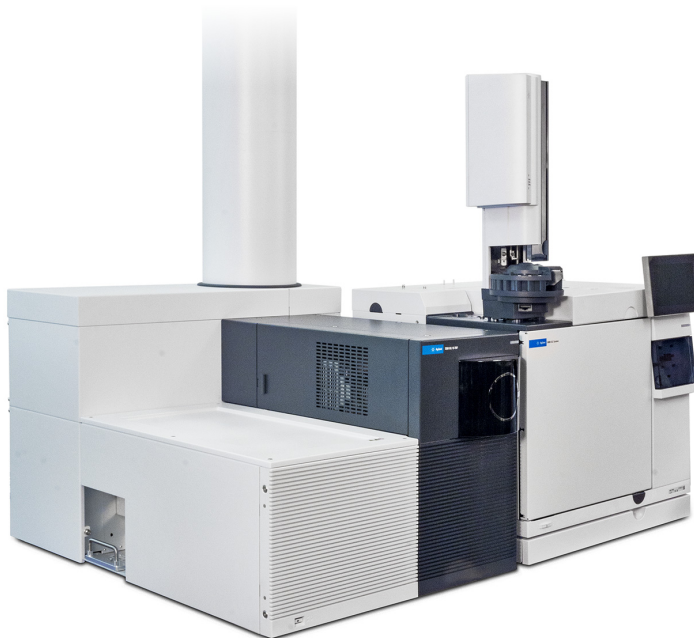


Agilent 7250 Accurate-Mass Quadrupole Time-of-Flight GC/MS System

Concepts Guide



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In This Guide...

The Concepts Guide presents “The Big Picture” behind the operation of the Agilent 7250 Accurate-Mass Quadrupole Time-of-Flight GC/MS System by helping you understand how the hardware and software work.

1 “Overview”

Learn how the 7250 Q-TOF GC/MS helps you do your job.

2 “Theory and Inner Workings”

Learn the concepts you need to understand how the 7250 Q-TOF works.

3 “Agilent 7250 Accurate-Mass Q-TOF Performance”

Learn how the 7250 Q-TOF exceeds performance measures.

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This chapter provides an overview of the Agilent 7250 Accurate-Mass Quadrupole Time-of-Flight (Q-TOF) GC/MS system, its applications, and its data analysis system.

System Description

The Agilent 7250 Accurate-Mass Quadrupole Time-of-Flight (Q-TOF) GC/MS is a stand-alone quadrupole time-of-flight mass spectrometer. It can be used with Agilent 8890 and 7890 Gas Chromatographs. The 7250 Q-TOF features:

- An independently MS-heated high efficiency, Low Energy Electron Impact (LE-EI) ion source capable of operating in standard (70 eV) or low energy (9 eV to 30 eV) modes
- Both 70 eV and 15 eV tune parameters are stored in the same tune file allowing use of both modes in different time segments for the same sample run
- Automated fast venting, that uses nitrogen to break vacuum thereby reducing the influx of air into the analyzer, resulting in lower stabilization times after pump down
- Independently MS-heated hyperbolic quadrupole mass filter, which can be heated to high temperatures, minimizing the contamination typical with low temperature analyses
- Single hexapole collision cell
- Ion-focusing slicer to improve resolution
- A 50% longer vacuum-insulated flight tube than on the 7200 Q-TOF provides increased resolution and uses a dual-stage ion mirror for improved mass accuracy
- A faster pulser than on the 7200 Q-TOF that allows extension of the mass range up to 3000 m/z
- A 5 GHz sampling rate with or without transient-level peak picking (TLPP)
- Analog detector
- Independently GC-heated GC/MS interface
- Full RoHS compliance
- Three turbomolecular vacuum pumps
- Rotary vane foreline pump
- An optional dry scroll foreline pump

The 7250 Q-TOF incorporates a hexapole collision cell blanketed with a nitrogen and helium gas mix, to improve the ion fragmentation prior to detection quantification. It also includes ion optics for focusing the ions prior to the flight tube and detector.

1 Overview

Q-TOF applications

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.

The 7250 Q-TOF can operate in either MS (TOF) mode or MS/MS mode. When operating in MS mode, the instrument can obtain high resolution, accurate mass measurements, and fast full spectrum acquisition. MS/MS mode provides high resolution, accurate mass measurements, and fast full product ion spectra with high sensitivity. These features make the 7250 Q-TOF a good tool for solving complex analytical problems, structural elucidation of unknowns, and confirmation of non-target compounds.

Q-TOF applications

The 7250 Q-TOF GC/MS combination can quantify trace organic compounds in complex matrices. The following applications use this type of quantification:

- Food safety and research
- Environmental contaminants studies
- Toxicology
- Forensics
- Metabolomics and Metabolomics
- Natural product research
- Human and animal doping studies
- Energy research and petrochemicals
- Homeland security

Paired with an Agilent 8890 or 7890 GC, the 7250 Q-TOF 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 in complex matrices
- Ability to meet stricter regulations on sample analytical limits for certain applications
- Simplified operation with Agilent's data analysis software
- Fast MS/MS operation
- Reproducible mass accuracy

The 7250 Q-TOF offers the improved sensitivity in GC/MS analysis that is required by many commercial and regulatory applications.

