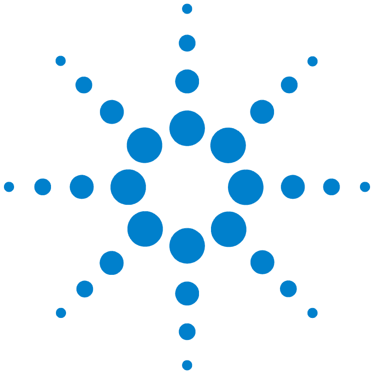


Agilent 7000 Series Triple Quadrupole GC/MS System

Concepts Guide

The Big Picture

Agilent Technologies

Notices

Manual Part Number

G7000-90031

Edition

Second Edition, October 2011

Printed in USA

Agilent Technologies, Inc.
5301 Stevens Creek Blvd.
Santa Clara, CA 95051

Software Revision

This guide applies to the Agilent MassHunter Workstation Software -- Data Acquisition for 7000 Series Triple Quadrupole program version B.03.00 or higher until superseded.

.

Warranty

The material contained in this document is provided “as is,” and is subject to being changed, without notice, in future editions. Further, to the maximum extent permitted by applicable law, Agilent disclaims all warranties, either express or implied, with regard to this manual and any information contained herein, including but not limited to the implied warranties of merchantability and fitness for a particular purpose. Agilent shall not be liable for errors or for incidental or consequential damages in connection with the furnishing, use, or performance of this document or of any information contained herein. Should Agilent and the user have a separate written agreement with warranty terms covering the material in this document that conflict with these terms, the warranty terms in the separate agreement shall control.

Technology Licenses

The hardware and/or software described in this document are furnished under a license and may be used or copied only in accordance with the terms of such license.

Restricted Rights Legend

U.S. Government Restricted Rights. Software and technical data rights granted to the federal government include only those rights customarily provided to end user customers. Agilent provides this customary commercial license in Software and technical data pursuant to FAR 12.211 (Technical Data) and 12.212 (Computer Software) and, for the Department of Defense, DFARS 252.227-7015 (Technical Data - Commercial Items) and DFARS 227.7202-3 (Rights in Commercial Computer Software or Computer Software Documentation).Safety Notices

CAUTION

A **CAUTION** notice denotes a hazard. It calls attention to an operating procedure, practice, or the like that, if not correctly performed or adhered to, could result in damage to the product or loss of important data. Do not proceed beyond a **CAUTION** notice until the indicated conditions are fully understood and met.

WARNING

A WARNING notice denotes a hazard. It calls attention to an operating procedure, practice, or the like that, if not correctly performed or adhered to, could result in personal injury or death. Do not proceed beyond a WARNING notice until the indicated conditions are fully understood and met.

In This Guide...

The Concepts Guide presents “The Big Picture” behind the operation of the Agilent 7000 Series Triple Quadrupole GC/MS System by helping you understand how the hardware and software work.

1 Overview

Learn how the 7000 Series Triple Quad helps you do your job.

2 Inner Workings – Triple Quadrupole MS versus Single Quadrupole MS

Learn the concepts you need to understand how the 7000 Series Triple Quad works.

3 Agilent Triple Quadrupole MS and Sensitivity

Learn how the 7000 Series Triple Quad achieves high sensitivity.

4 Agilent MassHunter Workstation Software – Instrument Control for 7000 Series Triple Quad

Learn concepts behind the design of the Agilent MassHunter Workstation Software – Instrument Control for Triple Quadrupole program.

Contents

1 Overview

2 Inner Workings – Triple Quadrupole MS vs. Single Quadrupole MS

3 7000 Series Triple Quad and Sensitivity

1

Overview

This chapter provides an overview of the Agilent 7000 Series Triple Quadrupole GC/MS components and how they help get the job done.

System Description

The Agilent 7000 Series Triple Quadrupole MS is a standalone triple quadrupole mass spectrometer for use with the Agilent 7890A GC system. The 7000 Series Triple Quad features:

- One split flow turbomolecular vacuum pump
- Rotary vane foreline pump
- Independently MS heated electron-ionization ion source
- Two independently MS heated hyperbolic quadrupole mass filters
- Single hexapole collision cell
- High-energy dynode (HED) electron multiplier detector
- Independently GC heated GC/MS interface

This configuration has advantages for many applications. The data is interpreted through the use of the MassHunter Workstation software, which provides quantitative and qualitative analyses of the data obtained.

The 7000 Series Triple Quad is the only triple quadrupole GC/MS combination that incorporates a hexapole collision cell blanketed with a combination of nitrogen and helium gas, to improve the ion fragmentation prior to final filtration and detection quantification.

Help for applications

The 7000 Series Triple Quad combination can quantify trace organic compounds in complex matrices. The following applications use this type of quantification:

- Food safety studies
- Environmental studies
- Drug discovery
- Toxicology
- Forensics

Paired with Agilent's 7890A GCs, the 7000 Series Triple Quad delivers sensitive, reproducible analyses of target compounds in complex matrices. This provides the following:

- Femtogram-level limits of detection and quantification
- Selective quantification of target compounds in high chemical background samples
- Improved signal-to-noise ratios (s/n) in complex matrices
- Ability to meet stricter regulations regarding sample analytical limits for certain applications
- Simplified operation with Agilent's data analysis software

The 7000 Series Triple Quad offers the improved sensitivity in GC/MS/MS analysis that is required by many commercial and regulatory applications.

Help for acquisition

The MassHunter Workstation Instrument Control software allows you to perform the following tasks from a single window:

Prepare the instrument

- Start and stop the instruments from the software
- Download settings to the GC and the Triple Quad in real time to control the instrument
- Optimize MS parameters automatically or manually through Agilent tuning programs and print an Autotune report
- Monitor the actual conditions of the instrument
- View the real-time plot for chromatograms and instrument parameters (both GC and MS) and print a real-time plot report
- View the centroid line spectrum of a peak or the mass range profile spectrum of a peak in real time

Set up acquisition methods

- Enter and save parameter values for the GC and the Triple Quad to an acquisition method
- Select and label the total ion chromatograms or extracted ion chromatograms that you want to appear in the real-time plot
- Set up time segments for each scan type and analysis where parameters change with the time segment or with the scans within the time segment
- Print an acquisition method report

Acquire data

- Enter sample information and pre- or post-programs (scripts) and run single samples interactively
- Enter and automatically run both individual samples and samples organized in a sequence of samples
- Set up pre- and post-scripts to run between samples in a sequence

- Set up and run a sequence to optimize MS acquisition parameters
- Print a sequence report
- View system events, including start and stop times, run events, and errors
- Print an event log report

To learn how to get started with the Agilent Triple Quadrupole GC/MS, see the 7000 Series Series Triple Quad GC/MS Quick Start Guide.

To learn more about how to use the Agilent Triple Quadrupole GC/MS with real samples and data, see the 7000 Series Series Triple Quad GC/MS Familiarization Guide.

To learn how to do individual tasks with the GC/MS, see the online help.

To learn more about the Agilent 7890A GC system, see the Agilent 7890A GC system documentation.

Help for data analysis

Quantitative analysis program

Agilent has designed the quantitative analysis program to help quantify very low amounts of material. The program has the following unique features:

- Imports information directly from the acquisition method
- Provides a curve-fit assistant to test all fits and statistics on curve quality
- Integrates with an automated, parameter-free integrator that uses a novel algorithm, optimized for triple quadrupole data
- Presents a batch results window to help you review and operate on an entire batch of data at once
- Automatically detects outliers
- Provides preconfigured templates for basic reporting and provides the capability to create custom reports in Microsoft Excel

Please refer to the Agilent MassHunter Workstation Software – Quantitative Analysis Familiarization Guide or the online help for the quantitative analysis program.

Qualitative analysis program

For fast method development, this software is used to quickly review the qualitative aspects of the data, such as the optimum precursor to product ion transitions.

Agilent designed the qualitative analysis program to present large amounts of data for review in one central location. With the program you can do these operations for any type of mass spectrometer data that you open:

- Extract chromatograms
- View and extract peak spectra
- Subtract background
- Integrate the chromatogram
- Find compounds

You can also set up methods to automatically do the tasks in the list, as well as others, when you open the data files.

Refer to the Agilent MassHunter Workstation Software – Qualitative Analysis Familiarization Guide or the online Help for the qualitative analysis program.

2

Inner Workings – Triple Quadrupole MS vs. Single Quadrupole MS

This chapter explains the inner workings of the 7000 Series Triple Quad.

The foundation for understanding the operation of a triple quadrupole mass spectrometer is the operation of a single quadrupole mass spectrometer. Therefore, an explanation of the workings of a single quadrupole mass spectrometer is presented first.

Single Quadrupole MS Operation

This section first reviews the fundamental aspects of the single quadrupole mass spectrometer. Understanding the operation of a single quadrupole mass spectrometer provides insight into the specific features of an 7000 Series Triple Quad.

Design for a single quadrupole mass spectrometer

Mass spectrometry is based on the analysis of ions moving through a vacuum.

The ionization of a sample occurs in the ion source that is shown, schematically, on the left in Figure 1. In this case, the source used is an electron impact ionization source, which ionizes the sample with a charged filament.

The ions are analyzed by a mass analyzer (mass filter) that controls the motion of the ions as they travel to the detector to be converted into actual signals.

