



ThermoFisher
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Critical On-line Process Monitoring using Ion Chromatography

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2022 Gulf Coast Conference

Process IC: Thermo Scientific Dionex Integral Process Analytical (PA) System

- Optimize process operations by improving process monitoring
- Easily migrate from lab instrument to plant floor
- Stand-alone sample preparer (SP) and stream selector (SS) modules
- Accommodates IC and HPLC instruments
- Dionex IC ease of use- eluent generation and electrolytic suppression
- Thermo Scientific™ Chromeleon 7 Process Analyzer software
- 35+ years of experience



Confidence in hardware, support, and results

Process analysis: industries and applications



Pharmaceutical/Biopharmaceutical – Reaction monitoring, collection based on purity, bioreactors, water purity, cleaning validation



Power – Ions in cooling water and steam condensate



Semiconductor – Water quality, critical components in plating baths, contaminants in rinse baths



Environmental/Utilities – Water treatment plant inflow/outflow (pesticides, by-products), remediation/reclamation process confirmation



Chemical/Petrochemical – Reaction process/endpoint determination, control reactant concentrations, waste stream discharges



Biofuels/Biorefineries – Critical media components and costly enzymes, SO_4 and Cl in final product



Food/Agriculture – Bottled water, food components, soft drink and juice formulation control

Over 35 years of experience with on-line IC and HPLC



**Process knowledge begins in the lab.
Process analytical technology (PAT) should too!**

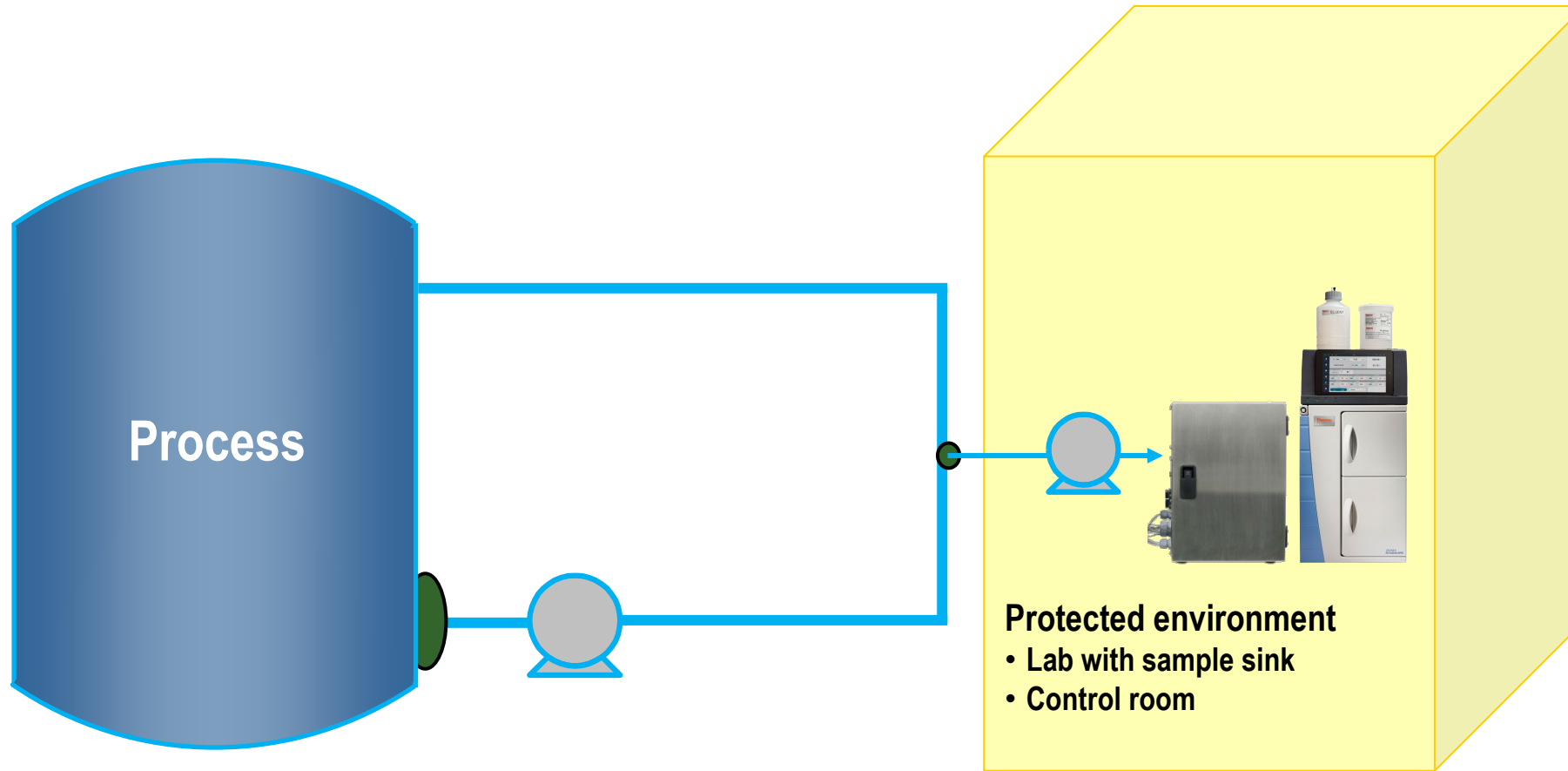


Migrate PAT with the process.

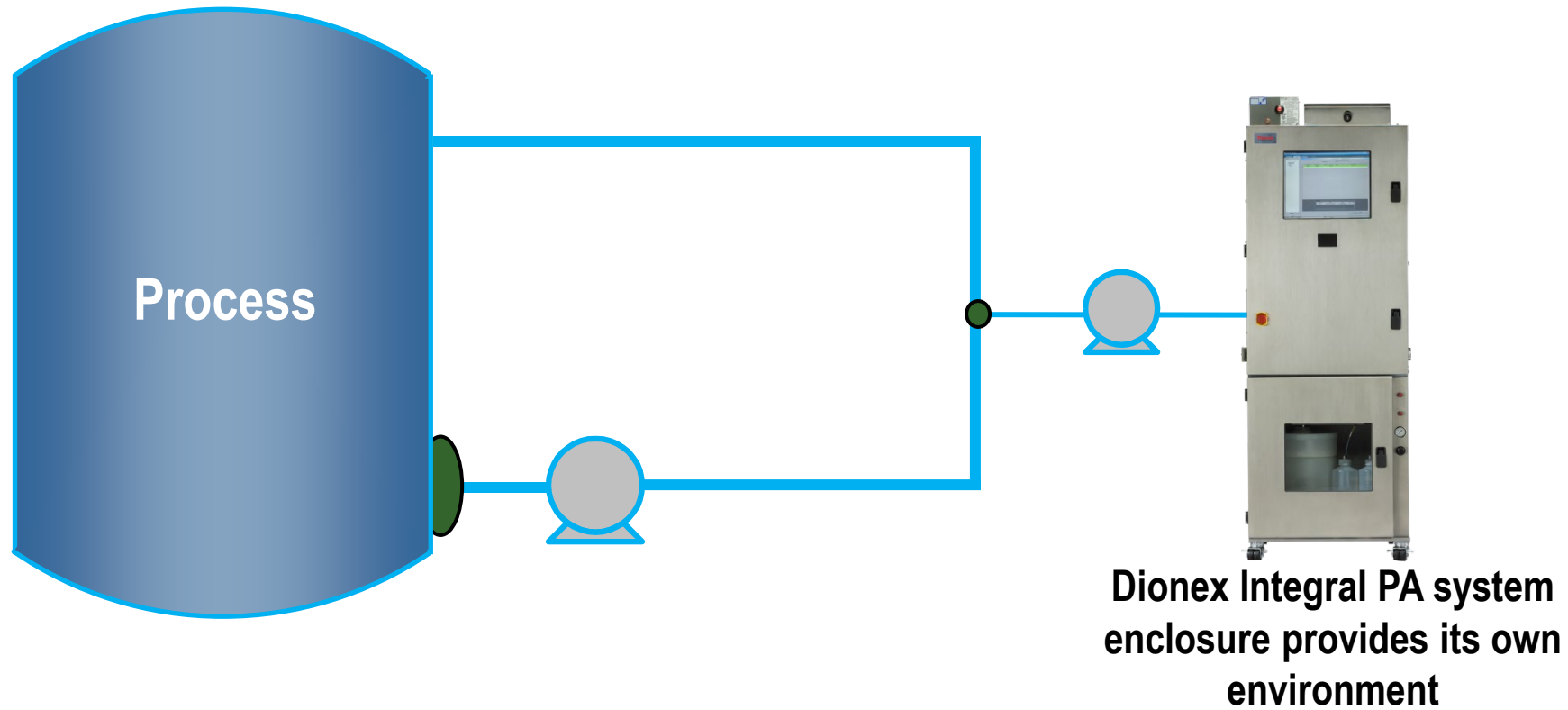
- More timely, frequent process analysis provides more process detail
 - Rapid identification of transient upsets and trends
 - Improved understanding of what impacts your process
- Enable use of process automation and control
- Reduced
 - Process variability
 - Process cycle times
 - Risk of exceeding regulatory limits
 - Risk of operator exposure to dangerous chemicals
- Improved product quality and yields

- Eliminate down time waiting on lab results
 - Increase process equipment usage
 - Decrease process cycle times
- Use labor to produce product, not delivering samples to the lab
- Eliminate equipment damage from corrosive process conditions
- Increased reaction yields
- Regenerate process resins on breakthrough; not time
- Eliminate production of out of specification product