Instrument control software

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

Prepare the instrument

- Start and stop the instrument from the software
- Download settings to the GC and the Q-TOF in real time to control the instrument
- Evaluate if the MS parameters are within the limits to produce the specified mass accuracy and resolution with a Checktune report
- Optimize MS parameters automatically (Autotune) or manually through Agilent tuning programs and print a tune 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 centroided line spectrum of a peak or the mass range profile spectrum of a peak in real time

Set up acquisition methods

- Enter and save the acquisition method parameter values for the GC and the Q-TOF
- Select and label the total ion chromatograms (TIC) or extracted ion chromatograms (EIC) 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 run both individual samples and automated multiple samples organized in a sequence
- Set up pre- and post-scripts to run between samples in a sequence
- Set up and run a sequence to optimize MS acquisition parameters

1 Overview

Data analysis software

- Print a sequence report
- View system events, including start and stop times, run events and errors and print an event log report

Please refer to the *Agilent MassHunter Software Data Acquisition Familiarization Guides*, the *online Help* for the *Data Acquisition* program, or the *Agilent 7250 Accurate-Mass Quadrupole Time-of-Flight GC/MS Operating Manual and Agilent 7250 Accurate-Mass Quadrupole Time-of-Flight GC/MS Troubleshooting and Maintenance Manual*, that can be found in the location specified in **"Reference Documentation"** on page 13.

To learn how to get started with the Agilent 7250 Q-TOF GC/MS, see the *Quick Start Guide*.

To learn more about how to use the Agilent 7250 Q-TOF GC/MS with real samples and data, see the *Agilent 7250 Q-TOF Acquisition Familiarization Guide*.

To learn how to do individual tasks with the GC/MS, see the *Online Help*.

To learn more about your Agilent GC, see the Agilent user documentation for your specific GC model.

Data analysis software

Quantitative analysis program

Agilent has designed the MassHunter Quantitative Analysis program to help quantify very low amounts of material with the following unique features:

- Imports information directly from the acquisition method
- Provides a curve-fit assistant to test all fits and statistics on the calibration curve quality
- Integrates signals with an automated, parameter-free integrator that uses a novel algorithm, optimized for Q-TOF 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 enables the capability to create custom reports in Microsoft Excel

Please refer to the *Agilent MassHunter Software Quantitative Analysis Familiarization Guides* or the *online Help* for the *Quantitative Analysis* program that can be found in the location specified in **"Reference Documentation"** on page 13.

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 MassHunter 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.

Please refer to the *Agilent MassHunter Software Qualitative Analysis Familiarization Guides*, *Training Videos*, or the *online Help* for the *Qualitative Analysis* program that can be found in the location specified in **"Reference Documentation"** on page 13.

Reference Documentation

Available on the 7250 Q-TOF installation of the MassHunter Software User Information. This documentation application is delivered to you as part of your MassHunter Software.

- *MassHunter Familiarization Guides for GC/MS* for an introduction to data Acquisition WorkStation, Qualitative Analysis, and Quantitative Analysis program features.
- *Qualitative Analysis Training Videos* for those seeking visual and audio lessons presenting a comprehensive use of the MassHunter Qualitative Analysis Navigator and MassHunter Qualitative Workflows.
- *On-line Help* for detailed information on how Data Acquisition WorkStation, Qualitative Analysis, and Quantitative Analysis works.
- *Demo data files and libraries* that allow you to perform all the analysis steps demonstrated in various familiarization guides.
- *Quick Start Guide* explains what documentation is included in the applications and what information is on each document.

Available on the 7250 Q-TOF installation of the User Manuals and Tools DVD. This documentation application is delivered to you with your 7250 Q-TOF instrument.

- *Concepts Guide* to learn more about how the 7250 Q-TOF GC/MS System works.
- *Quick Start Guide* explains what documentation is included in the applications and what information is on each document.
- *Hardware manuals* to learn how to operate and perform maintenance on the 7250 Q-TOF.

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Reference Documentation

2

Theory and Inner Workings

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This chapter explains the inner workings of the 7250 Q-TOF GC/MS.

The 7250 Q-TOF Mass Spectrometer

The Agilent 7250 Q-TOF is an orthogonal time-of-flight mass spectrometer. It performs MS/MS using a quadrupole and a hexapole, or collision cell, prior to a flight tube and detector. The sample is first ionized by the electron impact ion source. After ionization, the ions pass through the quadrupole analyzer, which consists of four parallel hyperbolic rods through which selected ions are filtered, based on their mass-to-charge ratio (m/z). A diagram of the 7250 Q-TOF mass spec is shown in **Figure 1**.