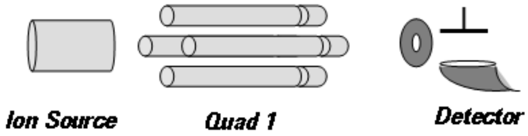


Figure 1 Schematic for single quadrupole mass spectrometer

The quadrupole mass analyzers consist of four parallel rods to which specific DC (direct current) and RF (radio frequency) voltages are applied. These rods filter out all ions except those of one or more particular *m/z* value, or mass to charge ratio value as determined by the voltages applied.

The RF is applied to all four rods, but the negative (–) rods are 180 degrees out of phase with the positive (+) rods. The rods are labeled + and – in reference to the DC voltages applied to them.

All ions that comprise the sample are generated at the source. However, when a specific set of voltages is applied, only ions of the corresponding *m/z* value may pass through the quadrupole to reach the detector. As the voltages are increased to other values, ions with other *m/z* values are allowed to pass through. A full MS scan is obtained by increasing the DC and RF voltages applied to the four rods over an expanded range of values.

How a single quadrupole mass spectrometer works

A conceptual model can be used to explain the theory of a single quadrupole mass spectrometer. See Figure 2.

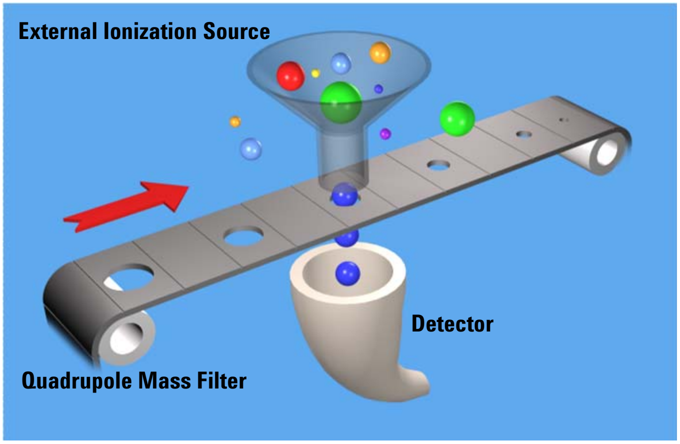


Figure 2 Conceptual model of a single quadrupole mass spectrometer

In the model:

- All of the ions contained in a sample are formed in the external ionization source and collected in a funnel. The balls of different colors and sizes represent different ions having different *m/z* values.
- The quadrupole mass analyzer is represented by a moving belt that serves to filter the ions as they pass through openings of various sizes. The ions pass from the funnel, through the filter, to the detector.
- The detector is represented by the collecting funnel below the filtering belt.

As the belt (the analyzer) moves, or the voltages on the rods are changed, ions with different *m/z* values are filtered through the mass spectrometer.

As the analyzer moves from a small *m/z* value to increasingly larger values, a full MS scan is created.

If the belt does not move, the detector continues to monitor the same single *m/z* value over the entire scan period. This type of analysis is known as selected ion monitoring, or SIM. It is the most sensitive operating mode for a single quadrupole mass spectrometer.

The scan period is selected (fixed) by the user. The user may set the dwell time to scan a specific mass range (for example, *m/z* 50 to 1,000) *or* to remain on one selected ion (SIM) *or* to move to several selected ions during the scan period. The quadrupole mass filter is not scanned over a range in the SIM mode. The required RF and DC voltages are set to filter a single mass for a specified time before moving to the setting for the next SIM.

Single quadrupole: SIM

To obtain the best sensitivity or quantitative measurement, the single quadrupole is operated in SIM mode (Figure 3). The duty cycle is the measure of the instrument’s time actually devoted to measuring signals. In SIM mode, the single quadrupole analyzes the signal of a specific *m/z* ion almost all of the time. This results in nearly 100 percent acquisition during the duty cycle.

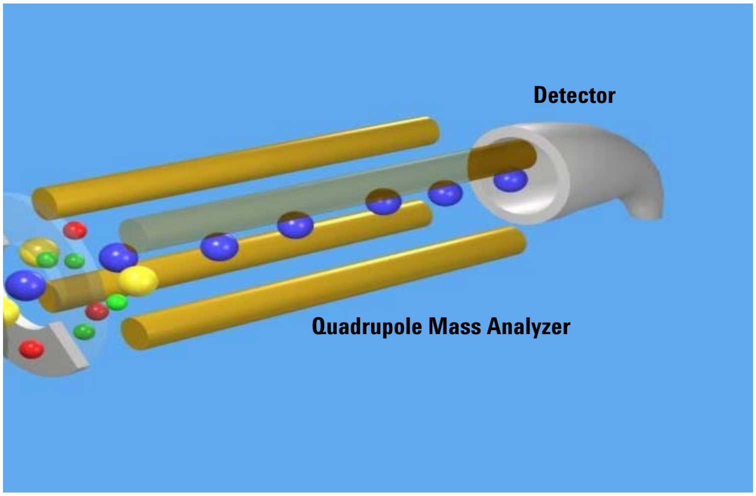


Figure 3 **Single quadrupole: SIM**

In this example:

1. All of the ions (+, –, and neutrals) are formed in the electron impact ionization source.
2. Ion optics guide the ions to the quadrupole mass analyzer.

   The Agilent electron impact ion source consists of a series of lenses and a repeller assembly that directs the ion beam into the analyzer.
3. In the analyzer, only ions of a particular *m/z* value, represented by blue balls, are allowed to pass through to the detector.
4. The detector completes the analysis.

This system has several advantages:

- Provides the best sensitivity for quantitation
- Increases selectivity
- Improves chromatographic specificity
- Provides no structural information

Single quadrupole: full MS scan

In a full MS scan, the quadrupole serves as a mass filter over time, and a scan is carried out by stepping through increasing DC and RF voltages. This provides filtering through the corresponding *m/z* values across a mass spectrum. See Figure 4.

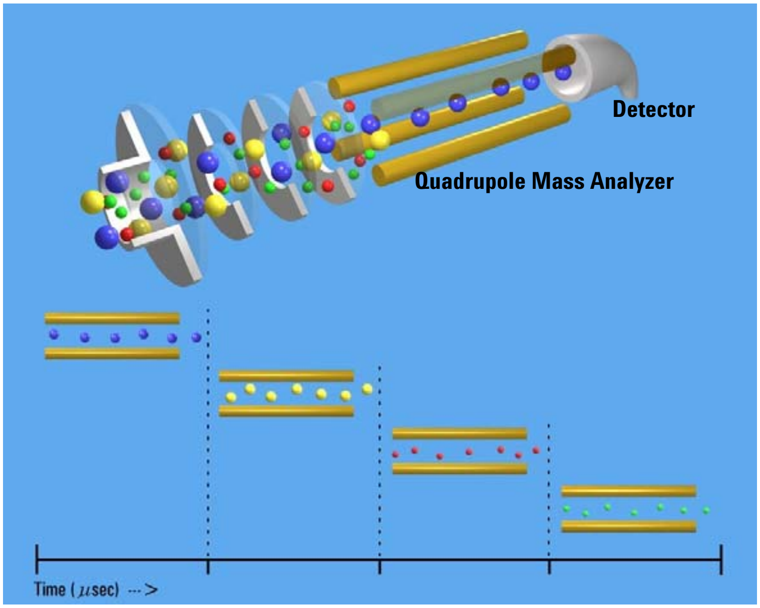


Figure 4 Single quadrupole: full scan MS

The full scan MS mode is less sensitive because the duty cycle for each *m/z* value is considerably less than 100 percent. The quadrupole mass analyzer scans sequentially, passing each *m/z* value in the selected mass range to the detector.

A full scan MS is still a useful mode of operation because it shows all of the ions that are being formed in the ion source. This alerts analysts to other compounds co-eluting with compounds of interest, and is helpful information for developing SIM acquisitions.

What about fragment ions?

Full scans with a single quadrupole instrument can also be used to study fragment ions. See Figure 5.

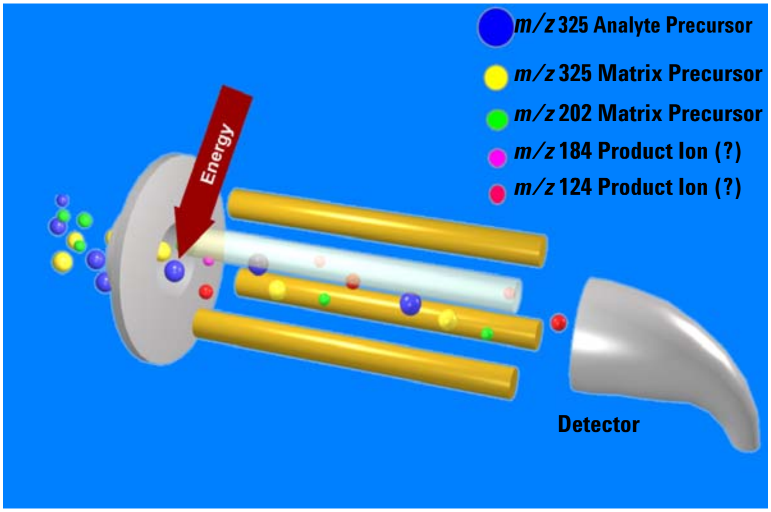


Figure 5 Fragment ions with single quadrupole MS

The diagram shows that fragment ions, also known as product ions, are formed by fragmenting or breaking apart precursor ions. Precursor ions formed in the ion source travel through the mass analyzer without change, unless extra energy is applied to their motion in a region where fragmentation can occur. If the ions run into gas molecules and the translational energy is high enough, these collisions convert the translational energy into molecular vibrations that can cause the ions to fragment. This is called collision-induced dissociation (CID).