On-line IC/LC with Dionex Integral PA Migration Path for PAT

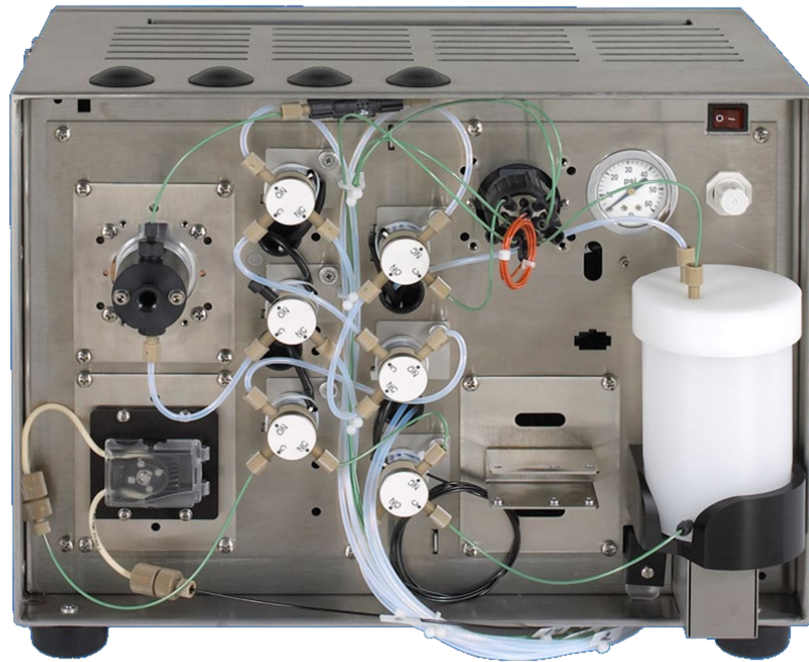


On-line IC/LC with Dionex Integral PA system enclosure



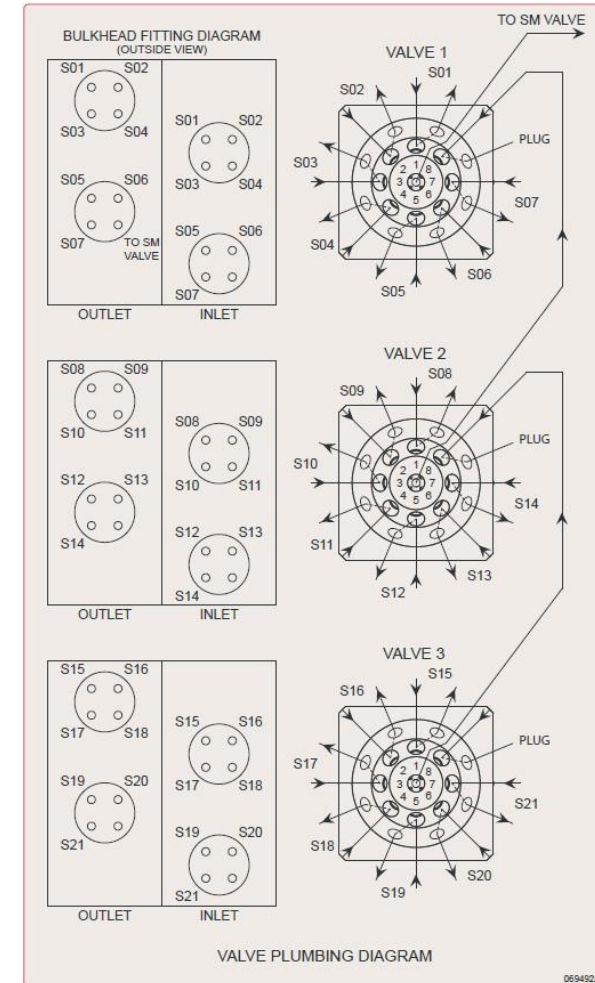
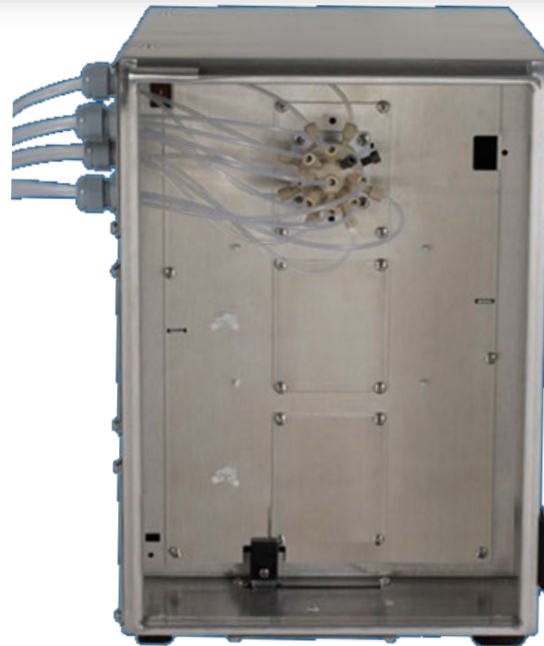
Thermo Scientific™ Stream Selector (SS) and Sample Preparer (SP) modules

Configurations and performance



Stream Selector (SS) module for Dionex Integral PA system

- Multiplex sample streams to single analyzer
- Up to 21 sample streams per analyzer
- Save cost by sharing analyzer across multiple streams
- Stand-alone module for lab, pilot plant, process



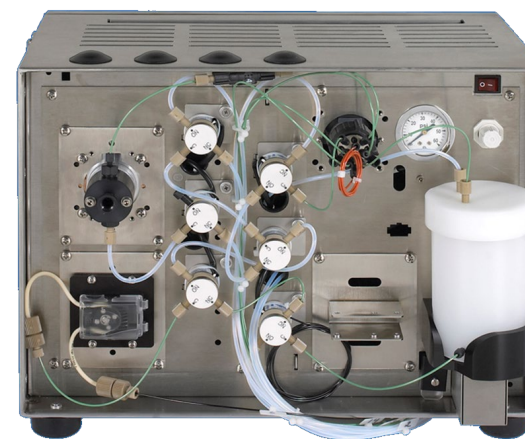
Sample Preparer (SP) module for Dionex Integral PA system

- Automated sample/standard preparation
 - Sampling
 - Dilution
 - Reagent addition
 - Analyte isolation/preconcentration (SPE)
- Automated calibration
 - Generate calibration curve from stock standard
- Stand-alone module for lab, pilot plant, process

- Available configurations
 - SP1 module: Concentration / direct injection
 - SP2 module: Dilution / direct injection
 - SPx module: Base unit for custom configurations



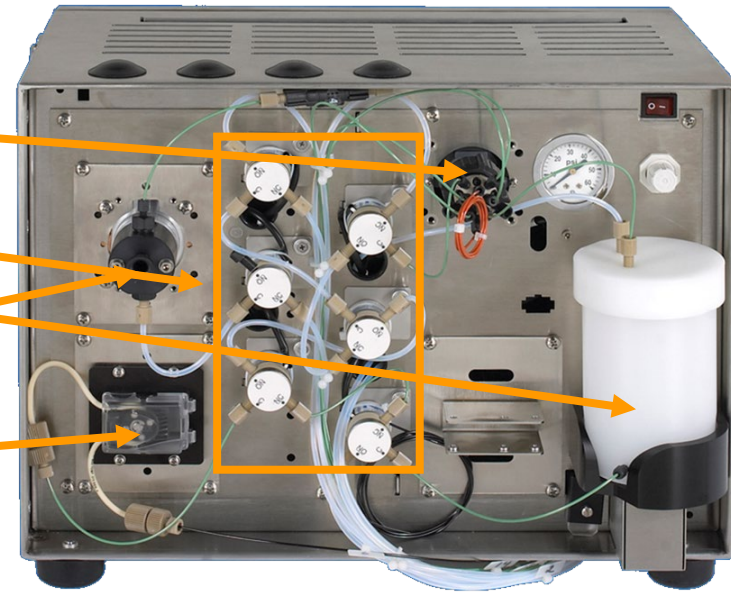
Vertical for external or stand-alone
(door removed)



Horizontal for internal mounting

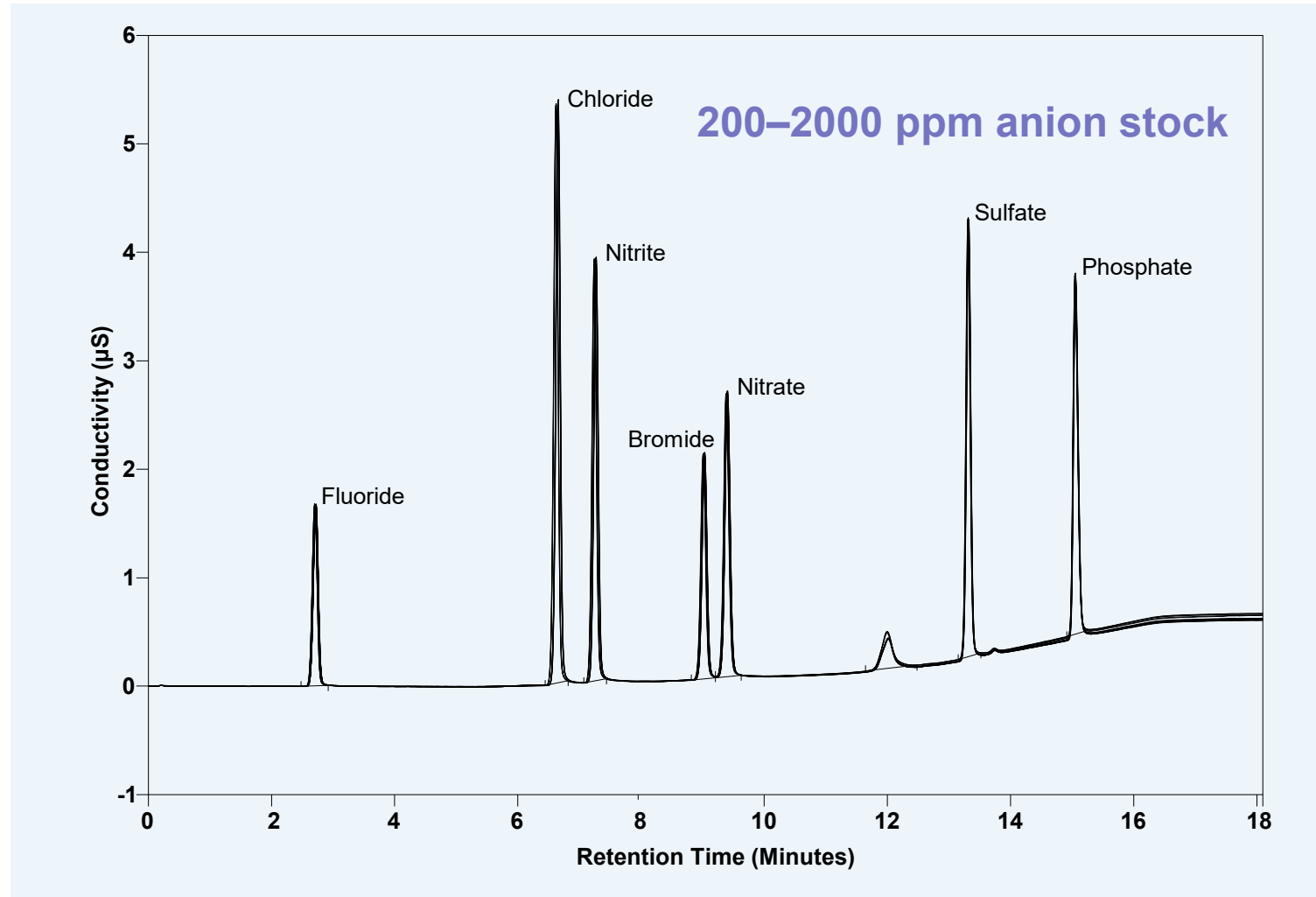
SP module configuration options

- Valves
 - PEEK & SST rotary valves
 - 2-position (10port, 6 port) and multi-position
 - 100-psi PEEK solenoid valves (up to 10)
- Dilution vessels with magnetic stirrer
 - 250 mL HDPE
 - 50mL PEEK, heated (up to 40° C)
- Pumps
 - Precision metering pumps
 - Peristaltic pumps
- Miscellaneous
 - Sensors
 - Leak detection
 - Sample flow
 - Ambient temperature
 - Pressure (gas or process)
 - Vial cooler for standard or reagent
 - TTL inputs, analog inputs, relays, DC power output



