

Configuring and optimizing an IC-MS system using a compact IC and a single quadrupole mass spectrometer

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Keywords

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Goal

The purpose of this document is to discuss from an ion chromatography point of view, the configuration, operation, and method optimization of an IC-MS system using a Thermo Scientific™ Dionex™ Integrion™ RFIC™ system with a Thermo Scientific™ Dionex™ Integrion™ RFIC™ system with a Thermo Scientific™ ISQ EC single quadrupole mass spectrometer.

Introduction

This technical note discusses the configuration, plumbing, and operation of the Thermo Scientific™ Dionex™ Integrion™ HPIC™ system, RFIC™ model, coupled to the Thermo Scientific™ ISQ™ EC single quadrupole MS system. This document is divided into eight sections and presented in the order below.

1. Installing the Dionex Integrion RFIC system with a CD Conductivity Detector, an extra 6-port valve, a Thermo Scientific™ Dionex™ SRD-10 Suppressor Regenerant Detector device, a Thermo Scientific™ Dionex™ AXP-MS Auxiliary Pump (with Thermo Scientific™ Dionex™ GM-3 gradient mixer (P/N 042126)), two 1000 psi backpressure coils (P/N 053765), and a Thermo Scientific™ Dionex™ AS-AP autosampler
2. Configuring the Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) for the Dionex Integrion RFIC system
3. Installing the ISQ EC MS with a foreline pump, nitrogen generator, liquid trap, and foreline vapor exhaust
4. Configuring the IC-MS modules using the Chromeleon Instrument Controller program
5. Creating Instrument Methods Using the Chromeleon Wizard editor
6. Optimizing the mass spectrometer

7. Calibrating the mass spectrometer
8. Creating Instrument Processing Methods Using Chromeleon MS Quantitation Templates

Installing the Dionex Integrion RFIC system

The Dionex Integrion HPIC system (RFIC model) with a Dionex AS-AP autosampler is configured with a CD conductivity detector, eluent generation, and the temperature control features for the column oven and detector-suppressor compartment. The Thermo Scientific™ Dionex™ AXP-MS auxiliary pump provides the deionized (DI) water needed as the suppressor regenerant. A second injection valve is used as a diverter valve between the CD cell out and the MS. This system has consumables device tracking through cable and radio frequency, optional manual controls by the Dionex Integrion HPIC system tablet, and can operate at pressures up to 5000 psi with eluent generation. Additionally, for all IC-MS applications, a Thermo Scientific™ Dionex™ SRD-10 suppressor regenerant detector device is recommended to stop the IC pump in the absence of regenerant flow.

To set up this system, first connect the Dionex AS-AP autosampler and the Dionex Integrion HPIC system according to Figure 1 and TN175 - *Configuring the Dionex Integrion HPIC System for High-Pressure Reagent-Free Ion Chromatography*.¹ A small piece of red PEEK tubing (< 5 in. of 0.005 in. i.d.) called a “jumper” in Figure 1 is installed in the IC Diverter valve connecting Ports 1 (L) to 3 (C). Install the AXP drivers included with the pump on the IC-MS instrument computer as described in the AXP pump operator’s manual.² The AXP pump provides MS calibrant at 0.05 mL/min flow during MS calibration. To aid in calibration and provide pulse damping, install a Thermo Scientific™ Dionex™ IonPac™ GM-3 gradient mixer (P/N 042126) and two yellow PEEK (0.003 in i.d.) backpressure coils (rated 1000 psi at 0.5 mL/min, P/N 053765) on the pump outlet. Run the AXP pump at 1 mL/min until liquid is flowing at a steady rate through the end of the tubing. It is recommended that the MS and the MS modules (nitrogen generator and the mechanical vacuum pump (foreline vacuum pump)) are not powered on until the IC is fully installed and configured by Chromeleon Instrument Configuration programs. Additionally, nitrogen gas flow is needed before connecting the IC flow to the MS.

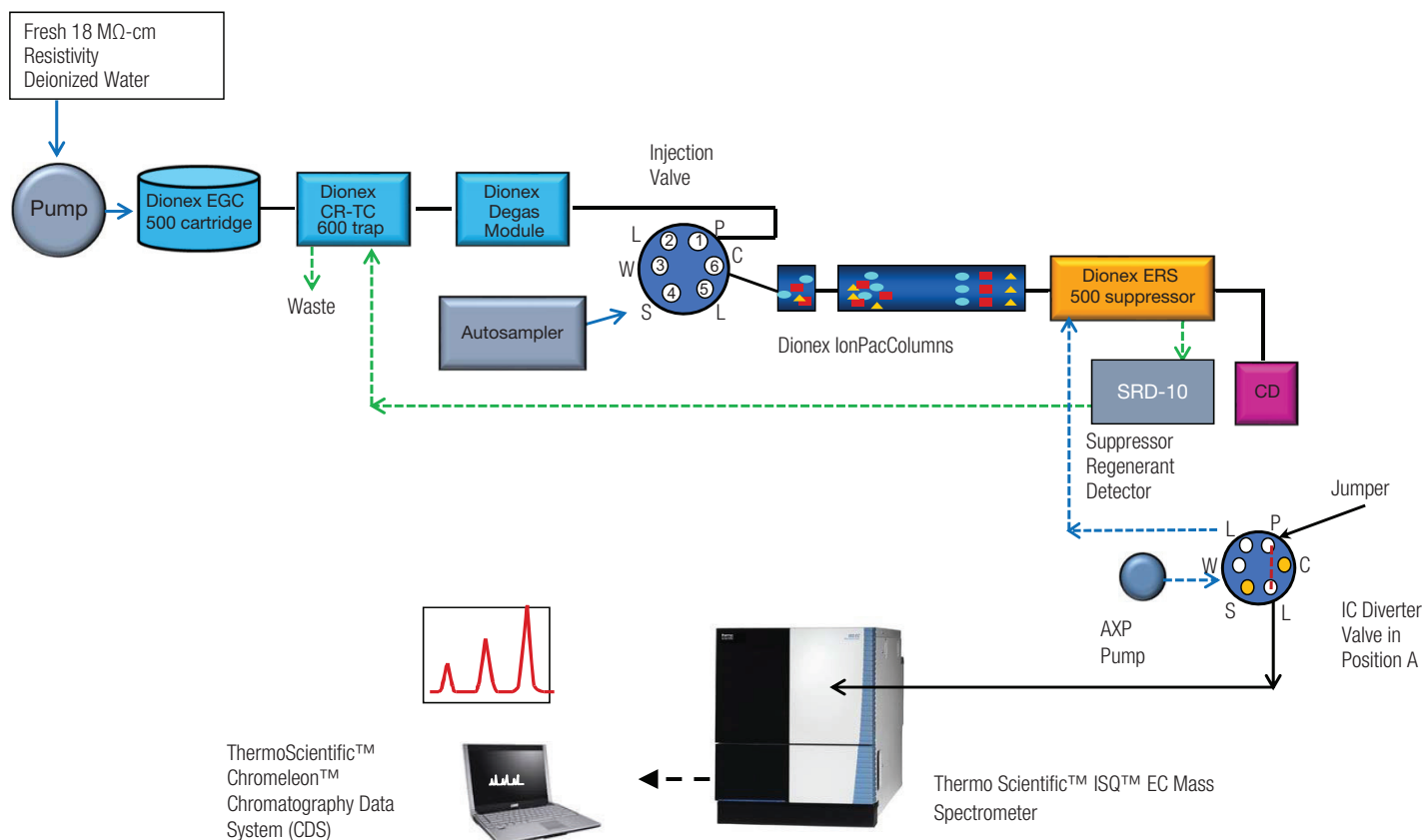


Figure 1. Flow diagram for IC-MS with diverter valve in “A” position

Consumables

In TN175,¹ the plumbing and Chromeleon CDS configuration of an Integrion RFIC system, Thermo Scientific™ Dionex™ IC PEEK Viper™ fittings, Consumables Device Monitor, conditioning and hydrating of columns, Dionex EGC 500 eluent generator cartridges, and Dionex CR-TC 600 continuously regenerated trap columns are thoroughly discussed, and therefore not discussed here. Instructional videos can also be found on the Chromeleon Console under the Consumables tab.

