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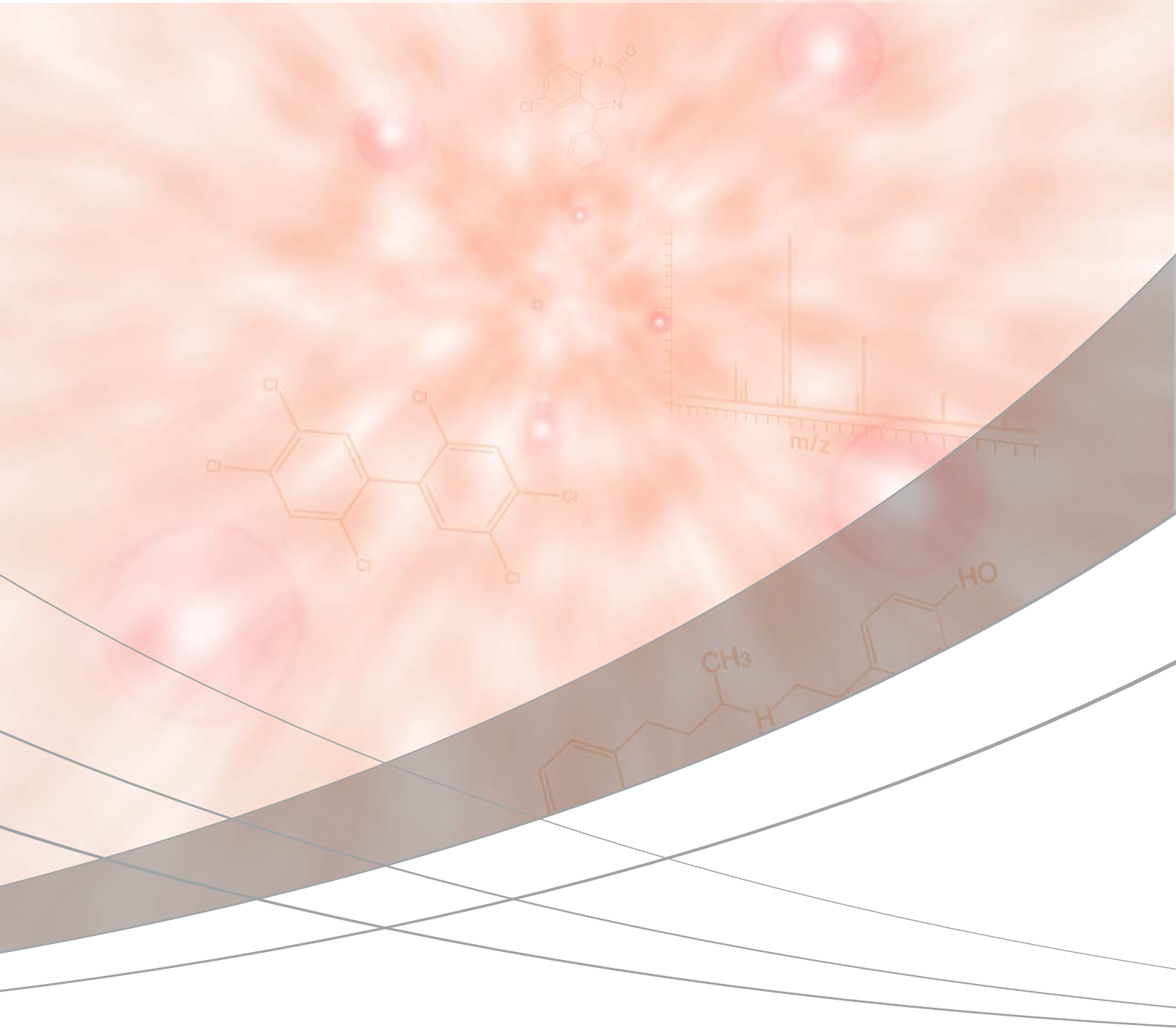
SHIMADZU

Excellence in Science

C10G-E080

Shimadzu's Fundamental Guide to

Gas Chromatography Mass Spectrometry (GCMS)



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MILESTONES FOR GAS CHROMATOGRAPHY & GAS CHROMATOGRAPHY MASS SPECTROMETRY (GC & GCMS)

Shimadzu Corporation focus on analytical and measuring instruments, medical systems, aircraft equipment and industrial machinery. Together with our global partners, we diligently strive to be a company that meets the challenges faced by society and develop products which contribute to the growth of industries and the enrichment of peoples' lives.

1875 — **Genzo Shimadzu Sr.** founds Shimadzu Corporation

1956 — **GC-1A**
Shimadzu's 1st GC system

1970 — **GCMS-9000**
Shimadzu collaborated with LKB, Sweden to produce the world's 1st magnetic sector GCMS.

1981 — **GC-8A**
Simple, Reliable and Compact GC

1982 — **GCMS-QP1000**
Quadrupole MS

1993 — **GCMS-QP5000**
Bench-top GCMS

2001 — **GC-2014**
Excellent performance and expandability to support all analysis

2004

2009 — **GC-2010 Plus**
The new Advanced Flow Technology enables high separation capability and fast analysis

GCMS-QP2010 Series
GCMS-QP2010
GCMS-QP2010 S
GCMS-QP2010 Plus
GCMS-QP2010 Ultra®
GCMS-QP2010 SE

2010 — **GC-2025**
Low environmental impact with high performance capabilities for capillary analysis

2012

GCMS TQ® Series

GCMS-TQ8030
Shimadzu's 1st GC-MS/MS Triple Quadrupole System

GCMS-TQ8040
Smart Productivity, Smart Operation and Smart Performance

GCMS-TQ8050
Enhanced SensitivityLeads to New GC-MS/MS Possibilities

2013 — **GC-2010 Plus Tracera**
The inclusion of a highly sensitive BID detector for ultra-trace analysis

2015

GCMS-QP2020
Delivering Smart Solutions

2016

2017 — **Nexis GC-2030**
The Next Industry Standard

NX model for GCMS-QP2020, GCMS-TQ8040 & GCMS-TQ8050
Nexis being the front-end GC

2018

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GC/GCMS Product Specialist
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Marketing Innovation Centre

Shimadzu produced our first Gas Chromatography Mass Spectrometry (GCMS) system in 1970 and has a long-standing history of GCMS technologies. With the current analytical trends and developments, we continue to pioneer new frontiers for GCMS. Notably, with our 2018 launch of NX model of the GCMS Series, Shimadzu aims to achieve superior performance, enhanced sensitivity, durable hardware and reliable operation for all our users and their applications.

We are thrilled to introduce our first-ever GCMS Fundamental Guide. This guidebook is part of Shimadzu' s Primer Series and aims to deepen your understanding on the essential GCMS principles. GCMS is essentially two pieces of technology, GC and MS, integrated together seamlessly. You could expert to learn not one but two sets of principle, and how they complement each other. This guidebook further illustrates our long history and innovative developments and serve as an excellent source of information for practical application tips.

We would like to express our gratitude for your eagerness to learn more about GCMS and taking the time to read this primer. We sincerely wish that it exceeds your expectation and provides you with a good foundation for GCMS.

Table of Contents

Abbreviations

APCI	Atmospheric Pressure Chemical Ionization
API	Atmospheric Pressure Ionization
APPI	Atmospheric Pressure Photoionization
CID	Collision-induced Dissociation
CLAM	Clinical Laboratory Automation Module
DUIS	Dual Ion Source
EI	Electron Ionization
ESI	Electrospray Ionization
GC	Gas Chromatography
GCMS	Gas Chromatography Mass Spectrometry
HILIC	Hydrophilic Interaction Liquid Chromatography
HPLC	High-Performance Liquid Chromatography
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
IEC	Ion Exchange Chromatography
IT	Ion Trap
IT-TOF	Ion Trap Time-of-Flight
LC	Liquid Chromatography
LCMS	Liquid Chromatography Mass Spectrometry
MALDI	Matrix-Assisted Laser Desorption/Ionization
MALDI-TOF	Matrix-Assisted Laser Desorption/Ionization Time-of-Flight
MRM	Multiple Reaction Monitoring
MS	Mass Spectrometry
MS/MS	Tandem Mass Spectrometry
MW	Molecular Weight
NPLC	Normal Phase Liquid Chromatography
PDA	Photodiode Array Detector
Q-IT	Quadrupole Ion Trap
Q-TOF	Quadrupole Time-of-Flight
RPLC	Reversed Phase Liquid Chromatography
RT	Retention Time
SEC	Size Exclusion Chromatography
SIM	Selected Ion Monitoring
SRM	Selected Reaction Monitoring
TIC	Total Ion Current
TOF	Time-of-Flight
TQ	Triple Quadrupole
UFMS	Ultra-Fast Mass Spectrometry
UHPLC	Ultra-High-Performance Liquid Chromatography
UV-VIS	Ultraviolet-Visible Spectroscopy

Symbols

μ	Micro
amu	Atomic mass unit
B	Magnetic flux density
E	Electric field
e	Elementary charge
g	Gram
k	Kilo
m	Mass
m/z	Mass-to-charge ratio
n	Nano
Pa	Pascal
V	Voltage
v	Velocity
z	Charge
ω	Oscillation frequency

Chapter 1

Basics of GC

Shimadzu's Fundamental Guide to GCMS begins with the basics of GC. This chapter includes a brief history of GC and its development and details the separation principle and instrumentation. Due to GC's unique characteristics, the instrument is often used for the analysis of small and volatile compounds and is widely applicable in many industries such as food, environmental testing, pharmaceuticals, petroleum, pesticides and fragrances.

Introduction

Chromatography is a technique that separates complex mixtures into its individual components for identification and quantification. It was first developed in the early 1900s by Russian botanist, Mikhail S. Tswett. He demonstrated the separation of colored plant pigments and termed this technique "chromatography". It was not until several decades later, around 1930s, where this technique sparked off further developments.

Scientist Archer J. P. Martin, who worked on paper partition chromatography, went on to develop Gas Chromatography (GC) with fellow scientist Anthony T. James. Their invention on GC was awarded the Nobel Prize in Chemistry in 1952 and it set the stage for many other developments such as Liquid Chromatography (LC) and Gas Chromatography Mass Spectrometry (GCMS).

GC is a technique that vaporizes the sample mixture into gaseous compounds and separates them based on the boiling point of the compounds and their differential adsorption on a porous solid or liquid support. It is commonly used for the analysis of low molecular weight and volatile compounds and is widely applicable in many industries such as in forensic science, food, environmental testing, pharmaceuticals, petrochemical, pesticides and fragrances. The following sections in this chapter details the separation principle and basic instrumentation of GC.

Principles and Applications

GC is also known as gas-solid or gas-liquid partition chromatography due to the distribution of compounds between the solid/liquid stationary phase in a column and the gaseous mobile phase. Figure 1 illustrates the separation of compounds in a GC. The sample mixture is injected, vaporized, and flows into the thermally-controlled column by an inert gas. The sample compounds can interact with the stationary phase through various intermolecular forces such as Van der Waals forces and dipole-dipole interactions. Some compounds tend to interact more strongly due to their polarity, thereby resulting in a higher concentration in the stationary phase compared to the mobile phase (i.e. higher partition coefficient, Equation 1). As a result, these compounds are strongly retained in the column and have longer retention time (RT) compared to compounds of weaker interactions with the stationary phase. As time passes, with continual flow of inert gas and a thermally-controlled column, the variations in the partition coefficients of the compounds (Equation 1) result in the separation of the compounds in a mixture. The separated compounds subsequently elute from the column and gets detected.

At the early forefront of GC development, Shimadzu embarked on this technology and developed the first GC in Japan in 1956. Subsequently, we developed newer and improved versions of GC and GCMS and achieved several key milestones. Click to learn more.

Click here

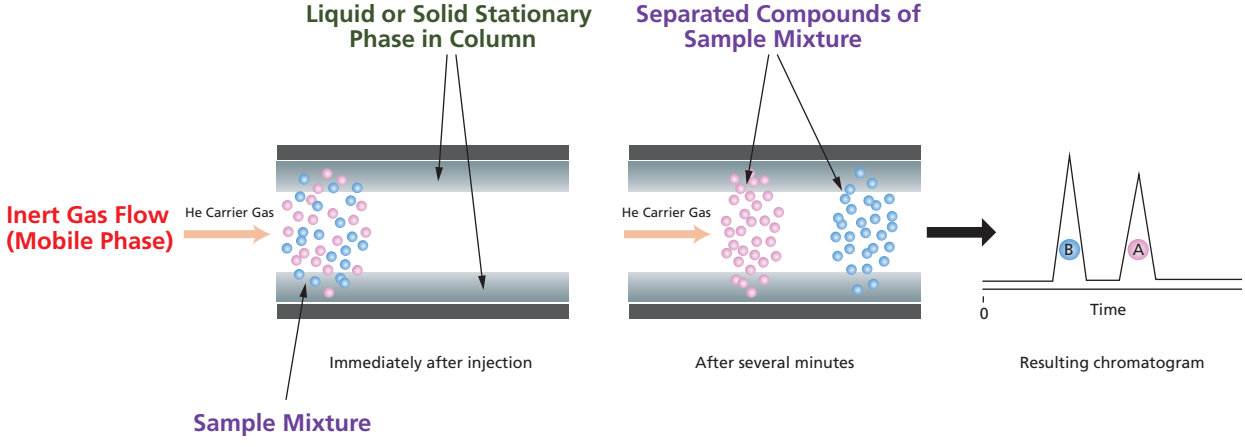


Figure 1. GC separation principle. The compound in red have a stronger interaction with the stationary phase and gets retained longer in the column. This results in the separation of the mixture where the red compound has a longer retention time than the blue compound ($RT_{red} > RT_{blue}$).

- Equation 1

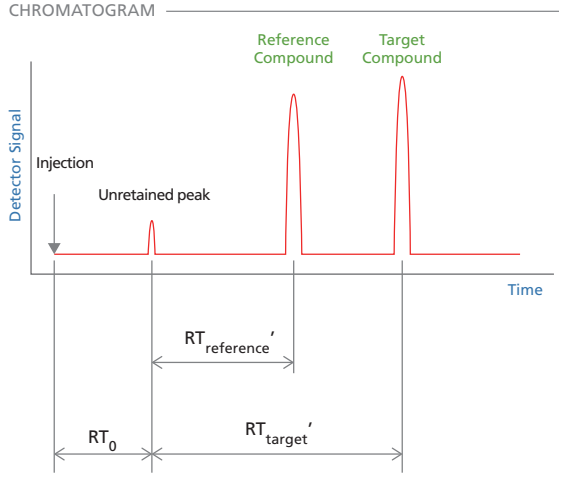
$$\textit{Partition Coefficient of Compound} = \frac{\textit{Concentration of Compound in Stationary Phase}}{\textit{Concentration of Compound in Mobile Phase}}$$

The separation of compounds in a GC mainly depends on two factors: (i) the polarity (i.e. interaction of the compound with the stationary phase in the GC column) and (ii) the boiling point of the compound (i.e. volatility). The lower the boiling point, the higher tendency of the compound being in the gaseous phase; thus, it travels faster in gaseous form through the column. Compounds with similar boiling points, elute with respect to their polarity, where compounds of weaker interaction with stationary phase elute first. Compounds with similar polarity elute in order of increasing boiling points, where compounds of lower boiling points have a shorter retention time.

The time taken for the compound to travel from the injection port to the detector is termed as retention time (RT). RT for a specific compound depends on various factors such as column type and dimensions, carrier gas type and flow, temperature and the analytical GC method used. Given the same analytical parameters, the same chromatogram and RT of compounds are typically expected. However, in reality, RTs of the same compound separated by GC columns of even the same manufacturing batch may differ slightly. Therefore, the use of relative retention or retention indices, a standardized form for comparison of GC retention data, can facilitate and allow GC to be an excellent tool for qualitative analysis. This standardized system is used for the comparison between different analytical parameters, and also for analysis conducted by different GC systems and laboratories. The use of retention indices in GC for qualitative analysis is well-established and is extensively used in many industries such as flavor and fragrance, pesticide and environmental testing.

Learn More: How to calculate relative retention?

Absolute RTs are affected by many parameters. The use of other retention values which are less dependent on parameters such as column dimension, carrier gas flow and analytical conditions are preferred. Therefore, relative retention, which depends only on the ratio of partition coefficient of the compounds, are commonly used for this purpose.



For unretained compounds, the time taken for it to elute is termed as the **gas hold-up time (RT_0)**. The time difference between the peak of an unretained compound and any compound is the **adjusted retention time (RT')**.
Relative retention can be calculated as shown below:
Adjusted Retention Time (RT') = Retention Time (RT) - Gas Hold-Up Time (RT_0)

Relative Retention (α)

$$= \frac{RT_{target'}}{RT_{reference'}}$$

$$= \frac{\textit{Partition Coefficient of Target Compound}}{\textit{Partition Coefficient of Reference Compound}}$$

where adjusted retention time of reference and target compound is $RT_{reference'}$ and $RT_{target'}$ respectively

Click here to learn more on retention index (Kováts Index) and Linear Retention Index (LRI).

APPLICATIONS OF GAS CHROMATOGRAPHY

Oil, Gas & Chemical

Analysis of sulfur, inorganic gases & light hydrocarbons

Flavor & Fragrance

Analysis of aromatics in perfume, wine and coffee

Environmental Testing

Analysis of volatile environmental pollutants

Pharmaceuticals

Impurities & residual solvent analysis

Forensic Toxicology

Steroid and drug analysis

Food & Beverage

Analysis of pesticides, additives & contaminants

GC is generally employed for the analysis of small and volatile molecules such as light hydrocarbons and volatile organic compounds. These analyses are required in almost every industry. Together with GC's easy-to-understand principles and simple interface, it serves many applications.

Click here to learn more:
Refer to Shimadzu GC application notes targeted for your analyses

Click here

However, not all analyses can be performed using GC. Figure 2 shows an illustration of the approximate molecular range of GC and LC. The molecular application range of GC is limited to small, volatile, non-polar and thermally stable compounds. Compounds that are not of this nature, such as semi-volatile, involatile and/or thermally-labile compounds, can go through various methods (e.g. pyrolysis, thermochemolysis and derivatization) to ensure compatibility for separation and analysis through GC. Derivatization, for example silylation and acylation, is commonly performed to reduce polarity, and increase thermal stability and volatility.

Besides GC, there are several other chromatographic and separation techniques such as LC (including ion exchange, size exclusion and column chromatography), supercritical fluid chromatography (SFC) and capillary electrophoresis. The choice of technique generally depends on the nature of the sample and the type of analysis required. GC and LC, the two most widely-used chromatographic techniques used in the industry, are frequently being compared. A concise comparison of GC and LC and the key features and differences are listed in Table 1.

GC is usually the method of choice due to its easy operation, high speed, resolution, sensitivity and reproducibility.

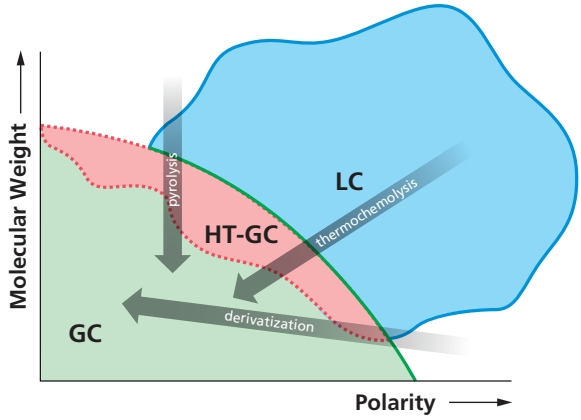


Figure 2. Molecular application range of GC.

With lesser variables and components such as solvents, columns and operating pressure, the GC system is less complex and requires less maintenance and operating cost. In all, it is a powerful technique and can achieve separation, identification and quantification of mixtures and compounds. GC can be coupled with various detection methods and the following section describes the instrumentation and components of GC.

Table 1. Comparison of GC and LC.

	GC	LC
Separation principle	• Partition between the gaseous mobile phase & solid/ liquid stationary phase • Polarity of compound • Boiling point of compound	• Partition between the liquid stationary & mobile phase • Polarity of compound • Other separation modes (e.g. ion exchange, size exclusion, reverse-phase) are available
Mobile phase	Inert gas	Solvent / buffer (liquid)
Pressure requirements	Requires lower pressure to operate (max 1200 kPa)	Require high pressure to operate HPLC & UHPLC* (30 – 140 MPa)
Sample requirements (Compound nature)	• Volatile • Thermally stable • Low molecular weight (e.g. alcohols, short-chain fatty acids, pesticides and VOCs)	• Soluble in liquid phase • Not limited by molecular weight or polarity (e.g. Proteins, peptides, amino acids and polymers)
Type of detectors	Consists of MS or ionization and conductivity detectors (e.g. flame ionization, thermal conductivity, photo-ionization, electron capture & barrier discharge ionization) • generally destructive in nature	Consists of MS or spectroscopy techniques (e.g. UV, fluorescence, refractive index, conductivity & light scattering) • generally non-destructive in nature

*HPLC: High Performance Liquid Chromatography UHPLC: Ultra-High-Performance Liquid Chromatography

Instrumentation

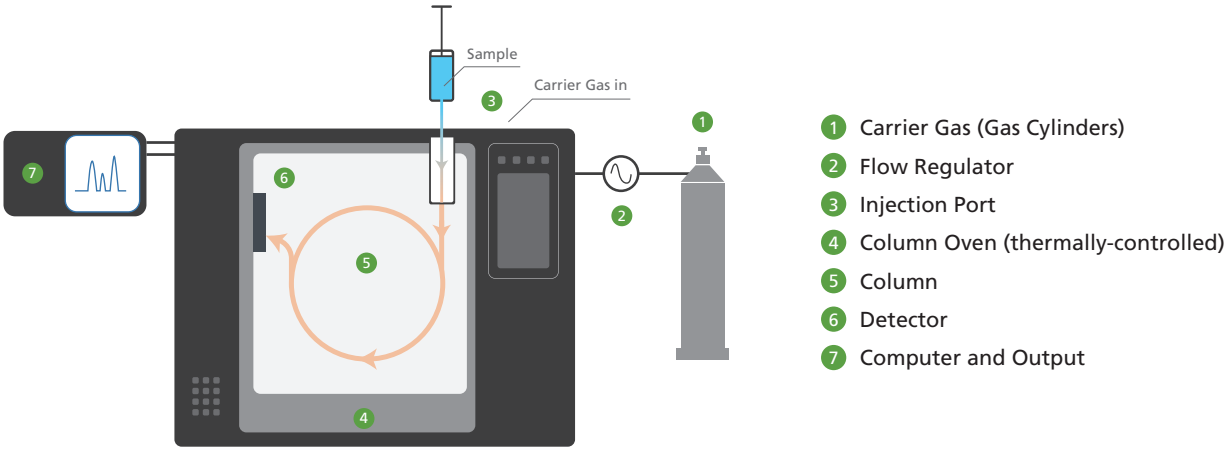


Figure 3. GC instrumentation.

A GC system consists of several components (Figure 3). The role of each component is critical to obtain a good separation and analysis. Carrier gas is required to provide a gas flow that transports the compounds through the column and to the detector. The purity and flow of the carrier gas is crucial to achieve good separation and reproducible chromatograms; gas filters and flow regulators are used to supply high-purity and constant-flow gas to the GC. Principally, the carrier gas needs to be inert and does not interfere with the separation and detection. Helium, hydrogen and nitrogen are some of the commonly-used carrier gases. These gases have different properties and characteristics and the choice essentially depends on the sample and the type of detector and analysis. These factors, such as the required separation resolution and efficiency, cost and compatibility with the detectors, should be considered when choosing carrier gases. Table 2 provides a tabulation of the pros and cons of the most commonly-used carrier gases.

Table 2. Pros and cons of the most commonly-used carrier gases.

Carrier Gas	Pros	Cons
Hydrogen (H_2)	• High diffusivity and linear velocities • Gets good separation efficiencies • Short analysis and run time (results in cheap operational cost)	• Flammable • Not completely inert (e.g. reacts with some compounds at high temperature)
Helium (He)	• Inert (safe) and non-flammable • Gives high resolution	• Expensive, not easily available
Nitrogen (N_2)	• Cheap and easily available	• Not suited for use in temperature-programmed GC analysis • Lower or poor separation resolution • Long analysis and run time

Helpful Tips

The purity of carrier gas used depends on the sensitivity required. For GC and GCMS, high purity gas is required. However, impurities from pressure regulators or other parts of the gas line (such as hydrocarbons, moisture and oxygen) can contaminate the gas line and instrument, cause column degradation and affect the accuracy of your analysis results, which may lead to instrument downtime. Therefore, an additional gas filter is essential.