Internal mounting

SP module performance data – 1:1000 dilution



Overlay of 30 consecutive runs, direct injection (10 μL) after dilution

SP module performance data – 1:1000 dilution

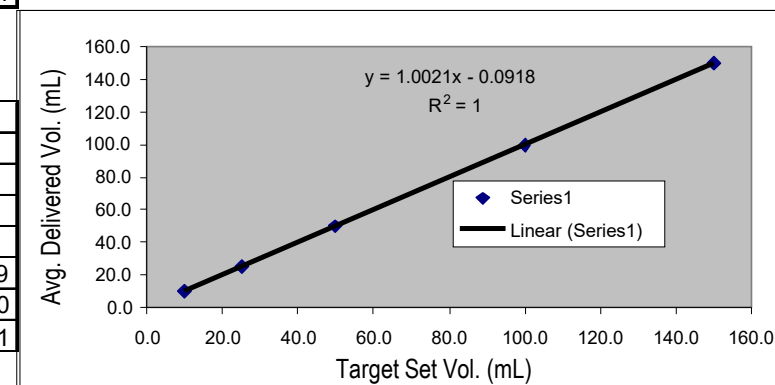
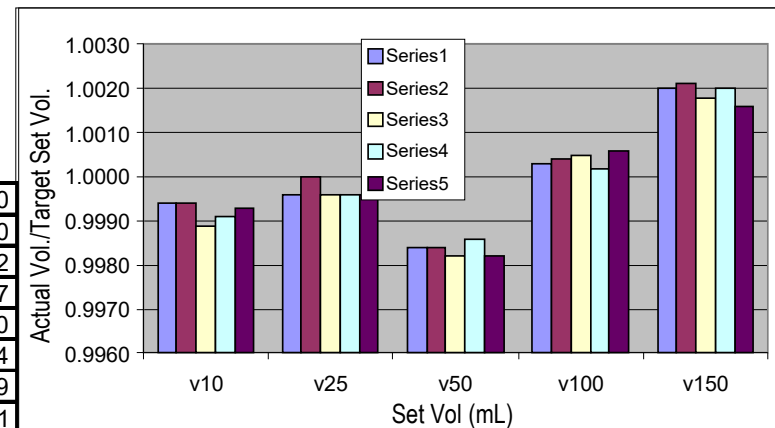
Peak name	Peak area RSD (n=30)	Retention time RSD (n=30)
Fluoride (200 ppb)	0.423%	0.277%
Chloride (1000 ppb)	0.377%	0.180%
Nitrite (1000 ppb)	0.391%	0.145%
Bromide (1000 ppb)	0.399%	0.082%
Nitrate (1000 ppb)	0.474%	0.074%
Sulfate (1000 ppb)	0.391%	0.034%
Phosphate (2000 ppb)	0.383%	0.027%

Passes general application specification of < 0.5% RSD for area

Dilution pump volume linearity

		Dilution pump				
		Volume delivered (mL)				
Test conditions	run#	10.00	25.00	50.00	100.00	150.00
Flow: 15 mL/min	1	9.99	24.99	49.92	100.03	150.30
Vol. per stroke: 0.2211 mL	2	9.99	25.00	49.92	100.04	150.32
	3	9.99	24.99	49.91	100.05	150.27
	4	9.99	24.99	49.93	100.02	150.30
	5	9.99	24.99	49.91	100.06	150.24
	average	9.99	24.99	49.92	100.04	150.29
	STDEV	0.002	0.004	0.008	0.016	0.031
	%RSD	0.022	0.018	0.017	0.016	0.021

run#	v10	v25	v50	v100	v150
1	0.9994	0.9996	0.9984	1.0003	1.0020
2	0.9994	1.0000	0.9984	1.0004	1.0021
3	0.9989	0.9996	0.9982	1.0005	1.0018
4	0.9991	0.9996	0.9986	1.0002	1.0020
5	0.9993	0.9996	0.9982	1.0006	1.0016
average	0.9992	0.9997	0.9984	1.0004	1.0019
STDEV	0.000	0.000	0.000	0.000	0.000
%RSD	0.022	0.018	0.017	0.016	0.021

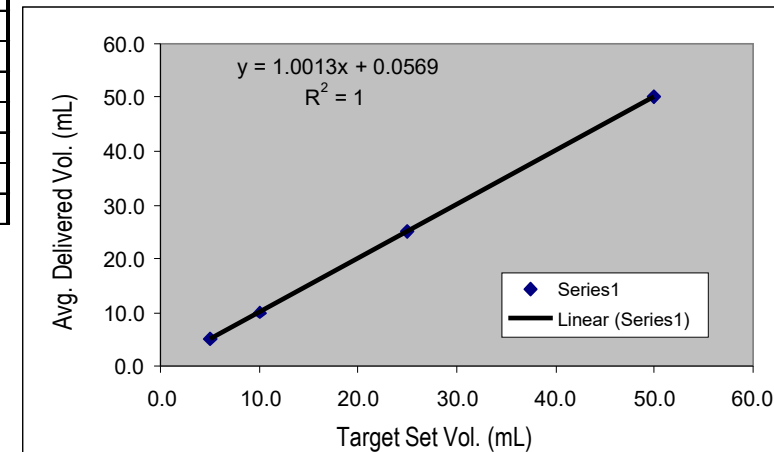
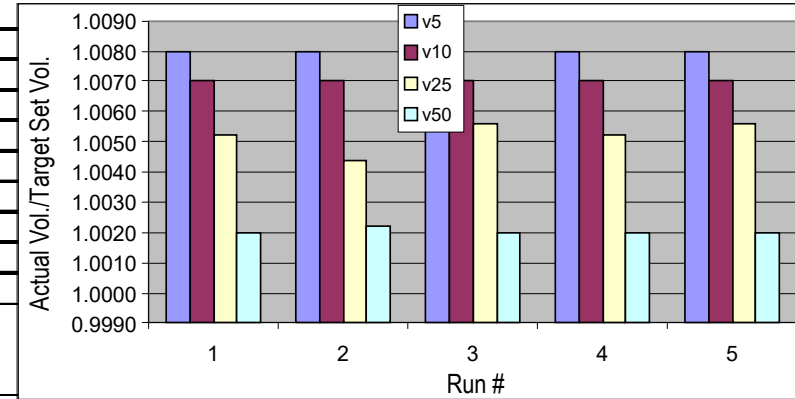


Meets target specs of <0.2% RSD (by 10x)

Loading pump volume linearity

Loading pump					
Volume delivered (mL)					
Test conditions	run#	5.00	10.00	25.00	50.00
Flow: 15 mL/min	1	5.04	10.07	25.13	50.10
Vol. per stroke: 0.2211 mL	2	5.04	10.07	25.11	50.11
	3	5.04	10.07	25.14	50.10
	4	5.04	10.07	25.13	50.10
	5	5.04	10.07	25.14	50.10
average		5.04	10.07	25.13	50.10
STDEV		0.000	0.000	0.012	0.004
%RSD		0.000	0.000	0.049	0.009

run#	v5	v10	v25	v50
1	1.0080	1.0070	1.0052	1.0020
2	1.0080	1.0070	1.0044	1.0022
3	1.0080	1.0070	1.0056	1.0020
4	1.0080	1.0070	1.0052	1.0020
5	1.0080	1.0070	1.0056	1.0020
average	1.0080	1.0070	1.0052	1.0020
STDEV	0.000	0.000	0.000	0.000
%RSD	0.000	0.000	0.049	0.009



Meets target specs of <0.2% RSD (by 10x)

Frequently asked questions – sampling interfaces

- United filtration: a good selection of bypass filters. Good for chemical / industrial samples.

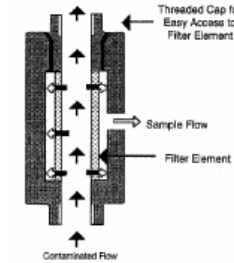
<http://unitedfiltration.com/stainless-steel-exotic-and-analyzer-filters/>

- Flownamics: well-known and well-regarded line of reactor probes.

http://www.flownamics.com/products_fisp.php

- Trace analytics: Dialysis and filtration probes:

<https://www.trace.de/en/products/sampling-systems/>



- GlobalFIA: some membrane-based units used for bioreactors.

<http://www.globalfia.com/components-store>



- Collins Swirklean filters: Used for high-solids, industrial and wastewater samples

<http://collins-products.com>

System configuration options

IC/HPLC with liquid, analyzer enclosure modules; external or internal SS/SP modules



- Thermo Scientific™ Dionex™ ICS-6000 HPIC™ system
 - Single- or dual-channel
 - Reagent-Free™ IC (RFIC™), isocratic, gradient
 - Analytical, microbore, capillary flow
 - Conductivity, PAD, UV-VIS



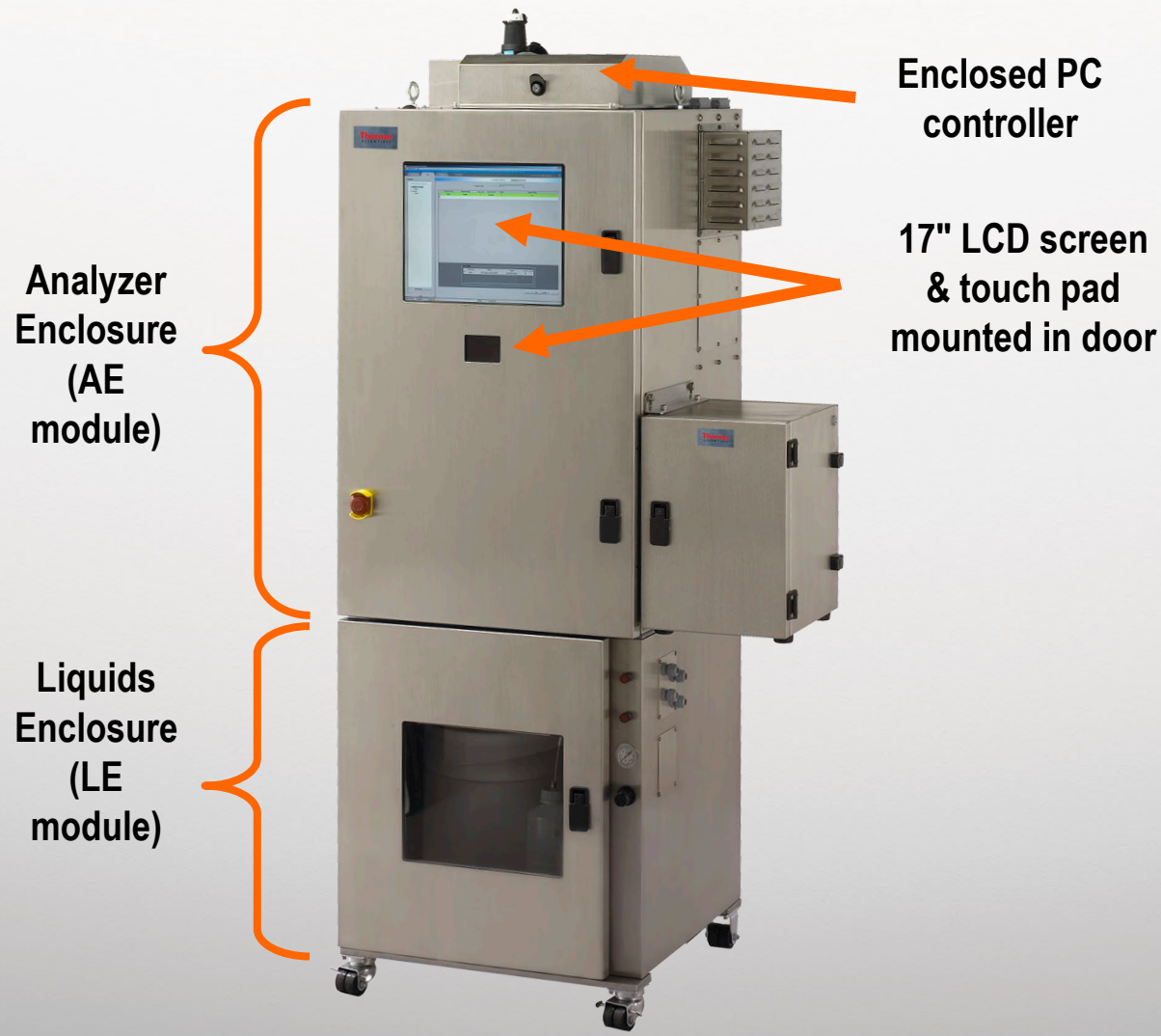
Single- or dual-channel
Dionex Integral
Migration System

