions:
see AN 630

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Method Detection Limits for HAAs by TSQ Endura MS Using IC-MS-MS

Analyte	Calculated MDL (ppb)
MCAA* (Monochloroacetic Acid)	0.105
MBAA* (Monobromoacetic Acid)	0.104
DCAA* (Dichloroacetic Acid)	0.044
DBAA* (Dibromoacetic Acid)	0.021
BCAA** (Bromochloroacetic Acid)	0.059
TCAA* (Trichloroacetic Acid)	0.033
BDCAA** (Bromodichloroacetic Acid	0.141
DBCAA** (Chlorodibromoacetic Acid)	0.214
TBAA** (Tribromoacetic Acid)	0.159
Dalapon	0.050
Bromate	0.059

*HAA5
** HAA9

IC-MS vs. IC-MS-MS

IC-MS vs. IC-MS-MS Results

Analyte	Regulated Limit (µg/L)	IC-MSQ Plus MS (LOD, µg/L)	IC-TSQ Endura MS (LOD, µg/L)	IC-TSQ Quantiva MS (LOD)
Perchlorate	MCL < 1000	0.080–0.155	0.005	attograms
Halo Acetic Acids	MCL: Total HAA5 < 60; MCAA < 70; TCAA < 20; DCAA : Not detected	~0.5–1	0.02–0.21	attograms
Acrylamide	50 µg/kg	0.2	Sub ppb to single digit ppb	attograms
Inorganic anions / cations	N/A	4–200 1–3	Sub ppb to single digit ppb	attograms

Units are normalized to µg/L for clarification

Summary

- IC-MS is recommended method 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
- TSQ Endura and TSQ Quantiva (MS-MS) offer specificity and sensitivity over single quadrupole methods (shown for HAAs with ppt LODs)

IC-MS Resources

- AN 151: Perchlorate in Environmental Waters Using IC-MS
- AN 243: Common Anions and Organic Acids Using IC-MS
- AN 269: ppb Levels of Common Cations and Amines by IC-MS
- AN 276: Fluoroacetate in Water by IC-MS
- AN 1000: Small Organic Acids in Sea Water by IC-MS
- AN 1001: Bisphosphonate Pharmaceuticals and Excipients by Capillary IC-MS
- Wang, L.; Schnute, W. Capillary Ion Chromatography Mass Spectrometry: Recent Advances in Instrumentation and Applications. Poster Note 111310, 2011.
- Chassaniol, K.; Brown, S; Wang, L.; Schnute, W. Specific and Selective MS Detection for Environmental Analysis by Ion Chromatography. Poster Note 110522, 2011.

IC-MS-MS Resources

- Slingsby, R., et al. Dual-Selectivity IC-ESI-MS for the Separation and Detection of Anionic and Cationic Arsenic Species. *Am. Lab.,* May, 2007.
- Wang, L., Yang, C., Schnute, B. Quantitative IC-MS/MS Analysis of Nitrogen Mustard Hydrolysis Products as Ethanolamines in Water Samples. Poster Note 87121, 2010. (TSQ)
- AN 622: Pathway-Targeted Metabolomic Analysis in Oral/Head and Neck Cancer Cells Using Ion Chromatography-Mass Spectrometry (Orbitrap)
- AN 630: EPA Method 557 – Analysis of Haloacetic Acids, Dalapon, and Bromate in Drinking Water by IC-MS/MS (TSQ)
- AN 1088: Thiosulfate and Pyrophosphate in Crayfish Wash Powder (TSQ)
- AN 1138: Untargeted Metabolic Profiling of Oral Cancer Cells Using Capillary Ion Chromatography Coupled with High-Resolution, Accurate-Mass Orbitrap MS
- Coming soon,… Polar Pesticides and Perchlorate

Thank you!