Fragmentation, or CID, can be carried out in a low-pressure region between the ion source and the mass analyzer. The outlet of the ion source is under vacuum, which is created by a two-stage vacuum pump. On the Agilent single quadrupole mass spectrometer, the region between the ion source and the quadrupole exhibits a gas pressure of about 10 to 20 × 10^{-5} Torr, which is well below atmosphere pressure (760 Torr). Under normal operation, a voltage is applied across this region to keep the ions passing through to continue on to the mass analyzer. Even if these ions collide with the gas molecules in this region, they usually do not have enough energy to fragment.

However, as the voltage is increased, the ions have more translational energy. Then, if the ions run into gas molecules (Figure 6), CID can occur. Even though this fragmentation does not occur where the ions are formed, this type of fragmentation is still referenced as "in-source CID."

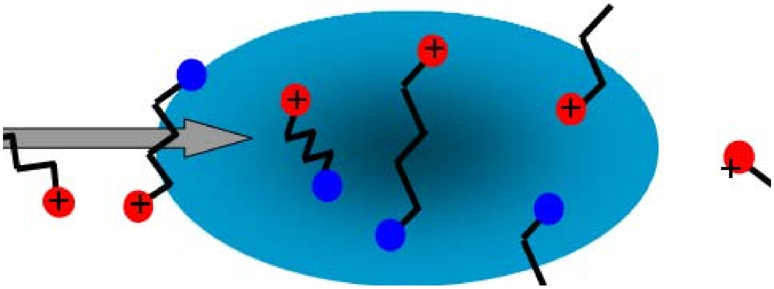


Figure 6 Ion fragmentation caused by collision-induced dissociation

A triple quadrupole mass spectrometer can do MS/MS, with fragmentation within its collision cell as described in the next section.

Triple Quadrupole MS Operation

The previous section regarding the operation of the single quadrupole mass spectrometer helps to clarify the principles of the triple quadrupole mass spectrometer.

Design of the 7000 Series Triple Quad

The triple quadrupole mass spectrometer consists of an ion source, followed by ion optics that transfer the ions to the first quadrupole. A diagram of the current 7000 Series Triple Quad is shown in Figure 7.

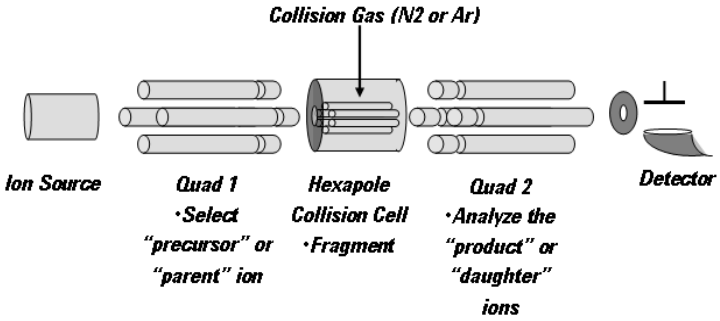


Figure 7 The 7000 Series Triple Quad innovative enhancements

As in the single quadrupole MS, the analyzers consist of four parallel hyperbolic rods through which selected ions are filtered. After passing through the first quad, the filtered ions then enter a collision cell where they are fragmented. The collision cell is typically called the second quadrupole, but in this case, geometrically it is actually a hexapole filled with nitrogen or another collision gas.

The fragment ions formed in the collision cell are then sent to the third quadrupole for a second filtering stage to enable isolation and examination of multiple precursor to product ion transitions.

Innovative enhancements in the 7000 Series Triple Quad

Ions enter the MS from the Agilent 7890A GC. One of several enhancements to the 7000 Series Triple Quad is found in the 7890A GC, which incorporates backflush technology, minimizing column bleed and providing better sample splitting. This results in less sample dilution at low flows and a reduction in chemical noise with the elimination of ghost peaks in the data.

After separation in the GC, the sample is transferred to an electron impact ionization source where ions are generated by a filament. The ion source contains dual filaments, which can be tuned separately and selected for use based upon their performance. The dual filament design allows the user to continue running with one filament even if the other needs to be replaced or cleaned.

Once the sample is ionized, a repeller directs the ions through a set of lenses and into the first quadrupole analyzer, where they are filtered based on their mass-to-charge ratio.

The ions passing through the first quadrupole analyzer are then directed into an improved collision cell, where they are fragmented. In the 7000 Series Triple Quad, the addition of a post-filter focuses the ion beam exiting the quadrupole, which ensures effective concentration of the ions exiting the quad.

The collision cell is actually a hexapole filled with a nitrogen and helium combination gas stream. Agilent innovation has led to the design of a collision cell that has axial acceleration for high-speed MS/MS analysis. The use of helium as a quench gas in the collision cell reduces noise from helium neutrals as well as enhances the efficiency of the fragmentation process. Agilent has shown that the addition of helium to the collision cell gas stream provides stabilization to high-mass ions, allows more control over the fragmentation process, and reduces neutral noise in the data.

Fragment ions formed in the collision cell are then sent through a prefilter, prior to the third quadrupole. Similar to the post-filter on the first analyzer, the prefilter focuses the ion beam into the quad. The third quadrupole provides a second filtering stage, which further concentrates the product ions.

Finally, the ions that pass through the third quadrupole are detected using a high-energy detector. Additional improvement in sensitivity is achieved in the 7000 Series Triple Quad through the triple axis high-energy dynode (HED). The HED uses an off-axis configuration that pulls the charged ion of interest away from the neutrals, allowing the neutrals to be eliminated by the turbo pump.

The split flow high-performance turbo pump provides vacuum and efficiently eliminates particles of carrier gas and unionized material to allow for accurate product quantification.

Once through the HED, the ions are quantitated by an electron multiplier detector. Gain normalized tuning of this detector provides consistent sensitivity over the life of the electron multiplier.

How a triple quadrupole mass spectrometer works

Triple quadrupoles provide the potential for MS/MS in several ways (see Figure 8).

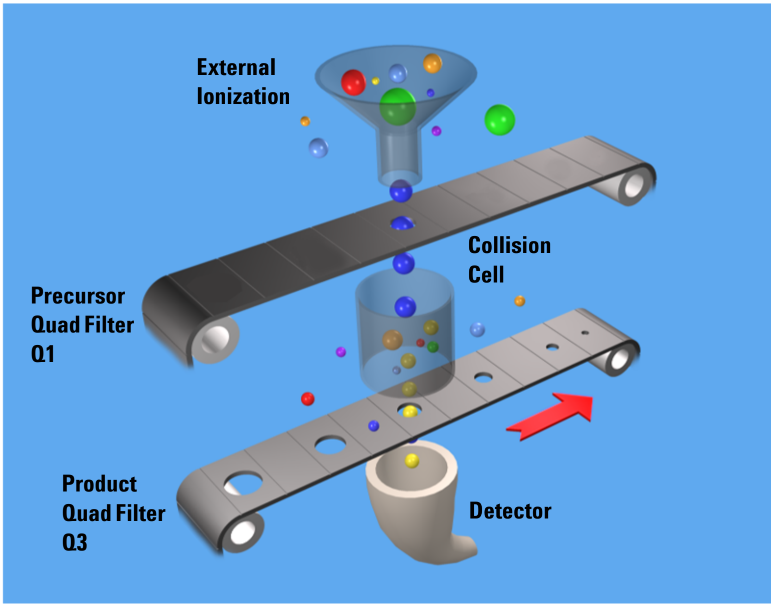


Figure 8 Conceptual model of a triple quadrupole mass spectrometer: With SIM, MS1 (Q1) set to pass the precursor ion *m/z* and SIM, MS2 (Q3) set to pass the product ion *m/z*.

Representing the quadrupole mass analyzers as moving belts, a collision cell can be placed between the belts to fragment the ions. The first belt can be fixed to select which precursor ion travels to the collision cell. Different types of collision cells can be used.

The cell can be another quadrupole, a hexapole (six rods like the one used in the 7000 Series Triple Quad), an octopole (eight rods), or even a transverse wave guide.

Whichever geometry is used, an inert, nonreactive gas is required for use as the collision gas. In addition, the voltages applied to the collision cell must be different from those applied to the quadrupoles to accelerate the movement of all of the ions so that their collision energy is sufficient to cause fragmentation.

In this example, a precursor ion is selected using the first quadrupole and is sent to the collision cell for fragmentation. The fragments are then scanned through the third quadrupole, resulting in a product-ion scan MS/MS. Since the fragment ions are pieces of the precursor, they represent portions of the overall structure of the precursor molecule. They are selected by the third quadrupole according to their m/z ratio in the same way the precursor ions are chosen by the first quadrupole. In this manner, a triple quad provides enhanced selectivity for accurate target compound analysis.

A full scan MS/MS using a triple quadrupole MS is also not the most sensitive mode for the same reason that a full scan MS using a single quadrupole is not the most sensitive mode of operation possible (first belt remains steady; second belt moves). The most sensitive mode of operation for the triple quadrupole MS instrument is to fix both belts and only monitor a specific precursor ion and a specific product ion. This mode is called selected reaction monitoring or SRM.