- Thermo Scientific™ UltiMate™ 3000 system
 - Single or dual channel
 - Isocratic, binary or quaternary gradient pumps
 - Micro or standard bore
 - SST or Titanium/PEEK for biocompatibility
 - RSLC (UHPLC) for high pressure and/or high flow
 - Multiple detection options
 - UV-VIS (single or multi λ , DAD), fluorescence, RI, CAD

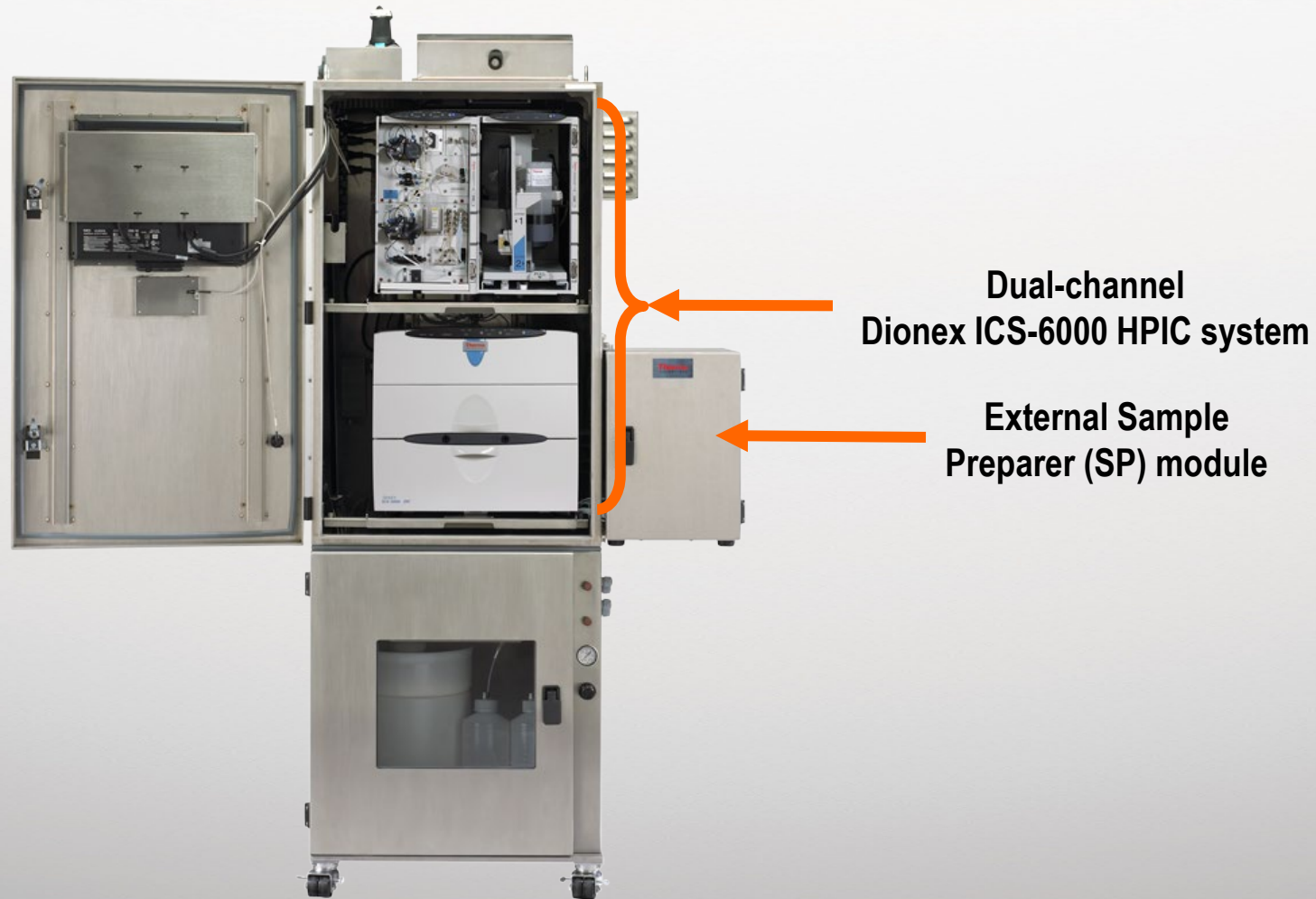


UltiMate 3000 Migration System

Dionex Integral PA system enclosure options



Dionex Integral PA system enclosure with ICS-6000 HPIC system



Dionex Integral PA system enclosure with UltiMate 3000 system

Purge controller options
for
explosion hazard areas



Single channel
UltiMate 3000 system

Internal
Sample Preparer (SP)
module

Hazardous environment implementations

- Allows operation of “general use” equipment in hazardous environments
- Implementation always involves customer engineering and plant safety review
- Example: Custom Pepperl+Fuchs purge implementation for C1D1





Increased speed

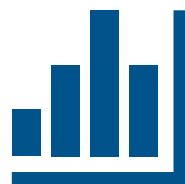
Tandem configuration
(2-pumps, 1-detector)

- Regenerate column 1 while performing separation on column 2

Parallel configuration

(2 complete LC systems)

- Inject sample on column 2 midway through analysis on column 1



Increased information

Dual system with complementary determinations

- Examples: Anions and cations or amino acids and carbohydrates



Increased selectivity (2-D IC/LC)

Channel 1 isolates sample

Channel 2 provides 2nd dimension

- Example: Heart cut on first ion-exchanger; re-focus and determination on second (perchlorate, bromate)
- Example: Capture MAb on Protein A; elute to reverse phase for purity

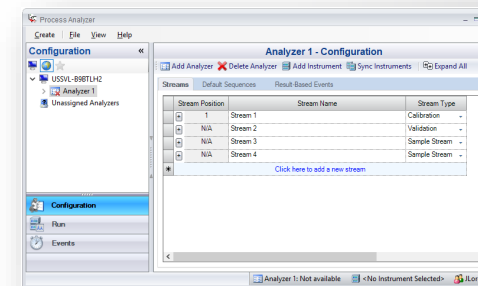
Thermo Scientific Chromeleon 7 Process Analyzer Software



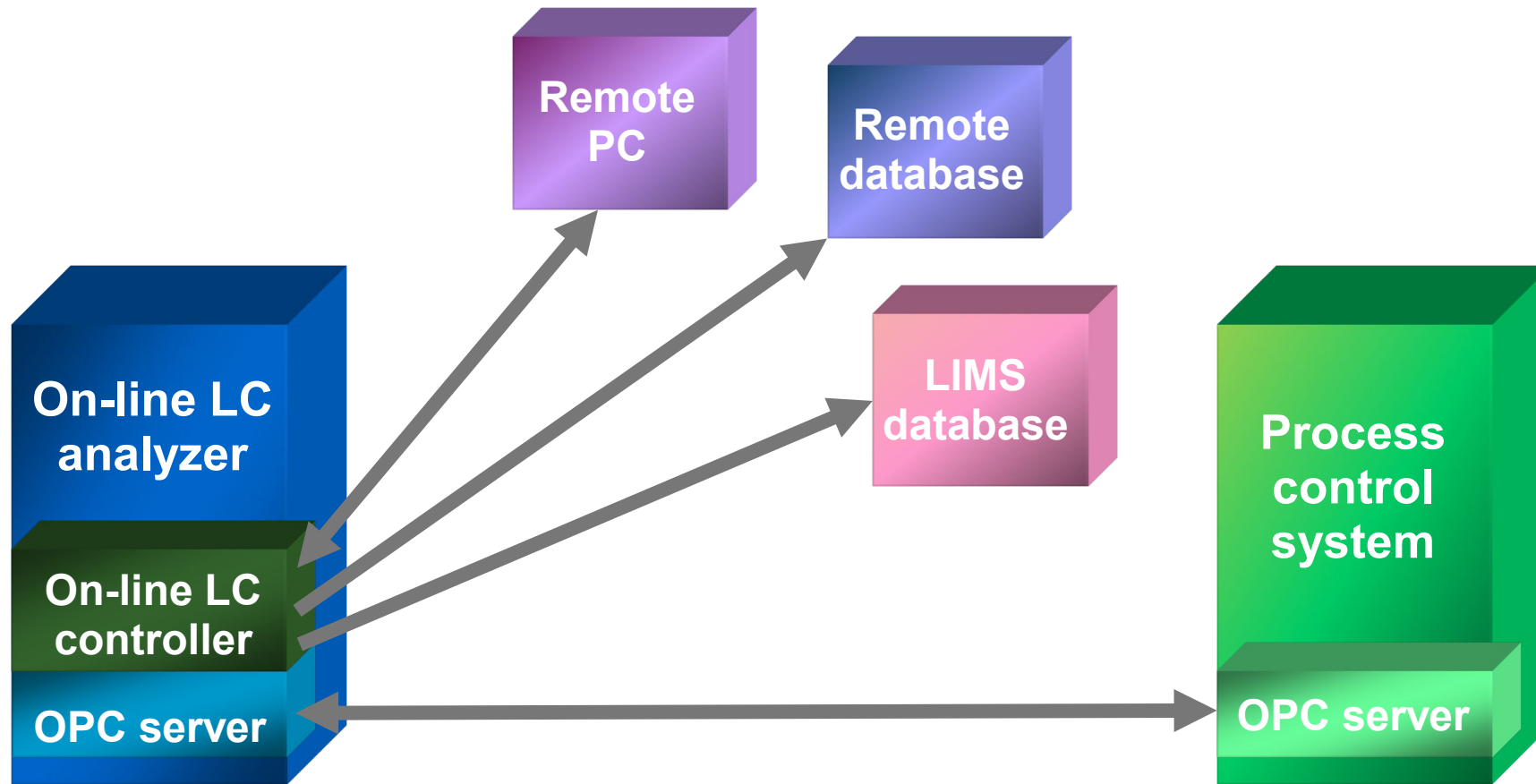
Chromeleon 7 Process Analyzer Software

- Control of Dionex Integral Process Analyzer
 - Up to four instruments in parallel per analyzer
- Based on Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) software, version 7.3
 - Electronically transfer methods from development to on-line monitoring
- Designed for regulatory compliance
 - Validated, security, e-signatures, audit trail, automated system suitability
- Intelligent analyzer control for results-based decisions

- User-customizable options
 - Results Based Events (RBE), alarms, alarm actions, control panels, reports
- Overlap sample preparation for faster sample throughput
- Supports Microsoft™ Windows™ 10 operating system
- Support for Open Platform Communication (OPC) will be added in upcoming revision