Click here to know more about Shimadzu Super-Clean Gas Filter Kits.

Learn More: Separation efficiency of a GC column and how carrier gases play a part.

Separation efficiency of a column can be determined by the number of theoretical plates (N). The larger N is, the more efficient the separation. N can be calculated by various formulae. Click or scan the QR code to learn more.

Click here

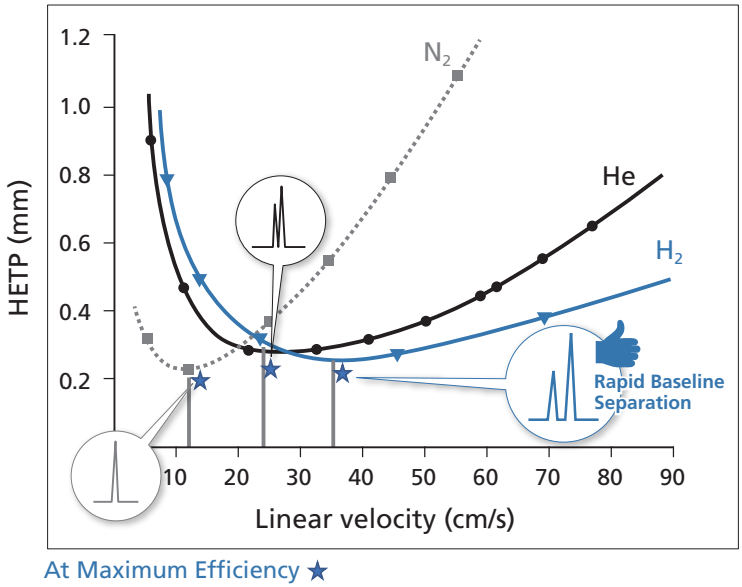
Another parameter that can similarly express separation efficiency is the Height Equivalent to a Theoretical Plate (HETP). The lower the value of HETP, the higher the separation efficiency. HETP is related to N: HETP = L / N, where N is the number of theoretical plates, L is the column length. For GC, the linear velocity of the carrier gas affects the separation efficiency. This association of HETP and linear velocity for the various carrier gas can be illustrated with the van Deemter equation and plot.

$$\textit{van Deemter equation: } HETP = A + \frac{B}{\nu} + C\nu$$

where ν refers to the linear velocity (flow rate) of the carrier gas, A, B and C are constants and accounts for eddy diffusion, molecular diffusion, and resistance to mass transfer term respectively.

From the van Deemter plots, N2 has the lowest HETP value and can achieve highest separation efficiency out of the three carrier gases. However, this maximum separation efficiency is only achieved at a low corresponding linear velocity (12 cm/s). A long run time is expected and for this reason, N2 is not commonly used. Furthermore, a slight change in linear velocities severely affect the HETP and separation efficiency. This property of N2 makes it unsuitable as a carrier gas for temperature-programmed GC analysis, where increased temperature results in decreased linear velocity. H2, which has the lowest overall HETP (flattest plot/gradient) and high linear velocities, are often preferred due to the short run time and good separation efficiencies.

van Deemter plot for GC capillary column



At Maximum Efficiency ★

^For capillary columns, there is an absence of eddy diffusion. The plots of HETP against linear velocity can be simply expressed by the Golay equation.

Sample is injected into the GC (i.e. injection port) via a syringe, autosampler or other sampling devices. High temperature (150 – 250°C, maximum 450oC) is usually applied to the injection port and GC glass insert to instantaneously vaporize the sample. However, care must be taken as too high a temperature may unnecessarily decompose or destroy the sample and cause unwanted peaks. For GC analysis, a few microliters (µL) of sample are usually sufficient, and sample is injected swiftly in a small plug to minimize band broadening.

There are various injection modes available, namely split, splitless and direct (on-column). These modes cater for the different sample concentrations and analyses. It ensures that the amount injected is satisfactory, the GC column is protected, and good chromatographic results are achieved. Figure 4 gives an overview of the 3 injection modes and its sample suitability. A GC injection port with a split vent is commonly utilized where the opening and closing of the split vent can accommodate both split and splitless modes.

Helpful Tips

The GC injection port is designed to accommodate temperatures ranging from 50 – 450°C. There are several types and grades of the injection port septum which suit the different temperature ranges and analysis type. The injection port septum will degrade overtime due to high temperatures and should be replaced regularly to prevent any leakages in or out of the GC system. These leakages can cause sample loss and/or contamination which ultimately affect the sensitivity and quality of the analysis.

Split

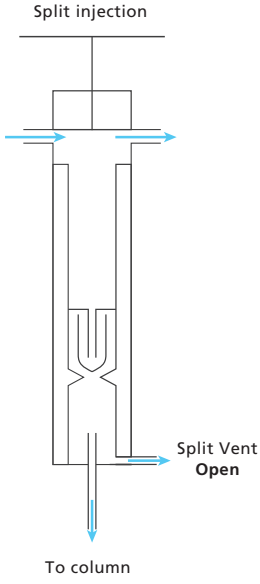
For high concentration analytes or involatile & residual matrices

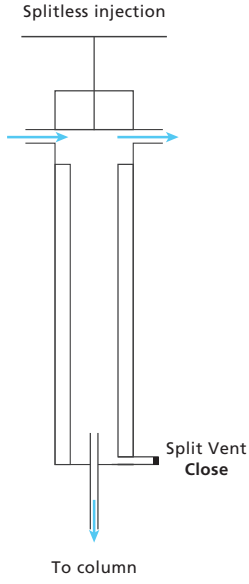
- To allow only a small portion of sample into the column by opening the split vent
- To avoid overloading of column and unresolvable peaks/ chromatogram

Splitless

For trace analytes or involatile & residual matrices

- To vaporize and introduce the entire sample into the GC column
- To allow accurate determination





Direct (on-column) For thermally labile, low volatility and/or reactive analytes

- To avoid contact with the hot injection port and go straight to GC separation

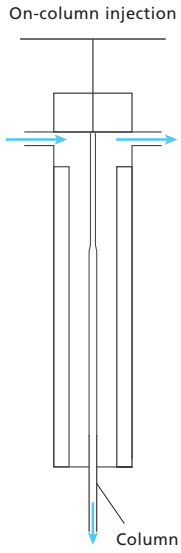


Figure 4. Schematic of a split, splitless and direct (on-column) injector.

Columns

Separation is mainly achieved using columns and temperature-controlled oven. There are various types of GC columns (Figure 5). Packed columns are one of the first columns used. These columns are filled with solid particles, either (i) a porous solid or (ii) a liquid-coated solid. For (i), the solid particles act as a stationary phase and analytes can be adsorbed on the surface of the porous particle. While for (ii), a form of gas-liquid chromatography is utilized where the liquid layer adsorbed on the solid particle acts as the stationary phase. These packed columns are not commonly preferred nowadays due to its limited applications and inefficient separation.

Today, capillary columns, which provides a more efficient separation, is widely adopted for GC analyses. These capillary columns are generally longer in length (≈ 30-60 m) and smaller in internal diameter. Furthermore, capillary columns provide a shorter run time (higher speed), requires lesser sample volume and gives a higher resolution. As shown in Figure 5, there are three types of open tubular (capillary) columns, (1) Wall-Coated Open Tubular (WCOT), (2) Porous-Layer Open Tubular (PLOT) and (3) Support-Coated Open Tubular (SCOT) columns. These capillary columns have the stationary phases only on the walls of the columns, and WCOT, PLOT and SCOT differ in the structure and layout of the liquid stationary phases. In WCOT columns, the liquid stationary phase is uniformly applied to or chemically bonded on the interior walls of the capillary as shown in Figure 5. This thin liquid layer interacts with the sample during separation. For PLOT and SCOT, it consists of a thin stationary layer that is similar to the composition of the packed porous solid column and packed liquid-coated solid column respectively.

In general, there are several column parameters that affect the separation, namely the column dimensions (e.g. length and internal diameter) and composition and thickness of the stationary phases. The selection of the type and composition of stationary phases depends on the analysis and most columns are made up of polymers. With different stationary phases, the interaction (e.g. Van der Waals, ϖ-ϖ, electrostatic-dipole interactions and hydrogen bonding) and polarity of the column can be altered to separate the compounds in the mixture. Dedicated columns are also available for some specific applications (e.g. acids, pesticides and polybrominated diphenyl ethers).

With these columns, GC can be operated in either isothermal or temperature-programmed modes. Appropriate temperature program is required to achieve separation and high resolution of analytes. Upon separation, the analytes elute from the column and generate a signal or response from the detector.

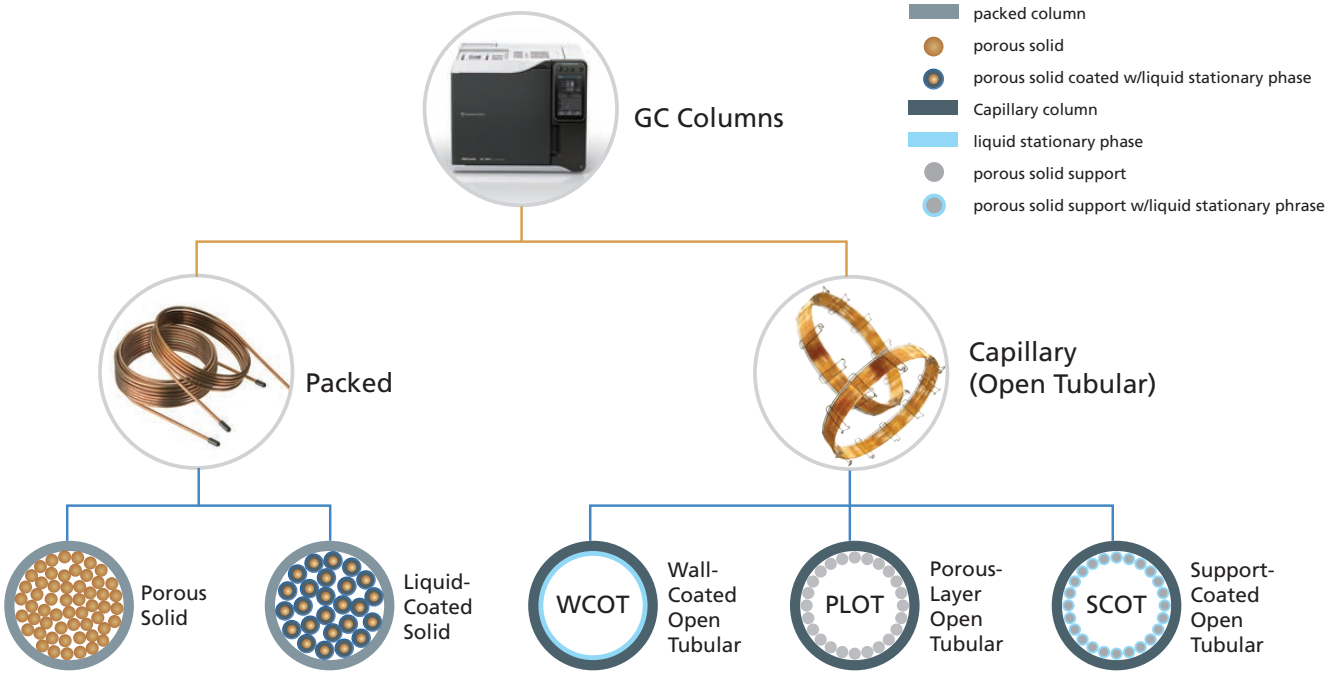
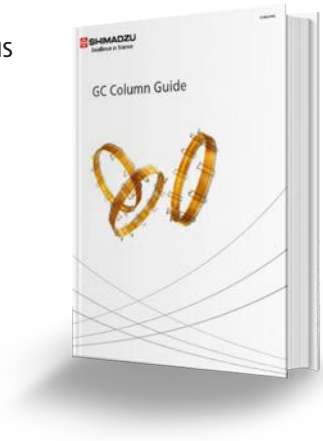


Figure 5. Types of GC columns – packed and capillary columns.

Click here to download Shimadzu's GC Column Guide:

A comprehensive selection of columns for your GC and GCMS analyses.



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Detectors

Detectors are used to determine the presence and quantity of the analytes in a mixture. It generally measures a physicochemical property and this data is converted into a signal and plotted against retention time to obtain a chromatogram. The peak area and/or peak height corresponds to the amount of compound present in the sample while the retention time can be used to distinguish the identity of the compound. An example of a chromatogram of a pesticides analysis using Flame Photometric Detector (FPD) is shown in Figure 6.

There are several GC detectors available. The ideal detector should possess these properties:

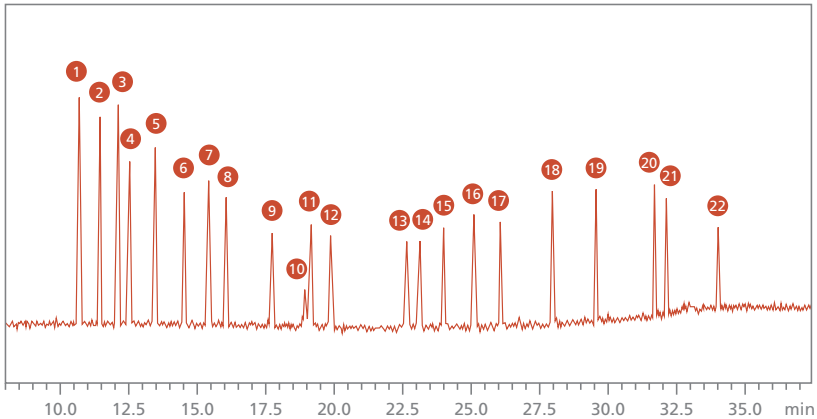
- Highly sensitive,
- Not affected by other variations,
- Excellent linearity,
- Able to quantify and identify,
- Non-destructive,
- Fast, stable and easy-to-use

However, all these ideal features are hard to find in a single detector. In this section, the characteristics of some commonly-used GC detectors such as thermal conductivity detector (TCD), flame ionization detector (FID), electron capture detector (ECD), flame photometric detector (FPD), flame thermionic detector (FTD) and sulfur chemiluminescence detector (SCD) are described, and the key features are highlighted in Table 3 and Figure 7 to assist in the selection of these general or specialized detectors for your analysis.

Based on their principles, detectors can be classified into either concentration or mass detectors. Concentration detectors measure the concentration of analytes present in the gas flow. This signal can be easily affected by the addition of make-up gases. On the other hand, mass detectors measure the total mass, or the analytes mass flow and the signal is independent of the amount of make-up gases. Flame detectors (e.g. FID and FPD), a type of mass detector, generally destroy the sample in the process of detection.

Detectors can also be grouped into universal or selective/specialized detectors. Universal detectors, for example TCD, detect all compounds with reference to the carrier gas. On the other hand, detectors such as ECD are selective due to its operating principle where it only works for certain groups of compounds (e.g. halogens). These detectors, universal or selective, have its pros and cons. The use of universal detectors may pose an issue for complex samples; while being too selective may cause some compounds to be omitted. Therefore, the use of detectors must be specifically chosen for your applications.

Apart from these commonly-used detectors, Shimadzu have also developed a new GC detector, a dielectric barrier discharge ionization detector (BID). It is a universal detector and comprises of a quartz tube, plasma generator and a separate charge collector (Figure 8). This technology enables the generation of an atmospheric non-equilibrium helium plasma with low heat. The noise is further reduced, and this allows the detections of trace components that are difficult to detect by other GC detectors (Figure 9a). Also, the use of BID can replace the conventional multi-detection methods for the analysis of permanent gases and light hydrocarbons (Figure 9b).



Splitless Analysis of 5 µg/L Organic Phosphorus Pesticide Standards for Each Component

Figure 6. Chromatogram for the splitless analysis of 5µg/L organic phosphorus pesticide standard using Flame Photometric Detector (FPD).

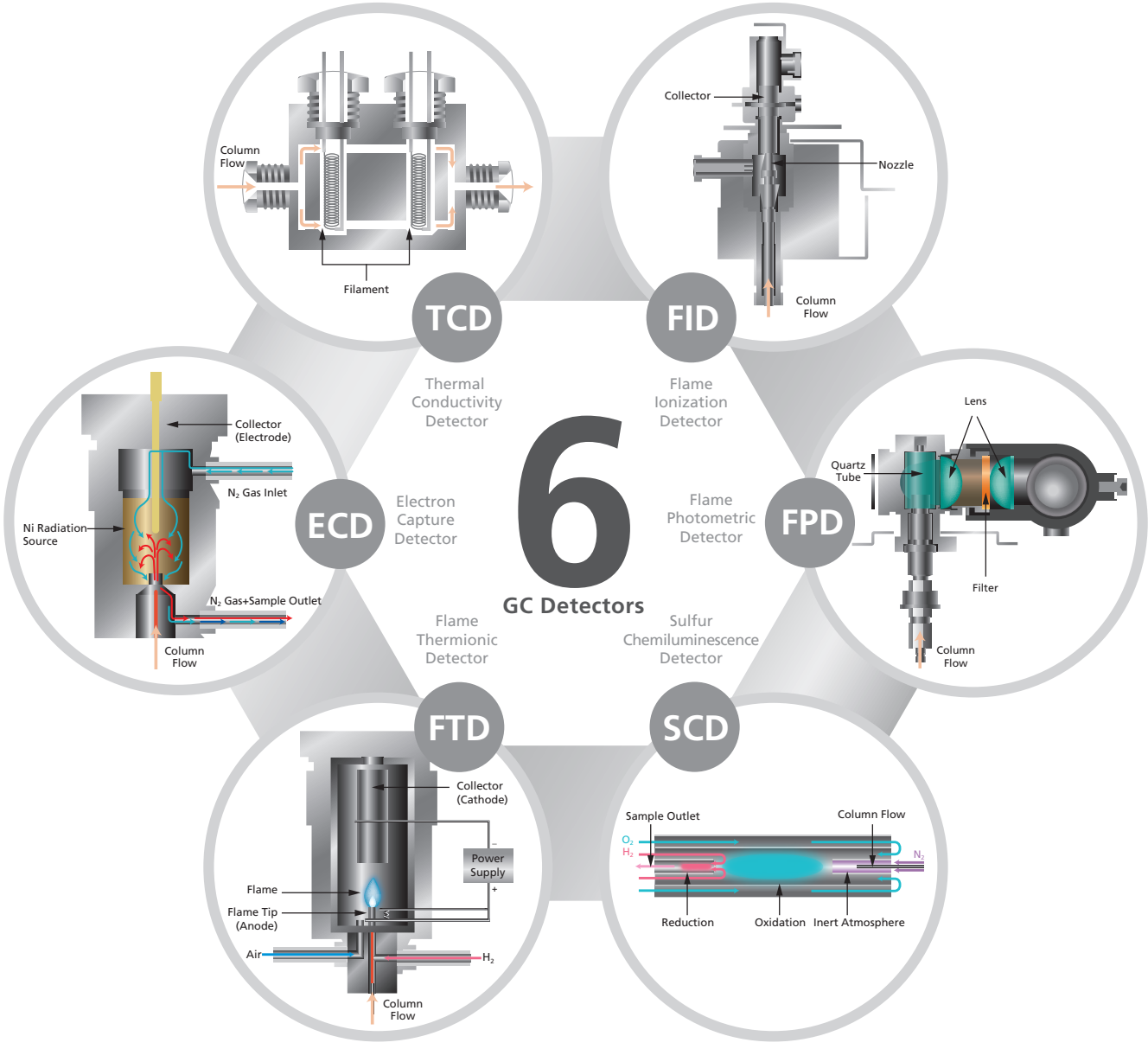
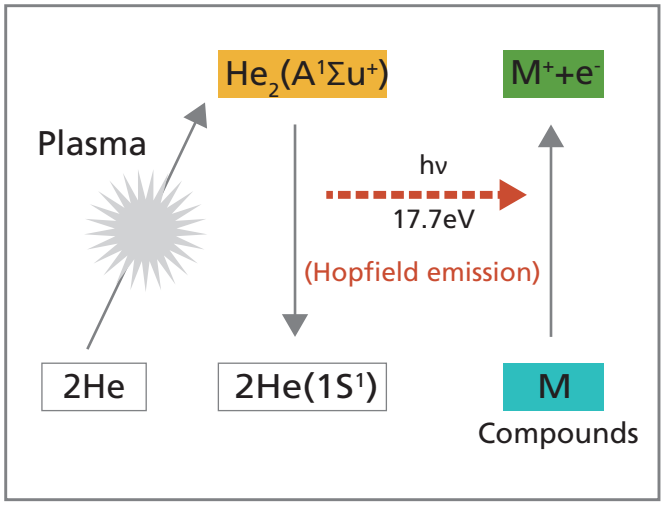


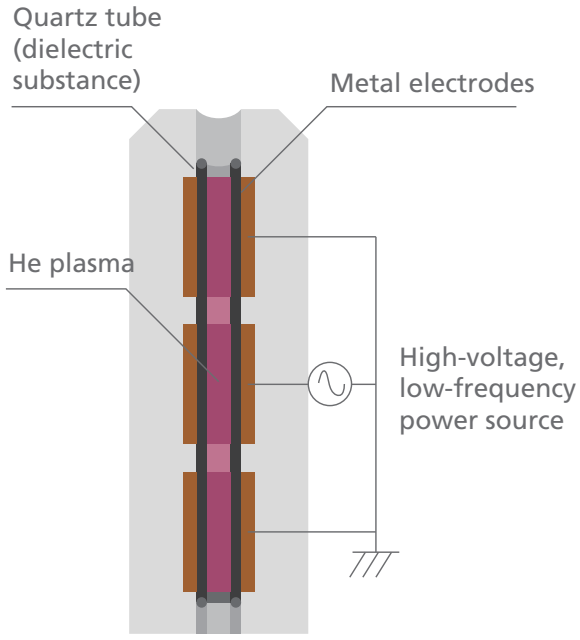
Figure 7. GC detectors: TCD, FID, ECD, FPD, FTD and SCD.

Table 3. Features and characteristics of common GC detectors.