In normal operation, a triple quadrupole MS instrument involves running multiple SRMs for the same precursor ions. This is called multiple reaction monitoring or MRM.

3

7000 Series Triple Quad and Sensitivity

This chapter shows how the 7000 Series Triple Quad reduces chemical and electronic noise and how each component contributes to enhanced instrument sensitivity.

How the 7000 Series Triple Quad Improves Sensitivity

Sensitivity is a performance standard for the 7000 Series Triple Quad. It is expressed as the signal-to-noise ratio (s/n). Triple quadrupole mass spectrometers exhibit multiple sources of noise, including interference from chemical and cluster backgrounds and electronics.

Sensitivity

In the design of the 7000 Series Triple Quad, sensitivity was addressed within all stages of instrumentation, from the ion source to the detector. See Figure 9.

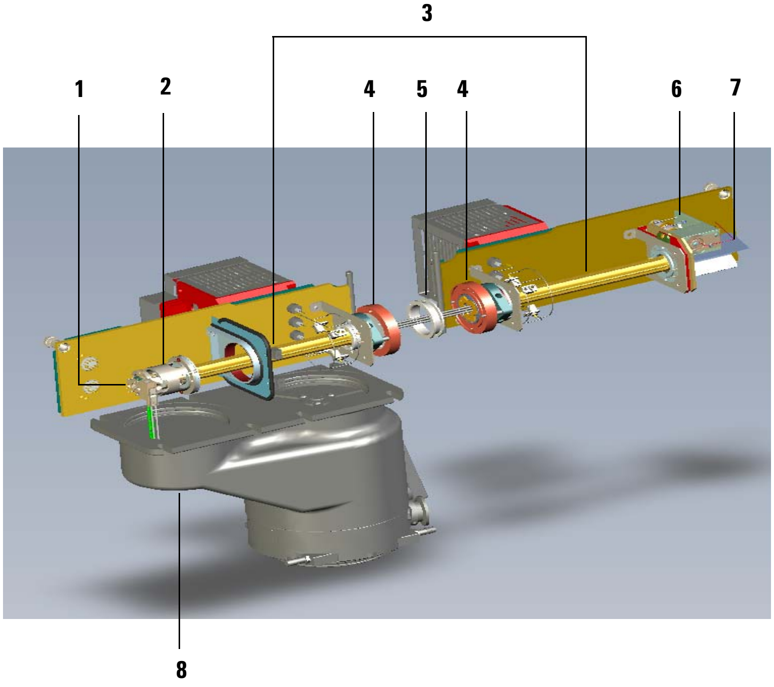


Figure 9 Sources of noise

How the 7000 Series Triple Quad instrument increases sensitivity

1. Sample enters the 7000 Series Triple Quad from the 7890A GC. The 7890A GC incorporates capillary flow backflush technology to produce better separation and reduce column bleed, providing a cleaner sample.
2. Electron ionization ion source incorporates dual filaments with tuning capabilities to optimize ionization and filament use.
3. Front and rear analyzers use hyperbolic quadrupoles to optimize ion transmission and spectral resolution.

4. RF quadrupole segments (pre- and post-filters) enhance ion transmission into and out of the collision cell.
5. High-pressure collision cell with linear acceleration optimizes MS/MS fragmentation while eliminating crosstalk, even at very low dwell times. A small-diameter high-frequency hexapole assembly assists with capturing and focusing fragmented ions. Helium quench gas assists in the fragmentation process while reducing the neutral noise in the data.
6. Off-axis high-energy dynode detector with log amp signal compression permits a high gain, long life, and low noise. This design allows neutrals to pass without hitting the detector.
7. Multiplier has a long life since only electrons impact its surface, never ions. Gain normalized tuning of the detector provides consistent sensitivity over the life of the multiplier.
8. Vacuum system incorporating the use of a split flow turbomolecular pump efficiently eliminates neutral materials prior to the detector.

Chemical noise reduction with MRM

MRM can only be performed with a triple quadrupole MS. In this operation, the front analyzer is run in SIM mode to monitor for a specific ion. After filtration in the first quadrupole, it is expected that only ions with a single *m/z* ratio will pass through (see Figure 10). After fragmentation in the collision cell, the third quadrupole is also run in SIM for a specific *m/z* range, to capture product ions resulting from the precursor. The third graph in Figure 10 shows how the data can be easily read for product identification and quantification.

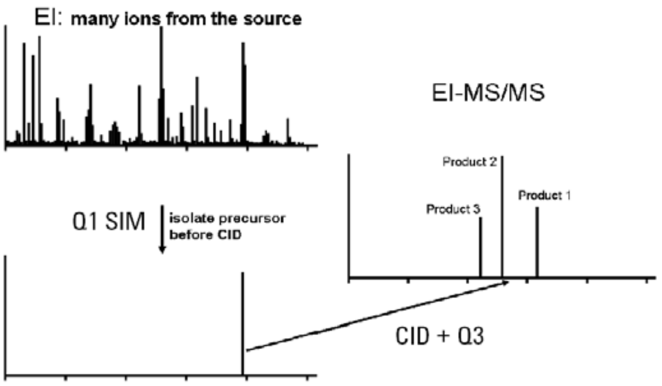


Figure 10 Sensitivity with MRM

The 7000 Series Triple Quad passes through four transitional steps in translating a signal in the MRM process (Figure 11).

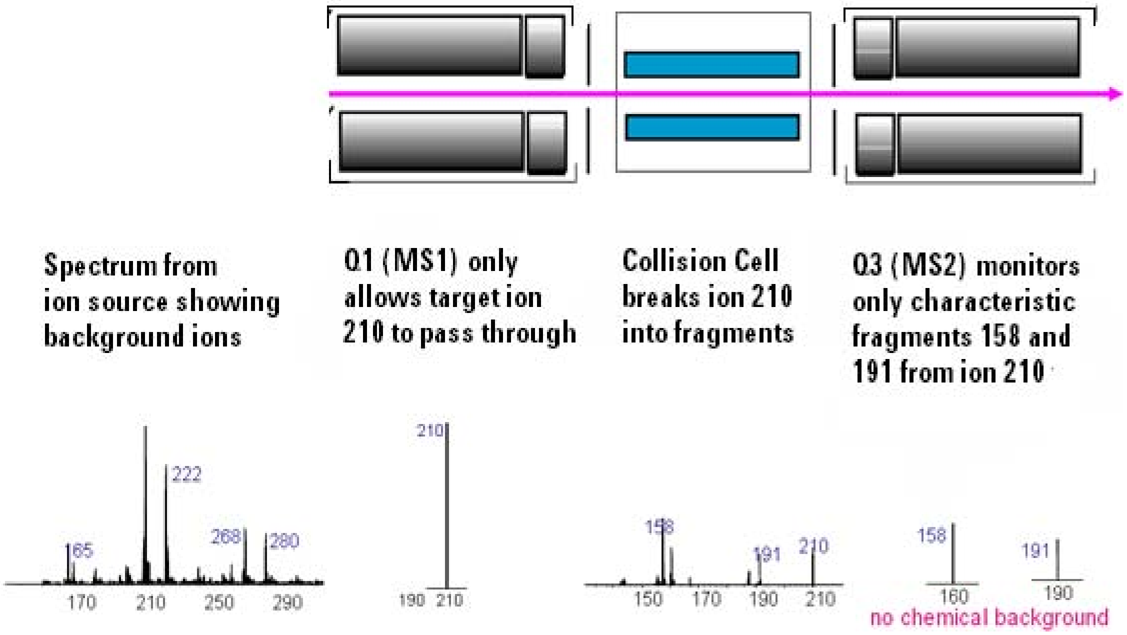


Figure 11 Multiple reaction monitoring (MRM)

Step 1 The spectrum at the far left represents everything that is being ionized at the ion source. A triple quad GC/MS reduces chemical noise for low-level quantitation in a dirty matrix more than a single quad GC/MS does.

Step 2 This step is accomplished by first selecting the chemical of interest at 210 from the co-eluting interferences seen in the rest of the spectrum. The second spectrum shows the result after passing through the first quadrupole, or Q1 (MS1).

Step 3 After Q1 (MS1), fragment ions are generated in the collision cell. The corresponding MS/MS spectrum is shown below the collision cell.

Step 4 Particular fragment ions can be selected to pass through the Q3 (MS2) quadrupole. These are selected for quantitation and confirmation.

The second stage of selectivity using the Q3 (MS2) quadrupole removes much of the chemical background. Typically, the chance of an isobaric interference at the same exact mass as the fragmentation ion is remote.

Sensitivity and reproducibility of the 7000 Series Triple Quad

Sensitivity in MS data is affected by detection limits, sample dilution, and sample contamination. Improvements in MS sensitivity are made through increased signal strength and a reduction in chemical noise.

The sensitivity specification for the 7000 Series Triple Quad is at femtogram levels. The instrument was developed for an injection of 100 fg of octafluoronaphthalene (OFN) to produce at least 100:1 RMS *s/n* for the transition of *m/z* 272 to the fragment ion *m/z* 222 using autotune parameters. This is demonstrated at customer sites upon installation. (See Figure 12).