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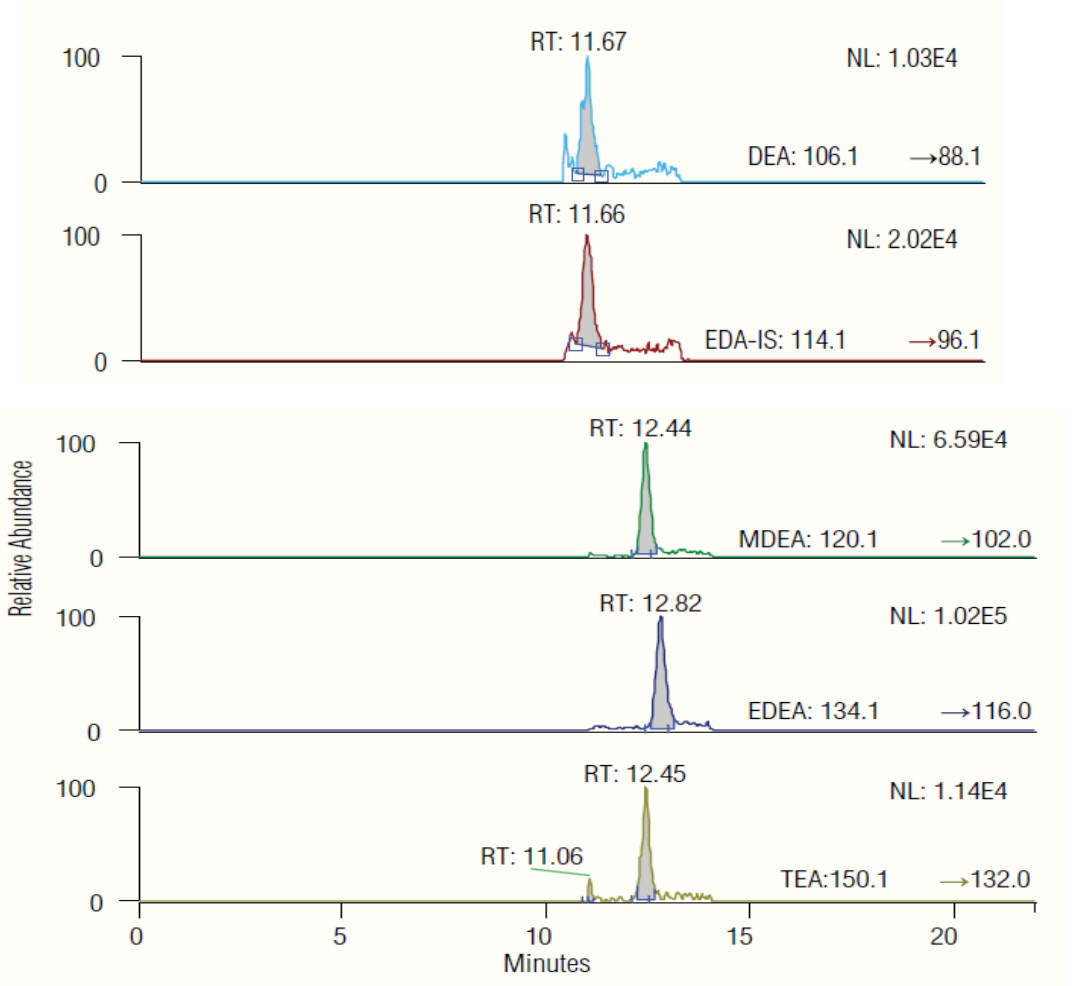
Transform Your Science

Other Applications

Quantitative IC-MS/MS Analysis of Nitrogen Mustard Hydrolysis Products as Ethanolamines in Water



DEA: Diethylamine
EDA-IS: D8 internal standard
MDEA: N-methyldiethanolamine
EDEA: N-Ethyldiethanolamine
TEA: Triethanolamine

Columns:	Dionex IonPac CG15/CS15 2 mm
Gradient (EG):	2 mM MSA (-4–8 min), 2–30 mM (8–18 min), 30 mM (18–22 min)
Flow Rate:	0.40 mL/min
Suppressor:	Thermo Scientific™ Dionex™ CSRS™ Cation Self Regenerating Suppressor, external water mode
Inj. Vol.:	20 µL
Detection:	A: Suppressed Conductivity, B: Electrospray Mass Spectrometry
MS Conditions:	TSQ Quantum Access MS, +ESI,
Makeup Solvent:	IPA at 0.2 mL/min
Scan:	SRM
Spray Voltage:	4K
Vaporization:	350 °C
Sheath/Aux Gas:	60 / 15 arbitrary units
Capillary Temp.:	300 °C

Analyte	Rt	Q1MS	Q3 MS	Collision Energy
DEA	11.7	106.1	88.1	10
		106.1	70.1	14
DEA-IS	11.7	114.1	96.1	11
		114.1	78.1	14
MDEA	12.4	120.1	102.1	13
		120.1	58.0	18
EDEA	12.8	134.1	116.0	13
		134.1	72.0	18
TEA	12.4	150.1	132.0	12
		150.1	88.0	17