On-line LC data integration with remote systems



On-line IC applications for high purity waters



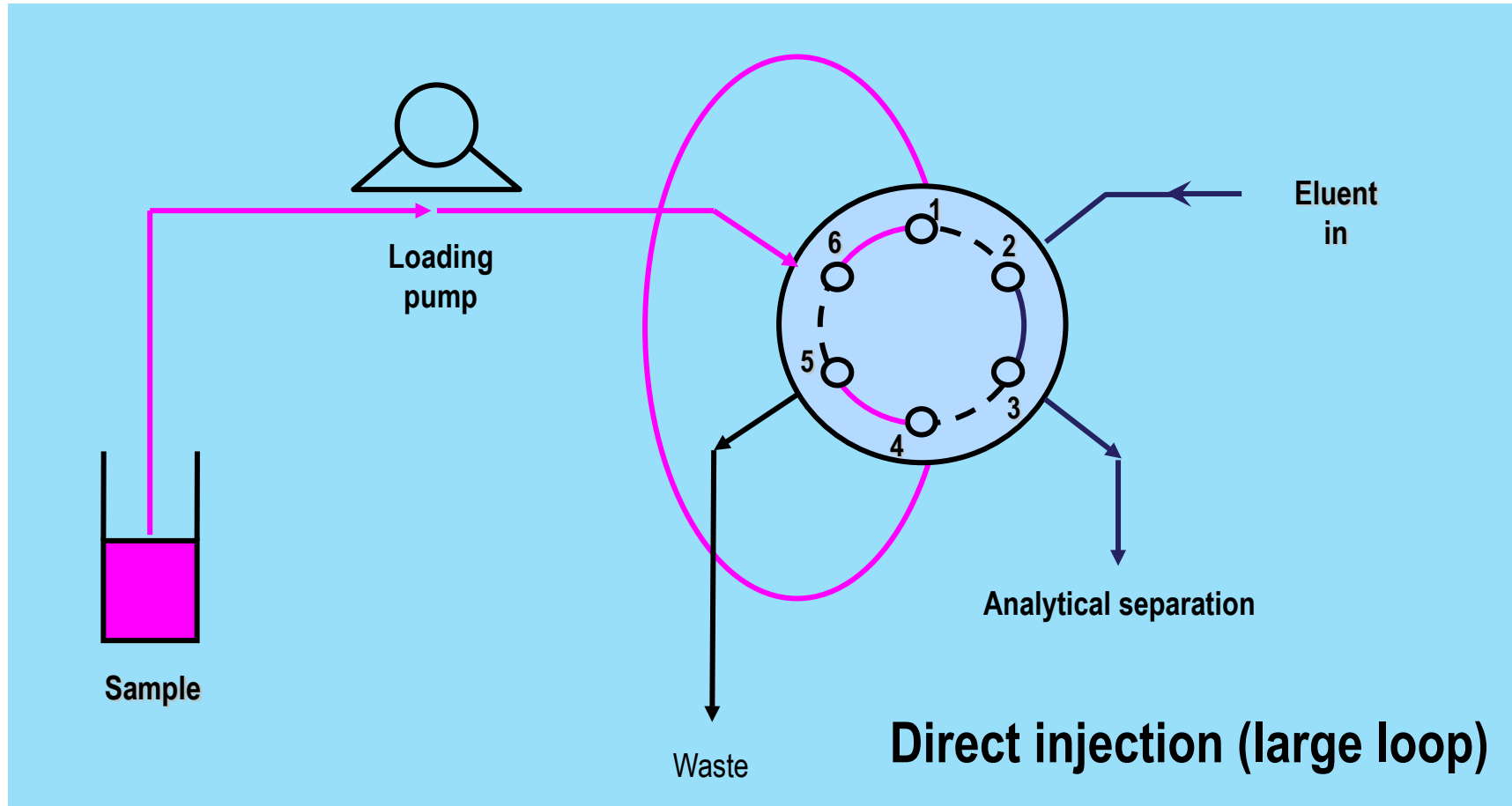
What is “high-purity” water?

- Power plant cooling waters
 - ppb-levels moving to ppt-levels
 - Matrix challenges from additives (amines, borate, lithium)
- Pharmaceutical grade
 - ppb-levels
- Semiconductor grade
 - ppt-levels to ppq-levels

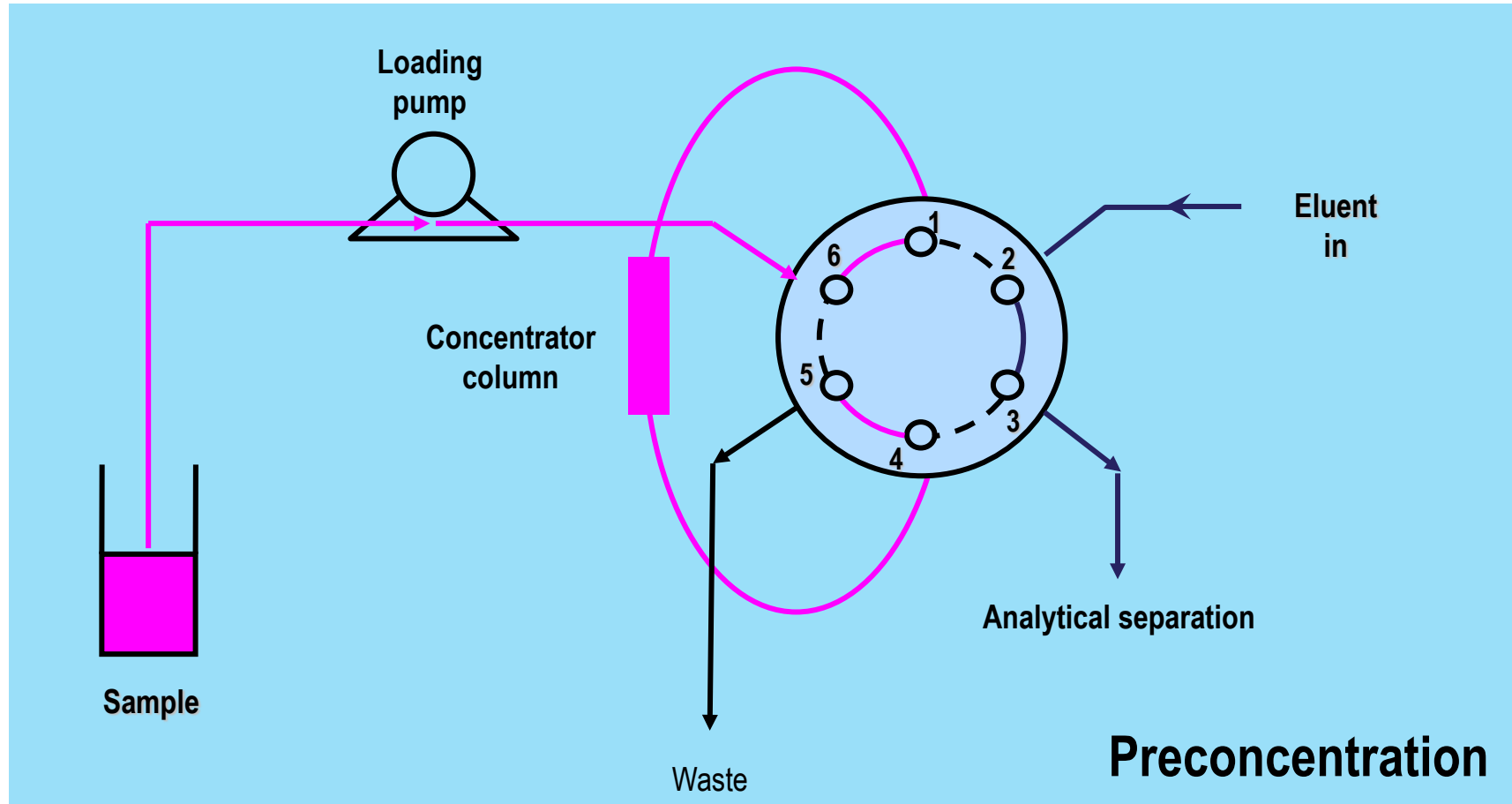
- Considerations for trace ion analyses
 - Don't contaminate the sample!
 - Grab samples
 - Continuous, closed streams
 - No dead legs allowed! They grow crud and bugs.
 - Filtration is rarely, but sometimes needed
 - Sample pressure and sample flow need to be considered

- **Direct injection vs. preconcentration**
 - Direct injection is appropriate for mid ppb-level determinations
 - Preconcentration is required for sub-ppb determinations
- **Preconcentration approaches:**
 - Deliver through sampling/loading pump
 - Deliver with carrier stream
 - Deliver with purified carrier stream
- **Calibration approaches:**
 - Stock dilution
 - Mass loading (Autoprep)

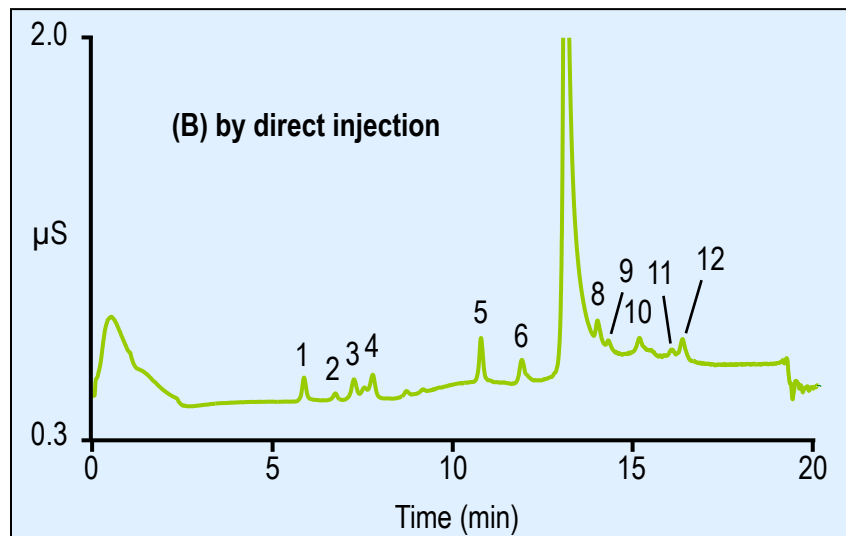
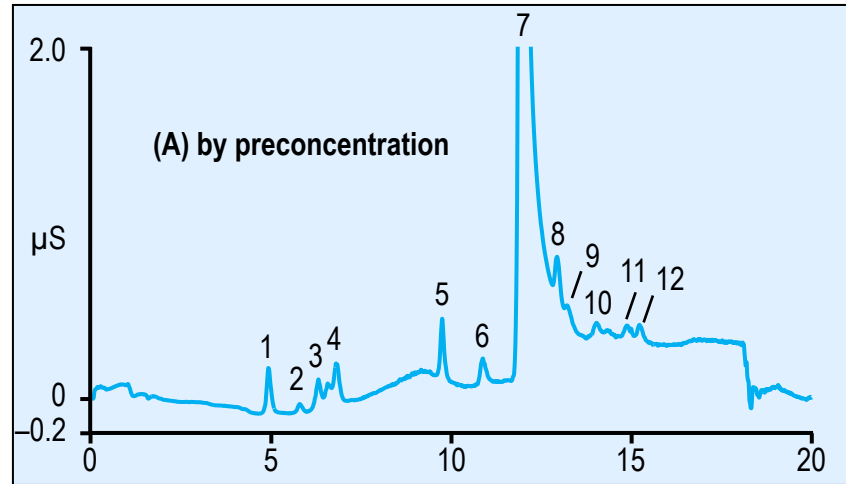
Plumbing approaches to trace analysis - ppb