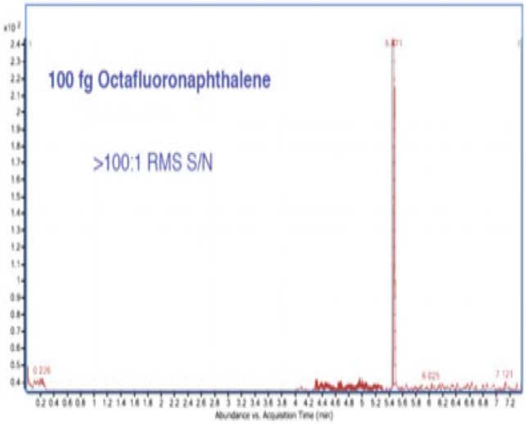


Figure 12 Analysis of 100 fg sample of OFN in MRM (272 : 222)

Triple quad GC/MS analysis is useful for identifying quantities of target compounds in complex matrices. The 7000 Series Triple Quad provides improved analysis in complex matrices. Figure 13 illustrates a chromatogram of two PCB congeners (PCB 153 and PCB 138) injected at 400 fg each on-column. Quantitation transition is performed at 360 —> 290 *m/z*, with the qualifier transition measured at 360 —> 325 *m/z* for simultaneous quantitation and confirmation at the lowest detection limit. Resulting data produce strong signals on a flat baseline.

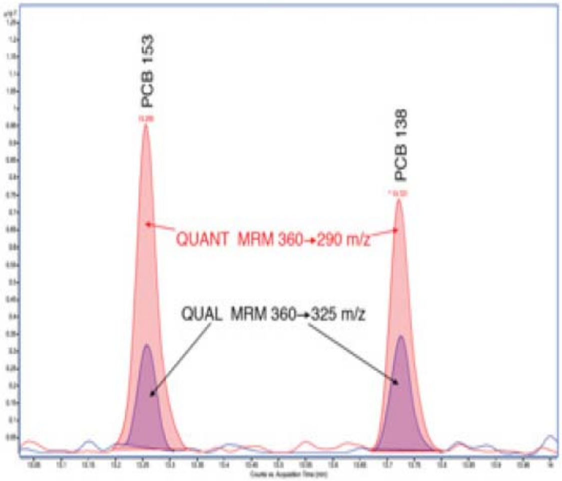


Figure 13 Identifying target PCBs in complex matrices

Another performance standard of the 7000 Series Triple Quad is high sensitivity for contaminated samples. Figure 14 illustrates HCB analysis in diesel fuel. Data from the single quad in SIM show a low signal-to-noise ratio, with many peaks and chemical background noise. In the second graph, the sample run in RMS mode results in a *s/n* of 86:1 with quantitative transition of 283.8:213.9 *m/z*. This demonstrates high sensitivity in a “dirty” matrix.

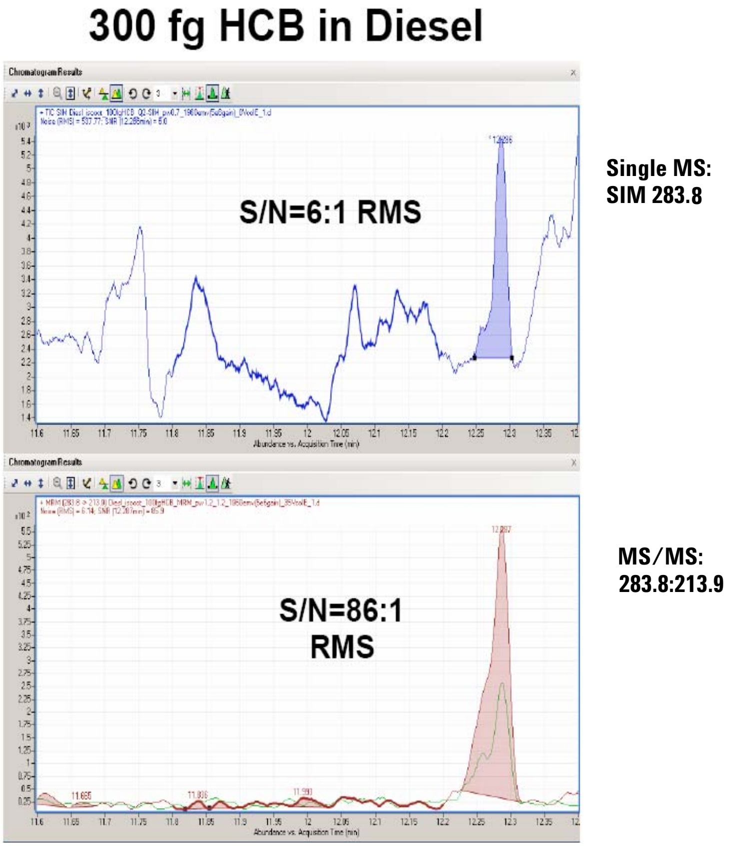


Figure 14 HCB analysis by 7000 Series Triple Quad in MRM mode

The 7000 Series Triple Quad produces clear data to help evaluate complex samples at lower levels. Figure 15 illustrates a chromatogram of multiple PCB congeners in mussel extract measured at 2 pg on-column. The resulting data provide strong signals on a flat baseline for clear data interpretation.

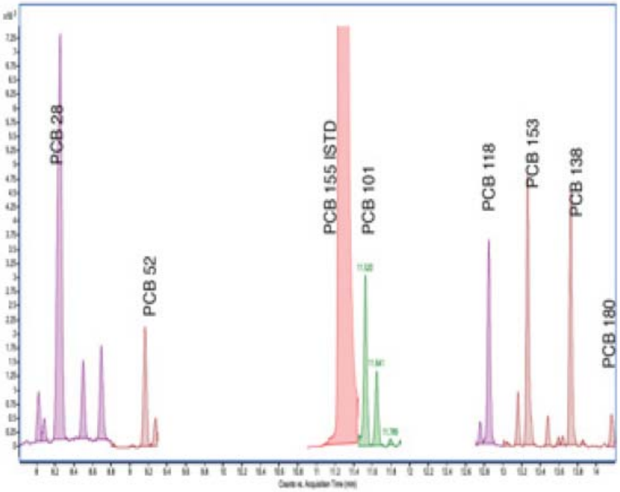
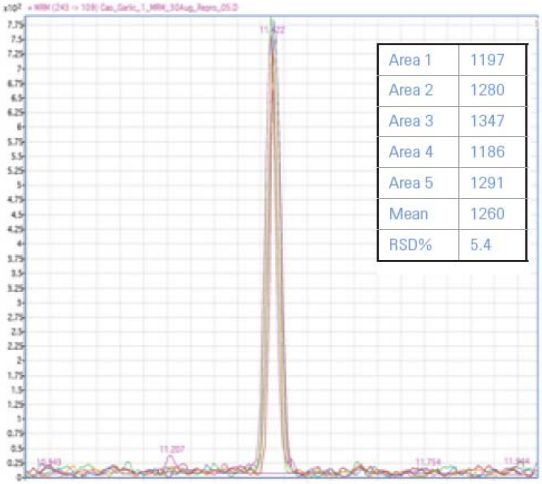


Figure 15 Detection of multiple PCBs at low detection limits

Reproducibility is an expression of how well the data agrees from test to test. Figure 16 illustrates the GC/MS results when the organophosphorous insecticide Cyanophos, spiked into garlic at 0.5 ppb, is analyzed in MRM mode. An overlay of five injections showing the quantitation transition of 243:109 *m/z* demonstrates strong reproducibility.



Area 1	1197
Area 2	1280
Area 3	1347
Area 4	1186
Area 5	1291
Mean	1260
RSD%	5.4

Figure 16 Reproducibility in 7000 Series Triple Quad data

How Each Component Works to Improve Sensitivity

This section describes in more detail how each of the components of the 7000 Series Triple Quad contributes to reducing noise (Figure 9).

Agilent 7890A GC capillary flow backflush technology

The capillary in the 7890A GC provides improved sample transmission, through its backflush technology. It is the same configuration that is used in Agilent's single quadrupole product. Through backflush, late eleuters are eliminated from the column, reducing sample contamination and the chemical noise that it creates. This technology is integral in the integrity and consistency of the MS data.

Electron impact ion source

The key components of the ion source are shown in Figure 17. The triple quadrupole uses the same front end ionization method as the single quadrupole mass spectrometer.

The EI ion source operates by electron impact ionization. Sample ions enter the source through the GC/MS interface. The sample is ionized in the ionization chamber, which is made up of the source body, repeller, and drawout plate.

A filament attached to the source body emits electrons into the ionization chamber through the guidance of a magnetic field. These electrons interact with sample molecules, ionizing and fragmenting them. The ionization source in the 7000 Series Triple Quad contains two filaments, which allows for a choice of filament depending upon tuning results.

Once the sample has been ionized, the ions are directed by the repeller through a stack of electrostatic lenses. The repeller contains a positive voltage, which pushes positive ions into the lens stack. There the ions are concentrated into a tight beam and pushed into the analyzer. Slots in the source body allow the vacuum system to pump away ions of carrier gas and unionized material as the sample ions enter the quad, thereby reducing neutral noise and improving sensitivity.