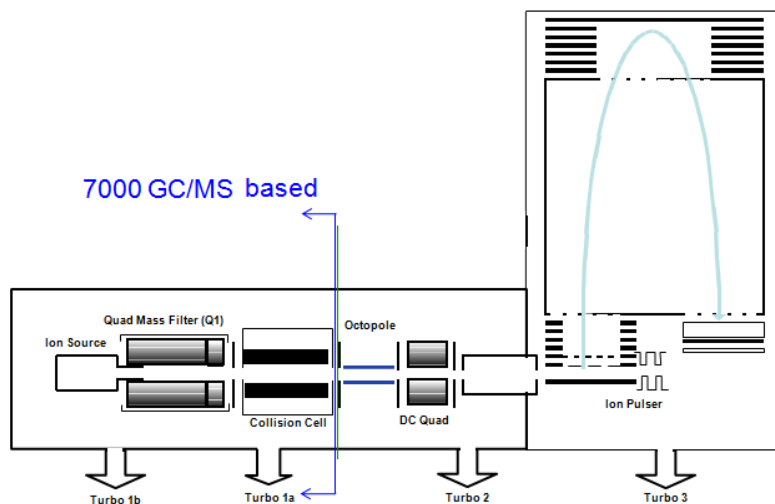


Figure 1. 7250 Q-TOF

The ions passing through the quad are then directed to the collision cell, where the entering precursor ions are further fragmented. The collision cell is a hexapole filled with a nitrogen and helium gas mix, and is designed for axial acceleration, which helps with high speed MS/MS analysis. The fragment ions, or product ions, are sent through a slicer, which helps to focus the ion stream before they are sent through a flight tube to the detector.

The acceleration pulse applied to send the ions up the flight tube is orthogonal to the direction that the ions are leaving the mass analyzer. This geometry minimizes the effect of the entrance velocity on the flight time, leading to higher resolution. Once the ions reach the end of the flight tube, they bounce off a

2 Theory and Inner Workings

The 7250 Q-TOF Mass Spectrometer

reflector, or dual-stage ion mirror, and travel in a reverse path back down to the bottom of the tube. The analog detector is located at the bottom of the flight tube.

The detector sends an analog voltage, proportional to the ion abundance as a function of time, to the 7250 data acquisition system. Here the analog signal is digitized and converted by an embedded microcomputer to a mass spectrum. This converted data is sent to the MassHunter software for data collection and analysis.

Sample Ionization Technology

In GC/MS, before the sample can be analyzed, it must be ionized in the ion source.

Electron impact ionization

In electron impact ionization mode, the sample stream enters an EI ion source from the GC/MS interface. Electrons emitted from a filament are guided by a magnetic field axially along with the ion beam. The high-energy electrons interact with the sample molecules, ionizing and fragmenting them. The positive voltage on the repeller pushes the positive ions into the lens stack, where they pass through several electrostatic lenses. These lenses concentrate the ions into a tight beam, which is directed into the quadrupole mass filter.

The 7250 Q-TOF ion source has two modes of ionization, 70 eV for classical fragment libraries and 15 eV for low energy ionization.

LE-EI ion source

The 7250 Q-TOF uses the an improved version of the high efficiency ionization source (HES) first used in the Agilent single and triple quadrupole mass spectrometers.

Agilent's HES technology provides a greater than 10 to 20 fold increase in ion creation relative to sources that ionize compounds in a orthogonal plane to the ion beam.

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 filament block containing the filament and a focusing lens.

A filament attached to the filament block emits electrons into the ionization chamber through the guidance of a strong magnetic field. These electrons interact with sample molecules, ionizing and fragmenting them. The long-lifetime, low-current filament in the EI ionization source of the 7250 Q-TOF is designed for easy replacement.

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

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LE-EI ion source

tight beam and pushed into the analyzer. Slots in the source body allow the vacuum system to pump away carrier gas and un-ionized material as the sample ions enter the quad, thereby reducing neutral noise and improving sensitivity.

Source body

The cylindrical ion source body holds the lens stack, and along with the repeller and the filament block, forms the ionization chamber. The ionization chamber is the space where the sample molecules are ionized. Slots in the source body help the vacuum system pump away carrier gas and un-ionized molecules.

Filament

The filament is located on the filament block. The filament carries an adjustable AC emission current. The emission current heats the filament causing it to emit electrons, which ionize the sample molecules. In addition, the filament has an adjustable DC bias voltage. The calibration of this voltage and the electron extractor lens voltage establishes the energy of the electrons. The filament shuts off automatically if there is a general instrument shutdown. The high efficiency of the 7250 ion source requires less emission current to produce a desired ion abundance.

Filament emission current

The filament emission current (Emission) has a typical operating range between 0.5 μA and 20 μA , with the maximum emission current at 40 μA .