Hydrating and conditioning the Dionex ERS 500e suppressor

Hydrate and condition the Dionex ERS 500e suppressor according to the instructions received with the suppressor or as stated in the suppressor manual.³ Install the suppressor in external water mode using the Dionex AXP pump to provide the DI water regenerant. The typical flow rate should be at 2–3× the flow rate of the Dionex Integrion pump.

Installing the Dionex SRD-10 suppressor regenerant detector device

The Dionex SRD-10 device is recommended for IC-MS applications to prevent non-neutralized eluent from entering the MS when the regenerant flow stops. The Dionex SRD-10 device is placed between the suppressor and the Dionex CR-TC trap column to detect an air bubble or air gap of more than 5 min. When these conditions are met, the SRD-10 detector triggers the Dionex Integrion pump to turn off through a TTL connection that then turns off the electrolytic devices. No flow continues to the MS. This only occurs if the Dionex AXP pump fails to deliver water to the suppressor regenerant channel. Because regenerant flow is necessary for a functioning suppressor, this also provides protection to the suppressor.

To install the Dionex SRD-10 device (as described in the Installation manual⁴), connect one end of the inlet tubing to the suppressor *Regen Out* port and the other side to the *Regen In* port of the Dionex CR-TC 600 trap column (Figure 2A). Connect the USB cable to the USB port on the back of the Dionex Integrion pump. Connect the red and black twisted pair cable to the 8-pin connector

(Red to TTL-1 In and Black to D-GND). Install the connector into the back of the Dionex Integrion IC system (Figure 2B). Install the SRD tubing to the *Regen Out* port on the suppressor and the *Regen In* port on the Dionex CR-TC 600 trap column. To verify that the Dionex SRD-10 device is working, first complete configuration as described in Configuring the Modules section. Then, turn-off the Regenerant pump, de-install the Dionex SRD-10 device, and blow out all liquid from the Dionex SRD-10 device using a compressed gas line. Reinstall the Dionex SRD-10 device, and after 5 min, the device will trigger the IC pump to turn-off. Restart the IC, but do not turn-on the suppressor until the Dionex SRD-10 tubing is refilled with DI water.

Installing the diverter valve

A second 6-port valve is installed on the Dionex Integrion HPIC system to act as an IC-compatible diverter valve. Install the tubing in the diverter valve as described in Table 1.

Starting the Dionex Integrion HPIC system

To start the system, turn on the pump and turn on the Dionex EGC 500 eluent generator cartridge as the system pressure approaches 2000 psi. Turn on the Dionex CR-TC 600 trap and Dionex ERS 500e suppressor when liquid is flowing through the devices. The system backpressure is dependent on the flow rate and type of column, but the system pressure must be above 2000 psi to support the Dionex EGC cartridges. Typically, columns with 4 µm resin particles operate above 2000 psi and, therefore, do not require backpressure tubing. However, if additional pressure is needed to achieve system pressures > 2000 psi, install yellow PEEK backpressure tubing (yellow PEEK, 0.076 mm i.d., 0.003 in i.d.) between the Dionex HP degas device and the injection port (Pump port position). Set the eluent concentration and temperature for the column oven, compartment oven, and cell as shown in the *Conditions* section in the application. Allow the system to equilibrate for 30 min or until the total conductivity is < 1 µS/cm. When the total conductivity reading of the IC is < 1 µS/cm, it is safe to connect the IC flow to an operating MS.

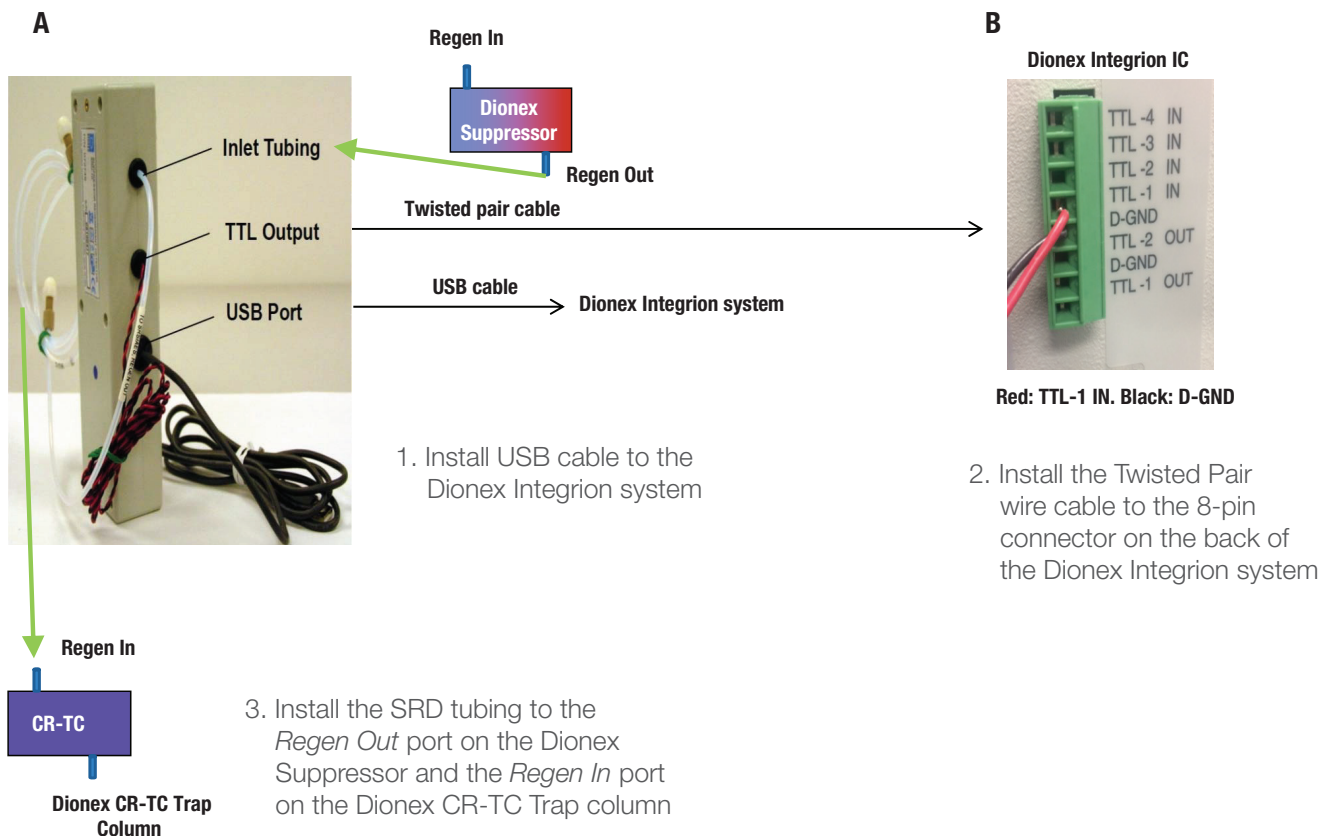


Figure 2. Installing the Dionex SRD-10 suppressor regenerant detector device

Table 1. Connections for the diverter valve

Port*	Tubing	Connecting	HP_Valve Position
Port P (1)	Black PEEK or IC PEEK Viper	From CD Out	
Port L (6)	6–12 in (15–30 cm) of Black PEEK, then Green PEEK	To waste	HP_Valve.B
Port L (2)	Black PEEK	From IC to MS valve (temporarily divert to waste container until IC total conductivity < 1 μ S)	HP_Valve.A

*Ports W (3), S (4), C (5) are not used. Install plugs into these ports to prevent an air gap.