Plumbing approaches to trace analysis - ppt



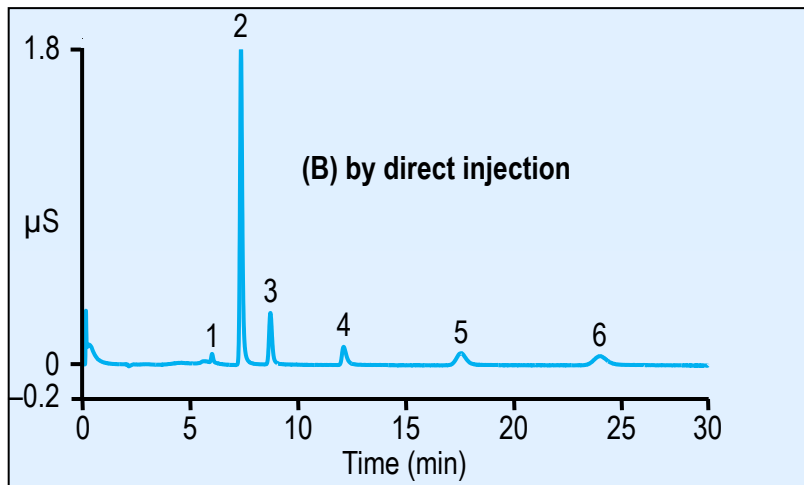
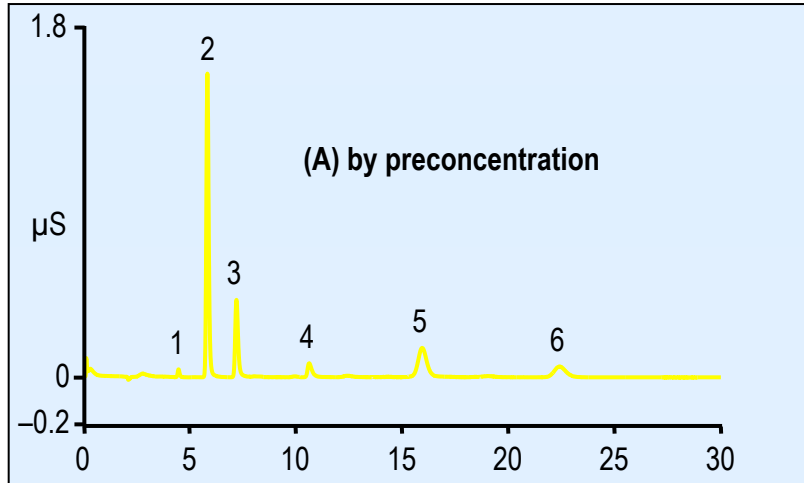
Anions in HPW: concentrator vs. large loop



Column: Thermo Scientific™ Dionex™ IonPac™ AS15, 5-µm
 Eluent: 7–60 mM KOH (EG)
 Temperature: 30 °C
 Flow rate: 0.7 mL/min
 Inj. volume: (A) 8 mL, pre-concentrated on TAC-ULPI
 (B) 1 mL
 Detection: Suppressed conductivity,
 Thermo Scientific™ Dionex™ ASRS™ ULTRA II,
 2 mm, recycle mode

Peaks:		A	B
1.	Fluoride	0.1	0.5 µg/L (ppb)
2.	Glycolate	0.2	1
3.	Acetate	0.2	1
4.	Formate	0.2	1
5.	Chloride	0.1	0.5
6.	Nitrite	0.1	0.5
7.	Carbonate	--	--
8.	Sulfate	0.4	2
9.	Oxalate	0.2	1
10.	Bromide	0.4	2
11.	Nitrate	0.1	0.5
12.	Phosphate	0.6	3

Cations in HPW: concentrator vs. large loop

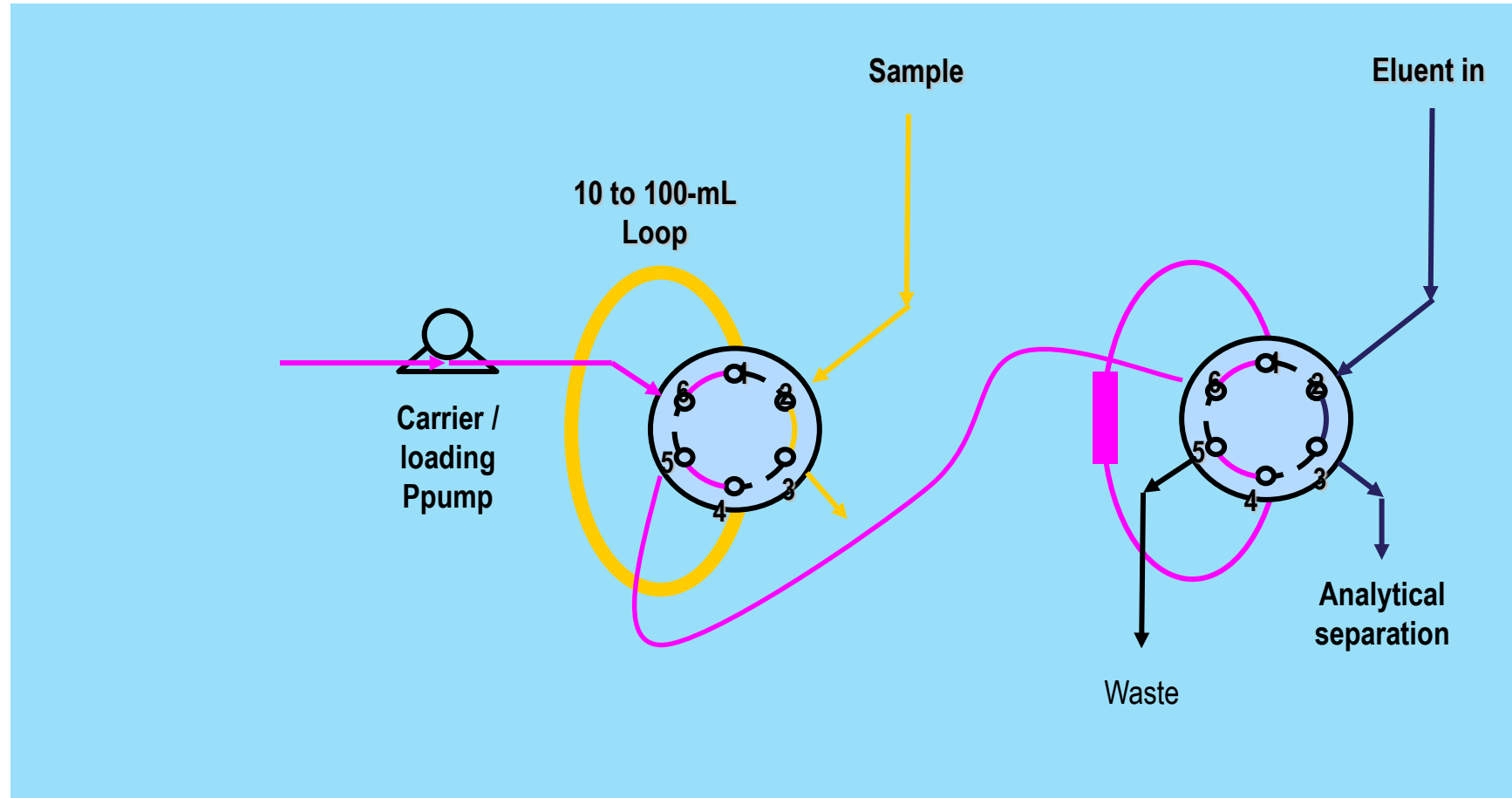


Column: Thermo Scientific™ Dionex™ IonPac™ CG16, CS16, 3 mm
Eluent: 30 mM MSA (EG)
Temperature: 40 °C
Flow rate: 0.5 mL/min
Inj. volume: (A) 8 mL, preconcentrated on TCC-LPI
(B) 1 mL
Detection: Suppressed conductivity,
Thermo Scientific™ Dionex™ CSRS™ ULTRA II, external water mode

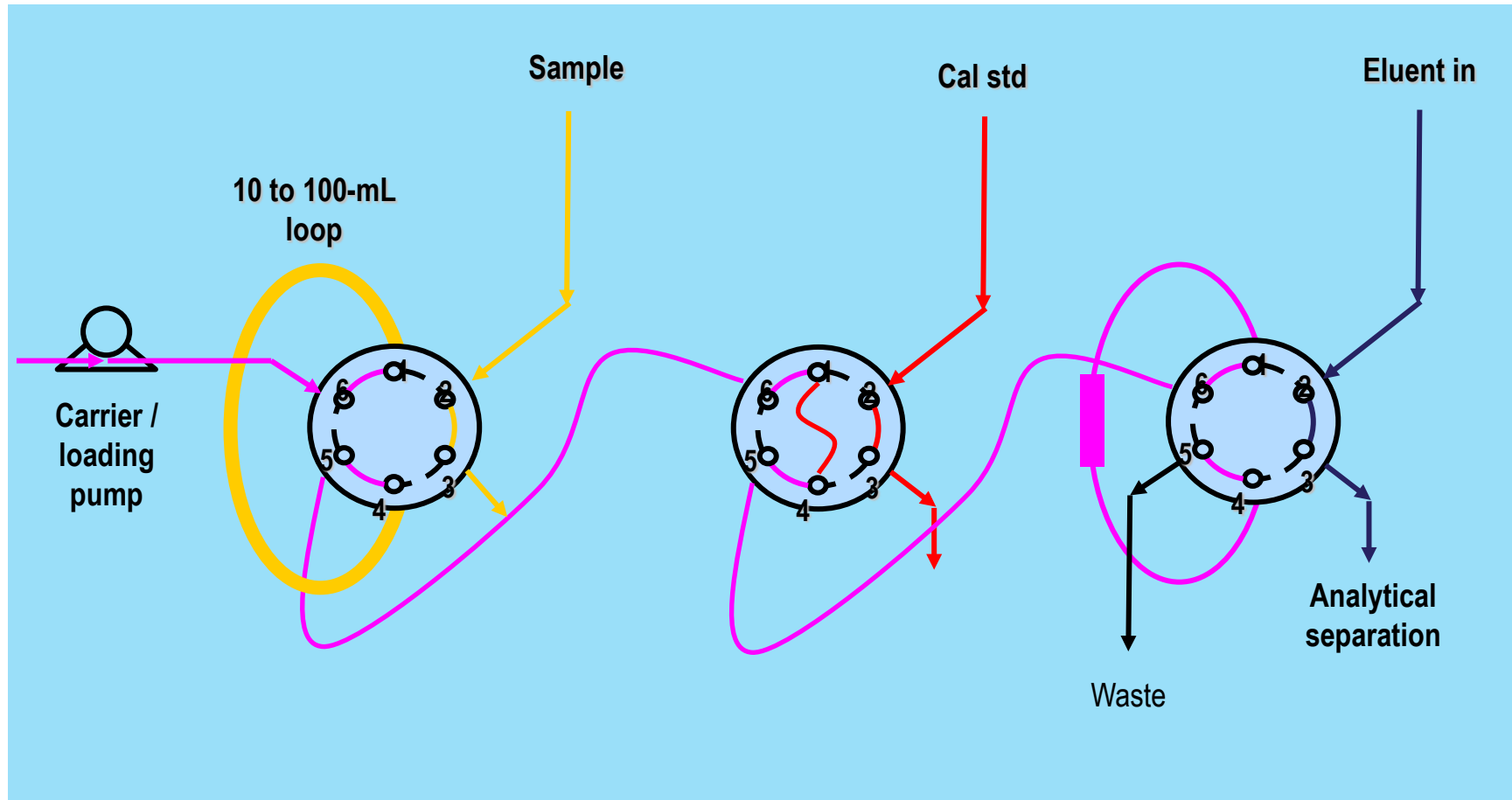
Peaks:		A	B
1.	Lithium	10	50 µg/L (ppb)
2.	Sodium	40	200
3.	Ammonium	50	250
4.	Potassium	100	500
5.	Magnesium	50	250
6.	Calcium	100	500