Electron energy

The electron energy is the amount of energy on the ionizing electrons. It is determined by the bias voltage; 70 VDC bias on the filament causes emitted electrons to possess 70 eV (electron volts). This value is adjustable from 70 to 200 eV, but for classical operation, set this parameter to 70 eV. For low energy EI this value is typically set from 12 eV to 15 eV.

Magnet

A strong magnetic field directs the electrons emitted by the filament into and across the ionization chamber. The magnet assembly uses permanent magnets with a charge of 800 gauss in the center of the field.

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LE-El ion source

Repeller

The repeller forms one wall of the ionization chamber. A positive charge on the repeller pushes positively charged ions out of the source through a series of lenses. The repeller voltage is typically set by autotune.

Extractor lens assembly

The extractor lens assembly forms another wall of the ionization chamber. The ion beam passes through a hole in the extractor lens. The assembly has longitudinal slots, that align with the slots in the source body, to allow carrier gas and un-ionized molecules to be pulled away by the vacuum system.

Ion focus

The voltage on the ion focus has an operational range from -50 to -200 VDC. In general:

- Increasing the ion focus voltage improves sensitivity at lower masses.
- Decreasing the ion focus voltage improves sensitivity at higher masses.
- Incorrect ion focus adjustment results in poor high mass response.

Entrance lens

The entrance lens is at the end of the ion source, prior to the entrance of the quadrupole mass filter. This lens minimizes the fringing fields of the quadrupole, which discriminate against high-mass ions. There is a permanent +4.4 volt voltage added to the entrance lens. The total voltage applied to the entrance lens is the sum of the entrance lens offset and entrance lens gain and the +4.4 volt permanent offset. Entrance lens voltage = +4.4 VDC + offset + (gain × mass).

Quadrupole Collision Cell MS/MS Technology

Quadrupole filtration

Understanding the operation of a single quadrupole provides insight into some of the features of a 7250 Q-TOF GC/MS system. This section reviews the fundamentals of a single quadrupole mass spectrometer.

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

As described in the previous section, the ionization of a sample occurs in the ion source. The ions are filtered by a mass analyzer that controls the motion of the ions as they travel out of the analyzer. In the case of a single quadrupole MS, the ions will travel to the detector to be converted into analog signals (**Figure 2**). In Q-TOF MS, an additional component (collision cell) is employed downstream of the quadrupole to enable ion fragmentation prior to the time-of-flight detection.

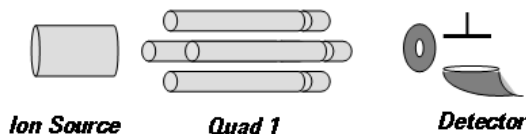


Figure 2. Schematic for single quadrupole mass spectrometer

The quadrupole mass analyzer consists of four parallel rods to which specific DC and RF voltages are applied. These rods filter out all ions except those of one or more particular mass-to-charge ratios, 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 a detector, in this case, the flight tube. As the voltages are altered, 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.

2 Theory and Inner Workings

Quadrupole filtration

A conceptual model can be used to explain the theory of a single quadrupole mass spectrometer. See **Figure 3**.

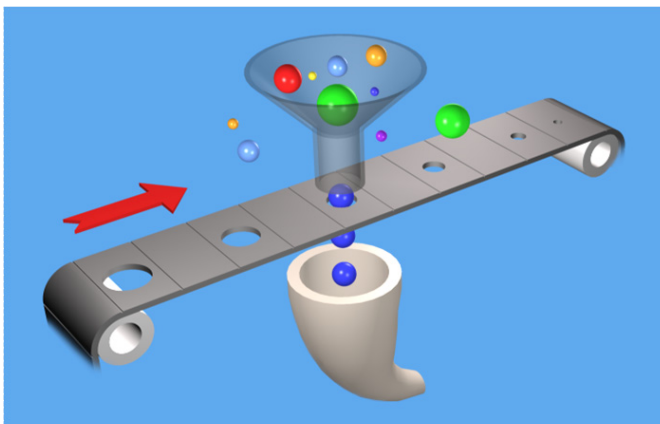


Figure 3. Conceptual model of a single quadrupole mass spectrometer

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, and are fragmented and focused before they are sent to the flight tube.
- The collecting funnel below the filtering belt represents the focusing electronics prior to the flight tube.

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 scan to a specific mass range (for example, m/z 50 to 1000) or to dwell on one selected ion (SIM) or to dwell on several selected ions during the scan period. The

2 Theory and Inner Workings

Quad mass filter

quadrupole mass filter is not scanned over a range in the SIM mode. The required RF/DC voltages are set to filter a single mass for a specified dwell time before moving to the setting for the next SIM.

The ions that pass through the quadrupole can either be measured by a detector, or sent through additional filtering methods for MS/MS analysis.