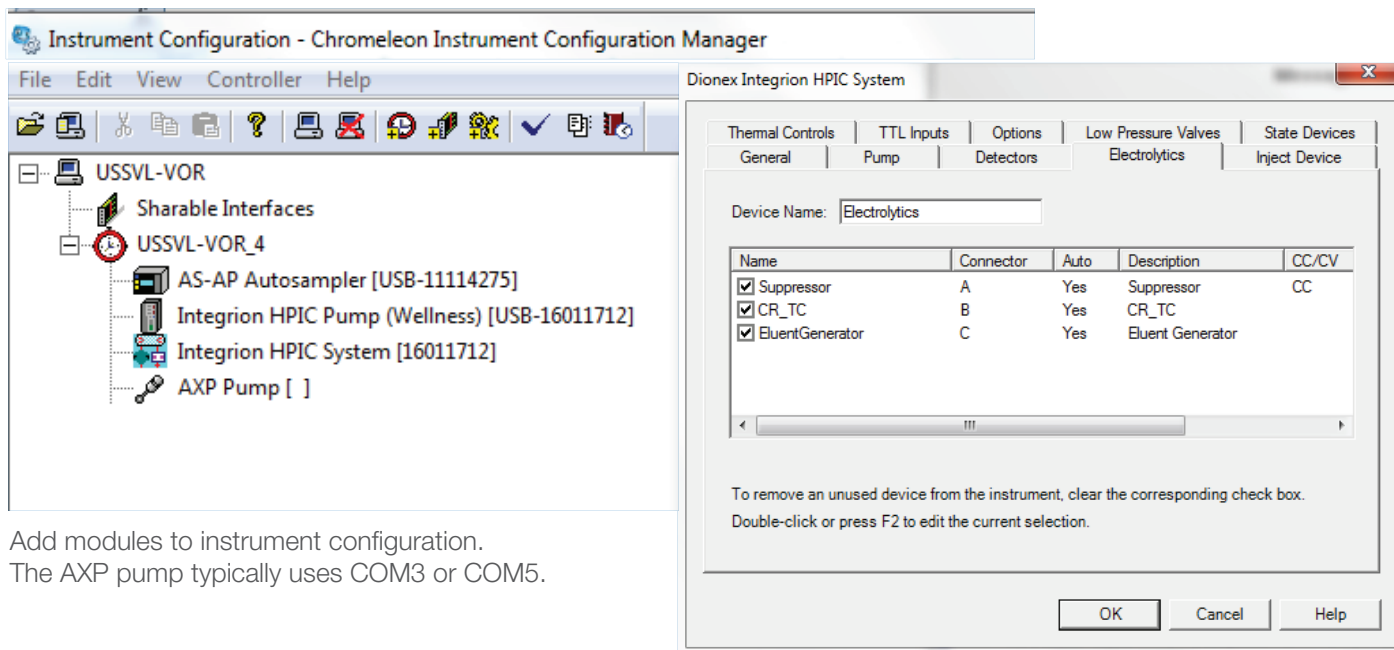
Configuring the Chromeleon CDS for the Dionex Integrion RFIC system

To configure the IC system, first start the Chromeleon Instrument Controller program and then select the link *Configure Instruments* to open the Chromeleon Instrument Configuration Manager. Right-click on computer name, select *Add an Instrument*, and enter an appropriate name (for example: Integrion_ISQ-EC_Amines). Add the following modules to this instrument configuration: *Integrion HPIC System*, *Integrion HPIC Pump Wellness*, and *Dionex AS-AP Autosampler* (Figure 3), as described previously in TN 175. Select the Electrolytics tab on the Integrion HPIC System module. The electrolytic devices are detected automatically (e.g. suppressor, eluent generator, and CR-TC).

Additionally, the configuration parameters are summarized in Table 2. The device configurations specific to IC-MS, such as assigning valve controls, activating the SRD-10 trigger, and configuring the AXP pump, are discussed in the following sections.

Integrion HPIC System module: assigning valve control

To assign control of the injection valves, select the Inject Device tab on the Dionex Integrion HPIC System module (Figure 4). Check the boxes for both valves, *Injection Valve* and *HP_valve*. Assign control of the injection valve to the autosampler, which will automatically assign control of HP_Valve to the Dionex Integrion HPIC system.



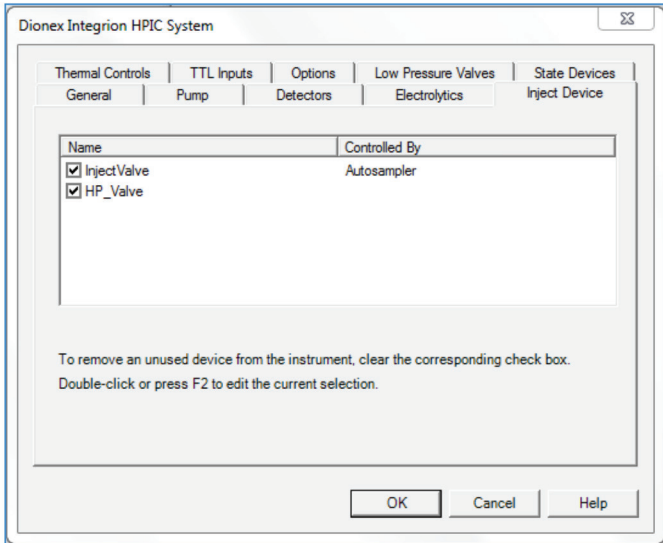
Add modules to instrument configuration. The AXP pump typically uses COM3 or COM5.

Select the Electrolytics tab on the Integrion HPIC System module. The devices are automatically selected.

Figure 3. Adding modules to the instrument configuration (electrolytic devices are detected automatically)

Table 2. Summary of the system configuration for the Dionex Integrion HPIC to ISQ EC mass spectrometer IC-MS system

Tab	Action	Result
Add Dionex Integrion HPIC Module		IC System
General	Link to USB address	
Pump		Flow rate and pressure limitations are displayed
Detectors		Automatically detected
Electrolytics		Automatically detects Dionex eluent generator cartridge, and Dionex CR-TC trap column, suppressor, and two auxiliary power supplies
Inject Device	Click boxes InjectValve and HP_Valve	Activates both valves for use with IC-MS applications. The HP_Valve is used as a diverter valve between the IC and MS instruments
	Double left-click on InjectValve	Opens the device configuration information on the injection valve
	Select Autosampler	Changes control of the injection valve from the autosampler to a programmed command by the Integrion IC
	HP_Valve	Used as a diverter valve
Thermal Controls		Thermal control options for column, detector, and suppressor are automatically detected.
Low Pressure Valves		Automatically detected
TTL Inputs	Double left-click on TTL_Input_1	Selecting TTL Input 1
	Select Inverted Mode	Directs the TTL connected device (Integrion pump) to turn off when regenerant flow is off for 5 min
	Click box of Pump On	Connects to pump
Options		Automatically detects Pump Degasser and Seal Wash pump
Add Pump Wellness Module		Monitors and allows display of Integrion pump pressure
General	Link to USB address	
Devices	Click pressure signal box	Activates pressure monitoring feature
Add Dionex AS-AP Autosampler		Delivers sample to IC injection valve
General	Link to USB address	
Sharing	Select Instrument	Select Instrument name(s). This option is available if more than one instrument is detected
Segments / Pump Link	Well Plate Sampler Segment Types	Select size and type of vials in each color segment, for example, 10 mL polystyrene vials or 1.5 mL vials for "Red", "Blue", and "Green"
Options	Injection Mode	Select Push
	Autosampler valves	If valves are present, assign function. Not used in this application.
	Select Buffer Size	1200 µL
	Select Syringe size	Typically 250 or 1000 µL
	Loop Size	Enter Injection Loop size (µL)
	Temperature Control box	Click on box to activate temperature control. Set temperature range: Application temperature
Add Dionex Auxiliary Pump Module		Pumps water through suppressor regenerant channel
General	Select COM3 or COM5	Connects communication from auxiliary pump to configuration
Pump Type	Select type of pump	AXP or AXP-MS pump.
Add ISQ EC IC-MS Module		Mass spectrometer module
Add module	Select Mass Spectrometry: ISQ EC IC-MS	Selects the correct module
General	Deselect Hardware inject synchronization	Do not select. Chromeleon controls injection
	Select ActiveLow for Remote Start	Setting for Dionex AS-AP autosampler



Assign control of InjectValve to Autosampler. By default the HP_Valve will be assigned to Integrion control.