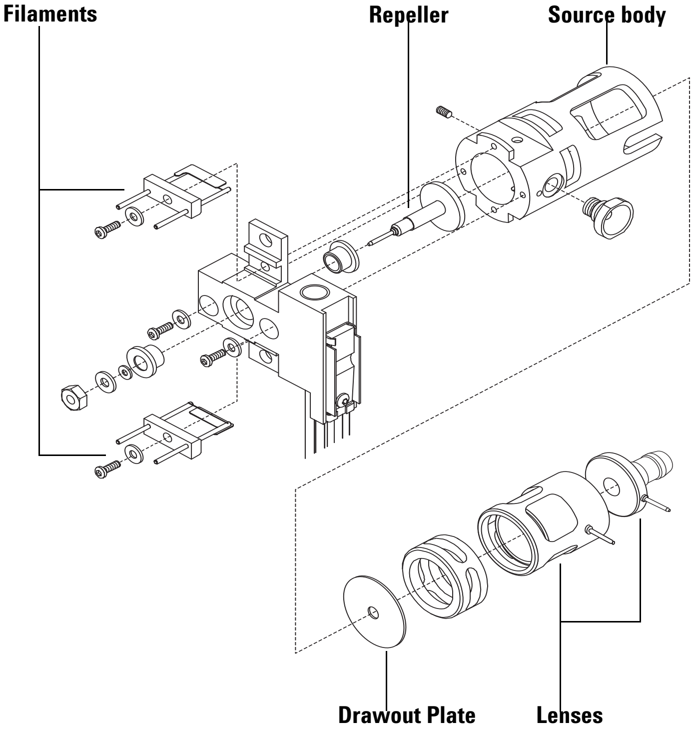


Figure 17 EI ion source

Quad mass filters

The quadrupoles consist of hyperbolic rods that optimize ion transmission and spectral resolution. The quadrupole configuration tends to generate less ion loss than circular rods.

The gold-plated quartz material allows the analyzer to operate at high temperatures and low vacuum, eliminating the contamination that occurs with lower temperatures.

Pre- and post-filters

The end section of the Q1 (MS1) quadrupole assembly also consists of short hyperbolic rods, but their RF voltages are only high enough to guide ions into the collision cell. A similar set of rods on the exit side of the collision cell are part of the Q3 (MS2) quadrupole. These short RF-only rods act as pre- and post-filters to the quads to ensure optimum ion transmission into and out of the collision cell.

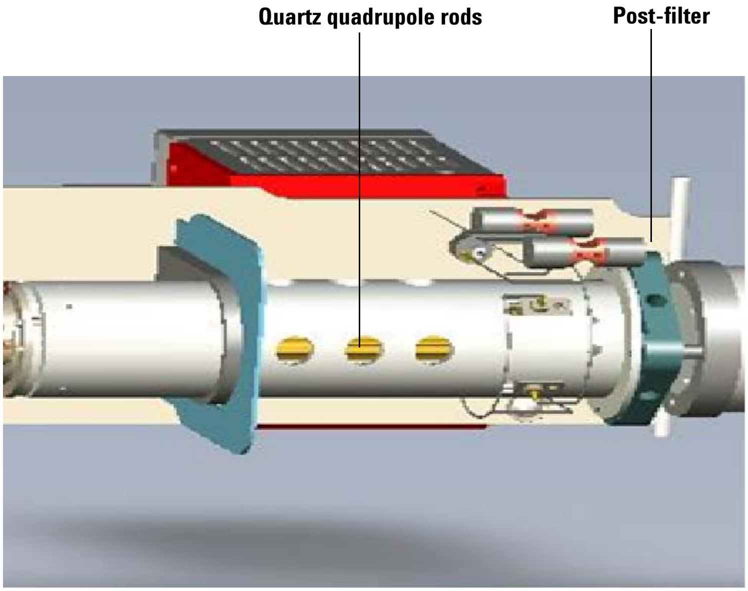


Figure 18 Q1 (MS1) quadrupole assembly

Collision cell

What is the collision cell?

The collision cell is another innovation. The collision cell collects parents of precursor ions and ion fragments, thermalizes the ion beam, and focuses the beam into the second analyzer. The collision cell is a high-pressure hexapole assembly with its linear acceleration adjusted to optimize MS/MS fragmentation while eliminating crosstalk even at very low dwell times (Figure 19).

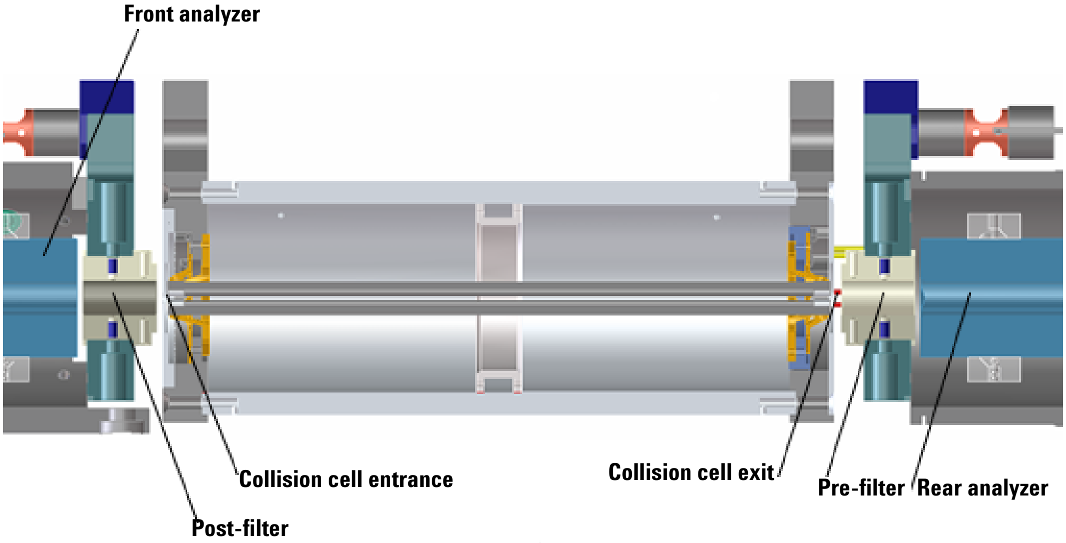


Figure 19 Collision cell technology produces higher sensitivity and faster responses without memory or cross-talk effects

The components that contribute to this higher sensitivity and faster response are:

- Small diameter hexapole collision cell
- High frequency hexapole collision cell
- Linear axial acceleration
- High pressure collision cell
- High speed digital electronics

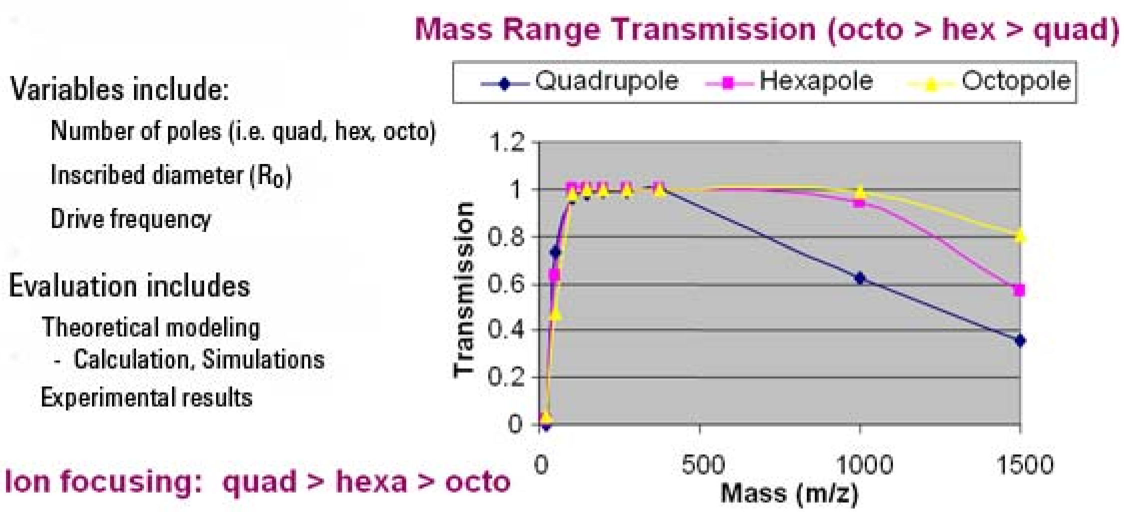
The collision cell contains nitrogen and helium. Helium has been shown by Agilent to provide more control over the fragmentation process, especially with higher mass ions. It was added to the nitrogen stream to reduce neutral noise by thermalizing metastables without letting them hit the detector. The helium is then eliminated by the vacuum pump along with carrier gas and unfragmented sample ions. The small diameter of the hexapole assembly assists in capturing fragmented ions.

Why a hexapole?

The geometry of a hexapole provides advantages in two domains: ion focusing and ion transmission (Figure 20).

- The first advantage is in ion focusing. Studies have shown that a quadrupole provides better ion focusing than a hexapole and a hexapole provides better ion focusing than an octopole. Therefore, ion focusing improves with a lower number of poles in the filter.
- The second advantage involves ion transmission across a wide mass range, or *m/z* bandwidth. In this case, the octopole is better than the hexapole, which is better than the quadrupole.

The hexapole is chosen after extensive modeling, simulation, and experimentation because it offers the best compromise between the focusing of a quadrupole and the ion transmission of an octopole.



Mass Range Transmission (octo > hex > quad)

Variables include:

- Number of poles (i.e. quad, hex, octo)
- Inscribed diameter (R_0)
- Drive frequency

Evaluation includes

- Theoretical modeling
  - Calculation, Simulations
- Experimental results

Ion focusing: quad > hexa > octo

Figure 20 Broad mass range transmission and improved transmission efficiency using a hexapole

Collision cell design

The collision cell hexapole consists of six resistively coated rods used to generate a potential difference across the length of the collision cell (Figure 21).