Quad mass filter

The quadrupole consist of hyperbolic rods that optimize ion transmission. 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-filter

The end section of the 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 is found on the exit side of the collision cell. These short RF-only rods act as filters to ensure optimum ion transmission in and out of the collision cell.

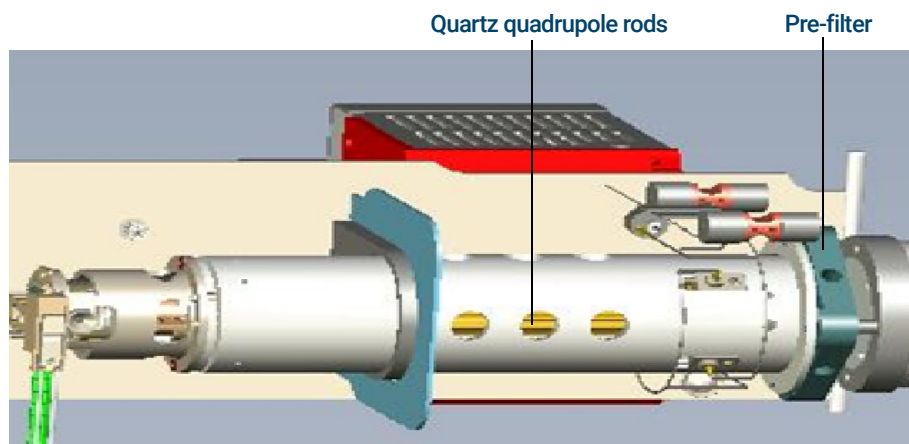


Figure 4. Quadrupole assembly

Ion fragmentation and collision cell technology

As charged ions move through the analyzer chamber, they can collide with each other and with the gas molecules present throughout the region. When the voltages increase along their path, ions have more translational energy, which causes fragmentation as they collide.

Because fragmentation patterns provide information about the original ions, a collision cell can be used to purposely fragment the ions that pass through the analyzer. These ions are called precursor ions, and their fragments are called product ions. The quadrupole can be tuned to select which precursor ion travels to the collision cell. Analysis of their product ions by the detector provides a means of chemical (analyte) identification of the precursor molecule.

Different types of collision cells can be used. The cell can be another quadrupole, a hexapole (six rods like the one used in the 7250 Q-TOF), 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 quadrupole to accelerate the movement of all of the ions so that their collision energy is sufficient to cause fragmentation.

In the collision cell, a potential difference along the length of the cell ensures that the precursor ions coming from the quadrupole or fragment ions generated in the collision cell are transmitted and not allowed to drift around at random, which helps to focus the ion stream before it is sent to the flight tube.

Collision cell

The collision collects precursor ions selected by the quadrupole mass filter and fragments them. The resulting product ions are transmitted to the flight tube. In the 7250 Q-TOF, 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. The small diameter of the hexapole assembly improves fragmentation.

The collision cell contains a nitrogen and helium gas mix, which is eliminated by the vacuum pump along with any remaining carrier gas. The small diameter of the hexapole assembly assists in colliding fragmented ions.

2 Theory and Inner Workings

Collision cell

Why a hexapole?

The geometry of a hexapole provides compromise to competing performance issues:

- Ion focusing improves with a lower number of poles in the filter. Studies have shown that a quadrupole provides better ion focusing than a hexapole and a hexapole provides better ion focusing than an octopole.
- Ion transmission improves with a higher number of poles in the filter 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 was chosen after extensive modeling, simulation and experimentation because it offered the best compromise between the focusing of a quadrupole and the ion transmission of an octopole.

Collision cell design

The collision cell hexapole consists of six resistively coated rods. A 5V potential difference established across the length of the collision cell (**Figure 5**) ensures that the precursor ions coming from the quadrupole, and the fragment ions generated in the collision cell, are transmitted and not allowed to drift around at random.

An additional voltage is superimposed to establish an appropriate collision energy for fragmentation.

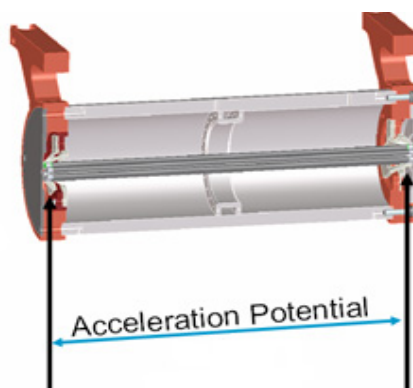


Figure 5. Collision cell design

2 Theory and Inner Workings

Collision cell

Length of time for collision cell flushing

A low degree of crosstalk can be demonstrated by examining how long it takes to evacuate ions from the collision cell. (See [Figure 6](#).)