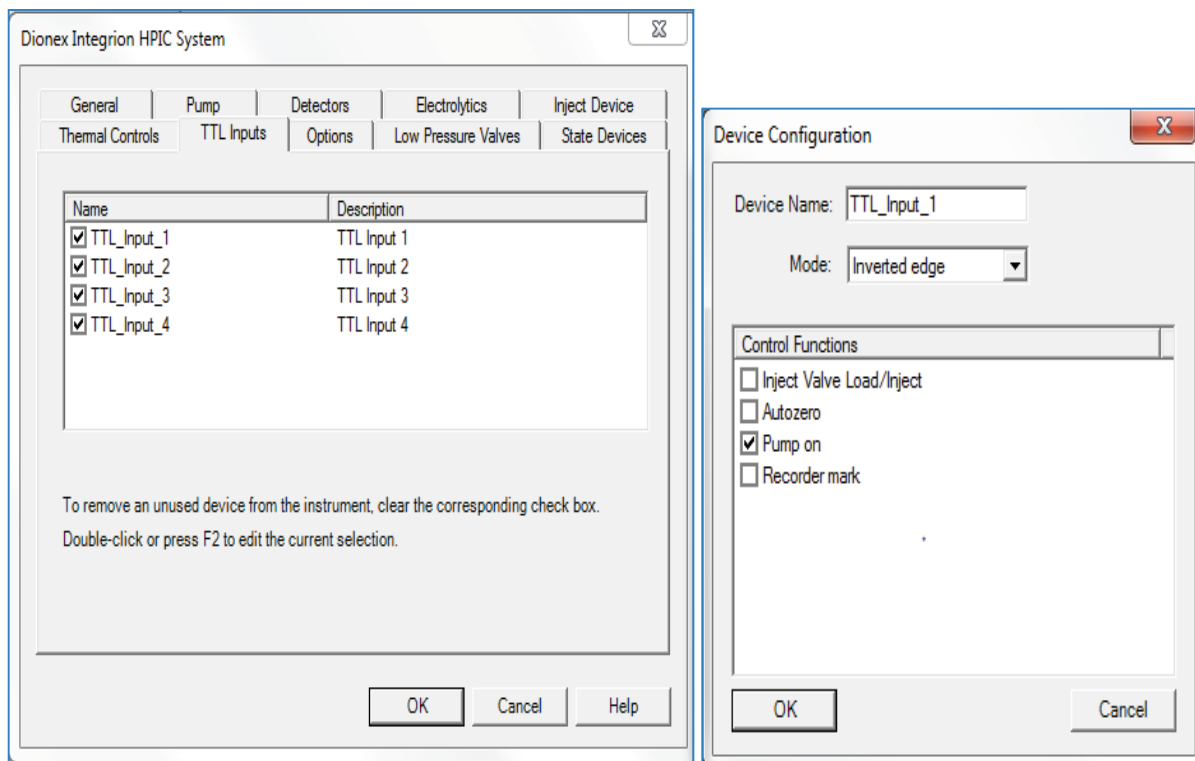
Figure 4. Assigning control of the HP_Valve to the Dionex Integrion HPIC system

Integrion HPIC System module: activation of the Dionex SRD-10 TTL controls

To activate the trigger for the Dionex SRD-10 device, first select the TTL tab on the Integrion HPIC System module. Then double-click on the *TTL_Input_1* text box on the left (Figure 5), which will open the Device Configuration window. Select *Inverted Edge* and *Pump on*. These commands will trigger the Dionex Integrion pump to turn off when the Dionex SRD-10 detects 5 min of an air bubble (no regenerant flow).

Adding the Thermo Scientific AXP or AXP-MS auxiliary pump module

The AXP or AXP-MS auxiliary pump is used to provide water regenerant to the suppressor regenerant channel. Open the computer program, Device Manager, to view the COM ports being used by the AXP pumps. To add the module into the configuration, select IC: Dionex modules, AXP pump. Select the COM USB or serial communication ports (typically COM3, COM5, or COM6) Select pump type as AXP or AXP-MS.



Start Instrument Configuration. Select *Dionex Integrion HPIC System* module. Select *TTL Input* tab: check boxes.

For the Dionex Integrion system, use *TTL_Input_1*, *Inverted Edge*, and *Pump On*. This directs the Integrion pump to turn off when regenerate flow is absent for 5 min.

Figure 5. Integrion HPIC System module: activating the Dionex SRD-10 device

- Exhaust line from the MS and the foreline pump to the in house exhaust system

Installing the ISQ EC mass spectrometer

The ISQ EC mass spectrometer includes an ESI source housing with a HESI-II probe, a liquid trap to collect condensate, and an external mechanical (oil, or rotary vane) vacuum pump, also known as “foreline” or “backing” pump. (The high-vacuum turbomolecular pump is located inside the MS.):

- Space sufficient for the IC-MS system and a computer monitor
- Power requirements listed in the installation guide and the ISQ EC Operator’s Manual, included with the instrument.⁶
- Nitrogen gas, described here generated from the recommended nitrogen generator. (Nitrogen gas flow between 90 and 110 psi is needed before connecting the IC flow to the MS.)

To install the ISQ EC mass spectrometer and mass spectrometer accessories, follow the instructions described in the ISQ EC Operator’s Manual. First make sure all the packing material has been removed from inside the MS and then install and condition the nitrogen generator according to the manufacturer’s instructions. Connect the nitrogen tubing to the rear panel of the mass spectrometer (Figure 6).

Add Ultra Grade 19 vacuum oil to the middle of the level window of the foreline pump and install the mist filter (Figure 7). Connect the tubing exiting the mist filter to the house exhaust system. Configure the foreline pump for the local site line voltage. Plug in the power cord from the foreline pump to the back of the MS (Figure 6). The foreline pump is now powered by the MS and turns on in sequence with the MS. Install the solvent trap line and collection bottle to the connector on the right-hand

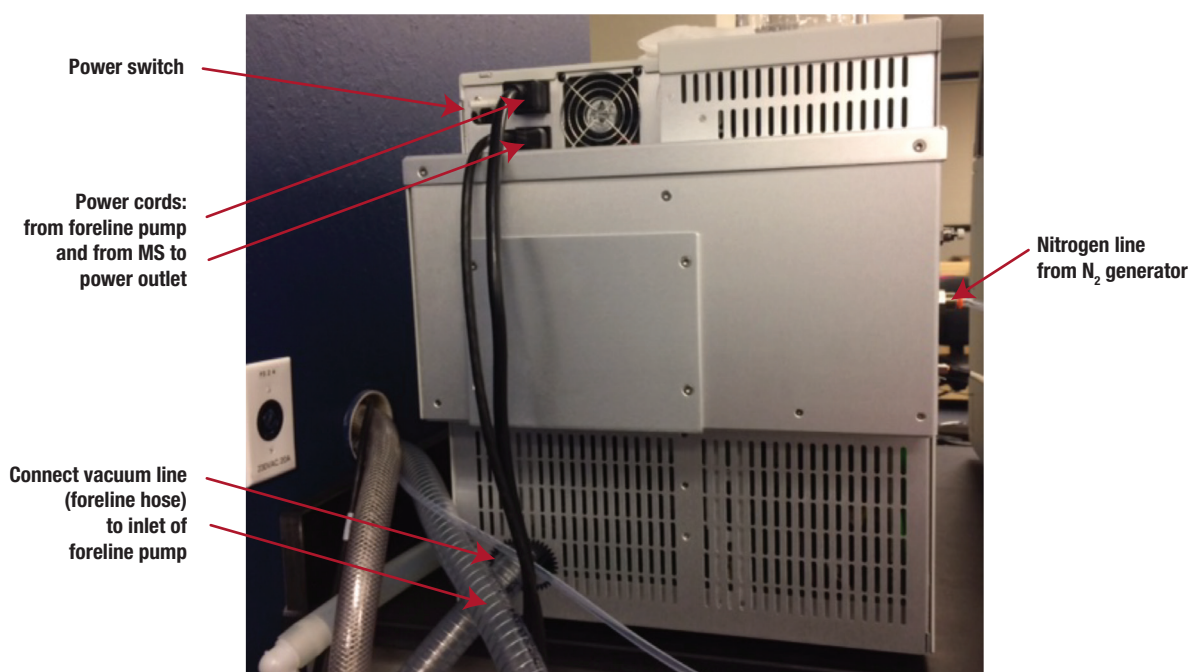


Figure 6. Power switch, power cords, and nitrogen and vacuum lines on the rear side of the ISQ EC mass spectrometer