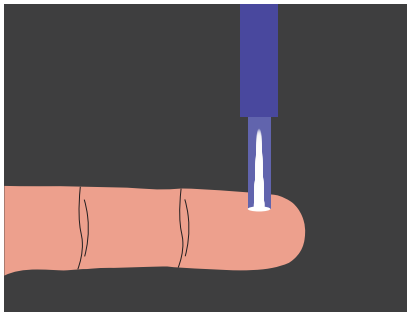
Detector	Principle of Detection	Type of Detector	Selectivity	Sensitivity
Thermal Conductivity Detector (TCD)	Based on the difference in thermal conductivity of gas flow, i.e. thermal conductivity of analytes as compared to the carrier gas (reference). This difference is amplified and recorded.	• Concentration detector • Can be affected by carrier gas flow • Non-destructive	• Universal (non-selective), e.g. organic compounds • Can also be used for the analysis of inorganic and permanent gases	• Acceptable sensitivity (ppm level), lowest sensitivity as compared to other detectors • Wide dynamic range (10^7)
Flame Ionization Detector (FID)	Analytes are burned in the air-hydrogen flame and produced ions and electrons. This generates a current and this positive signal is recorded to give an analyte peak.	• Mass detector • Independent of carrier gas flow • Destructive • Low noise	• Widely applicable, most commonly used for organic compounds (e.g. hydrocarbons, oxides of nitrogen & sulfur) • Does not respond to non-combustible gas (e.g. He, Ar, N_2, O_2, CO_2, CO and SO_2) and water	• Good sensitivity (ppb level) • Wide dynamic range 10^7
Barrier Discharge Ionization Detector (BID)	Analytes are ionized by the Helium-based, dielectric barrier discharge plasma. These generated ions produced a current; this signal is recorded to give an analyte peak.	• Mass detector • Independent of carrier gas flow • Destructive	• Universal • Suitable for a wide variety of compounds (e.g. inorganic gases and organic compounds), other than He and Ne	• High sensitivity (ppb level) • Good dynamic range (10^5)
Electron Capture Detector (ECD)	Electrons are generated by a source in the detector, and this current is measured (as reference). When analytes passed through, compound with high affinity tend to capture these electrons and caused a drop in the current. This difference in current is amplified and recorded to give an analyte peak.	• Concentration detector • Can be affected by carrier gas flow • Non-destructive	• Highly selective • Mainly used for electrophilic compounds such as halogens (F, Cl, Br, I), nitrogen and phosphorus (e.g. pesticides) • Cannot detect simple hydrocarbons	• Highest sensitivity (ppt – ppb level) • Good dynamic range (10^5)
Flame Photometric Detector (FPD)	Analytes are burned, and radiation are released in the process. This radiation, specific to the element (Sulfur: 394nm, Phosphorus: 526nm), is isolated and recorded for identification and detection.	• Mass detector • Independent of carrier gas flow • Destructive	• Suited for sulfur and organophosphorus compounds (e.g. pesticides and petroleum) • Can be used for elemental analysis such as tin, boron and arsenic.	• Highly sensitive for sulfur and phosphorus (ppt – ppb level) • Limited range (10^3)
Flame Thermionic Detector (FTD)	FTD has similar principles as FID. It uses a heated alkali-metal compound and analytes are ionized by the extraction of electrical charge from the alkali-metal surface. Ions are produced when the analytes are burned in a flame.	• Mass detector • Independent of carrier gas flow • Destructive	• Highly selective and used for nitrogen- and/or phosphorus- containing organic compounds	• Good sensitivity (ppb level) • Wide dynamic range 10^7
Sulfur Chemiluminescence Detector (SCD)	Sulfur-containing analytes are oxidized into sulfur dioxide (SO2), which is then reduced to sulfur monoxide (SO) in the presence of H2. SO reacts with ozone and the excited SO2* species emits radiation in the ultraviolet region (300-400nm) and is detected by a photomultiplier. The signal is linearly proportion to the sulfur quantity in the sample.	• Mass detector • Independent of carrier gas flow • Destructive	• Highly selective for sulfur-compounds • Little or no quenching	• Highly sensitive for sulfur compounds (ppt – ppb level) • Good dynamic range (10^6) • Linear and equimolar



Principal of Ionization Reaction



Cross Section Drawing of BID



Low-temperature plasma

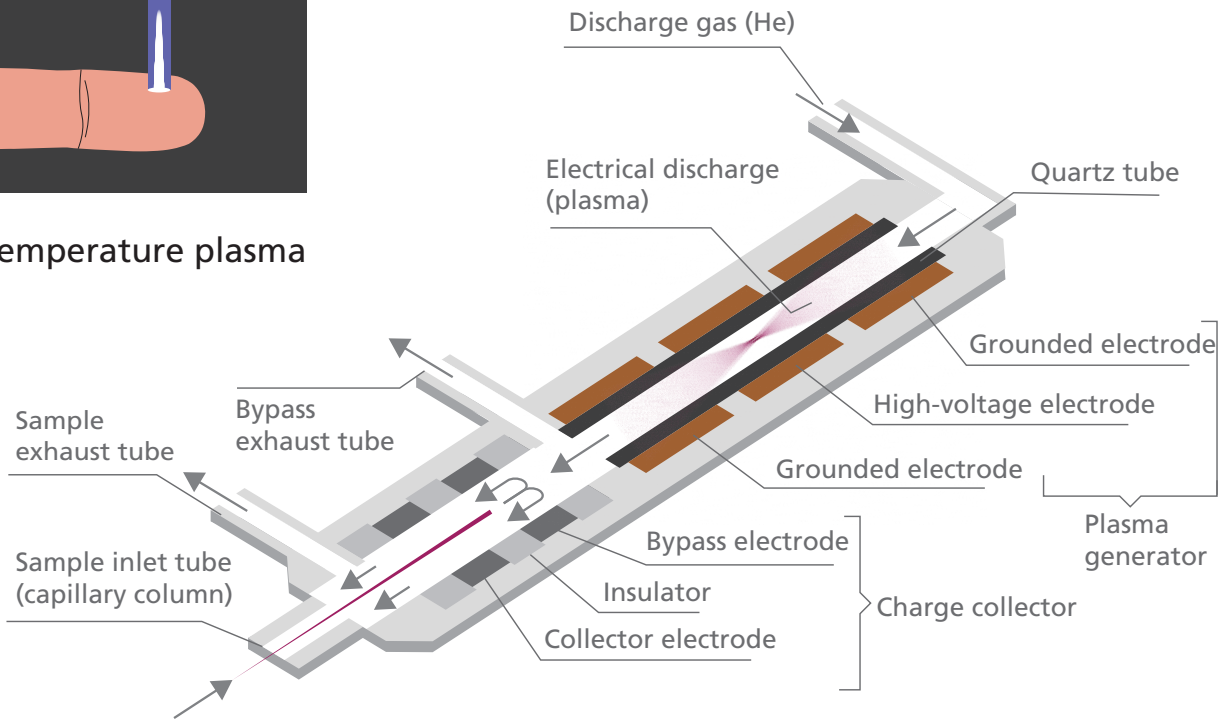


Figure 8. Principles and components of Barrier Discharge Ionization Detector (BID).

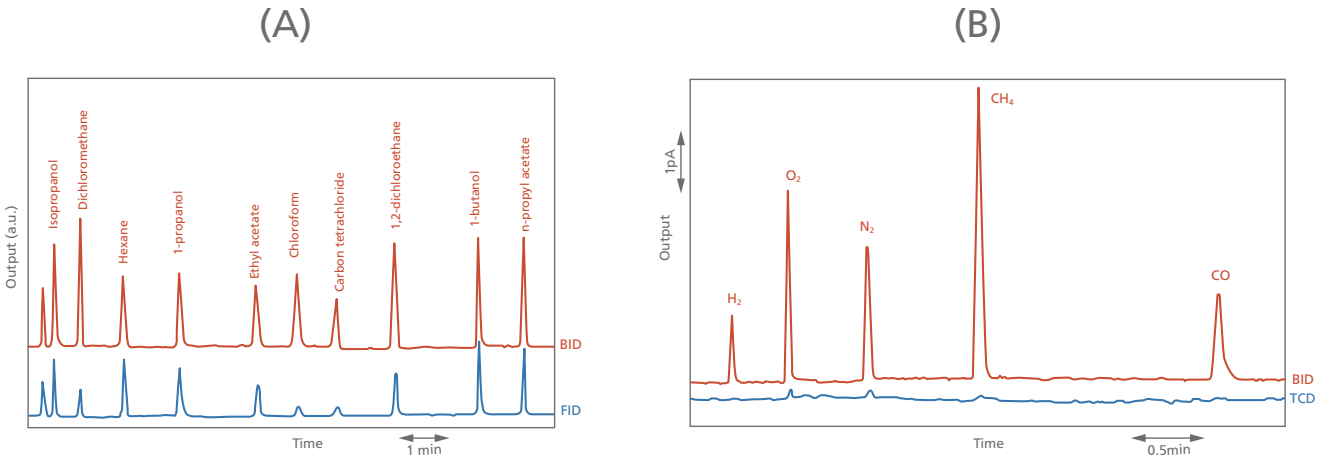


Figure 9. Comparisons of BID with other GC detectors: (a) BID and FID - Chromatogram of chlorine-containing sample and alcohol mixture (10 ppm concentration), (b) BID and TCD – Chromatogram of gas mixture (10 ppm concentration).

There are other GC detectors that are not as widely adopted such as the atomic emission detectors; this lack in usage may be due to the limited suitability, applications and cost of the detectors.

For the analysis of complex matrices and multi-component samples, universal detectors like TCD, and very selective detectors such as ECD may not be preferred. Issues such as co-elution or non-detection is possible and makes data analysis and interpretation complicated. These detectors also solely provide results such as retention time and peak intensity/area.

However, with the use of Mass Spectrometry (MS), it makes GC a more powerful instrument where the coupled instrument (GCMS) can differentiate co-eluting peaks, provide mass information and at the same time identify compounds with its library searching function. In a MS, the eluted gaseous analytes are ionized and accelerated into the mass analyzer. it separates all the ions based on their mass-to-charge (*m/z*) ratio and each intensity is recorded to give a mass spectrum. This intensity and *m/z* ratios can be used for both quantitative and qualitative purposes.

In summary, this chapter covered the basics of GC and touched on the principles, application and instrumentation. The various types of columns and detectors were further explored and discussed to provide comprehensive information on the applicability, options and flexibility of GC. Based upon the strengths of MS as a GC detector, it is evident that GCMS is a formidable instrument. The following chapters of the GCMS Fundamental Guide provide more insights on the principles, technologies and applications of GCMS.

New Approaches using GC-BID:

Click here to learn more on the principles of detection and various applications for the Barrier Discharge Ionization Detector (BID).

Click here

Chapter 2

Introduction to GCMS

GC coupled to MS is a powerful technique and a preferred method for the analysis of small and volatile molecules. This technique is also well-recognized for its ability in unknown compound analysis and multi-component quantitation. Chapter 2 introduces GCMS in greater detail: its principles, applications, instrumentation and technologies. Particularly, the generation of ions is crucial in all MS instruments. Electron ionization and chemical ionization are commonly utilized in GCMS as ion sources. This chapter discusses the mechanisms, processes and factors limiting the efficiency of these ionization processes.

Fundamentals

Mass spectrometry (MS) is a highly-sensitive detection technique that forms, separates and detects ions in the gaseous phase. When coupled to a GC, it immediately ionizes the gaseous eluted compounds, separates the ions in vacuum based on their mass-to-charge ratios (*m/z*) and eventually measures the intensity of each ion. These intensities are recorded to produce a series of mass spectra (Figure 10, blue) which displays the relative ion intensities against *m/z*. The eventual output of GCMS is the mass chromatogram (Figure 10, as represented in green and orange). A Total Ion Current Chromatogram (TIC) is a chromatogram created by summing up intensities of all mass spectral peaks belonging to the same scan.

MS is one of many GC detectors but unlike other detectors, it can perform both quantitative and qualitative analyses. GCMS separates and quantifies multi-component samples and complex matrices, as well as have the capability to identify unknown compounds. These strengths of GCMS are clearly depicted when comparing GCMS and other GC detectors, such as GC-FID (Figure 11).

Both FID and MS detectors can quantitate using the peak intensity or peak area and identify compounds using the retention time from the chromatograms. However, the unknown peak detected by both techniques, can only be further determined and identified easily using GCMS. Data such as the retention time, molecular weight and mass spectra obtained from GCMS can be retrieved and used for a spectral library search. With additional software, GCMS can calculate the accurate mass and estimate the molecular composition. This is extremely valuable for the unique identification of molecules, also known as qualitative analysis.

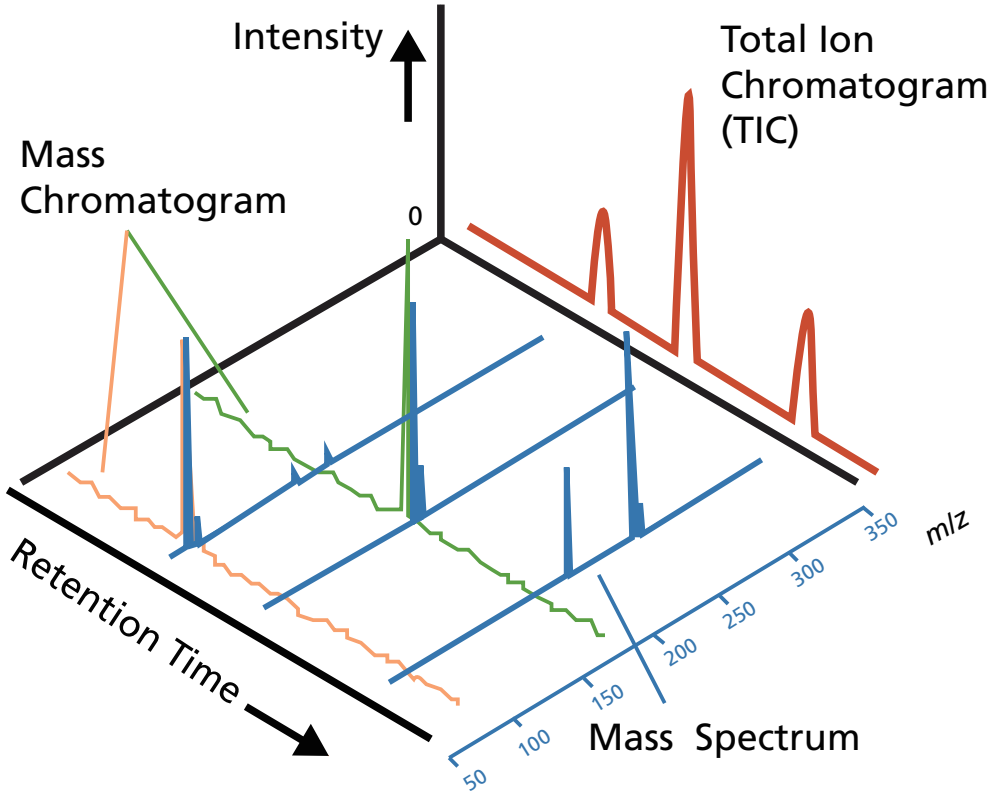


Figure 10: Typical GCMS mass chromatogram (green and orange), total ion chromatogram (TIC, red) and mass spectrum (blue)

Figure 11. Comparison of GC-FID and GCMS.

With this, GCMS provides added specificity and sensitivity, and the convenience of simultaneous multi-component analysis. This is applicable to many industries and applications today, for example, environmental, forensic, food and beverage, clinical, pharmaceutical and the chemical industries. It is commonly used for the direct separation and analysis of air samples and is often labeled as the accepted technique or gold standard for separation and analysis. However, MS do have some limitations as compared to other techniques. As discussed previously, the volatility and thermal stability requirements for analysis using GCMS is one of its major limitations. As GC separates based on the boiling point and interaction with the column, for very closely similar compounds or properties such as certain isomeric compounds (e.g. naphthalene and azulene), they cannot be easily separated and distinguished by GCMS. For these compounds, the separation may have to be conducted or further improved by 2D-GC or a more specialized column.

Learn more: Shimadzu GCMS application notes and technical reports for various industries.

Application Notes

Click here

Technical Reports

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Application Notebooks

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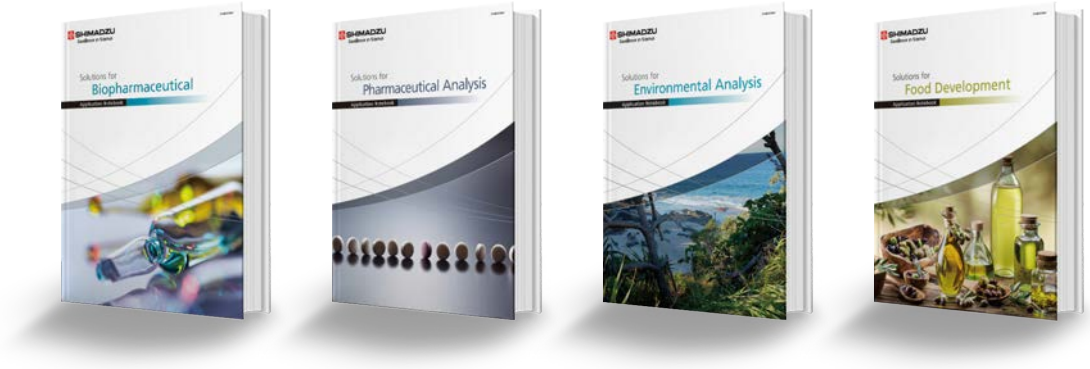
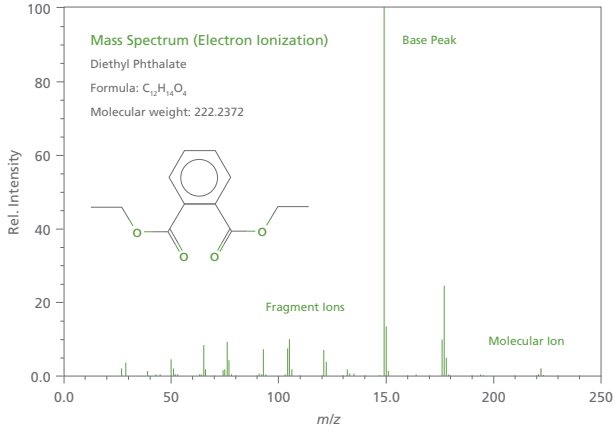


Learn more on Mass Spectrum.

A mass spectrum is a graphical representation of the ions from a MS. It illustrates the mass distribution of the ions. From the mass spectrum, we can obtain information about molecular weight, molecular structure and identify unknown samples. Shown below is a typical mass spectrum of diethyl phthalate when it undergoes electron ionization (EI) in a GCMS.

When a gaseous compound enters the MS, it is ionized (e.g. an electron can be removed from the molecule to form the molecular ion). For diethyl phthalate, the molecular ion is not stable, and it undergoes fragmentation to produce other smaller *m/z* ions (also known as fragment ions). These ions of various *m/z* are detected and recorded in the mass spectrum. The ion with the highest intensity (*m/z* 149 for diethyl phthalate) is highly stable and most abundant; the ion peak (whose intensity is taken to be 100%) is labeled as the base peak.

Given identical ionization conditions (e.g. electron energy in EI), the ionization process and fragment ions produced are the same, generating similar mass spectrum for the same compound. Fragmentation depends solely on the molecular structure of the compound. The acquired mass spectrum can be easily compared to a reference spectrum registered in a library MS database to determine the identity of the compound. Library search is an easy and useful tool for identifying a compound and a chromatographic peak. Click to know more about library search in GCMS.



Click here

Library Search: A software function to identify an unknown chromatographic peak by comparing the mass spectrum to reference spectra registered in MS libraries.

Hit Spectrum vs Reference Spectrum → Similarity Index → An Easy Tool for Identification

Instrumentation

The instrumentation of a GC system is described in Chapter 1. When coupling GC to MS, the GC components are roughly similar with slight changes. These modifications are necessary for successful connection and interfacing to the MS. Figure 12 shows these components and illustrates a typical GCMS system, where it is more complicated than the other GC detectors discussed.

MS does not just simply detect the compounds, it first generates ions, separates and then detects these ions. More specifically, the eluate (GC outlet) enters the MS and flows into the ion source, where ionization occurs. Once ions are generated, they are accelerated and directed to the mass analyzers and eventually gets detected and measured. MS includes an ion source, ion guide, mass analyzer and a detector. It also features the interface and vacuum pumping system. The remaining sections in Chapter 2 describes all these components, with emphasis on the ion sources, while Chapter 3 focuses on the various mass analyzer and tandem MS systems used in a GCMS.

GC and MS are quite similar in a way that both techniques involve gaseous compounds and high temperature. However, one major difference is the pressure requirement; GC operates at atmospheric pressure while MS requires low pressure and high vacuum state (10^{-3} to 10^{-4} Pa). To successfully overcome the pressure and connect the GC to the MS, the interface and vacuum pumping system play a crucial role.

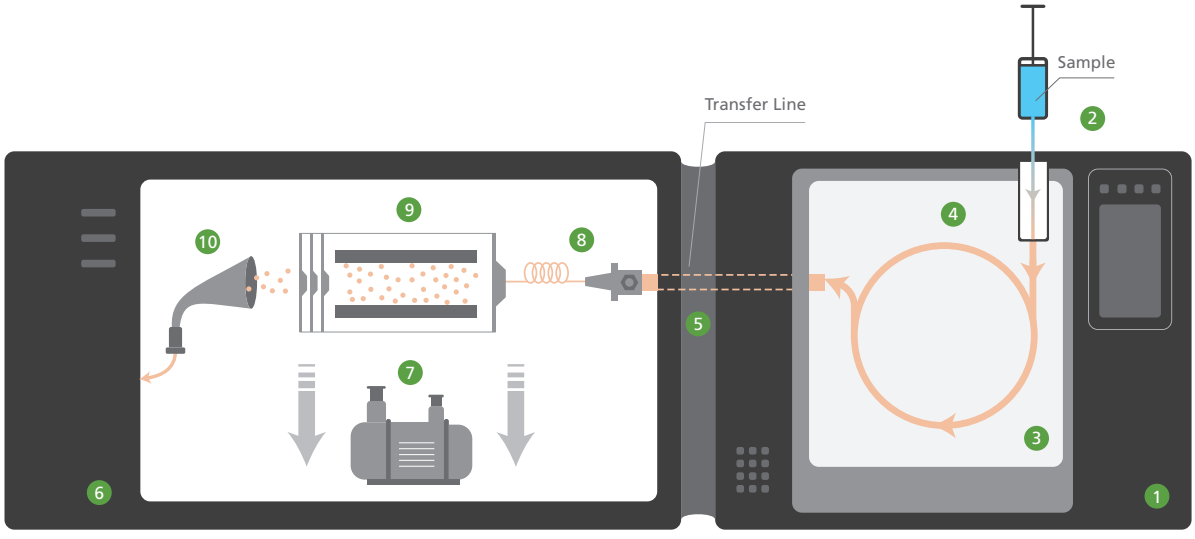


Figure 12. Typical GCMS instrumentation.

Interface and Vacuum Pumping System

The interface works as a bridge connecting the GC and MS. Together with the vacuum pumping system, they lower the pressure to meet the high vacuum requirement of MS. The interface is gas-tight and maintained at low and consistent pressure by pumps. Carrier gases can be removed at this step. With a heater, the interface temperature is kept high (e.g. 50 – 350°C) to ensure that the eluted compounds from the GC stay in the gaseous phase and only volatile compounds enter the MS.

Capillary columns are commonly used in GCMS. Its low pressure and low flow rate allow for easier interfacing and connection to the MS through the direct GCMS interface (Figure 13). This direct insertion of capillary column offers highest sensitivity with minimal loss of sample compounds. On the other hand, the use of packed columns in GCMS may pose an issue (this will be discussed further in the later section).

A vacuum pumping system is indispensable to achieve free flight of ions in a MS. The system can be made up of various setup and arrangement of pumps, for example, a single vacuum pump or a differential vacuum pumping system. With a single pump, the workload of achieving high vacuum is entirely on just one pump. In the case that the flow rate of the GC carrier gas is increased five times, the pumping capacity and speed needs to be similarly five times larger to achieve the same vacuum.

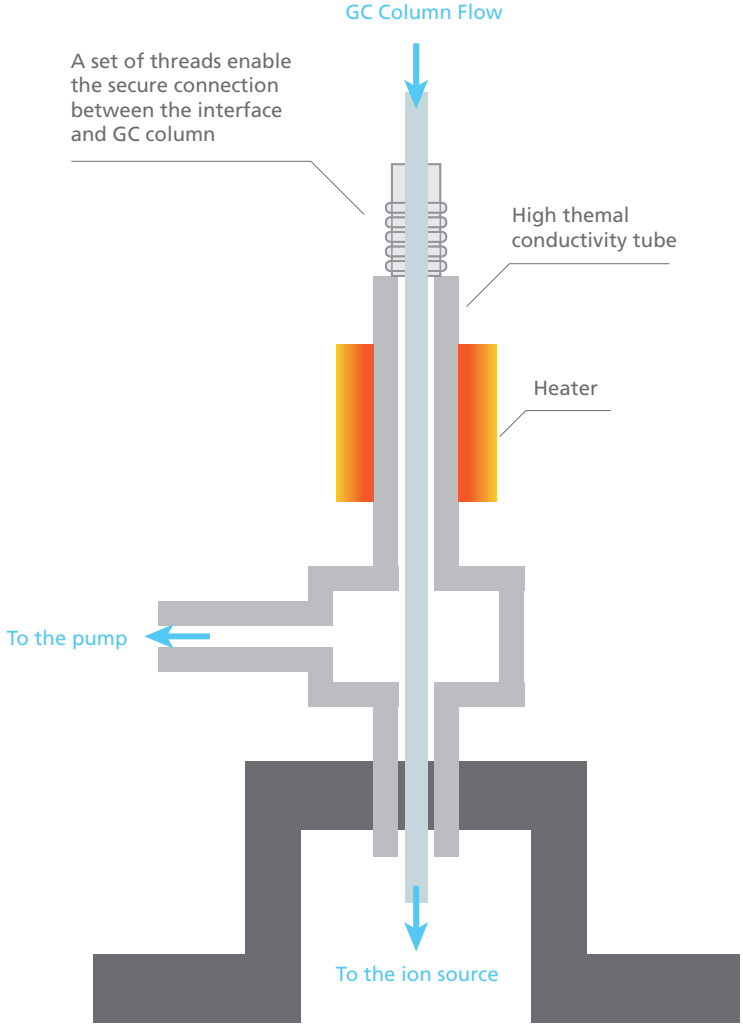


Figure 13. Direct GCMS interface.

Another system, differential pumping, obtains high vacuum in several stages (Figure 14). It is commonly used for large differences in pressure (e.g. atmospheric GC to high vacuum MS). With this phased approach, MS is divided into several vacuum chambers and gradually reaches the high vacuum required. This allows the pumps to be less loaded and the system to less easily affected. It can also afford more carrier gas (higher flow rate) in the GC.