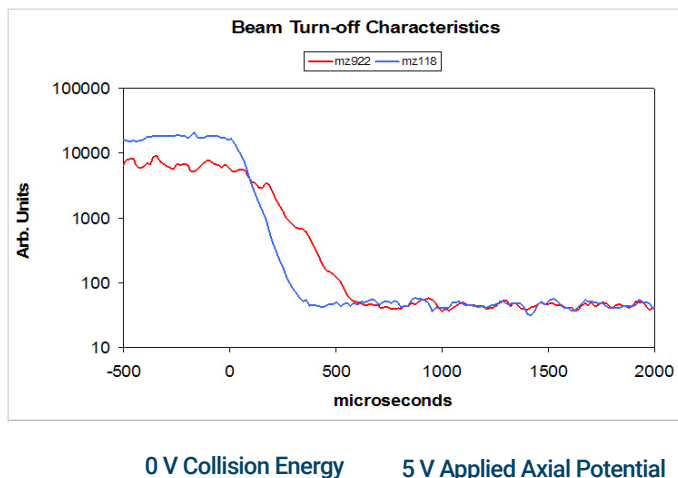


Figure 6. Collision cell clearing profile (500 pg Alprazolam, 20 ms dwell time)

The figure shows that the higher the mass 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 the low degree of crosstalk since the Y axis is logarithmic, showing complete clearance of the cell. This means that an inter-scan delay of 5 msec will be more than adequate to flush the collision cell of all ions.

Time-of-Flight MS Operation

The previous section discusses the theory behind ion separation using quadrupole mass spectrometry, and fragmentation with a collision cell. In quadrupole time-of-flight (Q-TOF) mass spectrometry, these methods are used for preliminary ion separation prior to detection at the end of the flight tube. Time-of-flight mass spectrometry measures the time it takes for ions to travel a known distance, and using this time value, determines the mass-to-charge ratio of the ions.

Ions are accelerated through a flight tube by an electric field. This acceleration results in an ion having the same kinetic energy as any other ion that has the same charge. The velocity of the ion depends on the mass-to-charge ratio. The time that it subsequently takes for the particle to reach a detector at a known distance can be measured. This time will depend on the mass-to-charge ratio of the particle (heavier particles reach lower speeds). From this time and the known experimental parameters, one can find the mass-to-charge ratio of the ion using the following relationships:

$$KE = 1/2 m v^2$$

$$v = d/t$$

$$t = m^{1/2} * d/(2KE)^{1/2}$$

Where **KE** = Kinetic Energy, **v** = velocity, **m** = mass, **d** is the distance traveled by the ion, and **t** is the time it takes for the ion to travel the distance **d**.

We can assume that the $d/2KE$ term of the above equation remains constant. Therefore, the mass of the particle can be determined by measuring the time the particle takes to travel the flight tube.

Consider the Q-TOF model in **Figure 1** on page 16. Ions that have been selected in the quadrupole, and fragmented in the collision cell are sent to the flight tube, where they are sent in an orthogonal direction up the tube. This means that they are sent in a direction perpendicular to their flight through the quadrupole and collision cell. The orthogonal direction minimizes the effects of ion generation and transmission on mass measurement and provides a uniform initial condition (approximately zero transverse velocity) for the ions being launched down the flight tube. Prior to launch down the flight tube, the nearly parallel beam of ions also passes through a slicer, a narrow slit that further discriminates the ion beam and constrains initial conditions.

The ion pulser is a stack of plates, each one (except the bottom-most plate) with a center hole. The ions pass into this stack from the side just above the bottom-most plate. To start the flight of the ions to the detector, a high voltage

2 Theory and Inner Workings

Proprietary INVAR flight tube

(HV) pulse is applied to the bottom-most plate. The applied pulse repels the ions and accelerates them through the stack of pulser plates, acting as a rapid-fire ion gun.

The charged plates of the pulser send the charged ions through the flight tube, which is about 1.5 m in length. Changes in temperature and humidity can alter pulse electronics. In addition, any collision of an ion with residual gas slows the ion on its path to the detector and affects the accuracy of the mass calculation. Therefore, the flight tube should be maintained at constant temperature and vacuum.

Proprietary INVAR flight tube

The 7250 Q-TOF flight tube is about 1.5 m in length and maintains vacuum pressure of about 10^7 Torr. It is vacuum insulated throughout the length of the tube. This eliminates the ion scatter that can occur at higher pressures and the temperature fluctuations that can change the flight distance of the ions. In addition, changes in temperature and humidity can change flight distance. The insulated flight tube helps minimize these effects and increase measurement accuracy.

The dual stage ion “mirror” at the end of the flight tube reflects the ions towards the detector. As it reflects, it refocuses the ions and minimizes the kinetic energy variations in arrival time. Ions with higher kinetic energies will penetrate further into the mirror, traveling a greater distance, helping them to reach the detector simultaneously. This reduces the variability in measurement and results in higher resolving power. Since the ions entered the ion pulser with a certain amount of forward momentum orthogonal to the flight direction in the flight tube, when they reflect off the mirror, they never return to the ion pulser, but reach the ion detector, as shown in **Figure 1** on page 16.