- Direct injection vs. preconcentration
 - Direct injection is appropriate for mid ppb-level determinations
 - ***Preconcentration is required for sub-ppb determinations***
- Preconcentration issues when loading sample:
 - Deliver through sampling pump: *Potential blank from pump*
 - Deliver with carrier stream: *Need clean carrier source*
 - Deliver with purified carrier stream: *Flow rate can be limiting*

Carrier delivery of sample



Autoprep / mass loading approach for calibration



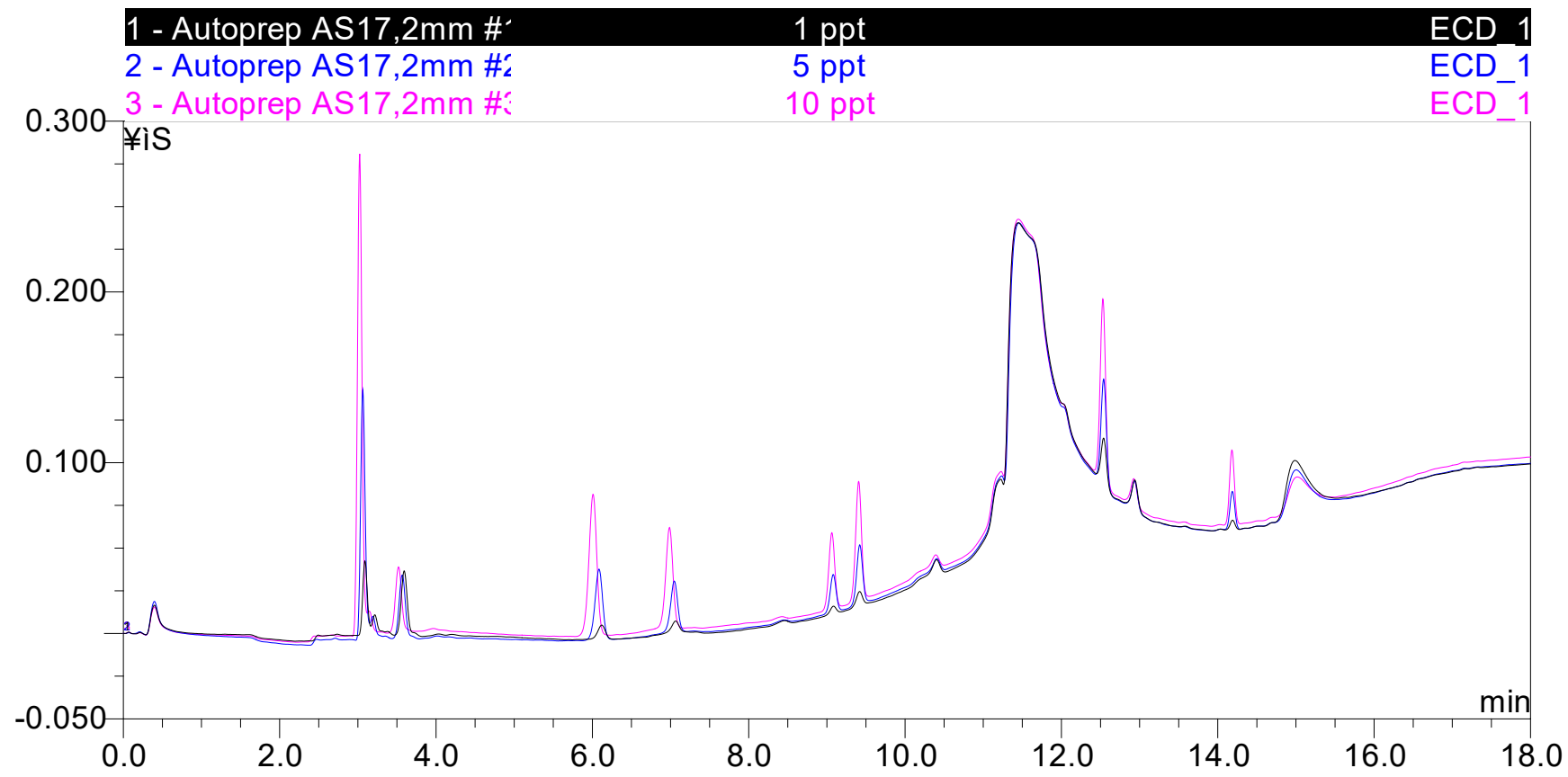
Dionex Integral PA system with ICS-3000 system semiconductor installation

- ICS-3000 system w/ Sample Preparer SP1 module
- Trace anions for ppt-level
- Autoprep with 40-mL sample
 - Carrier delivery of sample
 - Mass loading approach for calibration



Example of trace anions by Autoprep

20 mL preconcentration volume, AS17 with CRD



- Trace analysis possible with Autoprep configuration using 10-mL to 100-mL sample / carrier loop
- Need to load larger volumes (up to 75 mLs) for sub-ppt determinations
- Loop materials can vary, but performance tradeoffs
 - Perfluoroalkoxy (PFA) popular in semiconductor but leaches F for extended flushdown period
 - PEEK good for smaller volumes but SO₄ blank is a problem at <20 ppt levels
 - Polyethylene (HDPE) loop used successfully in customer installations; inexpensive solution compared to large quantity of PFA

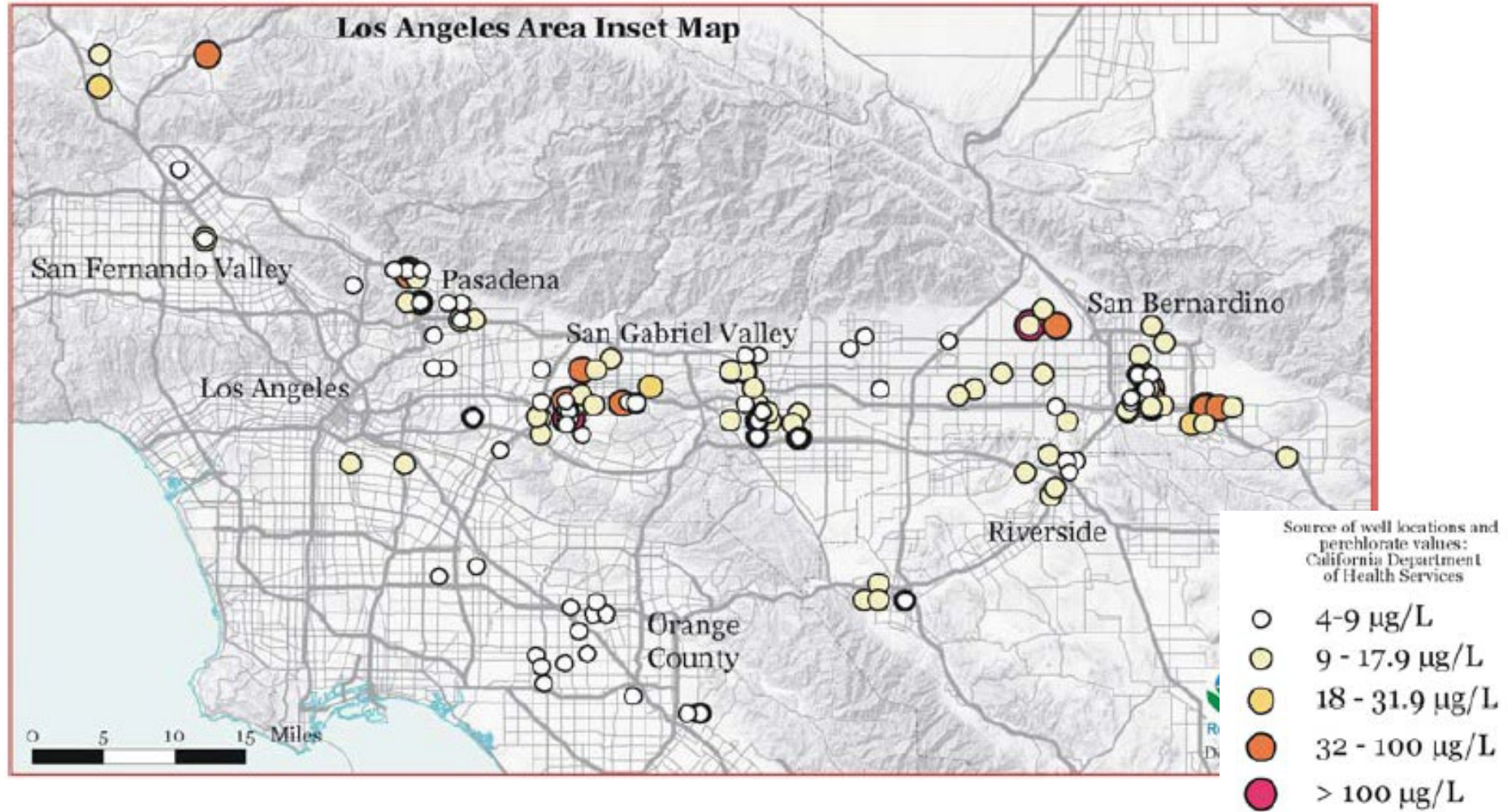
On-line IC application example in environmental

Monitoring perchlorate removal in ground water remediation



- Project summary:
 - Ground water contaminated with perchlorate
 - EPA pilot project to test remediation methods
 - On-line IC monitors perchlorate at ppb levels
- Goal:
 - Provide on-line monitoring of remediation process effectiveness