Two pumps are generally used in a differential-pumped GCMS (Figure 14). The turbomolecular pump (TMP) is the main pump that removes the carrier gas from the GC. It can achieve a clean vacuum and prevent the background of hydrocarbons. Its start-up and shut-down time is very short and efficient, giving easier maintenance and shorter downtime. Another alternative, a dual inlet TMP, also known as split-flow TMP, is gaining attention for having higher pumping capacity and enabling higher GC flow rates in GCMS. It requires two vacuum inlets, usually located at the ion source and mass analyzer. The second pump, rotary-pump (oil-rotary pump or oil free pump), works as the backup pump to remove the exhaust from the main pump. The oil-free pump serves as a better alternative to the oil-base as it gives similar performance and requires less maintenance.

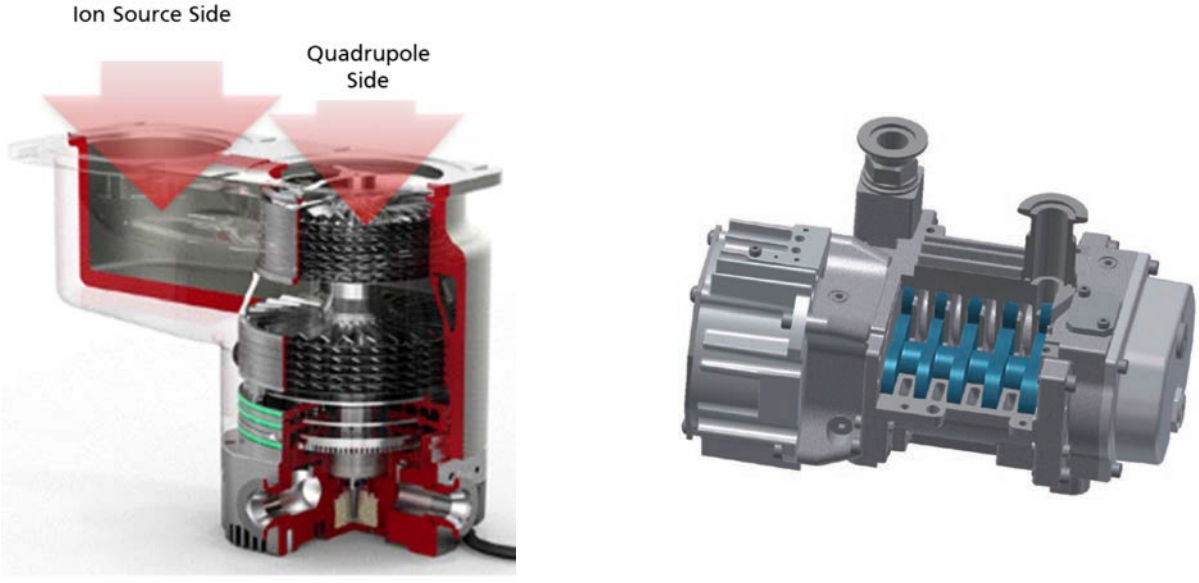


Figure 14. Illustration of a differential pumping system in a MS: differential turbomolecular pump (TMP) and an oil-free rotary pump

Learn More: Why does MS require high vacuum?

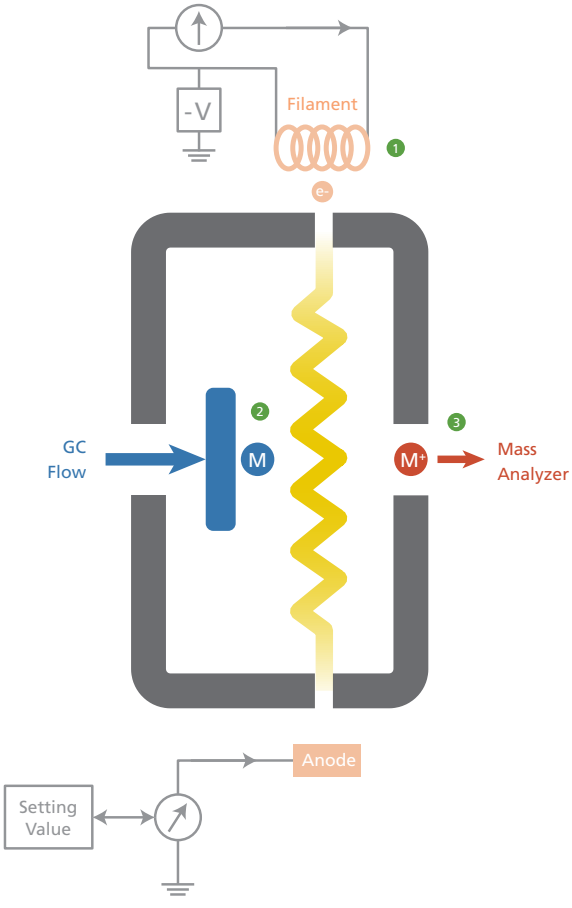
If the MS is in low vacuum, there exists other gases such as carrier and residual gases (e.g. helium, air and water) that can interfere with the ion path and affect the analysis. Target ions, created at the ion source, may collide with these gases on the way from the ion source to the detector. These unwanted collisions cause the loss of target ions and possible fragmentation, resulting in low sensitivity and irreproducible mass spectrum. The average distance of an ion's free flight without collision is defined as the mean-free path. To achieve high sensitivity and reliable data, a sufficiently long mean-free path is desired. A quadrupole MS is usually operated at around 10^{-3} to 10^{-4} Pa; this corresponds to about 5 – 50 m of mean-free path. With high vacuum, ions can reach the detector with minimal loss.

Ion Source

In GCMS, the ion source converts gaseous molecules into charged ions by means of electron bombardment or collision/reaction with a reagent gas. Electron ionization (EI) and Chemical ionization (CI) are the main ionization modes used in GCMS. The characteristics of each ionization method and the processes that occur in the ion source chamber are described in depth in this section. It serves as a guide to understand and select the most suitable ion source for your required analysis.

Electron Ionization

Electron ionization (EI) is a typical ion source for GCMS. As its name implies, electrons collide with gaseous molecules to form ions. The components in the EI chamber and the related processes are described in greater detail using Figure 15.



1. Electrons (70 eV) are produced by the heated filament and accelerated to the anode.
2. Gaseous compounds from GC flow collide with these high energy electrons.

$$M_{(g)} + e^- \rightarrow M^+_{(g)} + 2e^-$$

3. Compounds are ionized by the electron beam and undergo fragmentation. The molecular ion is rarely observed and fragments ion are usually detected. Ions are directed to the mass analyzer.

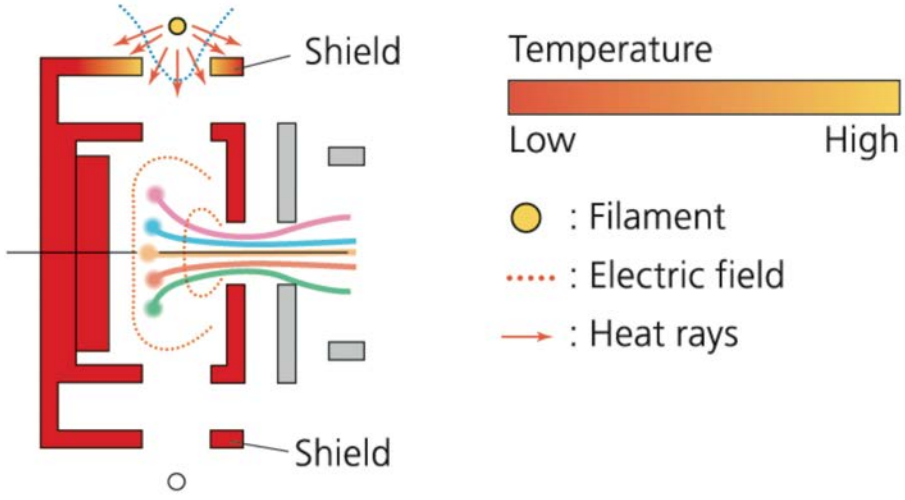
Figure 15: Election Ionization (EI) Ion Source. (Anode: A second filament is used as the anode in Shimadzu EI ion source and it allows automatic switching.)

Electrons are generated from a heated filament and accelerated by high voltage towards the ion source chamber. Gaseous molecules eluted from the GC collides with these electrons (i.e. electron beam of 70eV) in the EI chamber. From the collision, an electron is removed from the molecule to form the molecular ion (M^+). In some cases, the molecular ion is stable and does not undergo any further fragmentation. Almost always, the ionization in EI do not just stop at the molecular ion (M^+). There exists excess energy and meta-stable molecular ion (M^{+*}) can be produced. The instability of this M^{+*} ion and excess energy causes further fragmentation into smaller *m/z* ions (also known as fragment ions). Due to this reason, EI is commonly referred to as hard ionization where fragmentation is quite extensive and molecular ion is rarely observed. These ions (charged fragment ions) are produced and then accelerated to the mass analyzer.

An open-type ion source chamber is used for EI. It simply consists of a filament, an anode and the chamber as shown in Figure 15. The vacuum in the ion source is mainly determined by the carrier gas which is less than 10^{-2} Pa. With lesser interference from the GC carrier gases, it provides high chance for electrons and gaseous molecules to collide. Magnets may also be used in the ion source chamber to direct the electrons emitted from the filament to the gaseous molecules from the GC inlet flow. This increases the number of electrons entering the ion source and the number of collisions between the electrons and compounds. Thus, the use of magnets enhances the ionization efficiency. In essence, factors such as the ion source pressure, electron energy, temperature and design of ion source chamber are important in achieving the efficiency and reproducibility of EI.

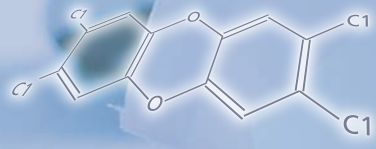
Learn More: Achieve Uniform Temperature in Electron Ionization Ion Source

The temperature in the ion source can be adjusted from 50 – 350°C and is usually heated and set at about 200°C. However, the heated filament and its electric potential can cause uneven distribution of temperature in the ion source. This affects the processes and collisions in the chamber. Shimadzu has overcome this issue by placing more distance between the filament and ion source chamber. In addition, a shield, that blocks out the radiant heat of the filament, is added to ensure that that temperature of the ion source remains uniform. With this improved design, a highly sensitive and stable ion source is developed for GCMS electron ionization.



High-sensitivity ion source for GCMS-TQ8050 NX

Boosted efficiency ion source

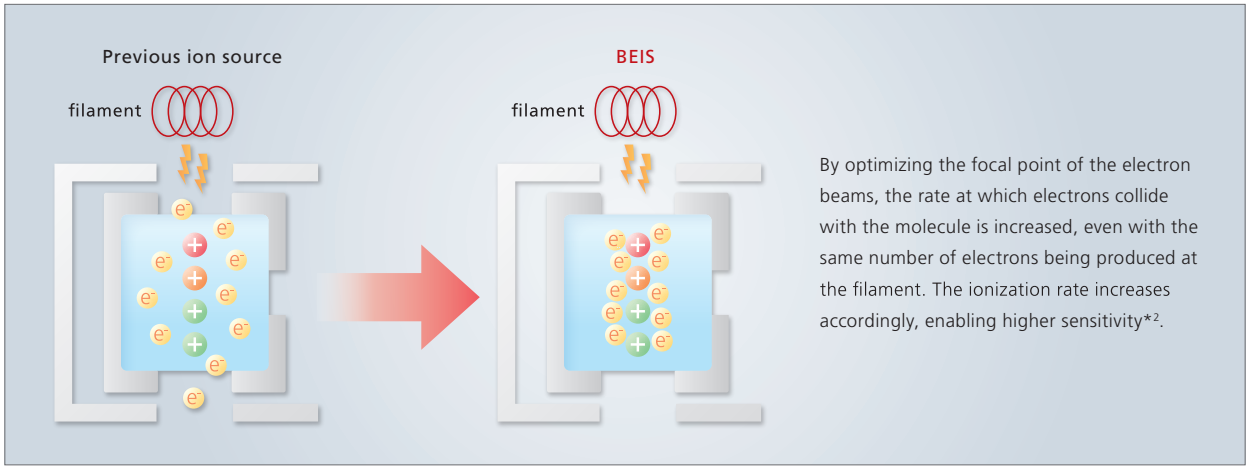


GCMS-TQ8050 NX

An ion source that dramatically increases the sensitivity of GC-MS/MS

As the capabilities of GC-MS/MS equipment have improved in recent years, it has come to be used for analysis of toxic compounds such as POPs (Persistent Organic Pollutants). Equipment sensitivity is of great importance for the analysis of low concentrations of these highly-toxic compounds,.

The BEIS (Boosted Efficiency Ion Source) maximizes ionization efficiency through optimizing the focal point of the electron beam in EI ionization. This achieves 4 times*[1] the sensitivity of previous ion sources, allowing reliable analyses of low concentrations that until now have not been possible. This is effective for analyzing POPs in environmental samples.



By optimizing the focal point of the electron beams, the rate at which electrons collide with the molecule is increased, even with the same number of electrons being produced at the filament. The ionization rate increases accordingly, enabling higher sensitivity*[2].

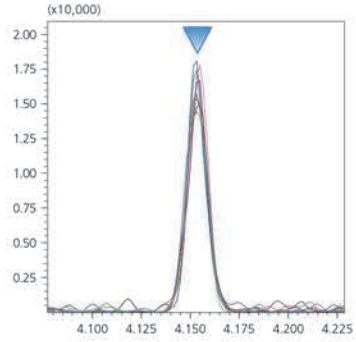
High-sensitivity ion source for GCMS-TQ8050 NX

Boosted efficiency ion source

Detection at the attogram level

Example: analysis of octafluoronaphthalene

With the increase in sensitivity, the instrument detection limit (IDL) is improved. The figure shows an example analysis of octafluoro-naphthalene. With an IDL of 0.14 fg, detection on the order of attograms becomes possible.

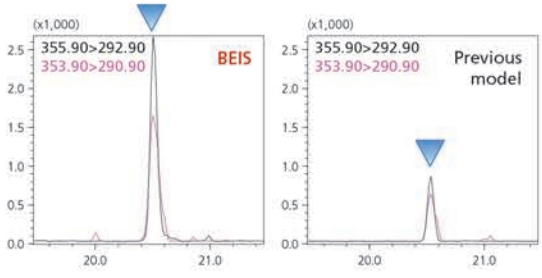


Analysis results for octafluoronaphthalene (1 fg, n=8)

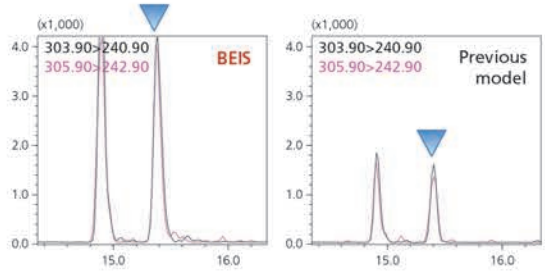
Reliable analysis of dioxins

Until now, analysis of dioxins in foodstuffs has been carried out using GC-HRMS (double-focusing GC-MS). However, with the increase in GC-MS/MS capabilities, the EU has issued regulations (EU589/2014,644/2017) which grant analysis methods using GC-MS/MS the same status in compliance regulations as methods using GC-HRMS. The BEIS therefore provides an optimal solution for those looking to move from GC-HRMS to GC-MS/MS for high-sensitivity analysis of dioxins in ultra-low concentrations.

Sensitivity comparison against a previous ion source



1,2,3,7,8-Pentachlorodibenzo-p-dioxin (25 fg/uL)



2,3,7,8-Tetrachlorodibenzofuran (25 fg/uL)

Compatible instruments

GCMS-TQ8050 NX

Standard specifications*3

EI MRM IDL (helium carrier):

1 fg octafluoronaphthalene *m/z* 272 → 222 IDL≤0.3 fg (n=8)

*1 The increase in sensitivity is dependent on the compound.

*2 Depending on usage, the lifetime of the filament may be shortened compared to previous models. Please contact a Shimadzu sales representative for details.

*3 As a general rule, standard specification checks are not carried out. If checks are required, please inquire about this in advance. In addition, the IDL is only checked when mounting the auto-injector.

The ionization voltage or the voltage difference between the filament represents the energy of the electrons emitted. This value can be adjusted but is generally kept at 70 eV, as the ion intensity is generally most intense at around 70 eV. When the energy used is decreased (<70 eV), the degree of fragmentation reduces, and the signal intensity of the fragments ions decreases (Figure 16). For energy below 10eV, ions normally cannot be produced. Besides fragmentation, molecules may undergo rearrangements to obtain more stable ions.

Ultimately in EI, the fragmentation process, distribution of ions and existence of the molecular ion depends on the compound, its bonds and stability. Given the same analytical conditions and parameters (e.g. 70eV), the ionization and fragmentation by EI is identical, giving reproducible mass spectrum. With the ability to compare and reference these generated spectral and databases, EI is preferred and used widely for both qualitative and quantitative analysis.

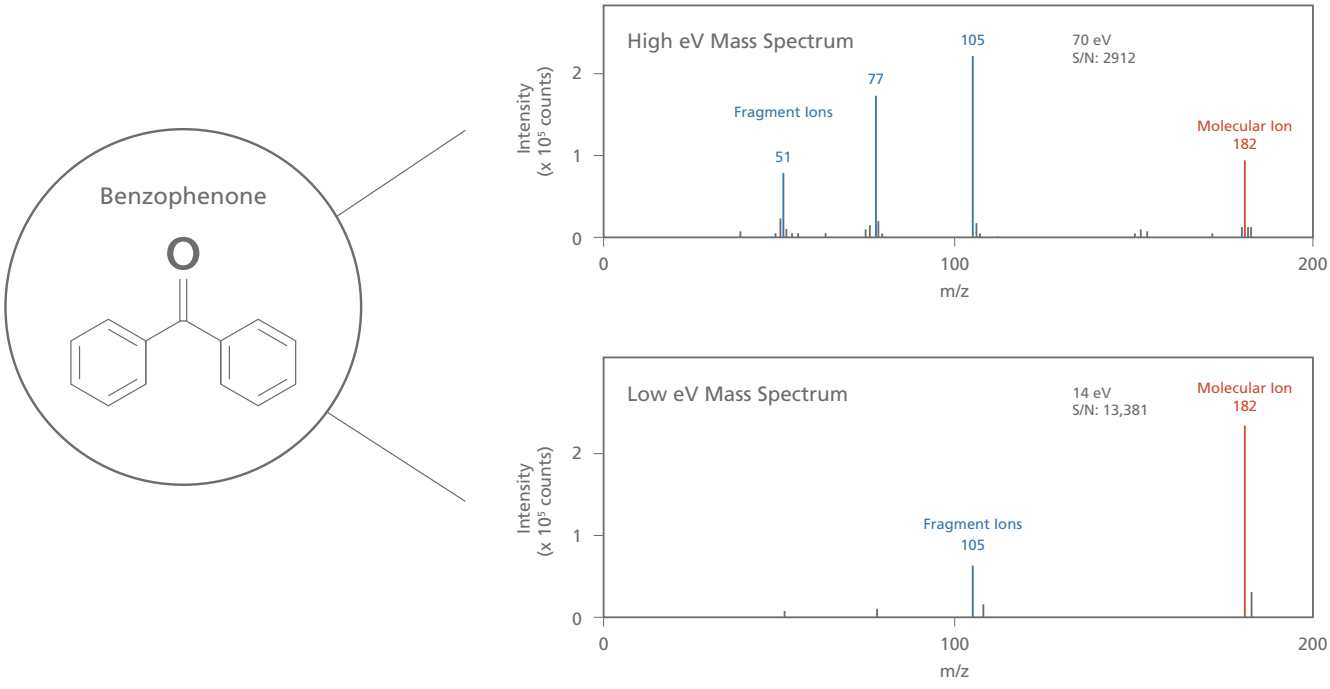


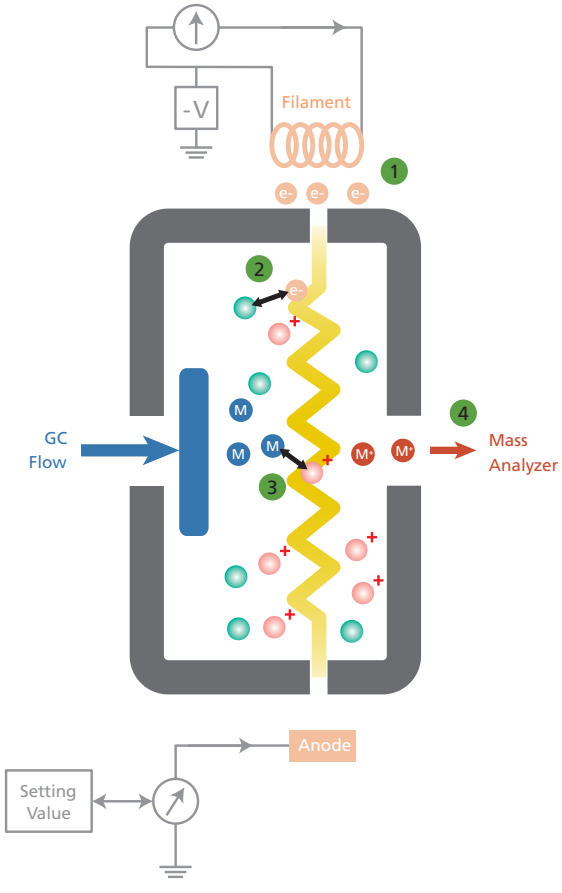
Figure 16. Mass spectrum of benzophenone at high (70 eV) and low (14 eV) electron energy.

Chemical Ionization

Chemical Ionization (CI), a soft type of ionization, is often employed in GCMS for the detection of molecular ion. CI exists in two modes: positive and negative and is usually used as a complementary ionization technique to EI. In Positive Chemical Ionization (PCI), positive ions are of interest and are generated and extracted in the ionization process. On the other hand, during Negative Chemical Ionization (NCI), negative ions are acquired and predominantly formed.

Positive Chemical Ionization (PCI)

Similar to EI, CI also requires electrons emitted from the filament. However, these high-energy electrons are released and accelerated into the chamber to collide with the reagent gases instead. PCI can be simply described in these three steps: (1) reagent gas molecules and these high-energy electrons collide and undergo electron ionization (EI), (2) reactant ions are formed from this ionization, and (3) sample molecules collide and react with these reactant ions to form ions. This indirect ionization of sample molecules is illustrated in Figure 17.



1. Emission of electrons from heated filament
2. Reagent gas collide with the high-energy e- to form reactant ions (Electron Ionization)

$$M + e^- \rightarrow M^+ + 2e^-$$

3. Indirect ionization – molecular reactions between reactant ions and sample molecules

$$M^+ + M \rightarrow M^+ + M$$

4. Sample ions ejected from the ion source

Key	Analyte	Reagent gas
Non Ionised	M	
Ionised	M^+	M^+

Figure 17. Positive Chemical Ionization (PCI), its processes and ion source chamber design.

Several molecular reactions can occur between the sample molecules and the reactant ions to form ions. These reactions, summarized in Table 4, can apply to a wide range of compounds. Usually, proton transfer reactions are predominant in PCI. For proton transfer to occur, the proton affinity (PA) of the sample molecule needs to be larger than that of the reactant ion. PA is defined as the tendency of a sample molecule to accept a proton.

As described, if the PA of the sample molecule M is larger than the PA of reagent gas (B), proton transfer between M and reactant ion (BH^+) will occur. Many organic compounds have proton affinity larger than 180 (larger than methane). In this case, most of these organic compounds can accept a proton and form ions when methane is used. Table 5 features some of these common reagent gases and its PA. The choice of reagent gases not only affects the type of reactions that occur, but also the generated ions and mass spectrum. Typically, all three reagent gases can produce the protonated ion $[M+H]^+$ by proton transfer. In addition to the protonated ion, the use of ammonia reagent gas may produce an adduct ion $[M+NH_4]^+$. The degree of ionization and fragmentation also differs based on the reagent gas properties; iso-butane and ammonia tend to have softer ionization than methane.

Figure 18 shows the mass spectrum of several compounds obtained using EI and PCI mode. As shown, CI softly ionizes sample molecules and is effective for confirming molecular weights while EI undergoes extensive fragmentation and produces many smaller *m/z* ions.

Table 4. Types of molecular reactions between reactant ions and sample molecules in PCI.