Detector

The detector records the ion abundance as a function of time for ions arriving at the detector. Fast electronics allow high sampling rates, and many data points within a given mass spectrum.

At the surface of the ion detector is a microchannel plate (MCP), which is a very thin plate containing a set of microscopic tubes that pass from the front surface to the rear of the plate. When an ion hits the front surface of the MCP, an electron escapes and begins the process of electrical signal amplification. As freed

2 Theory and Inner Workings

Detector

electrons collide with the walls of the microscopic tubes, an ever-increasing cascade of electrons travels to the rear of the plate. Roughly 10 times more electrons exit the MCP than incoming ions contact the surface.

These electrons are then focused onto a scintillator, which, when struck by electrons, produces photons. The photons from the scintillator are focused through two small lenses onto a photocathode in a photomultiplier tube (PMT). The photocathode converts photons back to electrons, and the electrons are subsequently multiplied by secondary emission in the dynode stage of the PMT. The electrical signal emanating from the PMT is read by the data acquisition system.

One benefit of converting from electrical current to photons and then back again to electrons is that the high DC bias voltage required at the MCP (typically -7000 V) can be electrically isolated from the data acquisition system, which typically remains at ground bias potential.

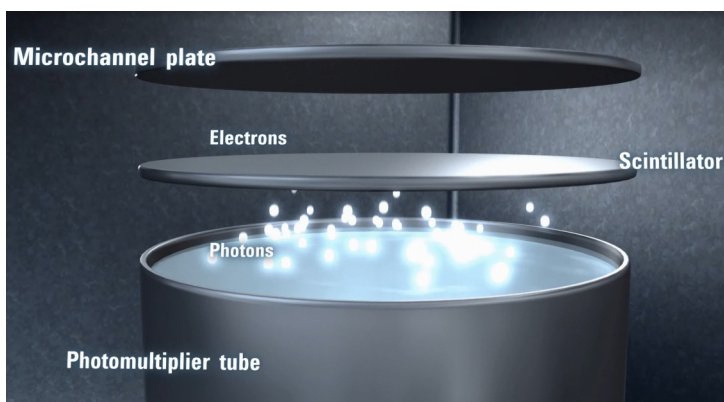


Figure 7. The process of conversion of electrons to photons by the scintillator

Pumping system

The vacuum system is a five-stage pumping system created by one split-flow and two additional turbomolecular pumps (see **Figure 8**) and a single foreline (roughing) pump. The vacuum system removes particles of carrier gas and any un-ionized molecules from the ion source outlet, the collision cell and the analyzer. In addition, it creates the constant low pressures necessary to focus the ions and propel them through the 1-meter flight tube with minimal ion scatter.

Vacuum quality affects mass accuracy, resolution, and overall data quality, because ion collisions with residual gas can alter the flight time of the ion as well as produce unwanted fragmentation. Accurate mass calculation depends upon accurate flight times. Therefore, the background gas pressure in the flight tube is very low and very consistent.

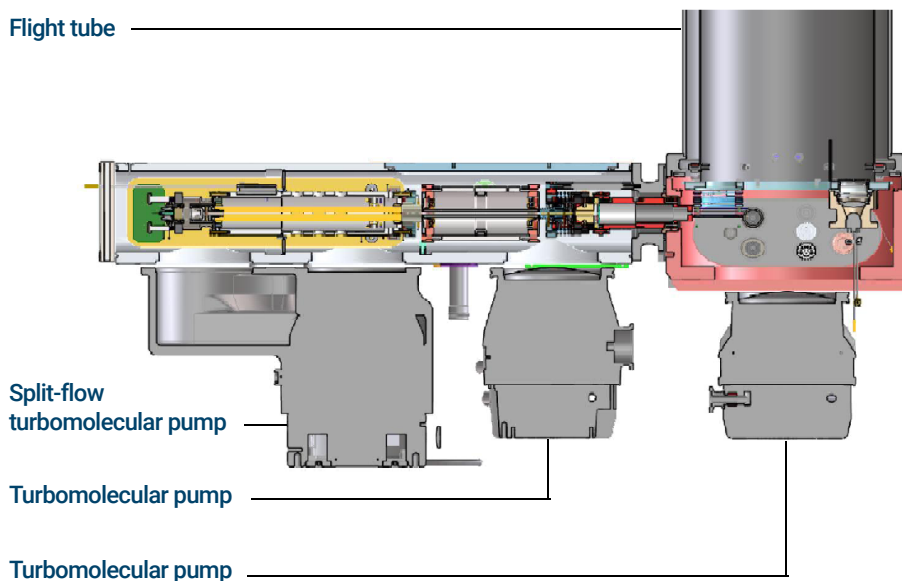


Figure 8. Vacuum system

Agilent 7250 Accurate-Mass Q-TOF Performance

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This chapter shows how the Agilent 7250 Accurate-Mass Q-TOF GC/MS reduces chemical and electronic noise and how each component contributes to enhanced instrument performance.