Figure 7. Foreline pump with mist filter

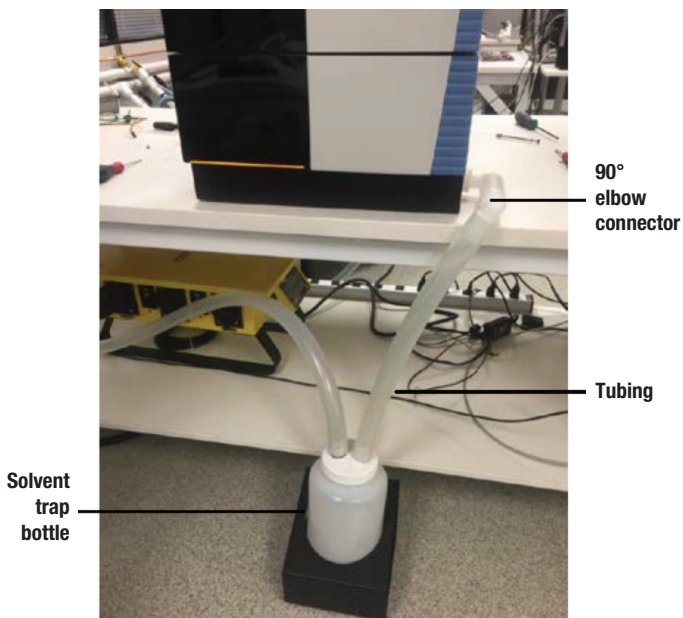
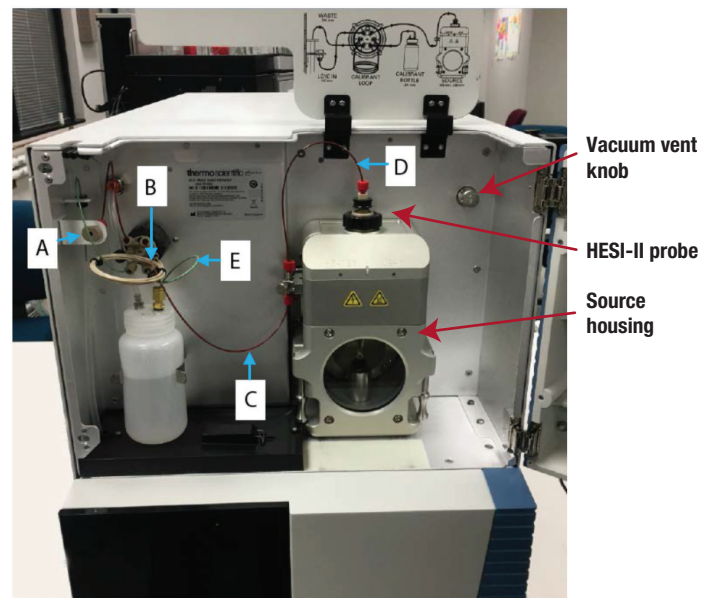


Figure 8. Solvent trap positioned below the MS⁷

side of the MS (Figure 8).⁷ Connect the free line from the collection bottle to the house exhaust line.

The source housing and the source cone may need to be installed (Figure 9).⁸ To install the source cone, follow the video instructions located on the website.⁹ First remove the PEEK tubing attached to the source housing, the grounding connector, and then the source housing. Install the source ion transfer tube and sweep cone (Figure 9).⁸ Verify that the source drain collar (similar to an



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

Figure 9. ISQ EC source housing and fluid path⁸

o-ring) is well seated in the MS drain. Install the source housing, grounding connector, and PEEK tubing.

To turn on the MS, first verify that the power is set to off. Connect the MS power cord to the wall outlet and switch the power on. The MS instrument automatically turns on the foreline pump, which will initiate the vacuum level needed for the MS. Caution: ensure that the foreline pump has been configured to the proper line voltage

before turning the instrument on. Damage to the pump or instrument may occur if there is a mismatch in voltages.

Electrospray ionization using the HESI-II probe

Electrospray ionization (ESI) is considered a soft ionization technique because it induces little fragmentation when the ions are put into the gas phase (or created in HPLC) from the water (solvent in HPLC).⁹ The ESI spray, which occurs at the HESI-II probe into the MS source, is optimized by adjusting the vaporizer and ion transfer tube (source cone) temperatures, and the sheath, aux (auxiliary), and sweep nitrogen gas flows to create a continuous ion stream into the MS. The very production of ions, the degree of ionization and its efficiency may depend on some or all of these parameters and be solvent and analyte-dependent. The advantage of RFIC ion chromatography over HPLC is that the composition of the IC effluent (pure water) is rather constant and thus the MS response of IC-MS is usually more stable and uniform than that of LC-MS.

A large negative or positive voltage is applied to the ESI needle (typically +3000 and -2000 V for IC in positive mode and negative mode, respectively).^{10,11} The HESI-II sheath and aux gases mostly vaporize the liquid

phase and create an aerosol, effectively transferring the ions into the gas phase. The gas-phase ions and small aerosol droplets are then directed inside the MS via an Ion Transfer Tube (ITT), wherein the aerosol is further dried up and the ions are desolvated by the heat and vacuum. Contrary to other chromatography detectors, only a portion of the plume enters the MS source cone. The vaporizer temperature, which sets the temperature of the aux gas, and the ion transfer temperature (not shown), which sets the temperature of the ion transfer tube, affect the rate of desolvation of the ionized liquid stream. The probe sprays the sample solution into a fine mist of charged droplets. The sheath gas (Figure 10) and heated auxiliary (aux) gas (Figure 11) help to spray, vaporize, and desolvate the sample solution. The ion transfer temperature controls the temperature of the ion transfer tube and completes the desolvation. The sweep gas (not shown here) provides a nitrogen gas counterflow from inside the sweep cone and out through its central orifice. This counterflow of the sweep gas helps to reduce the amount of non-vaporized droplets that can enter the ITT and then the MS, but mostly does not affect the transmission of ions that are already in the gas phase. The sweep flow, if employed, aids the robustness,

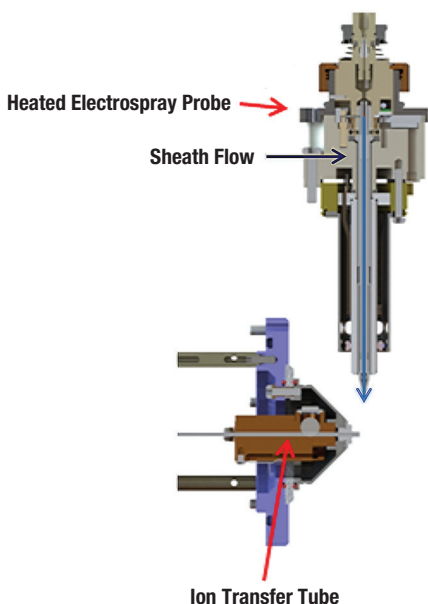


Figure 10. Sheath gas flow path in HESI-II MS probe¹²

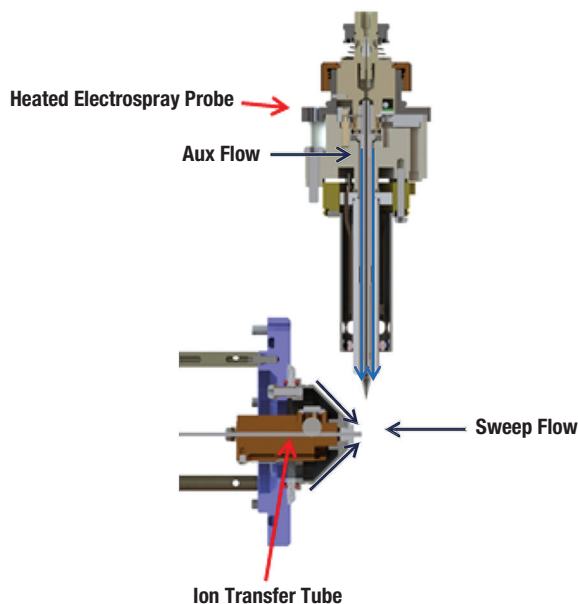


Figure 11. Auxiliary (Aux) gas flow path in HESI-II probe¹³

i.e. resistance of the system to heavy matrix, and reduces the frequency of the ESI interface cleaning.