Types of Reaction	Description
Proton Transfer	A proton (H^+) is transferred from the reactant ion $[BH]^+$ to the sample molecule (M) to form the protonated molecule $[M+H]^+$. $M + [BH]^+ \rightarrow [M+H]^+ + B$
Addition of Reaction Ion (Electrophilic Addition)	The reactant ion (B+) is added to sample molecule to form adduct ion [M+B]+. $M + B^+ \rightarrow [M+B]^+$
Hydride Abstraction	A hydride ion is abstracted from the sample molecule to form the [M-H]+ ion. $M + [BH]^+ \rightarrow [M-H]^+ + BH_2$
Charge Exchange	Charge exchange between the reactant ion [BH]+ and sample molecule (M). $M + [BH]^+ \rightarrow M^{+}* + BH*$

Table 5. Positive Chemical Ionization: common reagent gases and its properties.

Reagent Gases (B)	Reactant Ions (BH^+)	Proton Affinity (PA) of B (kcal/mol)	Examples of Generated Ions
Methane, CH_4	CH_5^+ $C_2H_5^+$	130.5 163.5	$[M+H]^+$, $[M+C_2H_5]^+$
Iso-butane, i-C_4H_{10}	$C_4H_9^+$	196.9	$[M+H]^+$, $[M+C_2H_5]^+$, $[M+C_3H_7]^+$
Ammonia, NH_3	NH_4^+	205	$[M+H]^+$, $[M+NH_4]^+$

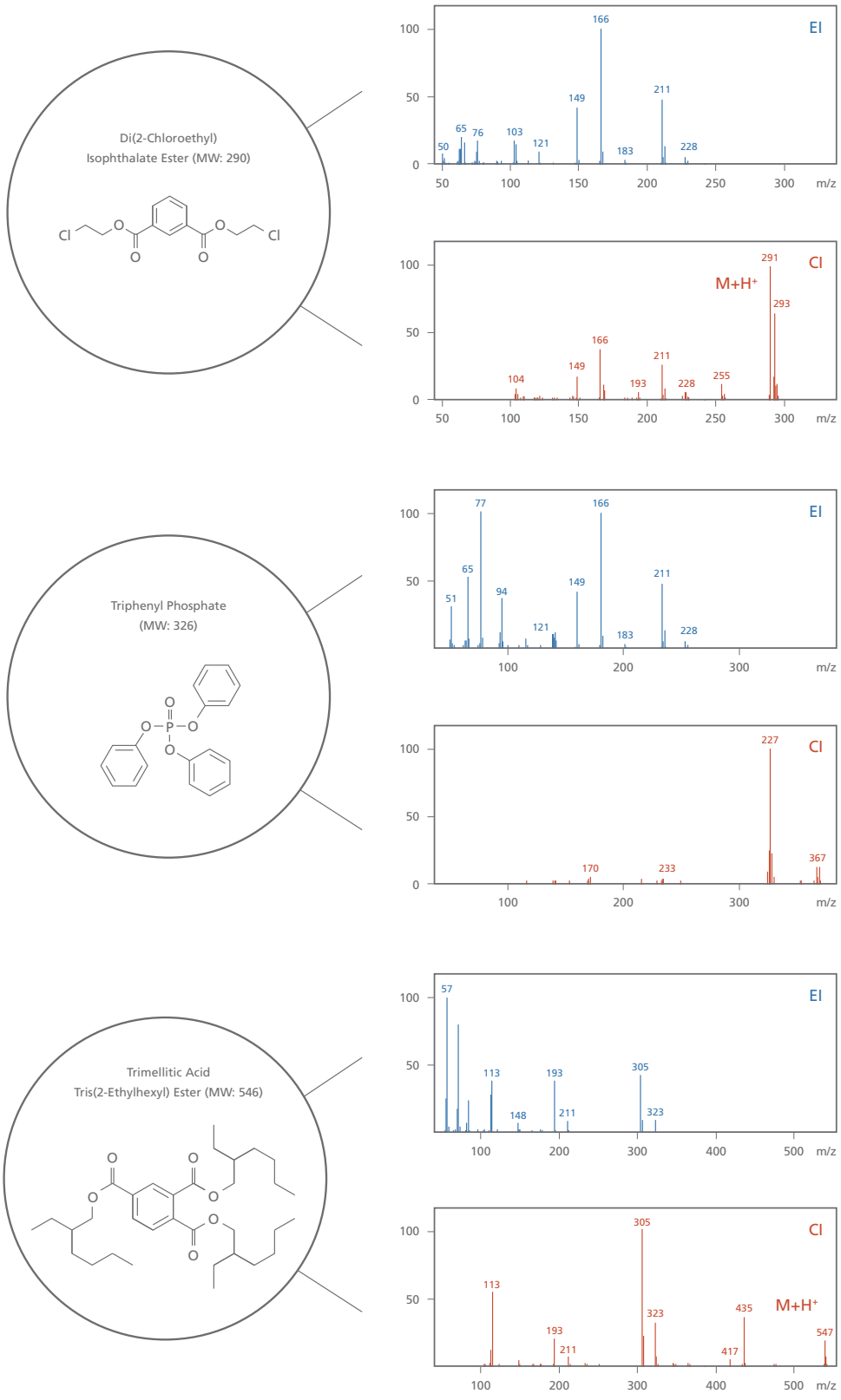


Figure 18. EI and CI mass spectra for di(2-chloroethyl)isophthalate ester, triphenyl phosphate and trimmellitic acid tris(2-ethylhexyl) ester.

The ionization efficiency of PCI can be attributed to the pressure in the ion source chamber. In order to achieve effective and reproducible ionization of the sample molecule, the reagent gas needs to be supplied sufficiently to the ion source and a pressure of about 10 – 100 Pa needs to be maintained. This ensures that there are sufficient reagent gas molecules.

Apart from having a closed or almost-closed system, there are other parameters that affect the efficiency of the ionization and the collision. Factors such as the initial electron energy of the electrons, the pressure and type of reagent gases and the temperature affects the mass spectrum generated. These conditions need to be fulfilled for PCI to occur.

Additional Information on Positive Chemical Ionization (PCI)

In the event that the pressure in the ion source chamber is insufficient or that the ion source is not correctly mounted, EI will take place instead of PCI. To check that the GCMS ion source setup and parameters are appropriate for PCI to occur, the mass spectrum of methane (a common reagent gas) can be acquired. The mass spectrum of methane under EI and PCI mode differ significantly. An EI spectrum of methane shows the base peak at *m/z* 16. Under the appropriate PCI conditions, many complex ions such as $[CH_4 + H]^+$ and $[C_2H_5]^+$ are produced. The possible reactions of methane molecule in PCI are shown below:

$$CH_4 + e^- \rightarrow CH_4^{+}*,\ CH_3^+,\ CH_2^{+}*,\ CH^+,\ C^{+}*,\ H_2^{+}*,\ H^+$$

$$CH_4^{+}* + CH_4 \rightarrow CH_5^+ + CH_3*$$

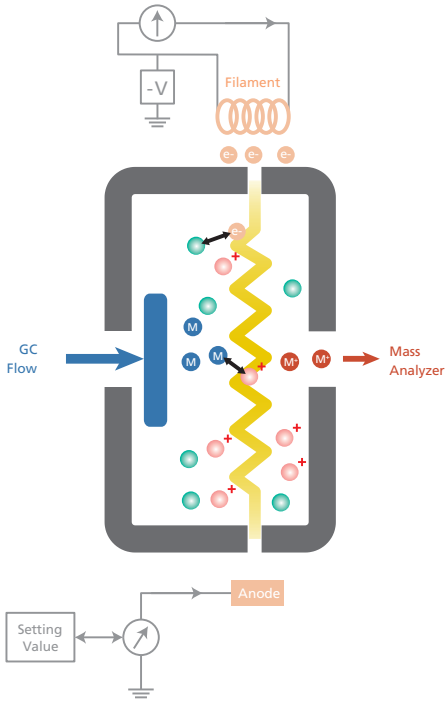
$$CH_3^+ + CH_4 \rightarrow C_2H_7^+ \rightarrow C_2H_5^+ + H_2$$

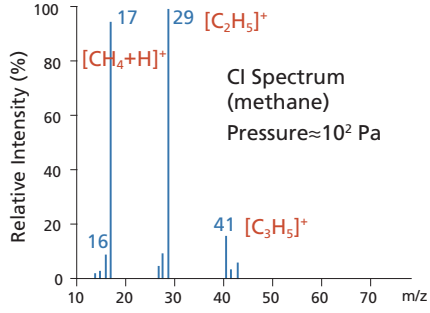
$$CH_2^{+}* + CH_4 \rightarrow C_2H_4^{+}* + H_2$$

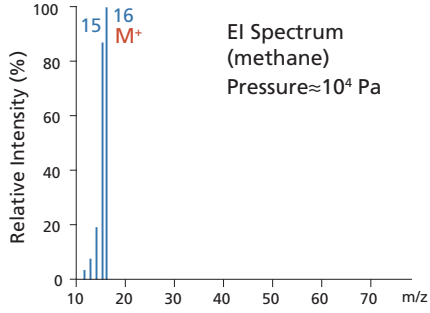
$$CH_2^{+}* + CH_4 \rightarrow C_2H_3^+ + H_2 + H*$$

$$C_2H_3^+ + CH_4 \rightarrow C_3H_5^+ + H_2$$

$$C_2H_5^+ + CH_4 \rightarrow C_3H_7^+ + H_2$$







Negative Chemical Ionization (NCI)

Negative ions are predominantly formed in Negative Chemical Ionization (NCI). The processes are initiated by a heated filament which emits electrons. These high-energy electrons collide with the reagent gases (also known as buffer gases in NCI) and are decelerated to form low-energy 'thermal' electrons. These 'thermal' electrons further collide with sample molecules (M), thus ionizing and forming negatively-charged ions (M-).

$$e^- (70eV) + B \rightarrow e^- (\text{'thermal' electron, 2eV})$$

$$e^- + M \rightarrow M^-$$

B: Buffer Gas, M: Sample Molecule

Similar to PCI, NCI is a soft ionization technique as these low-energy thermal electrons are not energized enough to extensively fragment the sample molecule. In some cases, fragmentation of sample molecules may occur when electrons with enough energy collide with these sample molecules. These processes are tabulated in Table 6, illustrating the different reactions when the sample molecule captures electrons of varied energy.

Not all compounds are suited for NCI. This ionization mode is highly-sensitive, selective and is mainly applicable for the detection of compounds with a large electron affinity (EA). The mechanism and processes in NCI is quite similar to ECD (Electron Capture Detector) and is commonly employed for the analysis of halogenated and organophosphorus compounds.

Table 6. Types of reactions between an electron and the sample molecule in Negative Chemical Ionization

Types of Reaction	Description
Resonance Electron Capture	An electron with low kinetic energy, (thermal electrons, 0 – 2eV) is directly captured by a molecule without fragmentation. This process forms the molecular ion (M^-). $M + e^- \rightarrow M^-$
Dissociative Electron Capture	Thermal electrons (0 – 15eV) is captured by the sample molecule and excess energy leads to fragmentation and formation of fragment ion [M-A]-. $M + e^- \rightarrow [M\text{-}A]^- + A$
Ion Pair Formation	Bombardment of an electron of energy more than 10eV causes the fragmentation of the molecule to produce a pair of positive and negative ions. $M + e^- \rightarrow [M\text{-}B]^- + B^+ + e^-$

Buffer gases (e.g. methane, iso-butane and ammonia) are required. These gases assist in the ionization by slowing down the velocity of the electrons and facilitating sample molecules in capturing these electrons. For this reason, the pressure requirement in the NCI ion source chamber is lower than in PCI, at about 1 – 10 Pa and a semi-closed chamber is required. The ionization efficiency and sensitivity of NCI is measured by the quantity of negatively-charged ions formed. The lower the pressure, the higher the sensitivity. Similarly, with lower temperature, the increased in probability of the sample molecule in capturing the electrons. The purity of the buffer gas also has an impact as these water and impurity molecules can compete for the electrons. This greatly reduces the sensitivity of NCI.

Comparing PCI and NCI, higher pressure of reaction gas is used in PCI for better sensitivity. On the other hand, NCI demonstrates higher sensitivity when low pressure is used. At low pressure, there is higher ion extraction rates for NCI and hence better sensitivity. The size of the opening where ions are released and guided from the ion source is bigger in the NCI chamber. Therefore, it is necessary to use appropriate ion source chamber when switching between these methods to achieve the highest efficiency and sensitivity.

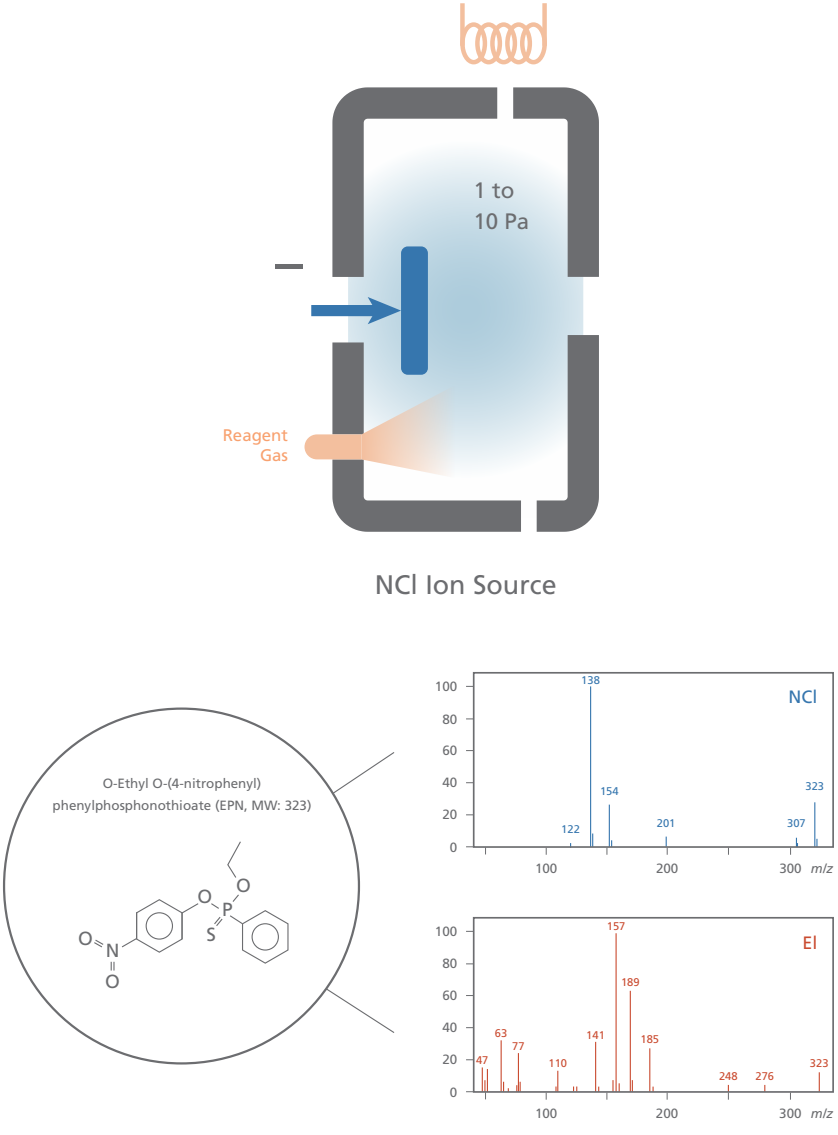


Figure 19. EI and NCI MS spectra and NCI ion source chamber.

Optional unit for the GCMS-NX series

SMCI Unit

SMCI stands for Solvent Mediated Chemical Ionization, a soft ionization method for GCMS. The headspace reagent gas from the sample bottle is introduced into the GCMS ionization unit to be ionized, which then causes chemical ionization (CI) of the target molecule via protonation.* Previous CI methods have required the use of flammable reagent gas cylinders, but SMCI can be carried out with a general organic solvent such as methanol or acetonitrile, together with nitrogen or argon gas. This results in greater safety and lower running costs.

Outside view

Inside view

SMCI unit＋GCMS-QP2020 NX

A safe and simple ionization method

Cylinders of flammable gas such as methane or isobutane are not used in this method, so it is easy and safe to install the equipment.

Can handle a large number of compounds

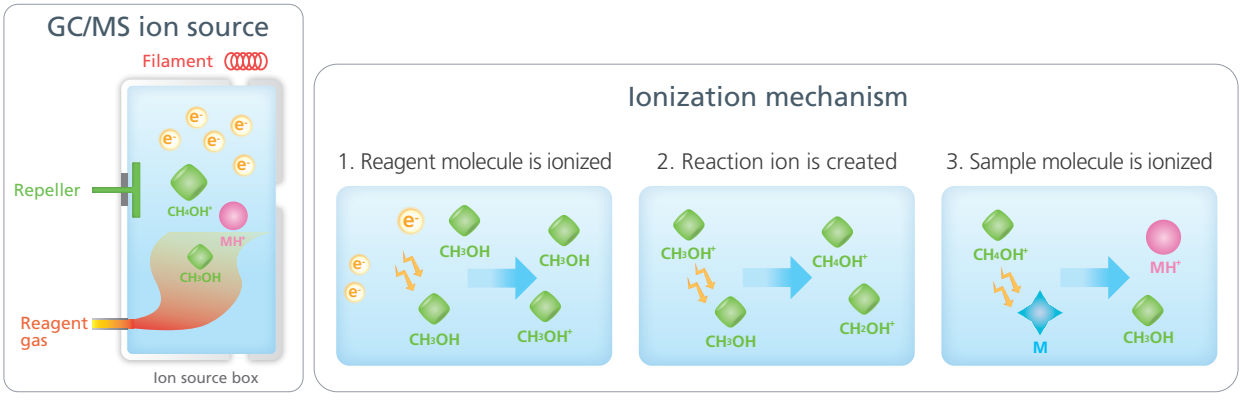
Compared to the CI substitution method, the SMCI method with methanol is less dependent on the compound, but can produce the same results. Because the SMCI method results in less fragmentation, it is very effective for verifying molecular weights for qualitative analysis.

Provides unique structural information to identify compounds

SMCI can provide structural information in addition to molecular weights. For example, using acetonitrile as the reagent gas with a TQ, it is possible to identify the position of double bonds in unsaturated fatty acids.

Low running costs

The reagent gas is less expensive than for other CI methods, so running costs can be reduced by over 80%.

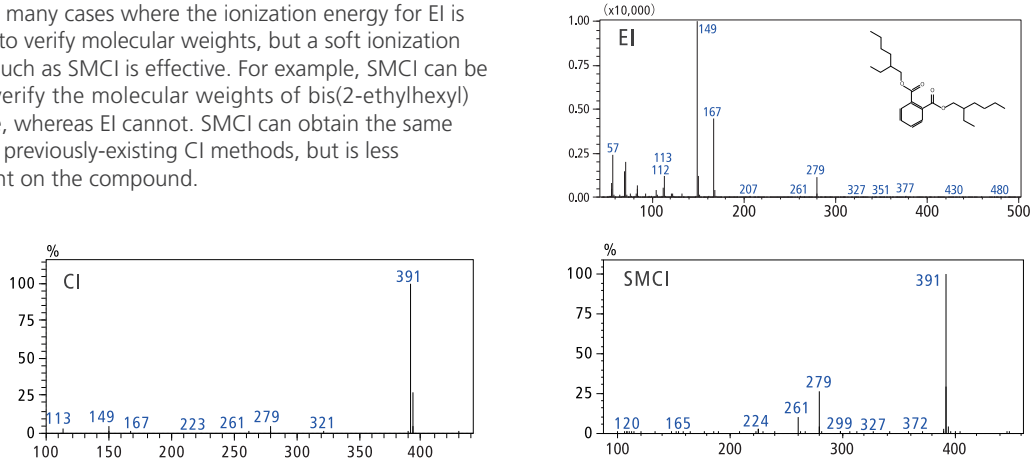


Principles of SMCI

*Patent pending

A CI method that can deal with various types of compounds

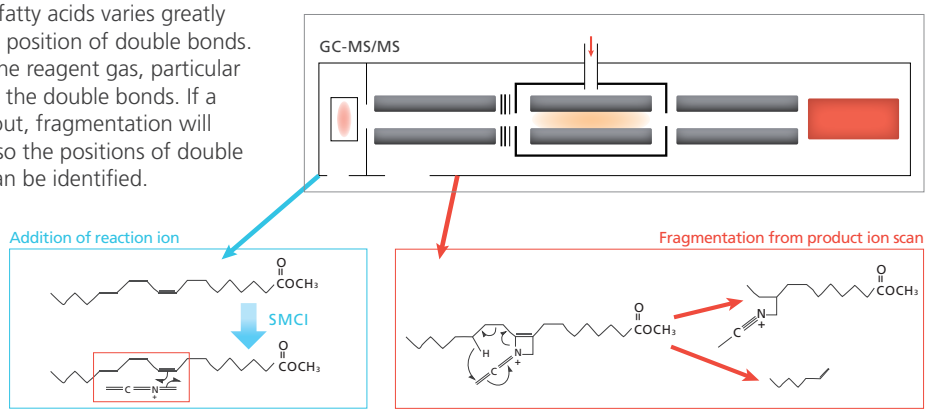
There are many cases where the ionization energy for EI is too high to verify molecular weights, but a soft ionization method such as SMCI is effective. For example, SMCI can be used to verify the molecular weights of bis(2-ethylhexyl) phthalate, whereas EI cannot. SMCI can obtain the same results as previously-existing CI methods, but is less dependent on the compound.



The mass spectrum of bis(2-ethylhexyl) phthalate (MW=390) obtained using different ionization methods

Identifying the position of double bonds in unsaturated fatty acids

The functionality of unsaturated fatty acids varies greatly depending on branching and the position of double bonds. Using SMCI with acetonitrile as the reagent gas, particular reaction ions selectively attach to the double bonds. If a product ion scan is then carried out, fragmentation will occur at these attachment sites, so the positions of double bonds in the original fatty acid can be identified.



Compatible GCMS models

GCMS-TQ8050 NX、GCMS-TQ8040 NX,GCMS-QP2020 NX

Recommended consumables

HPLC grade methanol or acetonitrile
Nitrogen or argon gas (99.99+% purity)

Comparison of Ion Sources

The ion sources in GCMS, that is EI, PCI and NCI, have been described in detail in the earlier sections. Together, the key features of these ionization modes are summarized in Table 7 to give a clearer comparison and idea in selecting the ion sources for your analysis and compounds.

Depending on the sample and objectives of the GCMS analysis, these ionization modes (i.e. EI, PCI, NCI) and its individual parameters need to be selected and optimized. For PCI and NCI, the selection of reagent/buffer gases is generally determined by trial and error. Generally, iso-butane is first considered, followed by ammonia. Methane is used in cases where the molecular weight of the sample compound is small.

Table 7. Summary of ionization modes (EI, PCI and NCI) in GCMS.

Ionization in GCMS	Electron Ionization (EI)	Chemical Ionization (CI)	
		Positive (PCI)	Negative (NCI)
Ionization Process	Direct process Bombard with high-energy electrons	Indirect process Reaction with reagent gases	Indirect process Interaction with buffer gases
Type of Ionization	Hard	Soft	Soft
Types of Ions Formed	Singly Charged Molecular ion rarely observed Mainly positively-charged ions	Single Charged Molecular ion observed Mainly positively-charged ions	Singly Charged Molecular ion observed Mainly negatively-charged ions
Compound Suitability	Universal, generally applicable for most compounds	Universal, generally applicable for most compounds	Highly selective for compounds with high electron affinities
Reagent Gas	No	Yes	Yes (Buffer Gas)
Type of Ion Source Chamber	Open	Almost Closed	Semi-Closed
Pressure in Ion Source Chamber	$< 10^{-2}$ Pa	10 – 100 Pa	1 – 10 Pa
Filament Control	Trap Current Control	Total Current Control	Total Current Control
Voltage Used	Positive	Positive	Negative
Parameters Affecting Efficiency of Ionization Process	Electron energy Temperature	Electron energy Temperature Pressure Type and Purity of Reagent Gas	Electron energy Temperature Pressure Type and Purity of Reagent Gas
Advantage/Strength	70eV EI – commonly used for mass spectral library database Able to gather structural information	Molecular ion can be observed	Molecular ion can be observed 100 – 1000 times more sensitive than EI and PCI.