How the 7250 Q-TOF Meets Performance Measures

There are several performance standards for the 7250 Q-TOF GC/MS. The most important are:

- Resolving power
- Mass accuracy
- Scan speed
- Sensitivity
- Dynamic range

Resolving power

Resolving power in mass spectrometry refers to the ability to distinguish between two peaks of slightly different mass-to-charge ratios (m/z) in a mass spectrum. High resolving power enables improved mass measurement accuracy and charge state identification of multiple charged ions, which leads to better compound identification. The vacuum-insulated flight tube and dual-stage ion mirror in the 7250 Q-TOF GC/MS provides consistently high resolution.

Mass accuracy

Mass accuracy is the ability with which the analyzer can accurately provide m/z information. In mass spectrometry, this is a function of stability and resolution. This performance standard is important because accurate mass detection reduces the risk of effort invested on the wrong molecule. The high sampling rate and multiple ion event data provided by the 5 GHz data acquisition system lead to highly accurate mass identification.

Scan speed

The scan rate of a mass spectrometer refers to how fast it samples the ion beam, that is, how many individual transients are compiled to produce a composite mass spectrum. Similarly, the spectral data acquisition rate (typically 1 Hz - 50 Hz or greater) sets the number of composite mass spectra acquired in a given interval of time. This is important for chromatography applications where at least one composite mass spectrum must be acquired in a time period less

3 Agilent 7250 Accurate-Mass Q-TOF Performance

Sensitivity

than the elution time of the chromatographic peak. Ideally, a minimum of 10 mass spectra are acquired for a single chromatographic peak. The fast electronics of the 7250 Q-TOF provides a maximum data acquisition rate of about 50 Hz. The number of transients used to compile a composite spectrum is dependent upon the mass range selected. Using a standard mass range of 20 - 1200 m/z , approximately 10,000 transients per second are acquired, i.e. approximately 10,000 transients at a spectral acquisition rate of 1 Hz and 200 transients at a spectral acquisition rate of 50 Hz. Each transient collected can contain up to 100,000 data points. The ability to acquire a mass spectrum comprised of many rapidly acquired individual data collection transients enhances data integrity by improved ion statistics.

Mentioned above, the number of acquired transients used to construct a mass spectrum is related to mass range for a given experiment. The mass (m/z) ranges available on the 7250 are:

- **Standard** 20-1200 m/z acquiring 9591 transients/spectrum
- **Low** 20-650 m/z acquiring 13091 transients/spectrum
- **Extended** 20-3000 m/z acquiring 6132 transients/spectrum

Sensitivity

Sensitivity in MS data is affected by many factors that include spectral acquisition rate, mass range, 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 of the 7250 with the LE-EI ion source is nearly an order-of-magnitude greater than the previous generation EI source, based on m/z 272 of OFN. In addition, the high separation, focusing, and fragmentation levels achieved by the quadrupole and collision cells, as well as the elimination of contaminants prior to the flight tube by the slicer and pumping systems, help to contribute to the high data integrity of the 7250 Q-TOF GC/MS.

Dynamic range

Dynamic range is a measure of the detection range of a detector and data acquisition system and describes the range of signal intensities over which accurate masses can be determined. It is the ratio of the largest to smallest detectable signal. The 7250 Q-TOF data acquisition system has an improved dynamic range, when compared to the 7200 Q-TOF.

3 Agilent 7250 Accurate-Mass Q-TOF Performance

7250 Accurate-Mass Q-TOF Design

7250 Accurate-Mass Q-TOF Design

In the design of the 7250 Q-TOF GC/MS, the performance measures were addressed within all stages of instrumentation, from the ion source to the detector.



Figure 9. 7250 Q-TOF performance

- 1 LE-EI ion source includes repeller, ion volume, high sensitivity extraction lens and filament.
- 2 Analyzer uses a hyperbolic quadrupole to optimize ion transmission and spectral resolution.

3 Agilent 7250 Accurate-Mass Q-TOF Performance

7250 Accurate-Mass Q-TOF Design

- 3 ADC electronics provide high sampling rates, improving resolution, mass accuracy, and sensitivity for low-abundance samples.
- 4 Dual-stage ion mirror improves second-order time focusing in the flight tube by extending the ion flight time provides high mass resolution.
- 5 Proprietary INVAR flight tube is 50% longer than previous model. It is vacuum-insulated and eliminates thermal mass drift from temperature changes, providing high mass accuracy and resolution.
- 6 Analog detector and high speed data acquisition system provides simultaneous high resolution and wide linear dynamic range.
- 7 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.
- 8 Vacuum system incorporating the use of three turbomolecular pumps efficiently eliminates neutral materials prior to the detector.

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7250 Accurate-Mass Q-TOF Design

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