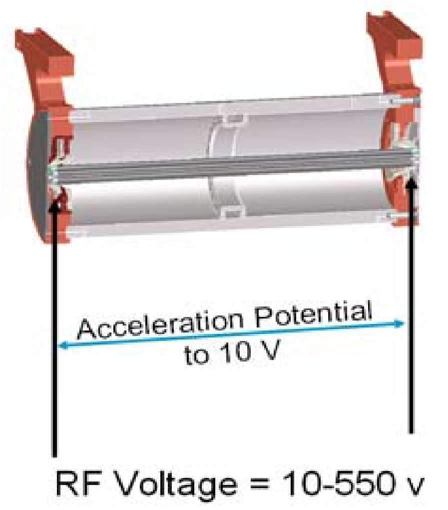


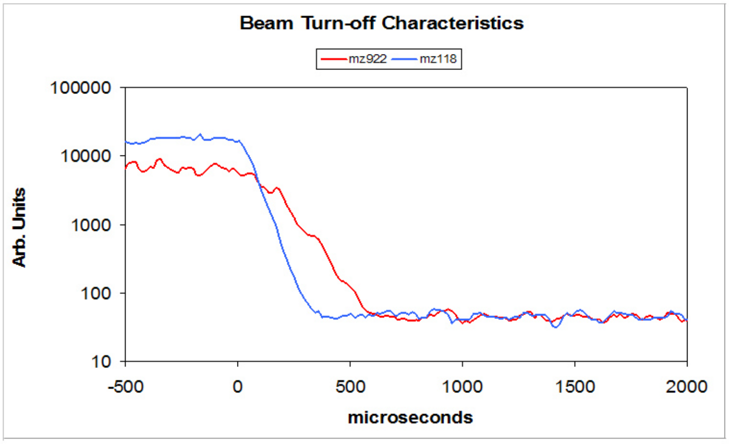
Figure 21 Collision cell design

A potential difference is always present. This ensures that the precursor ions coming from Q1 (MS1), or fragment ions generated in the collision cell, are transmitted and not allowed to drift around at random.

Sweeping out the ions in this manner avoids the issue of crosstalk, where residual product ions from a previous MRM experiment can interfere with the product ion spectrum of a subsequent MRM experiment (see Figure 22). A collision energy voltage is applied over the accelerating linear voltage to generate fragments or product ions.

Length of time for collision cell flushing

The low degree of crosstalk can be demonstrated by examining how long it takes to evacuate ions from the collision cell (Figure 22).



0 V Collision Energy 5 V Applied Axial Potential

Figure 22 Collision cell clearing profile (500 pg Alprazolam, 20 ms dwell time)

The figure illustrates a sample analysis that is typically performed with an LC triple quad MS. The model is useful to show that the higher the mass of the compound moving through the triple quad, the longer it takes to evacuate the collision cell. For example, *m/z* 922 takes about 600 µsec to evacuate the collision cell using the linear potential, while *m/z* 118 only takes 350 µsec. This also demonstrates a low degree of crosstalk since the Y axis is logarithmic, showing complete clearance of the cell. This means that an inter-scan delay of 1 msec will be more than adequate to flush the collision cell of all ions.

Detector

The detector assembly is unique to Agilent (Figure 23). It is a high-energy dynode coupled with an electron multiplier.

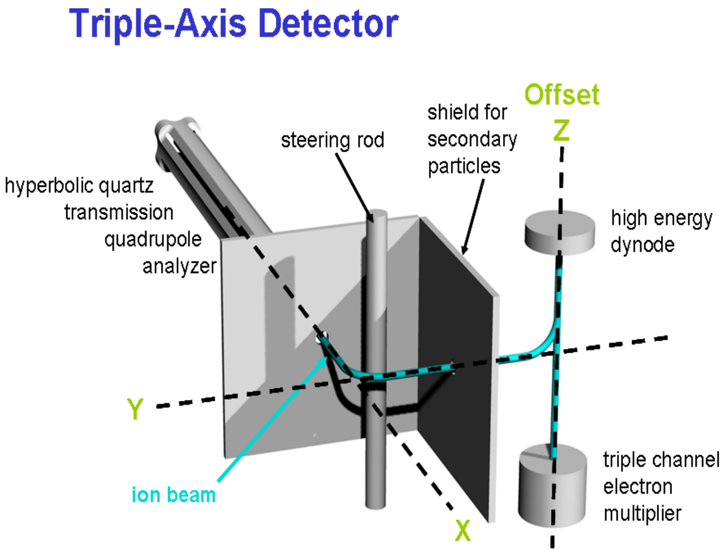


Figure 23 Detector components

The high-energy dynode is located off-axis from the center of the rear quad analyzer. This orientation reduces the possibility of neutral molecules impacting the detector while at the same time attracting the ions with high voltages. When the ion beam hits the dynode, the ions are converted to electrons before they impact the multiplier. These electrons are attracted to the more positively charged electron multiplier horn. The off-axis design of the detector allows neutrals to pass through and be eliminated by the vacuum system without hitting the detector.

The multiplier has a long lifetime since only electrons are allowed to impact it. Ions never impact its surface. Gain normalized tuning provides consistent sensitivity over the life of the electron multiplier. This also translates into consistency from MS to MS, and lab to lab.

Pumping system

A single split flow turbomolecular pump is used for the entire vacuum system. Sufficient vacuum for the entire process is achieved by partitioning the turbo pump to create multiple vacuum stages. The vacuum system removes particles of carrier gas and any unionized or unfragmented sample molecules from the ion source outlet, the collision cell, and both analyzers. This pump is backed by a single roughing (mechanical) pump (Figure 24).

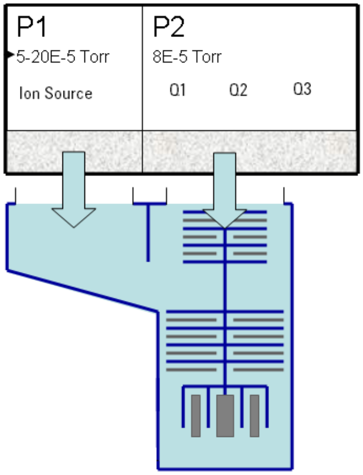


Figure 24 Vacuum system

4

Agilent MassHunter Workstation Software – Instrument Control for the 7000 Series Triple Quad

This section will help you understand the design and operation of the Agilent MassHunter Workstation Software or GC/MS Instrument Control for the 7000 Series Triple Quad.

Description

The Instrument Control program (Figure 25) has the following features:

- Showing the instrument at work through real-time plots
- Running multiple samples through the sequence table, a spreadsheet-like interface
- Controlling and monitoring instrument settings
- Tuning the instrument
- Setting up acquisition parameters for the GC and the Triple Quad
- Monitoring the chromatogram and mass spectra as samples are analyzed
- Setting up sequences of samples

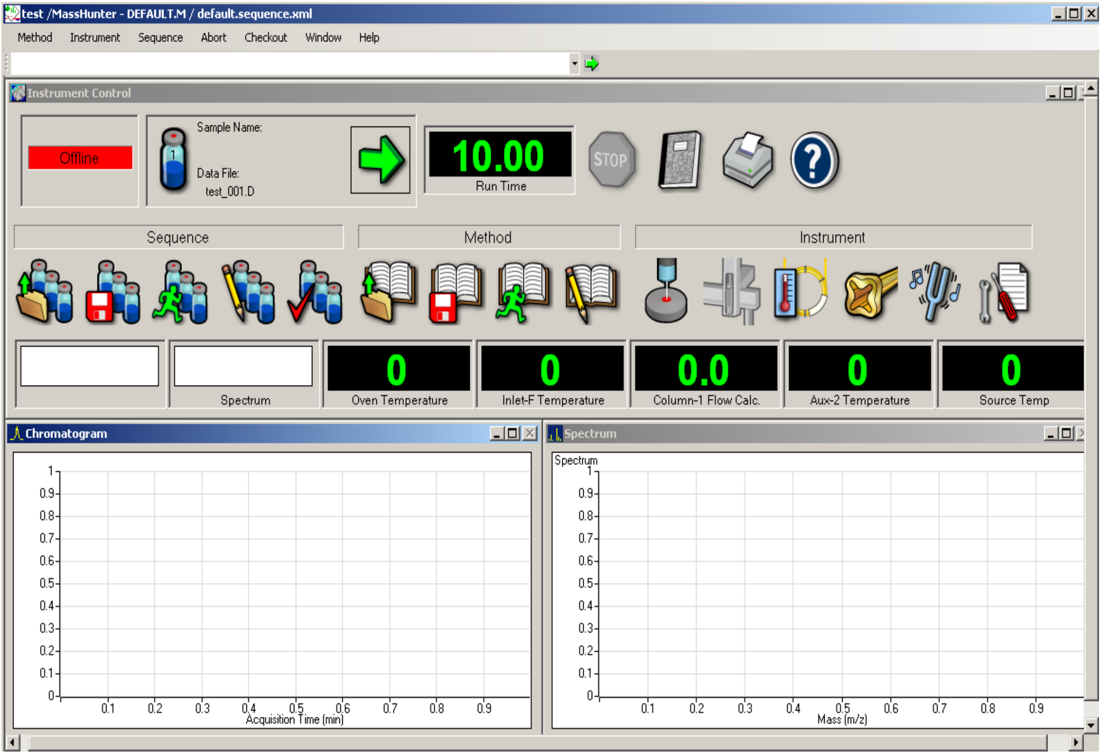


Figure 25 Instrument control

Tuning

Autotune

An autotune taking about 8 minutes can be used when an extensive tune is recommended (Figure 26). In this mode, everything is automatic. The tuning mix is delivered by the calibrant delivery system (CDS), which is switched on automatically during the tune.