There are pros and cons for each of these ionization modes. To accommodate the needs and demands of GCMS analysis today, manufacturers are looking to develop the 'ideal' GCMS ion source that have these features:

- Generates both molecular ion and fragment ions in a single analysis
- Capable of producing a mass spectrum for comparing with library database
- Fast, reproducible, robust, sensitive and low noise

To some extent, the 'ideal' ion source resembles an ionization mode that possess the characteristics of both EI and CI. With the technology and capability of the GCMS manufacturers, it is possible to design the ion source chamber and combine several ionization modes in a single ion source. This ion source serves to achieve the ideal features in a short and convenient manner.

Shimadzu has developed the Smart EI/CI ion source which is a single ion source that can easily switch from EI to CI mode, without compromising the sensitivity of the EI method. The Smart EI/CI ion source is fast, convenient and does not require any temperature stabilization. As shown in Table 8, the sensitivities of EI mode using the Smart EI/CI ion source is 100%. This can facilitate the collection and confirmation of both fragment ions and molecular ion with both the EI and CI data.

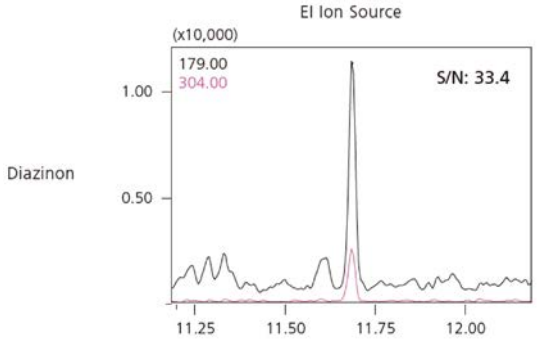
Upon leaving the ion source, these ions are accelerated and directed to the mass analyzers with the help of the ion guide. Ions are separated by their different *m/z* and travel towards the detector.

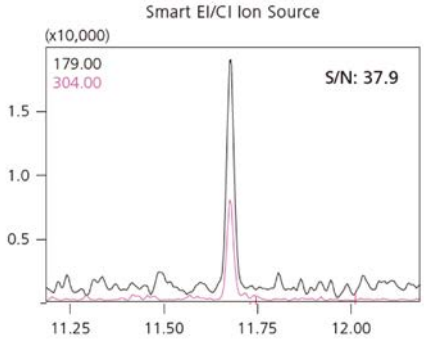
Table 8. Sensitivities of various ionization modes when using the EI, CI, Smart EI/CI and NCI ion source.

Type of Ion Source Used in Shimadzu	Sensitivities of Ionization Mode When Using These Ion Sources
EI Source	100% EI mode
CI Source	100% CI (PCI) mode, equipped with EI options
Smart EI/CI Source	100% EI mode, allows seamless exchange of EI & CI modes within a batch
NCI Source	100% NCI mode, equipped with both EI and CI (PCI) options
SMCI Source	100% solvent mediated CI or NCI mode (no reagent gas required)

Learn more on the Smart EI/CI Ion Source.

The quick switching of EI/CI modes in the same ion same analysis using the same ion source allows for faster and more convenient GCMS analysis. This ionization technique generates both molecular and fragment ions and is essentially useful in many applications. Download Shimadzu's Technical Report on "Usefulness of Smart EI/CI Ion Source Which Enables Both EI and CI Mode Measurements with The Same Ion Source" to find out on the key features and benefits.





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Detector

Electron multipliers are commonly used to detect ions. There are generally two main types used in MS: (a) discrete dynode electron multiplier and (b) continuous dynode electron multiplier. They operate in vacuum, adopt the same working principles and use dynodes, which are defined as electrodes that emit secondary electrons in a vacuum tube, or simply termed as amplifying devices.

A discrete dynode electron multiplier (Figure 20a) has about 10 – 25 individual dynodes arranged in succession. Negative voltage is applied to each dynode with the use of resistors where the applied voltage is more positive with each succeeding dynode. When an ion hits the first dynode, several electrons are emitted from the surface. This emission of secondary electrons repeats for succeeding dynodes and generates even more electrons and higher electric current. Eventually, this exponentially-amplified signal is measured for ions for each *m/z* and recorded into a mass spectrum.

The continuous dynode electron multiplier (Figure 20b) is generally shaped like a horn and made up of lead-silicate glass. Its amplification principle is similar to the discrete-dynode type, but electrons are emitted from the continuous inner surface of the dynode, instead of from a separate discrete metal dynode. The signal is amplified, and all triggered by just a single ion. If there are more ions hitting the dynode surface at the start, there will be more electrons generated and a corresponding higher signal will be recorded. The mass spectrum acquired will correspond to the intensity of the signal and the quantity of the ions. In the MS, the electron multiplier is usually positioned off-axis as shown in Figure 20 to reduce excessive noise and redundant ions (e.g. direct hit of neutral particles), giving lower noise and higher sensitivity.

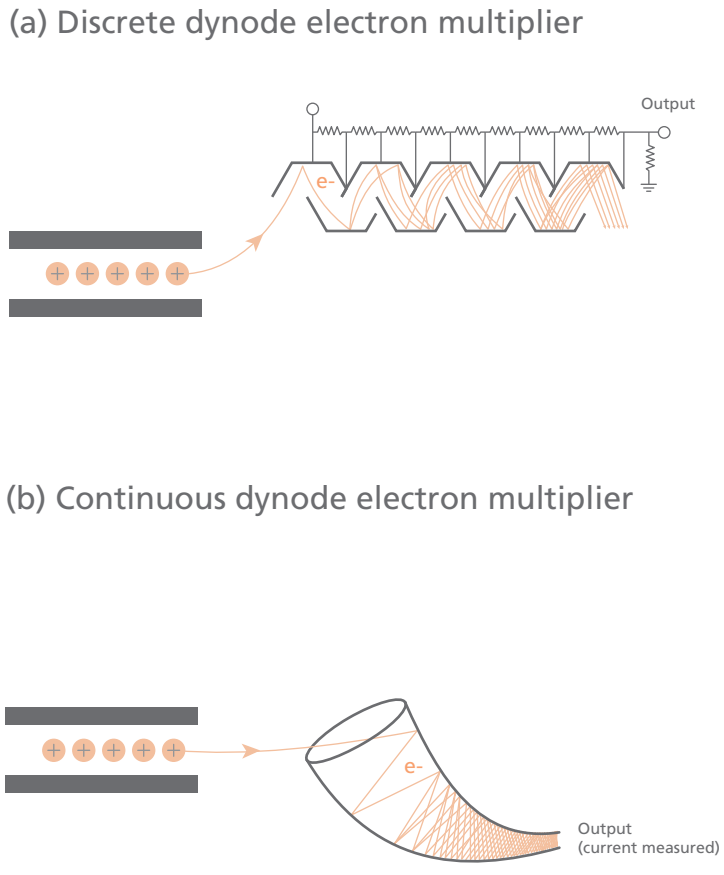
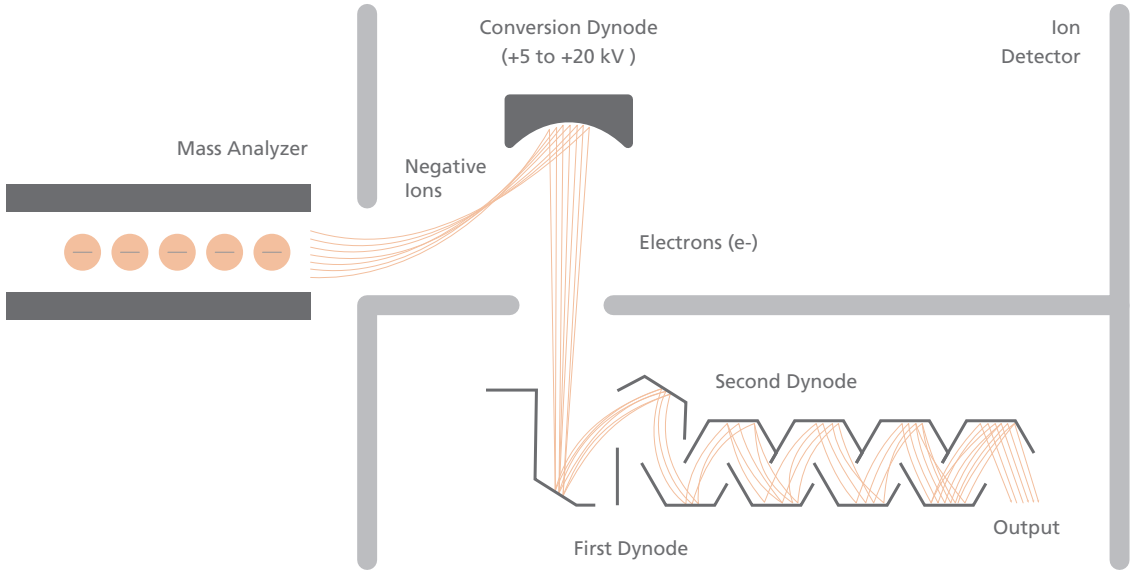


Figure 20. Electron multipliers: (a) Discrete dynode electron multiplier and (b) Continuous dynode electron multiplier.

Learn More: Conversion Dynode

Electron multipliers can detect both positive and negative ions in the same run and MS instrument. At times, a conversion dynode is placed in front of the electron multiplier. This conversion dynode, possessing high voltage of 5 – 20 kV with reverse polarity to the target ion, allows the detection of negative ions and increase the signal intensity of ions, particularly in the high mass region.



Detectors can be classified as either point- or array-detectors. The choice mainly depends on the mass analyzers used, and whether the ions are spatially resolved. Generally, point-detectors are suited for time-based MS where ions are separated temporally and gets detected sequentially at a fixed point. On the other hand, array-detectors go together with space-based MS where ions are spatially resolved and separated based on their deviation in terms of path radius or velocity. The various mass analyzers and their separating principle are discussed in greater detail in Chapter 3.

The setup of the discrete dynode and continuous dynode electron multiplier, shown in Figure 20, are examples of point-detectors. They are suited for ions separated by quadrupole MS and ion trap MS. Array detectors, such as microchannel plate (MCP), are commonly found in time-of-flight (TOF) MS. As illustrated in Figure 21, the MCP consists of many small channels all on a plate surface. Each channel operates similarly like a continuous dynode electron multiplier. With these added channels/detectors, it offers spatial resolution and simultaneous detection of ions.

Important Parameters to Note When Using a GCMS

If you have previously used a GC and this is the first time utilizing a GCMS, there are important features to understand and note prior to running and starting your GCMS analysis. Firstly, the choice of columns is particularly important in GCMS. The internal diameter and length of a GC column affects the vacuum pressure in the MS. Using a column of a larger internal diameter allows a higher flow rate of carrier gas and requires a more powerful and effective vacuum pumping system. Also, the type and material of column is another crucial factor. In a GCMS, the columns used are usually a capillary column (i.e. WCOT) and not a packed column. This is because the MS must be maintained at very low pressure of about 10-3 to 10-4 Pa. The use of packed GC columns with high flow rates is not fully compatible with GCMS as low pressures cannot be achieved easily. Furthermore, these packed columns may be damaged, and the column materials may cause an issue and be sucked into the MS during the analysis. PLOT column can be used but it is not recommended, additional accessories or modifications may be required for the use of PLOT columns in GCMS.

The GC carrier gas is another parameter to note when using GCMS. It is important to ensure compatibility with the sample, GCMS components and ion source. The use of hydrogen as carrier gases causes issue for GCMS as the ion source pressure are not calibrated properly by nitrogen in the presence of hydrogen. This would prove to be an issue for the low capacity diffusion and turbomolecular pumps to remove hydrogen from the ion source and thus affect the vacuum pressure. Also, hydrogen's low viscosity tends to cause peak broadening or tailing in GCMS. The use of a longer column or a column with smaller internal diameter is preferred to reduce the peak broadening/tailing effect. In all, these parameters need to be noted and modified to acquire sensitive and reproducible GCMS results.

In summary, Chapter 2 covered the fundamentals of GCMS which includes its applications and instrumentation. The individual components in GCMS, such as the vacuum pumping system, ion source and detectors, were discussed in great details to aid in your understanding of GCMS.

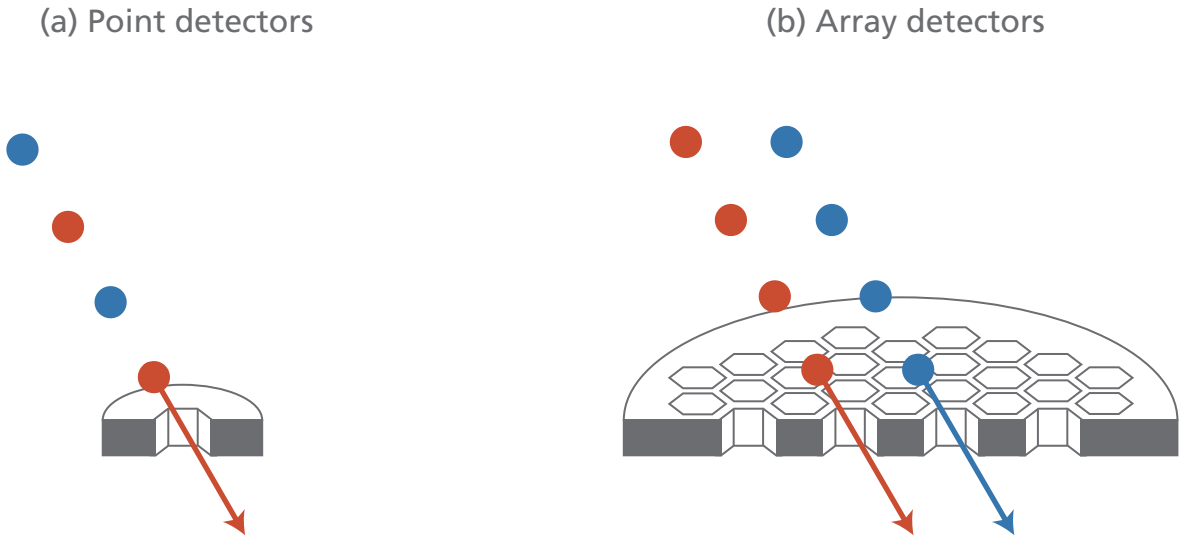
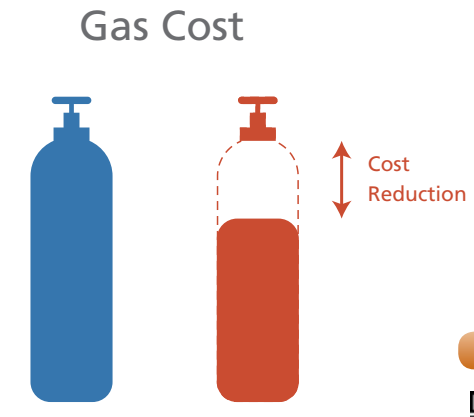


Figure 21. MS point- and array-detectors and microchannel plates (an example of array detector).

Learn More: Hydrogen as an alternative GCMS carrier gas

Most GCMS analyses utilize helium as the carrier gas. Alternatively, hydrogen can be used due to its good separation efficiency, high speed, low cost and easy-availability. With the use of Shimadzu high capacity dual-inlet turbomolecular pump, the pressure in GCMS (particularly at the ion source) can be successfully achieved and efficiently calibrated. By using method translator, the GCMS methods using helium can be easily converted to the methods using hydrogen carrier gas. Together with advanced flow control technology and gas generators, the optimal MS state can be achieved under all carrier gas conditions. Click to find out more on the use of hydrogen as an alternative GCMS carrier gas.



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Chapter 3

Mass Analyzers in GCMS and GC-MS/MS Systems

Thus far, we have only described mass spectrometry (MS) as a method used to measure the mass of atoms and molecules, but how does it measure mass? Many types of mass analyzers are available depending on the method preferred to separate ions. In this chapter, we shift our focus to MS and describe the principles and key features of various mass analyzers used in a MS and tandem MS systems.

Overview of Mass Analyzers

Normally when we measure mass (m), we use a mass scale or balance, which relies on the Earth's gravity. So, how do we measure the mass of a molecule, which is extremely small that its gravitational force is almost too negligible to determine easily? The first occurrence started in 1912, where the English physicist J. J. Thomson, utilized the fact that the flow of charged particles bends in an electric or magnetic field to develop an instrument that could separate charged particles by its mass number. In this instrument, a cathode ray tube, cations with identical mass-to-charge ratios (*m/z*) converged along the same parabola. When he measured the Neon (Ne) gas molecule, the parabolas for ^{20}Ne and ^{22}Ne (both are monovalent cations) were slightly different, which proved the existence of isotopes. Therefore, with the use of electromagnetic fields in a mass analyzer, ions can be measured and separated according to their *m/z*.

With this concept, a variety of mass analyzers have been developed but how exactly does each of these mass analyzers work? There are single mass analyzers such as the magnetic sector, quadrupole, ion-trap and time-of-flight (TOF) mass analyzers. Additionally, there are GC-MS/MS systems (also known as tandem and hybrid MS) that utilizes multiple mass analyzers. Triple Quadrupole MS/MS system is one of the more prevalent MS/MS systems in the industry.

These mass analyzers have different separating and operating principles and they can be classified by how the ions are introduced into the mass analyzers – continuous or pulsed mode. Continuous mass analyzers allow an uninterrupted supply of ions to enter while pulsed mass analyzers require the ions to be introduced only at a specific time point. In a pulsed mass analyzer, ions from a continuous flow (such as a GC flow) are usually accumulated and introduced in batches/pulses. The following sections elaborate on the principles and instrumentation of the single mass analyzers and MS/MS systems where various characteristics are compared, and pros and cons are listed for each of these mass analyzers.

Magnetic Sector MS

Magnetic sector, a continuous mass analyzer, has been used in GCMS historically the longest. As its name implies, the mass analyzer uses magnetic field to separate ions of different *m/z*. As shown in Figure 22, high voltage is applied to accelerate the ions into the mass analyzer. Ions are then exposed to the magnetic field and are deflected according to Fleming's left-hand rule[1]. The deflections experienced by the ions differ and are based on their *m/z* where ions of lower *m/z* will experience more deflection.

[1] Fleming's left-hand rule can predict the direction and force of the movement when there is an electric current moving in an applied magnetic field. As a result, ions are accelerated in a direction perpendicular to the current and magnetic field, resulting in a curved deflection path for the ions in the magnetic sector mass analyzer.

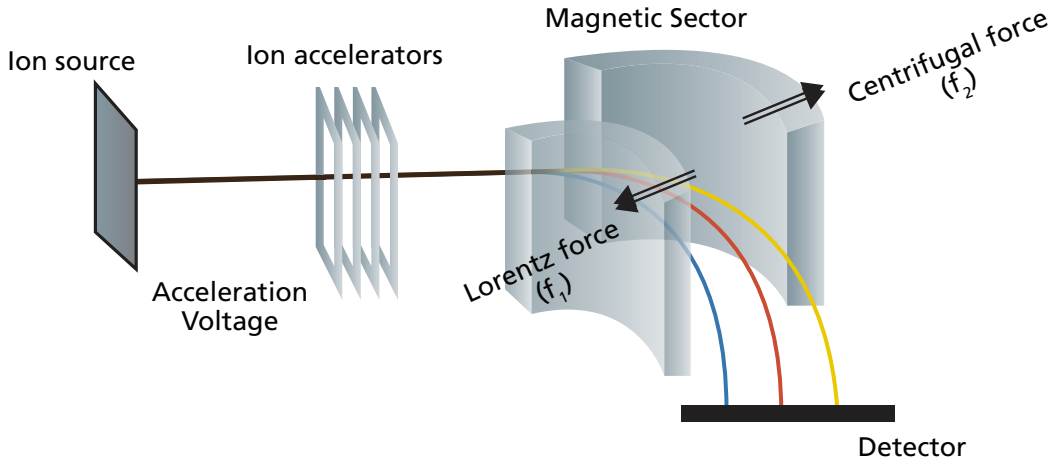


Figure 22. Schematic of a magnetic sector mass analyzer (mblue < mred < myellow).

This deflection experienced by the ions of a certain *m/z* can be simply expressed in mathematical terms. Ions experience a Lorentz force (f_1) from the magnetic field. As the ion moves and its direction changes, a centrifugal force (f_2) acts on the ion. For the ions to pass through the magnetic field region and reach the detector eventually, it must travel along a curved path of a given radius where f_1 and f_2 are balanced (Equation 2). The kinetic energy of ions accelerated by voltage V are calculated as shown in Equation 3. By eliminating the velocity of the ion (v), the equations are simplified to give Equation 4.

In theory, by keeping the ion acceleration voltage (V) constant and varying the magnetic flux (B) (or keeping B constant and varying V), a detector placed on the corresponding path radius (r) could detect any mass (m), given the same charge. However, in practice, only one ion detector is used in the magnetic sector MS and both the acceleration voltage (V) and curve path radius (r) are kept constant while the magnetic flux density (B) is scanned. This means that ions with different masses all pass along the same path through the magnetic field, one after another, and reach the detector. One mass spectrum is obtained from each scan of the magnetic field. In other words, the magnetic sector mass analyzer function by ion transmission and scanning mode.

The key characteristics of magnetic sector mass analyzer are its high resolution and wide dynamic range. Besides the described single magnetic sector mass analyzer, there are also models of MS with both the electric sector and magnetic sector in a single MS, which is known as a dual-focusing MS. This dual-focusing setup is able to focus and converge ions of different energy and identical mass thereby obtaining even higher mass resolution than the single-focusing model. The measurement range of a magnetic sector mass analyzer is typically about 10 to 10,000, though it depends on the acceleration voltage and instrument design. Resolution of about 2000 can be obtained using a single-focusing magnetic sector model and several tens of thousands can be attained using a dual-focusing magnetic sector. Before the recent introduction of the high-performance TOF MS, the dual-focusing magnetic sector was the only MS capable of such high-resolution measurements.

However, to further improve the performance of the magnetic sector MS, the strength of the magnetic field needs to be raised. This means increase in cost and space as a larger magnet and instrument are required. This limits the development of magnetic sector. With its extremely high vacuum requirement of 10^{-7} Pa and low scan speed as compared to other mass analyzers, it is limited in its usage. Nevertheless, it is notably used in high-resolution analysis such as dioxins analysis. Quadrupole MS, which is easier to use, is coming into broader use in many industries today.

$$f1 = Bzev = \frac{mv^2}{r} = f_2 \quad \text{– Equation 2}$$

$$KE_{ion} = \frac{1}{2} mv^2 = zeV \quad \text{– Equation 3}$$

$$\frac{m}{Z} = \frac{eB^2 r^2}{2V} \quad \text{– Equation 4}$$

B: magnetic flux density, m: mass of ion, z: charge of ion, r: path radius
e: elementary charge, v: velocity of ion, V: acceleration voltage applied to ions

Quadrupole MS

Quadrupole mass analyzers are most extensively employed in GCMS. It is ideal due to its compact design, high sensitivity, low cost and easy operation and maintenance. As its name implies, quadrupole MS consists of four parallel cylindrical metal rods inside a vacuum chamber, positioned equidistant from the center axis (Figure 23). These rods are electrodes with a hyperboloidal interior surface. The quadrupole mass analyzer function by scanning of ions and allowing ion transmission. In other words, ions are transmitted and detected sequentially from the lowest to highest *m/z* in the selected *m/z* range.

To begin with, ions generated from the ion source are continuously flowed and accelerated in the z-direction (Figure 23, green arrow) by a relatively weak voltage of only a few dozen volts. These ions pass through a tiny orifice and enter the quadrupole. As depicted by the blue (+) and red (-) rods in Figure 23, direct current (D.C.) and high frequency alternating current or radiofrequency (RF) are applied to the four rods where diagonally-opposite rods possess the same voltage polarity and adjacent rods are of opposite voltage polarity. With the voltages applied to the rods, an electric field with a rapidly varying phase is generated within the mass analyzer. Consequently, ions passing through this electric field oscillate in the x- and y- directions.

With an appropriate set of DC and RF voltages, certain ions of a specific *m/z* range maintain a stable oscillation and pass though the quadrupole to reach the detector. The path of these ions follows that of the resonance ion (as indicated by the purple path in Figure 23). On the contrary, the oscillation of the non-target ions (of other *m/z* values) become unstable, causing them to collide into the rods or fly out of the system and not get detected (Figure 23, non-resonance ion). In doing so, the quadrupole mass analyzer acts like a mass filter where only selected m/z ions pass through the mass analyzer.

When these DC and RF voltages are varied, the m/z range are "scanned" and the ions are transmitted to the detector. The quantity of ions that reach the detector is converted to an electronic signal and output to a computer. The data and mass spectrum of the selected *m/z* range are captured.