Configuring the IC-MS modules using the Chromeleon Instrument Controller program

Adding the Thermo Scientific ISQ EC single quadrupole mass spectrometer

To add the ISQ EC module for IC-MS, select Mass Spectrometry: ISQ EC IC-MS. Select the *Hardware inject synchronization* check box, for Remote Start select *ActiveHigh*, and click on OK (Figure 12). Save the configuration and close the Instrument Configuration program.

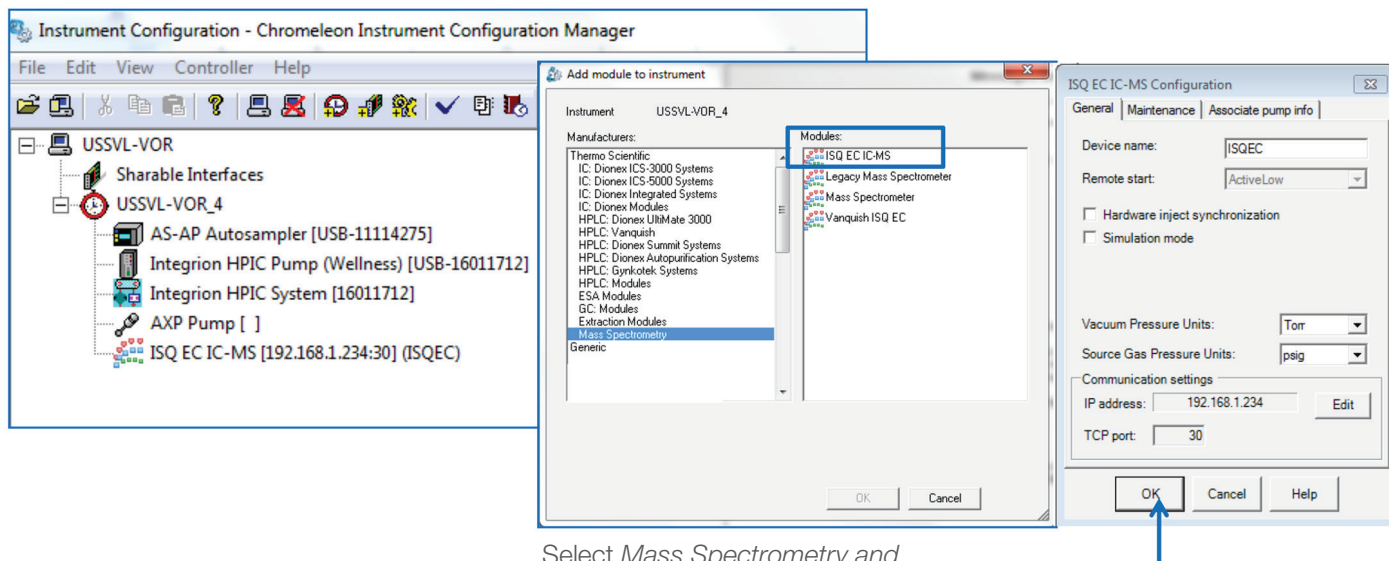
Creating an IC-MS instrument method

To create a new instrument method using the Chromeleon Instrument Method Wizard editor, select *Create, Instrument Method*, and select an instrument. Enter the values from the Chromatographic and MS

Conditions sections of the Thermo Scientific application document. Save the instrument method.

Creating a High Conductivity Trigger in the Instrument Method

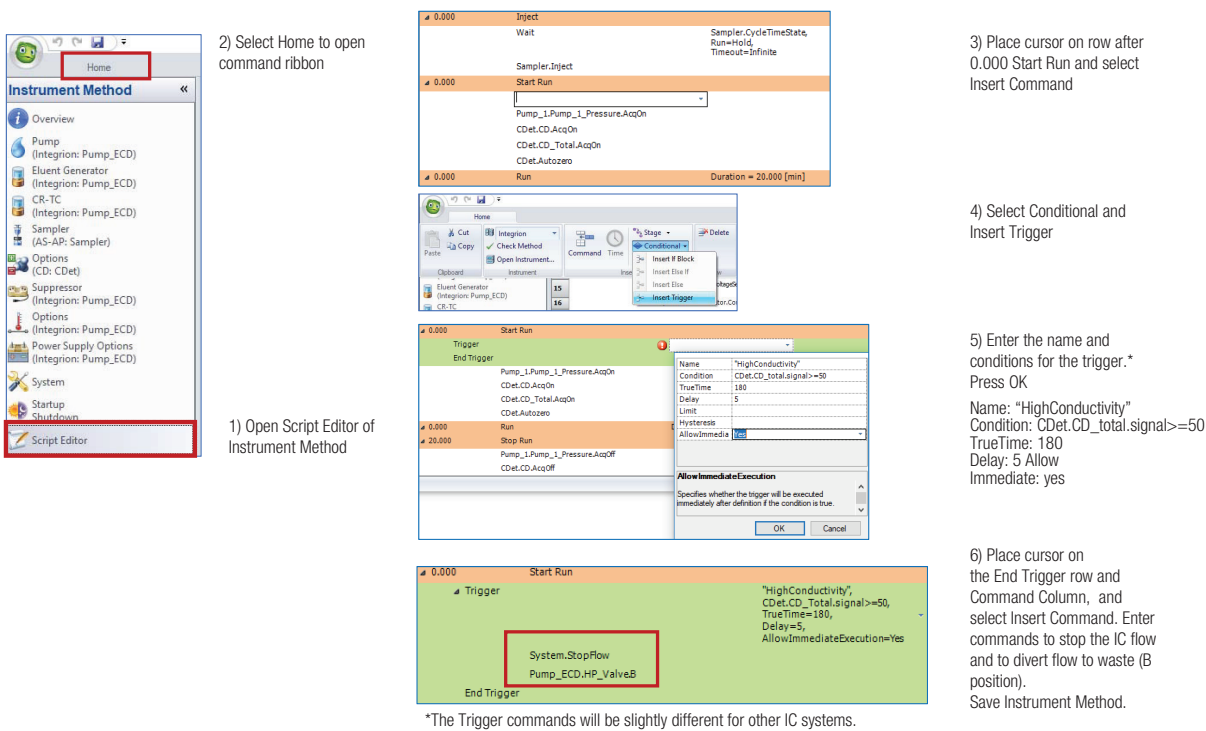
In addition to the Dionex SRD-10 device, create a high conductivity trigger in the Instrument Method script as a fail-safe to protect the MS when the suppressor fails to operate properly. The trigger conditions selected are 50 μ S for 180 s. When these conditions are met, the trigger activates commands to turn off the Dionex Integriion IC system eluent pump (System.StopFlow) and to rotate the diverter valve to the waste position (HP_Valve.B). When the pump turns-off, it turns-off the eluent generation cartridge, Dionex CR-TC trap column, and the suppressor. Create the high conductivity trigger as outlined in Figure 13. To be effective, the high conductivity trigger should be inserted into all IC-MS Instrument Methods. These conditions and commands



Select *Mass Spectrometry* and *ISQ EC IC-MS* module

1. ActiveLow setting is needed when using the Dionex AS-AP autosampler.
2. Hardware inject synchronization is not needed when using Chromeleon CDS software.
3. Select OK to close the system configuration.

Figure 12. Add the ISQ EC mass spectrometer module to the instrument configuration.