Manual tune

A manual tune of user-defined ion masses with six corresponding profile masses is available.

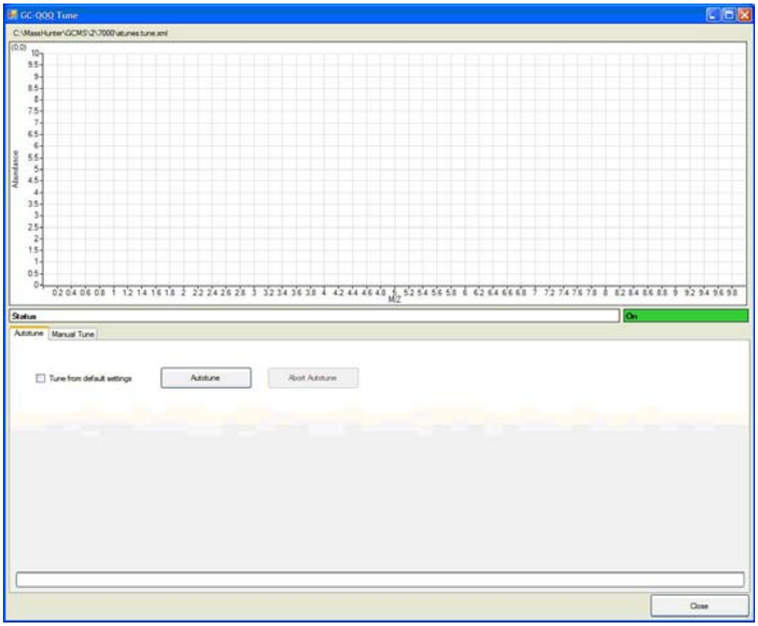


Figure 26 Autotune in progress

A Lens 2 DC voltage ramp with RF Off is shown at the top right. An automated version of this is also available for the Tuning Mix with autotune.

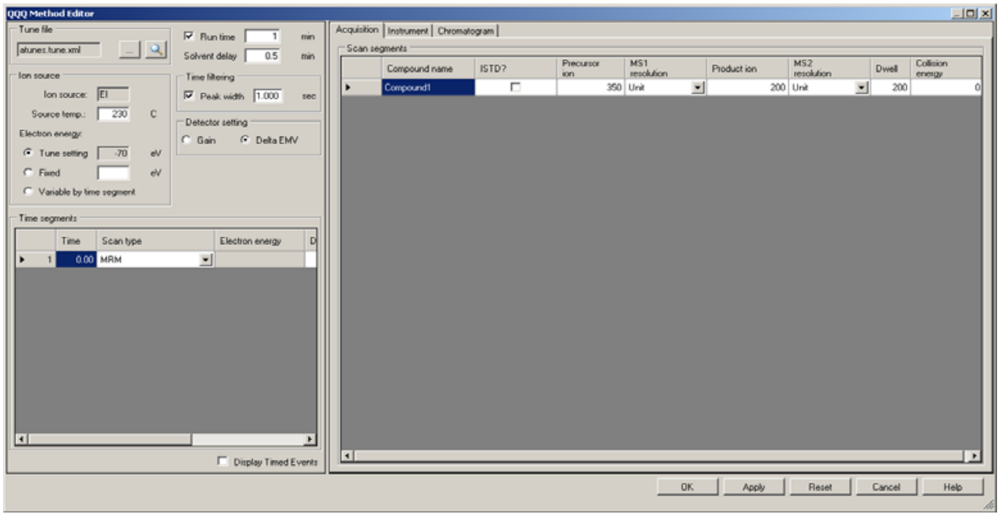
Tune reports

Tune reports are also available.

Acquisition

The 7000 Series Triple Quad GC/MS can be controlled and monitored from the Instrument Control panel, which is the window used for accessing acquisition settings and sequence lists (Figure 27, Figure 28, and Figure 29).

The real-time plot pane also can show the MS and GC results in real time.



Tune file: atunes.tune.xml

☑ Run time: 1 min
Solvent delay: 0.5 min

Ion source
Ion source: EI
Source temp.: 230 C
Electron energy:
● Tune setting: -70 eV
○ Fixed: eV
○ Variable by time segment

Time filtering
☑ Peak width: 1.000 sec

Detector setting
○ Gain ● Delta EMV

Time segments

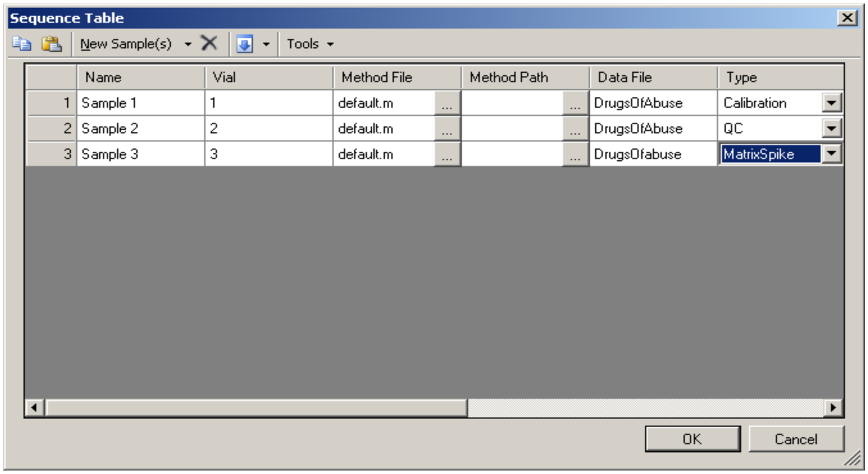
	Time	Scan type	Electron energy
1	0.00	MRM	

☐ Display Timed Events

Scan segments

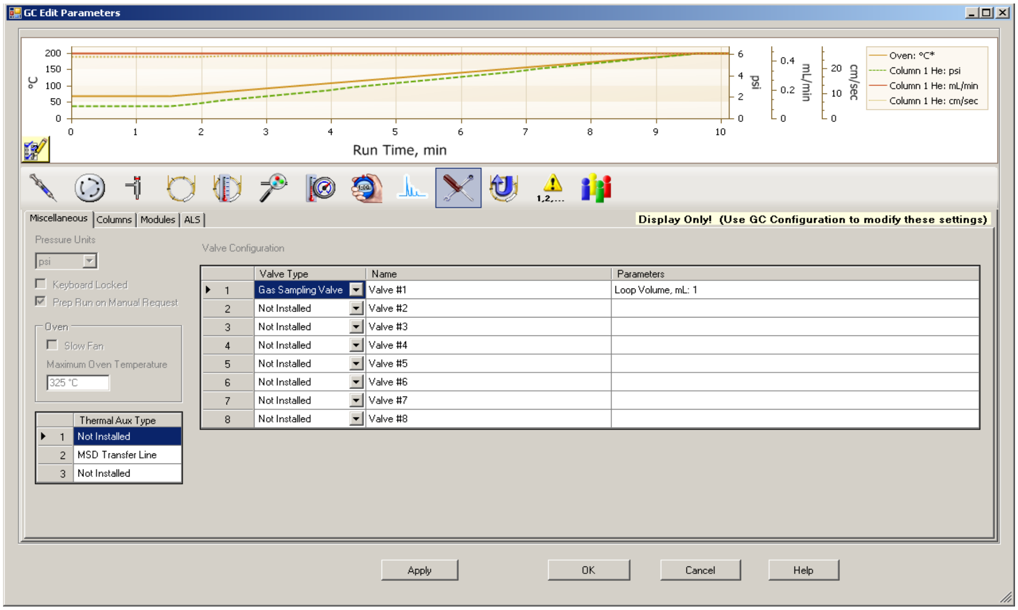
Compound name	ISTD?	Precursor ion	MS1 resolution	Product ion	MS2 resolution	Dwell	Collision energy
Compound1	☐	350	Unit	200	Unit	200	0

Figure 27 MS acquisition settings



	Name	Vial	Method File	Method Path	Data File	Type
1	Sample 1	1	default.m		DrugsOfAbuse	Calibration
2	Sample 2	2	default.m		DrugsOfAbuse	QC
3	Sample 3	3	default.m		DrugsOfabuse	MatrixSpike

Figure 28 Sequence table



Display Only! (Use GC Configuration to modify these settings)

Pressure Units: psi

☐ Keyboard Locked

☑ Prep Run on Manual Request

Oven

☐ Slow Fan

Maximum Oven Temperature: 325 °C

	Thermal Aux Type
1	Not Installed
2	MSD Transfer Line
3	Not Installed

Valve Configuration

	Valve Type	Name	Parameters
1	Gas Sampling Valve	Valve #1	Loop Volume, mL: 1
2	Not Installed	Valve #2	
3	Not Installed	Valve #3	
4	Not Installed	Valve #4	
5	Not Installed	Valve #5	
6	Not Installed	Valve #6	
7	Not Installed	Valve #7	
8	Not Installed	Valve #8	

Figure 29 GC acquisition settings

www.agilent.com

Second Edition, October 2011

Agilent Technologies