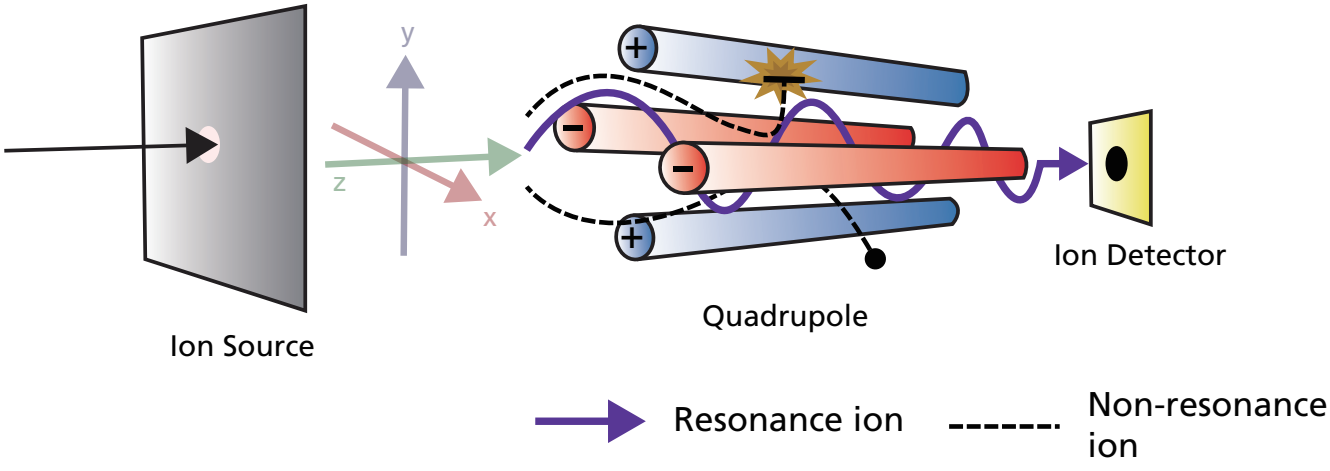


Figure 23. Quadrupole mass analyzer: how it works.

The ion path and oscillations within the quadrupole mass analyzer is based upon the Mathieu Equation (Figure 24) regardless of the ion's initial velocity or position. Figure 24 illustrates how the Mathieu Equation is solved and indicates the Mathieu Stability Diagram for the stable regions for the ions in a quadrupole mass analyzer. As illustrated in the shaded areas in the graph in Figure 24, the conditions required for stable ion oscillation are determined by the mass and oscillation frequency of the ion. The region of stability is different for ions with different mass. If the voltage is varied while keeping the ratio between the direct current voltage (y-axis) and high-frequency alternating current voltage (x-axis) constant, a straight scan line is obtained. This scan line passes through respective regions of stability for ions with masses m_1, m_2 and m_3. Consequently, these ions are passed through the quadrupole consecutively in the same order. A mass spectrum is obtained for ions with masses ranging from small to large. Based on Figure 24, the mass resolution can be altered by changing the slope of the scan line and shifting the line upward or downward.

Scan and Selected Ion Monitoring (SIM) modes

For a single quadrupole mass analyzer, it can operate in two modes: (A) Scan and (B) Selected Ion Monitoring (SIM) as illustrated in Figure 25. In the scan mode, mass spectral data are acquired in sequence at specific intervals. The voltages of the quadrupoles are configured such that the entire mass range specified is scanned sequentially with appropriate dwell time[2] for each *m/z*. As illustrated in Figure 25 (A), the blue, followed by red and lastly yellow ions passed through the quadrupole mass analyzers sequentially and gets detected. The result is a record of the ion abundance in the specified range of the mass spectrum. In SIM mode, the mass spectrometer is set to measure only the specified mass. As shown in Figure 25 (B), only the selected *m/z* (e.g. red ion) is monitored, passed through the quadrupole and gets detected. With this SIM mode, it has sufficient dwell time[2], avoids the effects of unwanted analytes and impurities, and thus offers high sensitivity.

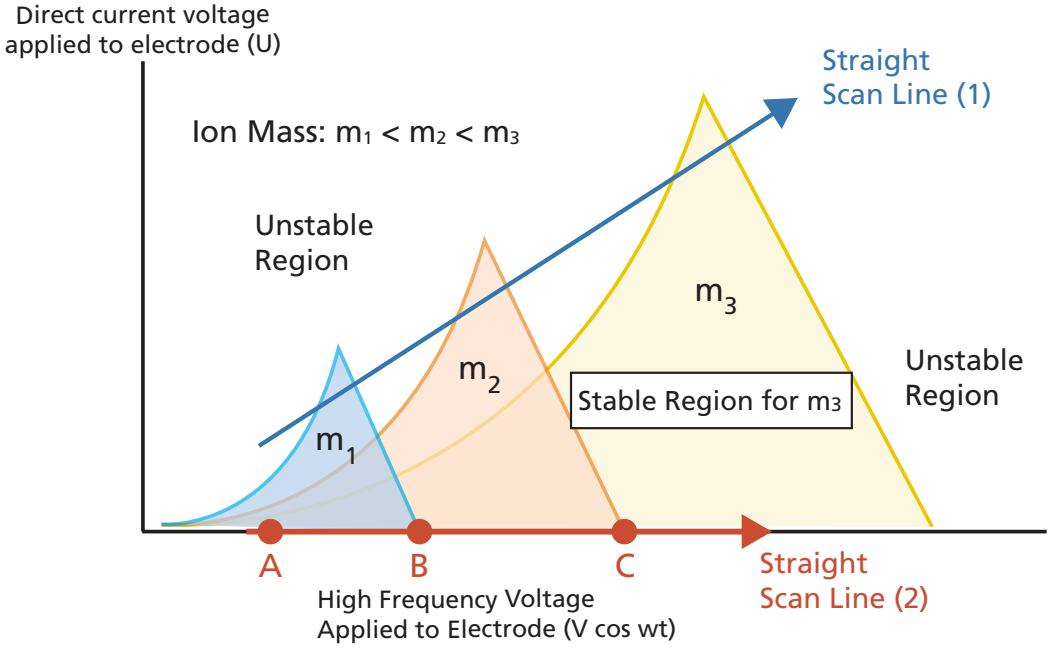


Figure 24. Mathieu Equation and Mathieu Stability Diagram for the stable regions for ions in Quadrupole MS system.

The choice of modes depends on the objectives and requirements of the GCMS analysis. If the sample components are unknown, scan mode is usually used as it captures the ion abundance and provides a full scan of the sample in the specified range of the mass spectrum. On the other hand, SIM mode is usually preferred for the quantitative analysis of known compounds as its sensitivity is at least tens to hundred times better than that in the scan mode.

Since the separating principle of quadrupole MS is rather straightforward, the instrument is comparatively easy to operate and maintain. Also, it is compact in design, robust and relatively inexpensive. Consequently, quadrupole GCMS systems are widely adopted as a general-purpose analytical instrument. Furthermore, unlike other MS which require high vacuum levels, quadrupole MS can adequately function at low vacuum levels (≈ 10^{-2} to 10^{-3} Pa). The drop in vacuum level caused by the interface to chromatography has minimal effect on the mass separation performance, making it best suited for interfacing with chromatographic techniques (such as LC and GC).

In summary, quadrupole MS demonstrates good scan speed and sensitivity. With a high scan speed of 15,000 amu/second, it measures at a much higher scan speed than the magnetic sector MS. Its mass range can reach up to 2,000 *m/z* which enables qualitative analysis in a practical range of molecular masses. In addition, it allows high-speed polarity switching, which facilitates simultaneously monitoring of multiple selected ions of different polarity. With the use of the SIM mode in a quadrupole MS, it can deliver a high-sensitivity quantitative analysis of a large number of target compounds, making it a widely recognized system among MS.

[2] Dwell time is the time allocated for acquiring the data of an ion of a particular *m/z* in a mass spectrometer. The longer the dwell time, the greater the number of target ions detected. In simultaneous multi-component analysis, dwell time may be shortened for each target component to capture all target compounds.

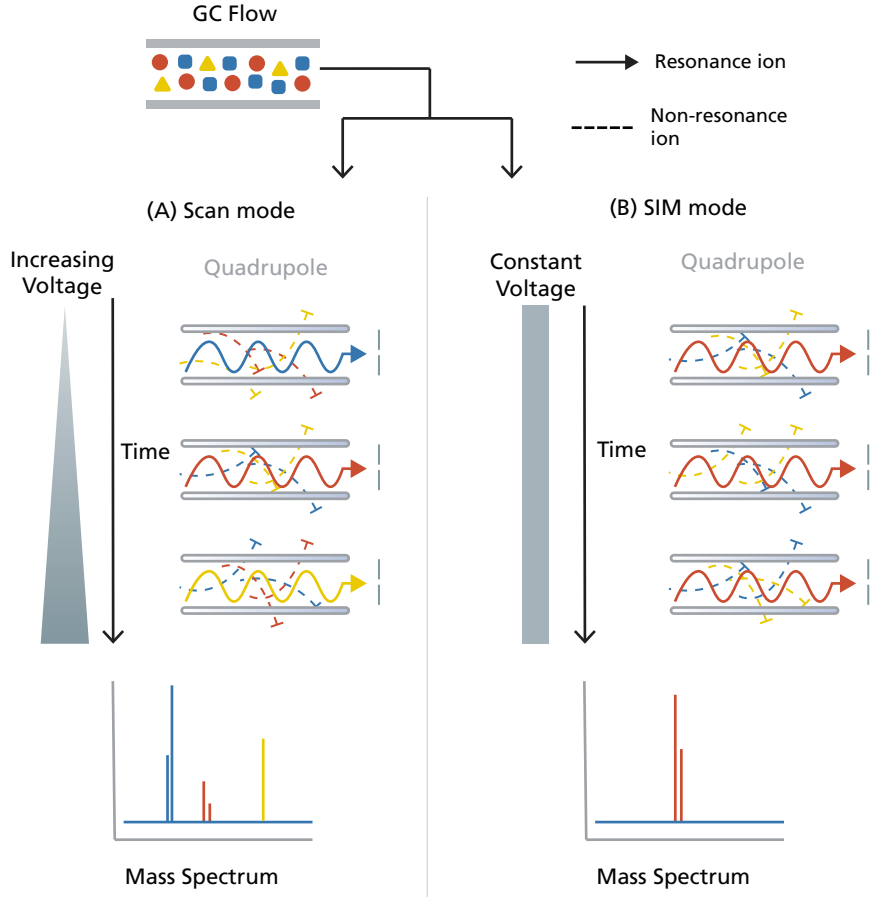
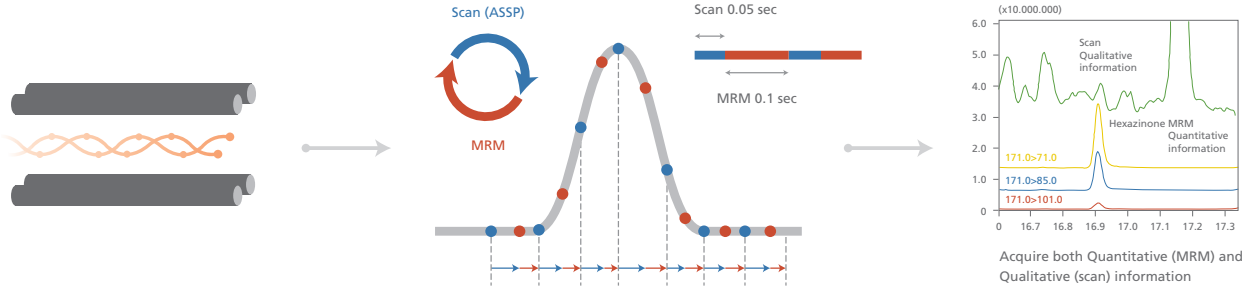


Figure 25. Schematic of (A) Scan and (B) Selected Ion Monitoring modes in quadrupole mass spectrometers.

Learn more on Shimadzu High-Speed Scan Control Technology.

With Shimadzu High-Speed Scan Control Technology and Advanced Scanning Speed Protocol (ASSP®), Shimadzu GCMS can achieve high-speed data acquisition and minimize sensitivity deterioration at the same time. With this technology, there is no need to fret on which modes to choose for GCMS. Scan and SIM data can be acquired at almost the same time by fast, alternate switching between the scan mode and SIM mode. Highly sensitive SIM data of Shimadzu Fast Automated Scan/SIM Type (FASST) is useful in case traditional scan data is insufficient in sensitivity, and scan data of FASST catches the unknown compounds which are usually overlooked in traditional SIM mode. Acquire both qualitative information and high-sensitivity data simultaneous in a single analysis. This technology is also featured in triple quadrupole mass spectrometers.

Click here



Time-of-Flight (TOF) MS

Unlike magnetic sector and quadrupole, TOF MS is a pulsed and non-scanning mass analyzer. It has a simple construction as shown in Figure 26, consisting of an accelerator, a field-free region, a reflectron and a detector inside a high-vacuum chamber (also known as a flight-tube). TOF MS separates and detects ions by the varied time of flight[3] for ions of different *m/z*.

Ions generated in the ion source are accumulated and introduced in pulses to the flight tube. These ions are accelerated by applying a high acceleration voltage between the electrodes. The corresponding kinetic energy of the ion is described in Equation 5. Given a constant acceleration voltage as well as kinetic energy, each ion flies at its unique velocity inside the flight tube to reach the ion detector where ions with smaller *m/z* travel faster than ions with larger *m/z*.

[3] Time of flight refers to the time taken for the ions to travel through a field-free region of a fixed distance.

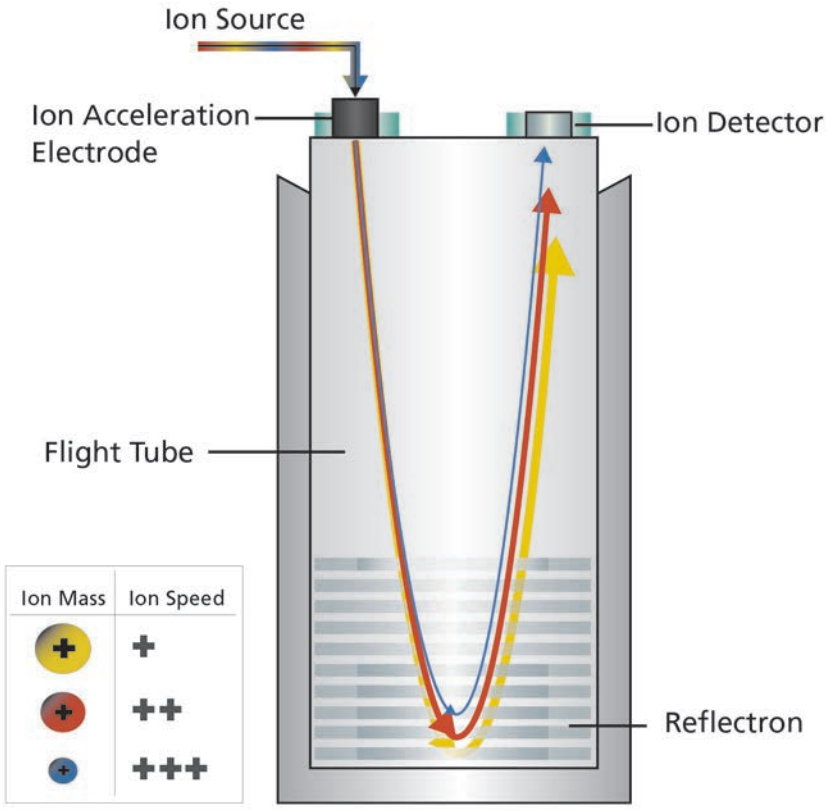


Figure 26. Schematic of a TOF MS.

$$KE_{ion} = \frac{1}{2} mv^2 = zeV \quad \text{– Equation 5}$$

$$T = \frac{distance}{velocity} = \sqrt{\frac{m}{z}} \times \frac{L}{\sqrt{2eV}} \quad \text{– Equation 6}$$

T: time of flight m: mass of ion v: velocity of ion z: charge of ion
e: elementary charge V: acceleration voltage applied to ions L: flight distance in TOF

As shown in Equation 6, the time of flight (T) is proportional to the square root of *m/z*, i.e. for a fixed flight distance (L), ions with smaller *m/z* reach the detector sooner than those with larger *m/z*. Therefore, by keeping all other parameters constant, the time of flight (T) can be converted directly to *m/z*, and in turn generate a mass spectrum. Since there is no limit for time of flight in a TOF MS, it can theoretically measure an unlimited mass range. This coupling of TOF with GC provides another alternative for the full capture of spectral information and high-resolution MS.

There are other mass analyzers such as the ion trap, Fourier-transform ion cyclotron resonance (FT-ICR) and orbitrap MS. The ion trap MS is generally based on an ion trapping mechanism and pulsed MS, it employs the same principle as the quadrupole MS and the motion of ions within the ion trap mass analyzer follows the Mathieu Equation. For a generic ion trap MS (Figure 27), it separates and detects the masses by discharging ions with unstable oscillations from the system. Target ions of interest are trapped in the MS and only discharged to be detected.

There are pros and cons to using ion trap MS. SIM cannot be utilized in ion trap. Furthermore, pulsed mode is required and only a limited quantity of ions is trapped, resulting in a narrow dynamic range. The advantages of such a mass analyzer is that it provides high sensitivity in scanning analysis as all the trapped ions are detected. It also allows the trapping a of specific ion where further fragmentation and trapping can be arranged.

As mentioned, there are other similar trapping type of MS such as the FT-ICR and Orbitrap. In the FT-ICR setup, the use of both the electric and magnetic field generates the stable oscillation and motion of the ions. To detect the ions, the selected ions are accelerated such that its radius of oscillating motion increases, the oscillation becomes unstable and eventually gets removed. By specifying the cyclotron frequency, it can be Fourier transformed and the ion mass can be deduced. For Orbitrap MS, it only requires the use of electric field to trap and separate the ions. Overall, these MS systems generally demonstrate excellent mass resolution and accuracy.

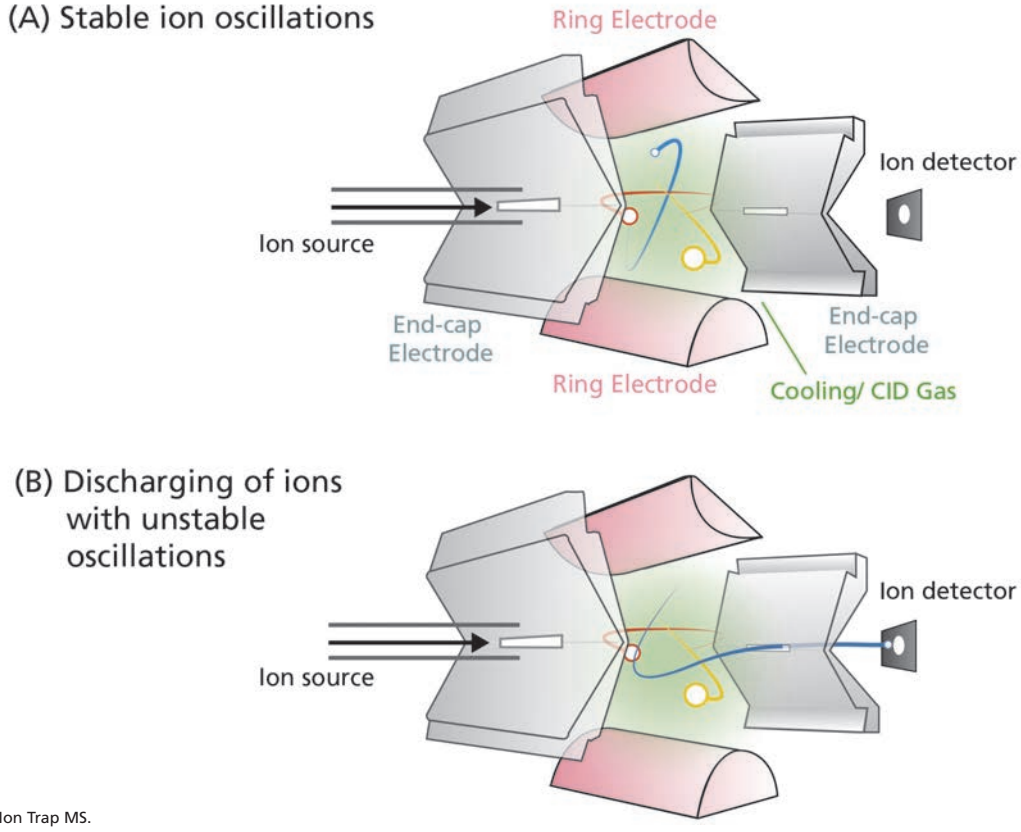


Figure 27. Ion Trap MS.

Comparison of Mass Analyzers in GCMS systems

Mass spectrometers are now used for an extremely diverse range of applications. Each mass analyzer, with its own characteristics, got its pros and cons. It is crucial to understand the different principles, features and characteristics of these mass analyzers and choose the most suitable one for your analyses. Some of the key advantages and limitations of these single mass analyzers are listed in Table 9. In terms of performance, simplicity, cost and ease-of-operation, quadrupole mass analyzer has been the superior choice for most applications and have been dominating the GCMS industry.

Table 9. Advantages and limitations of the various mass analyzers.

Mass Analyzer	Description	Advantages	Limitations
Magnetic Sector	Scanning Continuous	• High resolution • High dynamic range • High reproducibility • High sensitivity	• Expensive and bulky • Slow scan speed • High vacuum required
Quadrupole	Scanning Mass Filter Continuous	• Compact and simple • Relatively cheap • Good selectivity (SIM) • Moderate vacuum requirement	• Limited mass range • Low resolution • Little qualitative information
Time-of-Flight (TOF)	Non-scanning Pulsed	• High sensitivity and ion transmission • High resolution • Excellent mass range • Fast scan speed	• Requires pulsed introduction to MS • Requires fast data acquisition
Ion Trap Orbitrap	Trap Pulsed	• Small and compact • High sensitivity • Good resolution	• Limited dynamic range • Limited trapping volume • Limited resolution • Requires pulse introduction to MS

Introduction to MS/MS Systems

MS is a very useful and powerful tool in quantitative and qualitative analysis. Furthermore, it can identify analytes based on *m/z* and provide accurate mass information on elemental composition, isotopic analysis and structural information. However, there are limitations for a single mass spectrometer. A single MS may not provide sufficient information in cases where sensitivity and chromatography resolution is inadequate. This is particularly the case when working with complex sample matrices, trace target analytes or hard-to-separate compounds (e.g. isomers). With such limitations and difficulties, a technique that provides a higher selectivity, specificity and sensitivity and gives additional unique mass and structural information of the target analytes is required.

MS/MS serves as a solution for the challenges faced by a single MS analysis. It allows the identification and further confirmation of compounds. Also known as a tandem[4] or hybrid[5] MS, a MS/MS system (Figure 28) consists of two mass analyzers connected in series with a collision or fragmentation cell in between. Like the single MS system, the MS/MS system can be coupled to a GC for chromatographic separation prior to MS analysis.

Figure 28 illustrates the basic components in a MS/MS system. Ions are separated in the first mass analyzer (MS1). The separated ions (also known as precursor ions) then enter the collision cell and undergo fragmentation, resulting in the generation of fragment ions also known as product ions. These product ions further undergo separation in the second mass analyzer (MS2). With an additional collision cell and MS2, the MS/MS system provides detailed mass information and allows the reduction of interferences and background noise, giving superior selectivity and sensitivity. The following sections describe the characteristics and processes that takes place in a MS/MS system that give the instrument these enhanced features.

[4] Tandem MS refers to MS/MS systems that use the same mass analyzers (e.g. Triple Quadrupole).
[5] Hybrid MS refers to MS/MS systems with different MS systems (e.g. Quadrupole-TOF).

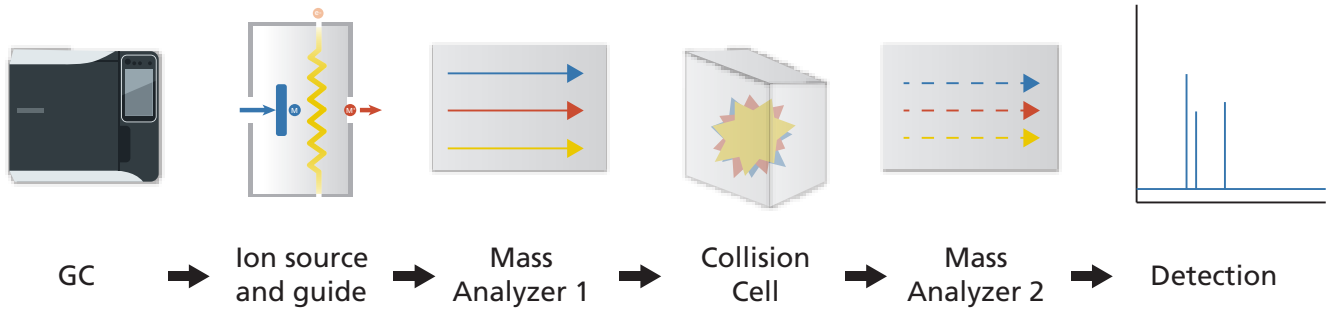


Figure 28. Basic GC-MS/MS instrumentation.