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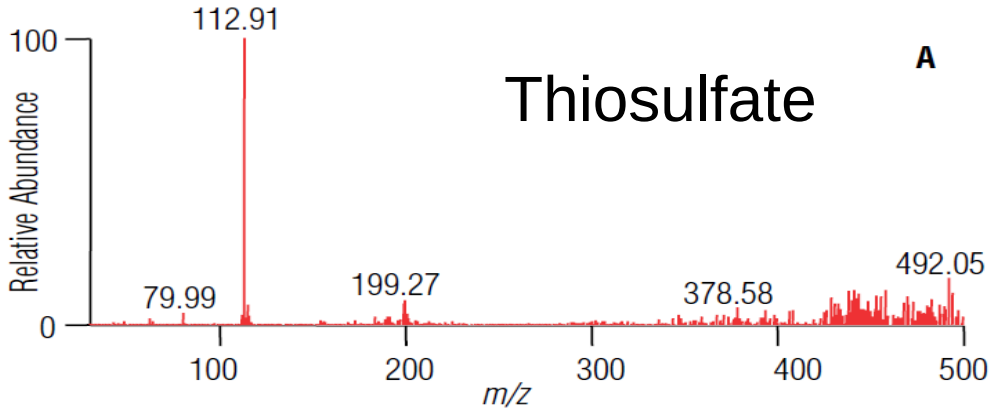
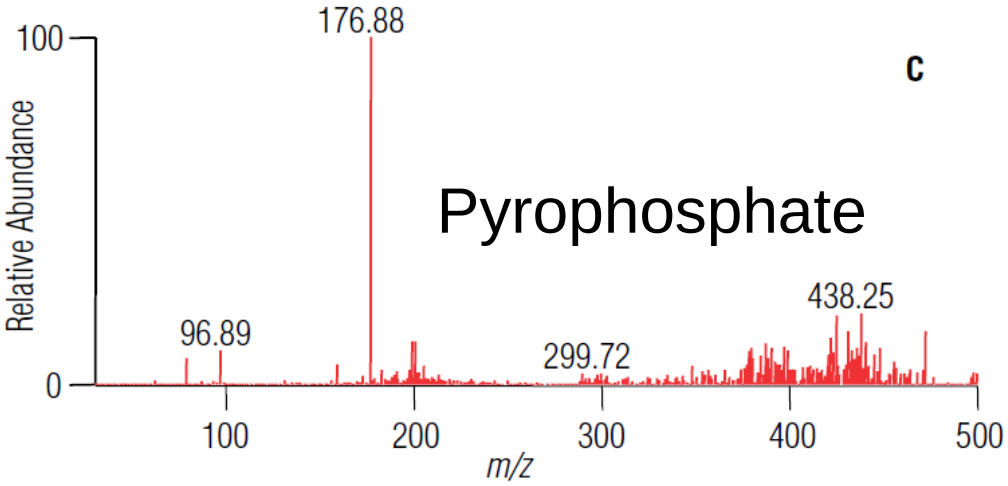
Thiosulfate and Pyrophosphate in Crayfish Wash Powder





Columns:	Dionex IonPac AG19/AS19, 2 mm i.d.
Eluent (EG):	KOH
Gradient:	6.5 mM KOH (0–15 min), 6.5–40 mM (15–30 min), 40–67 mM (30–37 min), 67 mM (37-39 min), 6.5 mM (40-46 min)
Flow Rate:	0.25 mL/min
Temp:	30 °C
Suppressor:	Thermo Scientific™ Dionex™ ASRS™ Anion Self Regenerating Suppressor, external water mode
Inj. Vol.:	25 µL
Detection:	1-Suppressed conductivity, 2- Electrospray Mass Spectrometry
MS Conditions:	Vantage TSQ MS, -ESI,
Spray Voltage:	3K
Vaporization:	350 °C
Sheath Gas:	40.0 bar
Ion Sweep Gas:	0 bar
Aux Gas:	5.0 bar
Collision Gas:	0 mTorr
Sample Prep.:	100 mg powder/100 mL DI, filter, Dionex OnGuard RP, OnGuard Na
Sample:	A: Wash Powder 1 C: Wash Powder 2