2) Select Home to open command ribbon

1) Open Script Editor of Instrument Method

3) Place cursor on row at 0.000 Start Run and select Insert Command

4) Select Conditional and Insert Trigger

5) Enter the name and conditions for the trigger.* Press OK
 Name: "HighConductivity"
 Condition: CDet.CD_total.signal>=50
 TrueTime: 180
 Delay: 5 Allow
 Immediate: yes

6) Place cursor on the End Trigger row and Command Column, and select Insert Command. Enter commands to stop the IC flow and to divert flow to waste (B position). Save Instrument Method.

*The Trigger commands will be slightly different for other IC systems.

Figure 13. Creating the HighConductivity Trigger (> 50 µS for 180 s) in Script Editor

are specifically for the Dionex Integriion HPIC system. Other systems have slightly different commands.

IC-MS analyst creating a new method, the easy mode can create suitable starting conditions.

The ISQ EC Instrument Method Editor in Chromeleon CDS has two panes: the upper pane sets the parameters for the ESI ion source, and the lower pane sets the parameters for the MS analyzer. For the ESI ion source, there are two modes: Easy mode (also called AutoSpray) and Advanced. For the MS analyzer, there are three modes: Basic, Component, and Scan. For a new

The Easy (AutoSpray) mode provides starting conditions for an inexperienced MS analyst or a new method. First enter the liquid flow rate because the optimum conditions are affected by the flow rate. (One can also link the IC pump speed to the MS in the configuration. In that case, the pump flow will display automatically.) To set the conditions, move the slider buttons up or down

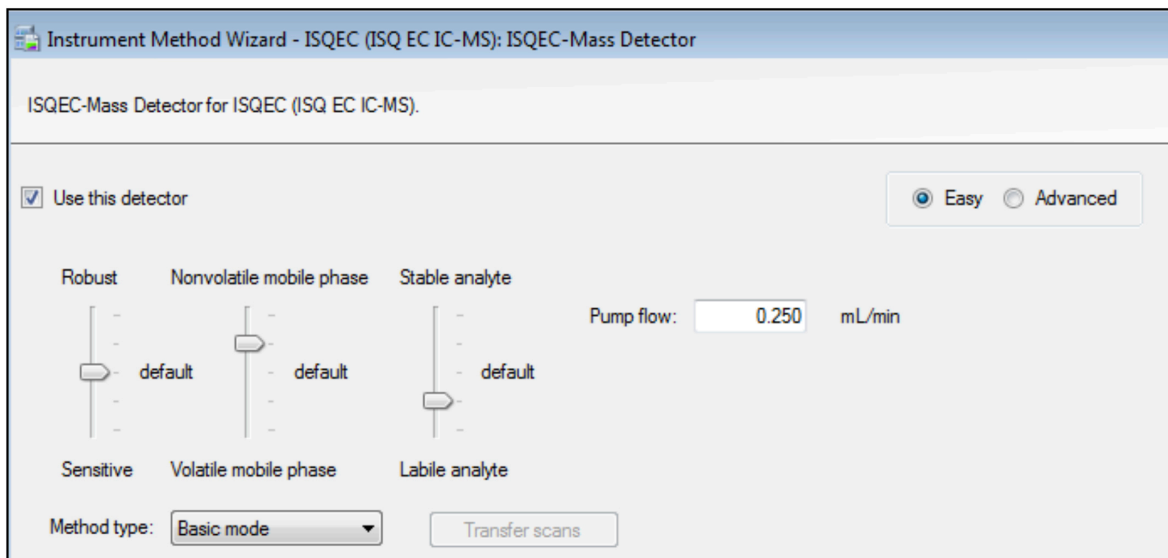


Figure 14. Recommended starting conditions using the Easy mode in the Chromeleon Method Wizard editor

(Figure 14). To see what numerical method parameters correspond to each slider's position, hover the mouse pointer over the slider. The Robust/Sensitive parameter impacts the sweep gas; typically, settings are at the default to sensitive (0.5 psi to 0 psi). Generally, the lowest sweep gas results in the most sensitivity; however, IC applications often require some sweep gas.

The Nonvolatile/Volatile Mobile Phase parameter impacts sheath gas, aux gas, and vaporizer temperature, which are typically set from above default (middle position of the slider) to the maximum for IC-MS applications. The Stable/Labile analyte setting affects the ion transfer temperature. This parameter is often a compromise between the sensitivity needed for a small volatile analyte ion, such as ammonium, or a larger less volatile ion, such as triethanolamine or perchlorate; therefore, the optimum setting can vary across the whole range.

Adding scan and acquisition rates in Basic MS mode

Enter the name, mass or mass range, ion polarity, and CID voltage (Collision Induced Voltage, CID V) values into the scan list (Figure 15). For small ions, such as ammonium and fluoride, CID V may be needed to break up adduct formation. In other cases, the adduct may be needed for quantitation so the CID V is low or not used. Enter in the peak width at 50% peak height into the *Min baseline peak width* text box. Typical values are 10 to 15 s with 6 to 10 points on a peak for IC applications.

The method parameters set by the sliders in the Easy mode can be transferred to and viewed in the Advanced mode, wherein all the method parameters are displayed as numerical values and can be edited individually by an experienced user. Likewise, the MS scan parameters set in the Basic mode can be transferred into and edited in

the Component and Scan modes. The Scan mode of the MS analyzer is the most advanced and gives full and fine control of the MS method.

Methods of optimizing the MS

There are several ways to further optimize the MS for the application:

1. Infusion of 10–50 mg/L single analyte standards using a syringe pump with Real Time Scan mode.
2. High flow infusion of 10–50 mg/L single analyte standards using a syringe pump into the IC eluent stream at the application conditions. Real Time Scan mode is used to monitor the effects of changing the parameters.
3. Sample Loop injection by the IC into the MS. The instrument program is adjusted incrementally to change the vaporizer temperature in 50 °C steps, ion transfer temperature in 50 °C steps, sheath gas in 10 psi steps, aux gas in 2 psi steps, and sweep gas at 0, 0.2, and 0.5 psi. The ions of interest are evaluated in a synthetic standard at expected concentrations in the sample.

The advantages of using Real Time Scan mode^{1,2} are that bare ion and adducts of the ions are observed in the Full Scan and SIM modes and the CID voltage can be modified during the optimization. The sample is introduced manually or by a syringe pump. The optimization may take 1 to 15 min per analyte to complete the experiments.

The advantages of changing the MS and ESI variables within the IC method³ are that the ion suppression effects of the ions are included in the method development. This method development technique is done automatically through the Chromeleon CDS sequence, but experiments may take longer to complete. After completing the

Scans				
	Scan Name	Mass List or Range (amu)	Ion Polarity	Source CID Voltage
▶*			Positive	0.0

Acquisition rate	
Min. baseline peak width:	<input type="text" value="15.0"/> s
Desired scans per peak:	<input type="text" value="10"/>
Acquisition rate:	<input type="text" value="0.7"/> Hz