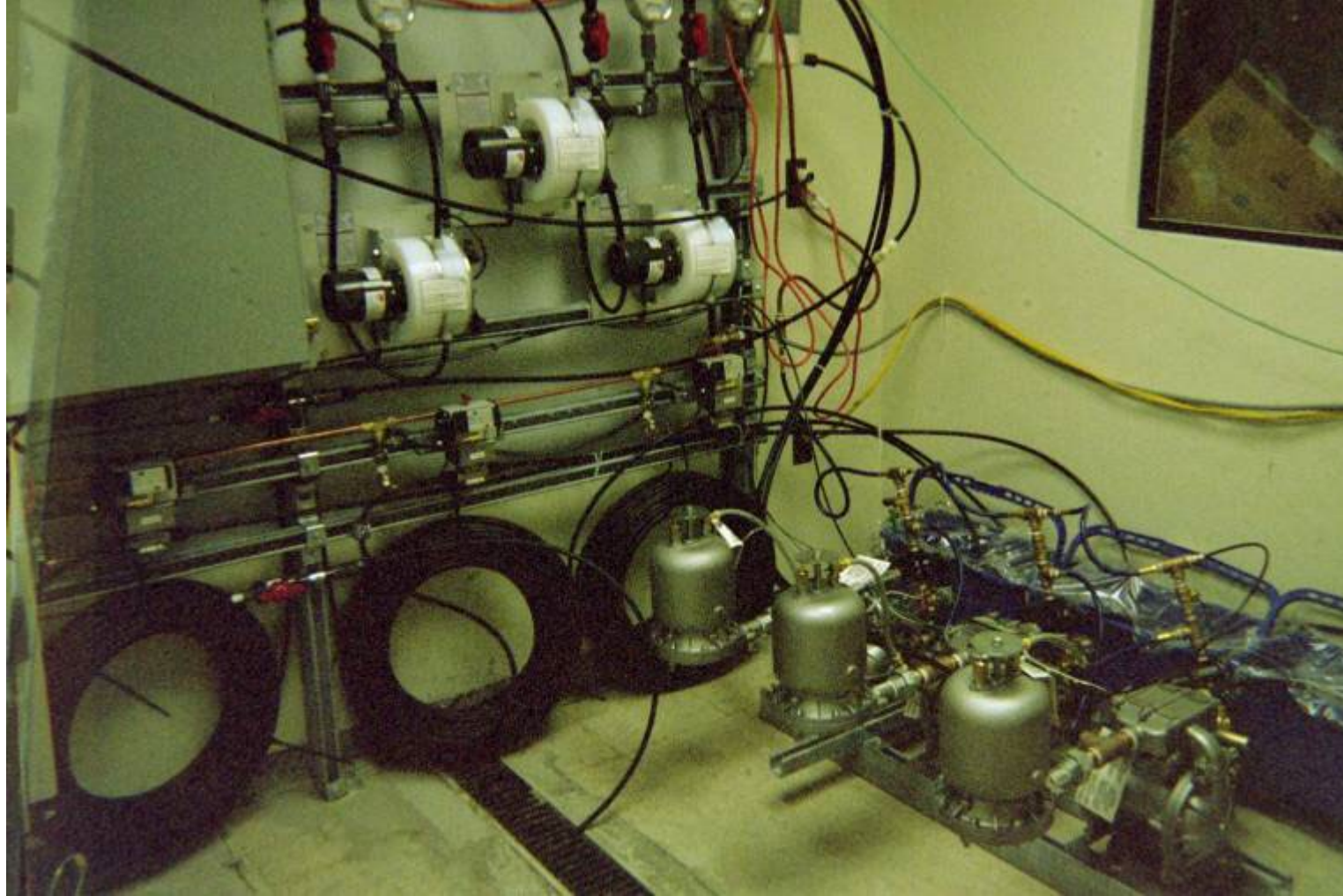
Cal DHS / EPA target locations



Southern California remediation site



Sampling pumps, valves, and filters



Designed and fabricated by Shaw Environmental, Inc. (Lawrenceville, NJ)

- Allen Bradley LSC 5/05 PLC
- RS View software
- Matrikon data manager
- Chromeleon PA software and workstation
 - Chromeleon OPC server
 - Analyzer status
 - Analyzer control
 - Analysis results reporting
 - Meilhaus ME630 16Ch Relay TTL I/O Board
 - Valve control
 - Pump solenoid control
 - Filter motor control

Motorized tangential filters

- Sample sumps, filters, and valves controlled by analyzer program
 - Timing defined by user
 - Steps and timing can be different for each sample
- Filters set for intermittent duty cycle
 - Analysis on 30-minute cycle
 - Filters ran warm unless bypass sample flow was maintained at high flow rate

On-line LC application example in water utility

Bromide in water utility feed stream

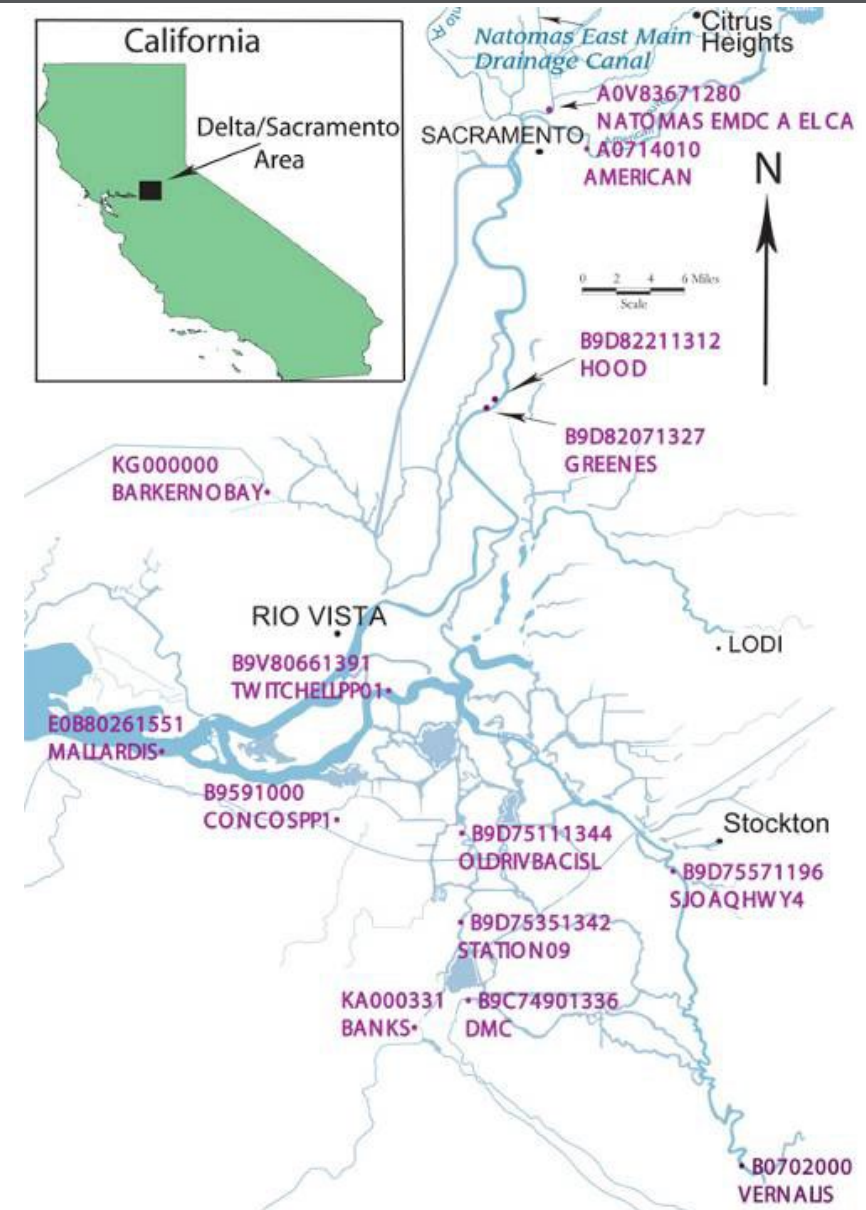


Monitoring bromide in the California aqueduct

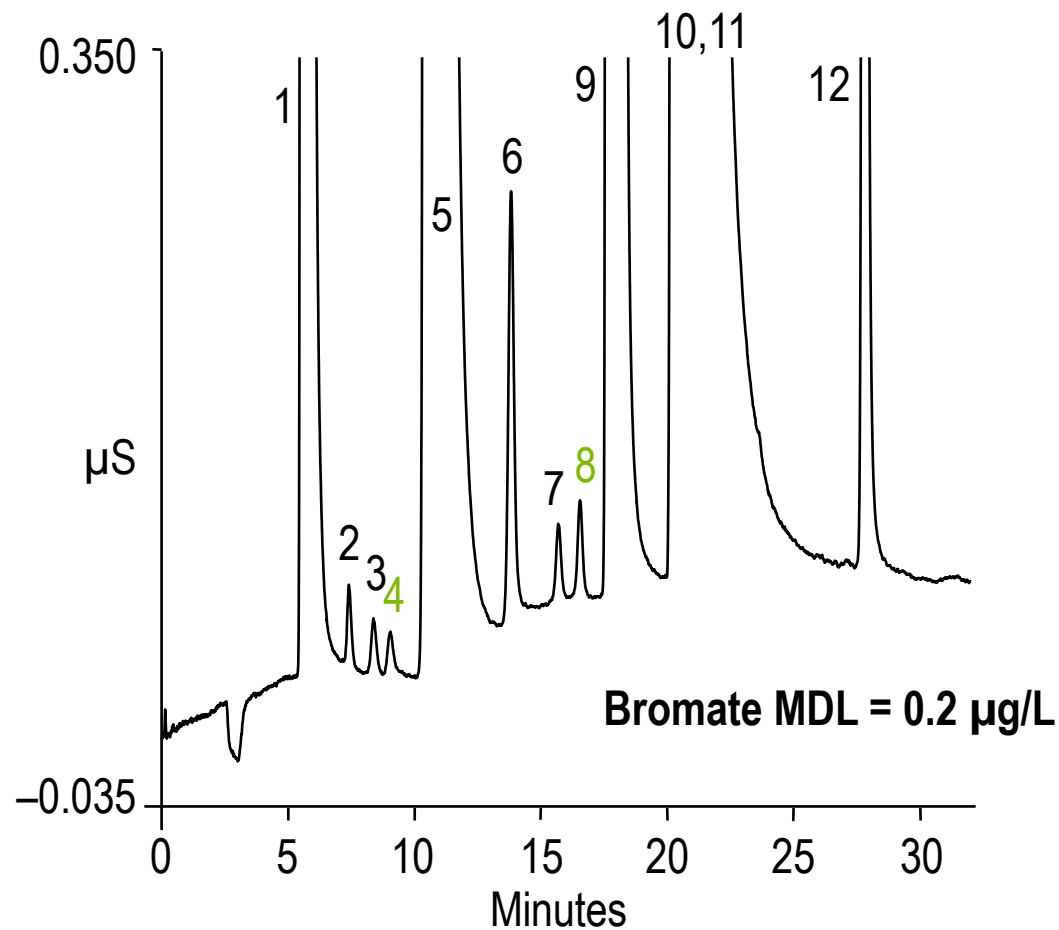
- 2/3 of water consumption occurs south of Sacramento
- 2/3 of precipitation occurs north of Sacramento
- The California Delta (near Sacramento) is the crossroads for transportation from storage to points-of-use
 - Subject to high salinity and bromide from seawater intrusion
 - TOC levels can elevate from broad land areas and agricultural runoff
 - MQWI program of the CA DWR monitors quality for downstream municipal customers

MQWI monitoring stations

- 11 sites
- Weekly & monthly manual sampling
- 4 on rivers
- 6 in delta
- 1 urban
- Program in place to make near-real-time quality results available to “customers”



Bromide and bromate in drinking water



$$\text{MDL} = \text{SD} \times t_s (n = 7), t_s = 3.14$$

Column:	Thermo Scientific™ Dionex™ IonPac™ AG19, AS19, 4 x 250 mm	
eluent :	Potassium hydroxide: 10 mM from 0 to 10 min, 10–45 mM from 10 to 25 min	
Eluent source:	EGC II KOH cartridge with CR-ATC	
FlowRate:	1.0 mL/min	
Temperature:	30 °C	
Suppressor:	Thermo Scientific™ Dionex™ ASRS™ ULTRA II, 4 mm, autosuppression external water mode, 300 mA	
Injection vol.:	500 μL	
Peaks:	1. Fluoride	1 mg/L (ppm)
	2. Formate	–
	3. Chlorite	0.005
	4. Bromate	0.005
	5. Chloride	50
	6. Nitrite	0.005
	7. Chlorate	0.005
	8. Bromide	0.005
	9. Nitrate	10
	10. Carbonate	25
	11. Sulfate	50
	12. Phosphate	0.2

- Dionex Integral systems based on 35+ years on-line IC/HPLC experience
- Unmatched versatility and value
 - Both IC and HPLC options
 - *Integral Migration Path: On-line IC/LC whenever and wherever needed*
 - Lower investment risk; reconfigurable for future systems / applications
 - Single- or dual-channel capabilities in one enclosure
 - Coordinated multi-system operation for unattended operation
 - Scheduled reporting for timely, automated results
- Numerous examples of successful on-line IC/LC applications
 - Significant return on investment