Figure 15. Scan and acquisition rates in Easy mode

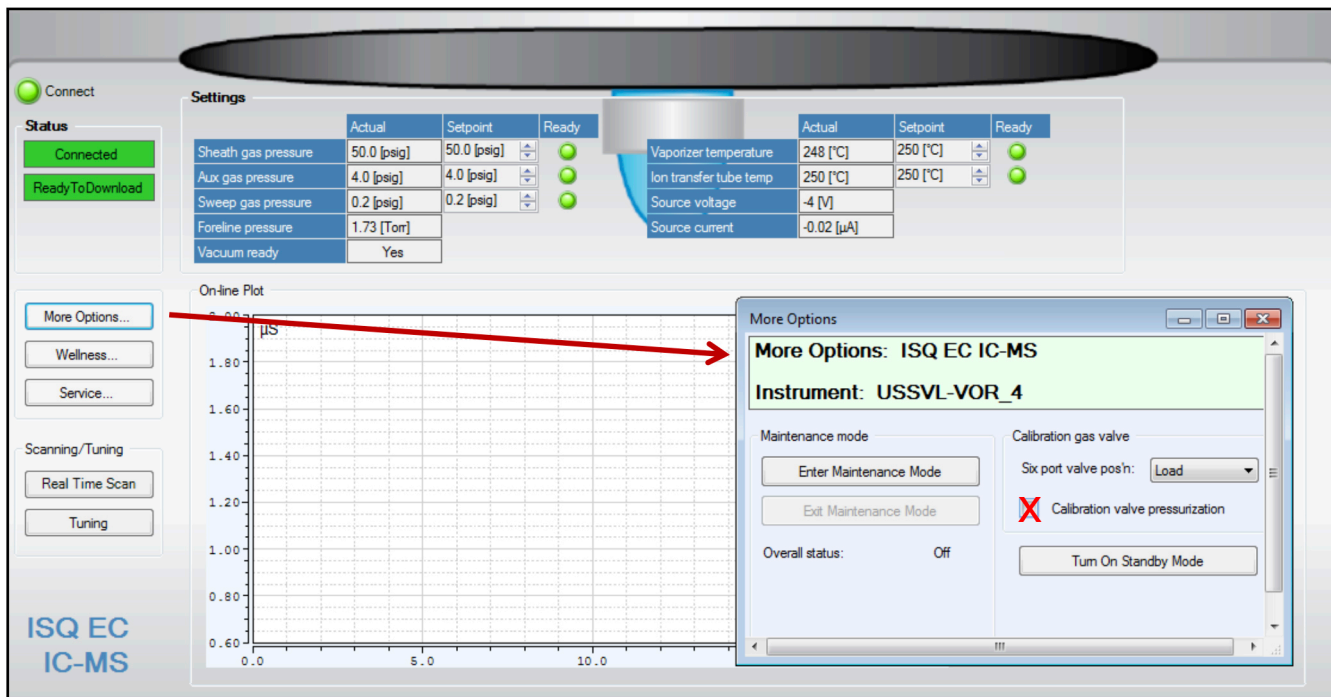


Figure 16. Flushing the calibration valve

experiments, enter the optimized temperatures, gas flow, and voltages into the Chromeleon Instrument Method Wizard editor.

Tuning the mass spectrometer

The MS tuning process requires a DI water flow rate at 0.05 mL/min; therefore, the AXP-MS pump is used for this function. Place the diverter valve in “B” position to place the suppressor in recycle mode. As previously discussed (second paragraph in section Installing the Dionex Integrion RFIC system), the AXP pump was modified with a gradient mixer and backpressure tubing to provide pulse damping during MS calibration. Run the AXP pump at 1 mL/min until liquid is flowing at a steady rate through the end of the tubing. Set the pump to 0.05 mL/min and run for 15 min to stabilize the flow. Connect the tubing to the MS inlet.

To flush the MS sample loop, press the More Options button on the left side of the ISQ EC panel (Figure 16). Another window will open. Toggle the 6-port valve position to *Load*, and select the *Calibration Valve Pressurization* check box. Allow liquid to flow for about 30 s, and then unselect the *Calibration Valve Pressurization* check box and close the window. The MS sample loop has been filled and flushed with calibration solution.

To autotune the MS, first check that the calibration container has sufficient solution. Preload the conditions by clicking on the Real Time Scan button and checking the calibration box and then close the window. Then, select the Tuning button on the left side of the ISQ EC panel. Select the ESI Positive tune button. After the positive tune is complete and passes, if the application is in negative mode, select the ESI Negative tune button. When the autotune is finished, place the diverter valve into “A” mode, which places the suppressor in external water mode and directs the eluent flow to the MS.

Starting the IC-MS system

If not previously done, open the Chromeleon Instrument Console and enter the IC conditions in the (Integrion) Pump_ECD panel and the AXP pump flow rate into the Pump panel (2× eluent flow). Equilibrate the IC until the total conductivity is < 1 μS/cm. After the IC has reached a total conductivity of 1 μS/cm or lower, select the ISQ EC panel, enter the MS gas conditions, and set the vaporizer to 150 °C. Monitor the ISQ EC panel until an acceptable vacuum is achieved, typically ~2 torr, and the vaporizer temperature is 150 °C by the appearance of a green light next to the vaporizer ready status. Enter the MS parameters of the instrument method into the panel. After vacuum has been achieved, and the temperatures and gas levels are responding to the set conditions,

set the diverter valve to "A". In this valve position, the eluent flow will be directed to the MS. Connect the tubing leaving the diverter valve to the MS injection valve. Nitrogen gas flow is required before the vaporizer temperatures can be set above 150 °C and liquid flow is required to prevent damage to the HESI-II probe. The source voltage and source current values displayed in the ISQ EC panel are only relevant when the MS is scanning. (Figure 16 shows the ISQ EC panel of the IC-MS system running but not scanning.)

Running a sequence by approving Consumable Tracking

The ISQ EC mass spectrometer is controlled by Chromeleon CDS software, resulting in a complete IC-MS system that is run on one software platform. Therefore, create a sequence in the typical way using Chromeleon Wizard editor, select the IC-MS method with optimized MS filters, and run the sequence. The Consumable Tracking Feature is a new program on Integrion systems that tracks the consumable information, (lots, serial number, etc.), warns against incompatible installed devices, and records usage on the consumables (number of injections on the columns and suppressors and amount remaining on the eluent generator cartridges). However this monitoring requires an action to either approve or correct an incompatibility between devices before allowing a sequence to start. Any installation of a new consumable device will initiate the "Approve Consumables" prompt message. To approve consumables, select the Consumables button above the tabs on the Instrument Console, select inventory, and approve the consumables. The doors on the instrument must be closed to activate this feature.

Creating a processing method

For the processing method to work properly, the sample or standard must have been run with an instrument program that contains the same MS filter (channel) to be used in the processing method. An IC-MS processing method is created after generating data by selecting the MS Quantitative template. Select the MS Component Table tab and enter or upload the components. To complete the component section by connecting the component to the MS instrument method filter, double click on one component, select extracted ion chromatogram, select the green chromatogram icon, and select the base peak and filter for the component.

For data processing, select the MS Quantitation channel and use the MS Filter options to view the MS data. Use the MS Component option for the SIM quantitation.

Placing the ISQ EC mass spectrometer in Standby or Shutdown modes

Standby

Fill up the DI water bottles to ensure that the IC has sufficient water to run at low flow rates. Set the IC pump flow to 0.1 mL/min, the suppressor to 2 mA, eluent concentration to 2 mM, and AXP pump flow rate to 0.2 mL/min.

Wait 3 min (void volume time), and then select the More Options tab on the ISQ EC panel and press the button labeled Turn On Standby Mode. Set the IC HP_Valve to B position (divert to waste). Disconnect the MS from the Chromeleon panel by clicking on the green Connected button. The MS can now be powered down or left in this mode. Standby can also be done manually by setting the MS vaporizer temperature to 0. For a faster cool down, the gas flow is maintained at the running conditions. As the vaporizer temperature approaches room temperature, set the MS detector sheath gas and aux gas to 2 psi and sweep gas to 0 psi.

Shutdown

To shut down the IC-MS system, first pump DI water through the tubing from the IC diverter valve to the MS for 3 min to flush any residual eluent and sample in the lines and the HESI-II probe. Then turn off the eluent generator, suppressor, AXP pump, and Integrion pump. Set the HP_Valve to B (divert to waste). To prevent contamination of the suppressor and column, remove the tubing from the column to the suppressor *Eluent In* port. Plug both the tubing and *Eluent In* port with plug connectors.

To shut down the MS, wait 3 min (void volume time), select the More Options tab on the ISQ EC panel, and press the button labeled Turn On Standby Mode. Wait until the vaporizer temperature is below 100 °C, and set the ion transfer temperature to the lowest temperature (150 °C). Open the MS vacuum vent knob for 15 s and then close it (leave in the close position so that it is ready to restart). Disconnect the MS from the Chromeleon panel by clicking on the green Connected button. The IC and

the MS systems, vacuum pump, and nitrogen generator can now be safely turned off. The Chromeleon Server Program can also be stopped.

Additional resources

IC-MS applications using the ISQ EC mass spectrometer can be found on the Thermo Fisher Scientific AppsLab Library of Analytical Applications.¹⁴ More in-depth discussions on MS theory and operating information can be found in the HESI-II product manual and the ISQ EC Mass spectrometer operating manual.^{6,10}

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