Collision-induced Dissociation (CID)

Collision cell, as its name suggest, is the location where collisions and fragmentation take place. Fragmentation of precursor ions occurs, and this generates product ions which gives unique MS data for each compound. Collision-induced dissociation (CID) is a common and preferred method for fragmentation and Figure 29 illustrates the CID processes that occurs in the collision cell. Besides CID, there are other less common alternatives to induce fragmentation such as electron capture dissociation, surface-induced dissociation and photodissociation.

For CID to happen, the precursor ions of *m/z*, selected by MS1, enter the collision cell filled with chemically inert gas (e.g. He, Ar, Xe and N_2). Collisions between the precursor ions and inert gas are induced by applying an oscillatory field (giving a 'shake'). Collisions cause conversion of kinetic energy into molecular excitation (internal energy) that result in chemical bond breakage to generate product ions. The degree of fragmentation and product ion species depend on the energy supplied because some bonds require higher activation energy than others for breakage.

The supplied energy is termed as collision energy (CE). With a CID collision energy of 0 volts, the precursor ion generally does not undergo fragmentation and its molecular ion is of highest abundance with no or minimal product ions. As CE increases, the abundance of the molecular ion decreases, and fragmentation occurs to generate a variety of product ions. At even higher collision energies (> 50 eV), the degree of fragmentation is more extensive resulting in the mass spectrum showing no molecular ion and higher abundances of product ions of lower *m/z*. For each transition from precursor to product ion, the collision energy needs to be optimized to acquire high-abundance signal of the target compound.

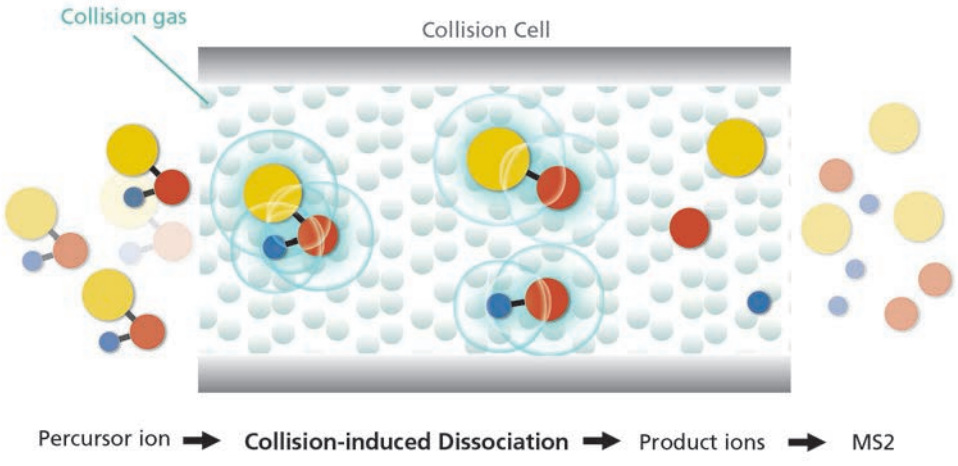


Figure 29. Illustration of CID in the collision cell of a MS/MS system.

Various MS Modes for MS/MS System

In the earlier section, the scan and selected ion monitoring (SIM) modes of a single quadrupole MS were illustrated using Figure 25. Likewise, in MS/MS systems, each of the mass analyzers (MS1 and MS2) can either adopt the scan or SIM (fixed) mode. The different arrangements allow the instrument to operate at various scan and monitoring modes (Figure 30) such as (a) product ion scan, (b) precursor ion scan, (c) neutral ion scan and (d) selected reaction monitoring. It is important to note that these modes available in MS/MS systems depends on the mass analyzers used. Some of these modes (e.g. precursor ion and neutral ion scan) may not be available in time-based[6] MS.

For a long time, Selected Reaction Monitoring (SRM) used to be the term historically preferred by IUPAC, while instrument vendors including Shimadzu preferred the alternative term, Multiple Reaction Monitoring (MRM). Now IUPAC recommends that the term SRM be used to describe the technique applied to a single target and MRM for plurality of SRM. In this document hereafter, the technique is referred to as MRM regardless of the number of precursor/product pairs monitored simultaneously.

Prior to performing MRM, product ion scan is usually conducted to determine the product ion of highest abundance. In conclusion, these scanning and monitoring modes in MS/MS can not only remove noise and interference but also selectively deliver a higher specificity and sensitivity analysis.

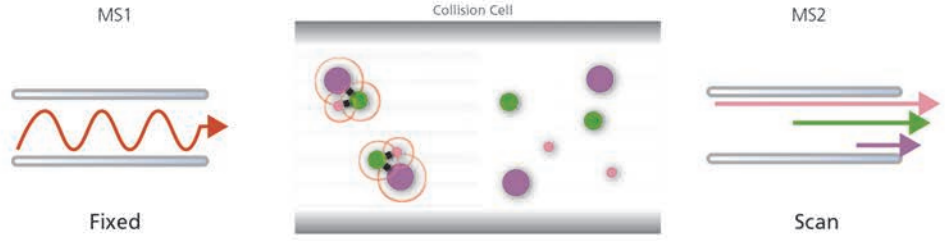
[6] Time-based MS refers to the mass spectrometry where ions are separated temporally and gets detected sequentially at a fixed point. Examples of time-based MS are like ion trap and orbitrap MS. On the other hand, space-based MS separates ions spatially based on their deviation in terms of path radius. Examples of space-based MS are magnetic sector and quadrupole MS.

For every single compound and individual transitions in the MRM mode of a GC-MS/MS instrument, collision energies are optimized to give enhanced sensitivity, specificity and selectivity. The use of MRM mode enables trace analysis of compounds in complex matrices. Watch the short video on MRM Optimization Tool for GCMS. Learn more on the efficient MRM method setup and automatic optimization of MRM transitions.

Click here

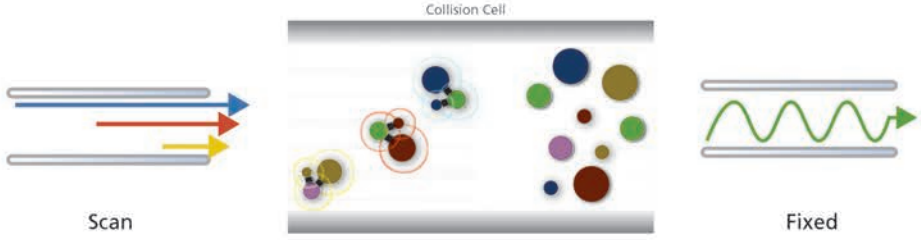
(A) Product Ion Scan:

MS1 is fixed at selected *m/z* while MS2 operates at scan mode. This scan acquires all the product ions from the fragmentation of a selected precursor ion. The intensity and *m/z* of all product ions are captured and displayed in the mass spectrum.



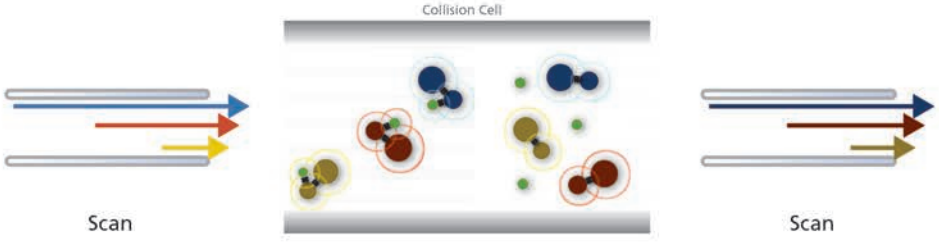
(B) Precursor Ion Scan:

MS1 operates at scan mode while MS2 selects the product ion of a particular *m/z* formed by CID in the collision cell. This mode is especially useful for determining the precursor ions that produce fragment ions of a particular *m/z*.



(C) Neutral Loss Scan:

MS1 and MS2 operates at scan mode while keeping a specific *m/z* difference. This scan can determine the precursor ions that lose a specific neutral molecule (e.g. hydroxyl group and phosphate group) during fragmentation.



(D) Selected Reaction Monitoring (SRM):

The transition of a selected precursor ion to a selected product ion is monitored where MS1 and MS2 are fixed at the specific *m/z*.

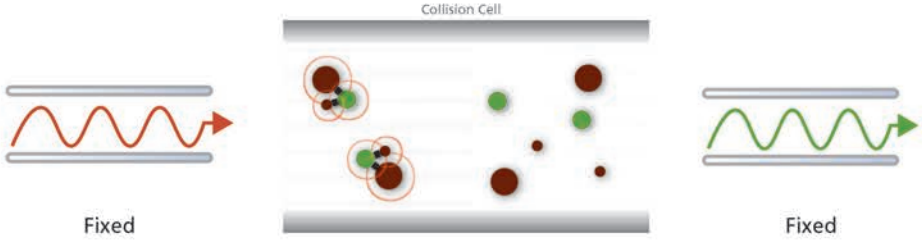


Figure 30. Types of scan and monitoring modes in MS/MS.

Types of MS/MS Systems and Their Key Characteristics

With the inclusion of two mass analyzers in a MS/MS system, several tandem and hybrid configurations consisting of quadrupole, magnetic sector and/or TOF MS can be obtained. Key examples include triple quadrupole MS, dual-focusing MS and quadrupole time-of-flight MS. The separating principles of the individual mass analyzers remain even when they are built in a MS/MS system. The following sections elaborate on the key characteristics of two of such systems and discuss in detail their applications, strengths and limitations.

Triple Quadrupole MS

The simplest and most common MS/MS system is the Triple Quadrupole Mass Spectrometry (TQMS). It consists of three quadrupoles arranged in series (Figure 31) with the first and third quadrupole acting as MS1 and MS2 respectively and the middle quadrupole as the collision cell. With the use of precursor ion scan, neutral loss scan and MRM, TQMS can achieve superior selectivity, specificity and sensitivity with minimal background. TQ MS is an excellent instrument for quantitative analysis and is commonly employed for routine targeted analyses. On the contrary, TQMS is not commonly employed for untargeted analyses as it falters in terms of mass accuracy and resolution as compared to other types of MS/MS. Also, prior knowledge of the compound (e.g. molecular ion mass) is required to utilize the high sensitivity MRM modes in TQMS.

Until recently, dual-focusing GCMS, consisting of both magnetic and electric field in magnetic sector mass analyzers, has been the preferred mass spectrometer for the analysis of dioxins in food. However, with the improved quantitative accuracy of triple quadrupole GCMS, results obtained using the high-resolution dual-focusing GCMS and high-sensitivity triple quadrupole GCMS are comparable. With its relatively low cost and easier-to-use features, triple quadrupole GCMS is increasingly being used for dioxin analysis. Click to learn the details on the analysis of dioxins in food and feed using Triple Quadrupole GCMS.

(1) Determination of Polychlorinated Dibenzo-p-dioxins and Dibenzofurans (PCDD/Fs) in Foodstuffs and Animal Feed Using a Triple Quadrupole GCMS-TQ8040 System with Smart MRM® Transforms Laboratory Analysis

Click here

(2) Analysis of Dioxins in Foods and Feeds Using GC-MS/MS

Click here

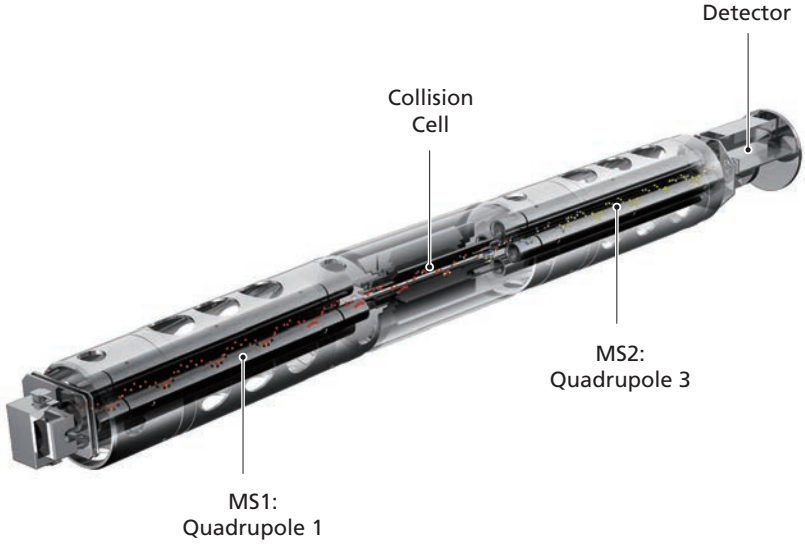


Figure 31. Instrumentation of Triple Quadrupole Mass Spectrometry (TQMS).

Scan to find out more on the use of Triple Quadrupole MS in MRM mode for these applications.

(1) Determination of Organochlorine Pesticides and Polychlorinated Biphenyls Using GC/MS/MS Operated in the MRM Mode

Click here

(2) Determination of N-Nitrosamines by US EPA Method 521 using Triple Quadrupole Gas Chromatography Mass Spectrometry

Click here

Quadrupole Time-of-Flight (Q-TOF) MS

By switching the last quadrupole mass analyzer in a TQMS to a TOF mass analyzer, the Q-TOF hybrid MS is obtained. With the inclusion of a TOF MS, this hybrid system provides excellent dynamic range, high mass resolution and mass accuracy. In addition, it can perform good quality quantitative analysis. With the full scan and full ion transmission capability in Q-TOF MS, it captures all ions in a single run and allows the reinvestigation of data for new and unknown compounds without the need for reacquiring. With these properties, it is commonly used for high-resolution accurate-mass analysis such as the identification of unknown compounds in complex matrices (environmental samples and food) and metabolomics research.

In summary, a variety of GCMS and GC-MS/MS systems are described. Each has its own key features, advantages and drawbacks. With all things considered, it is evident that there is no universal MS or MS/MS for all applications and analyses. Together, Chapter 3 provides important insights on GCMS and GC-MS/MS systems that helps you gain a better understanding and to find the most suitable GCMS (or GC-MS/MS) system for your needs.

Chapter 4

Challenges, Trends and Developments of GCMS

Despite possessing several limitations, GCMS has progressively evolved to become a routine analytical instrument. Chapter 4 aims to discuss these constraints and challenges of using GCMS, as well as the needs of the industry today. This chapter further describes several of these solutions and current trends aimed to support the sample preparation and introduction to GCMS. Shimadzu continues to innovate and build key technologies to meet the present needs of the industry and future challenges. Notably, Ultra-Fast Mass Spectrometry (UFMS) was developed to achieve high-throughput, high-efficiency and high-sensitivity MS analysis.

Overview

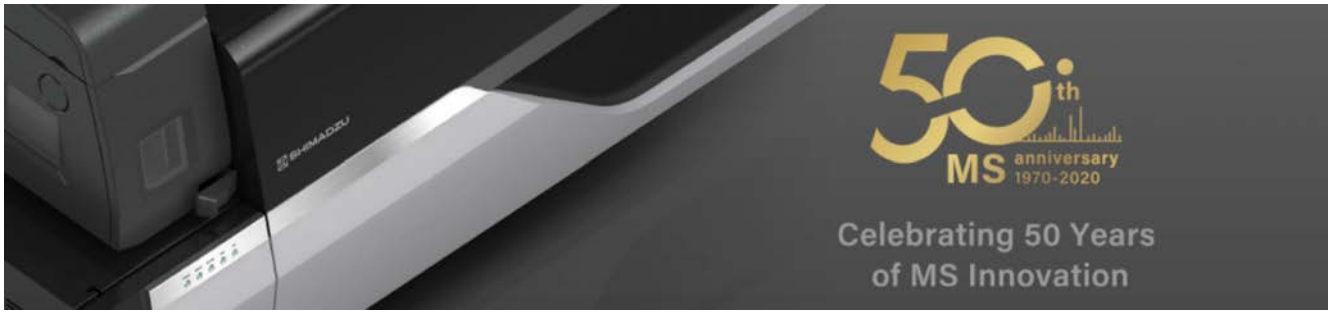
GCMS technology is applied in various applications for many years and has been in the forefront of the analytical field for a long time. Its usage, popularity and relevance in the industry is mainly because of its speed, sensitivity, ease-of-use, robustness and availability of mass spectral libraries. With capabilities in both quantitative and qualitative analysis, GCMS has progressively become an essential and routine analytical instrument in many industries.

Refer to Shimadzu's comprehensive Mass Spectral Database and Libraries

Click here

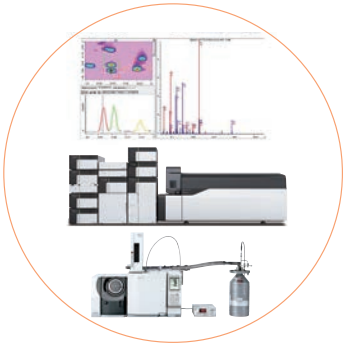
However, GCMS has its own limitations. As discussed in the earlier chapters, GC and GCMS are mainly applicable to volatile and thermostable compounds. Compounds that do not possess such properties (i.e. involatile and/or thermolabile compounds) require further sample preparation such as derivatization. This sample pretreatment process is sometimes tedious and time-consuming. Furthermore, GC is limited in terms of chromatographic separation. Its separating principle is dependent on the polarity and boiling point of the compounds; isomers and compounds with similar properties may be difficult to separate. Even with these constraints, GCMS is still widely adopted and is sometimes preferred over LCMS due to the variations in LCMS ionization (e.g. electrospray ionization) and the complex liquid chromatographic separation.

With increasing adoption of GCMS, as well as to meet the demands of the industries, developments are ongoing where instrument companies are looking to widen the scope of GCMS, accelerate and simplify the GCMS workflow. The current developments and trends of GCMS are focused on achieving high-speed, high-throughput and high-efficiency analysis. To attain these outcomes, GCMS instrument providers have thoroughly investigated the workflow (i.e. sample pretreatment, sample introduction, separation and data acquisition and analysis). A variety of GCMS accessories, technologies, hardware and software have been improved and developed to streamline, condense and/or automate the entire GCMS process. The final chapter of the Fundamental Guide to GCMS aims to provide an in-depth section on the current trends and developments. Together, Shimadzu continues to innovate and develop key GCMS technologies to overcome present and future challenges for GCMS applications.

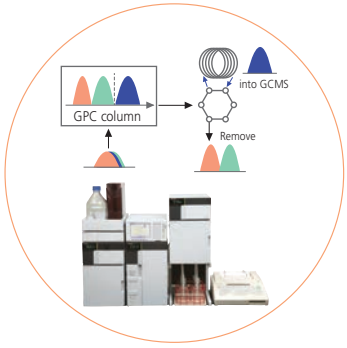


Current Trends: GCMS Configurations and their Applications

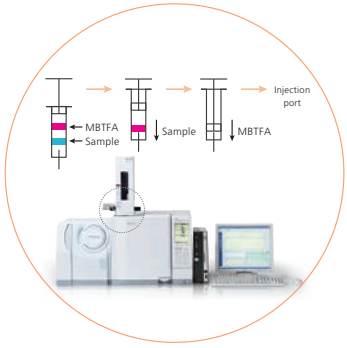
Several GCMS configurations are designed to provide users the ease-of use, high-speed, versatility and automation capabilities. These configurations and accessories, discussed in this section, can be categorized into three groups based on their functions.



2-Dimensional GCMS
2D-GCMS



Gel Permeation Chromatography
GPC-GCMS



On-Column
Derivatization

Sample Preparation and Further Chromatographic Separation
(Online or On-Column Configurations)

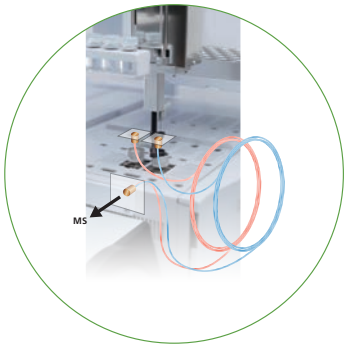
High Speed, High Efficiency & High Throughput

Sample Introduction

Purge & Trap, Multimode, Thermal Desorption, Pyrolysis, Multi-functional Autosampler and Compatibility to Other Techniques (ITEX and SPME-Arrow)

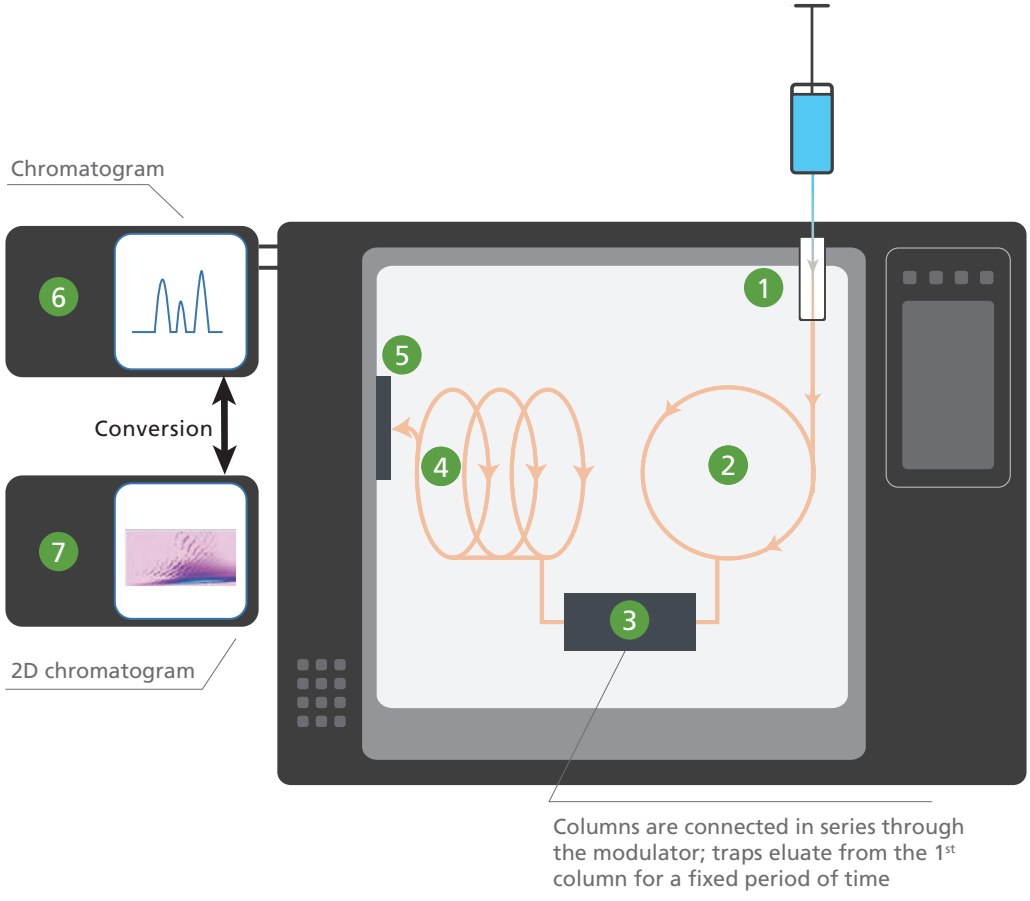
GCMS Operation

Twin Line
MS System



Multi-Dimensional GC (MDGC) and 2-Dimensional GCMS (2D-GCMS)

Multi-Dimensional GC (MDGC), also commonly recognized as 2-dimensional GC or GCxGC, is suitable for complex samples and compounds that cannot be resolved in a single GC column (e.g. co-eluting compounds). As 2D-GC utilizes two columns of different stationary phases, it involves two mechanisms of separation. An example of a 2D-GC system is shown in Figure 1Figure 32 where the first column is of a non-polar phase. Compounds are first separated by boiling point and undergo further separation in the second column of polar stationary phase. Such 2D-GC configurations can be applied for the analysis of petroleum products, fragrance and optical isomers, as well as trace compounds in complex samples where peaks are hidden by major peaks in a 1D-GC system. With this versatile system, samples can be resolved/separated with ease.



1. Injection unit
2. 1st GC Column (non-polar)
   Separation by boiling point (comparatively slow analysis)
3. Modulator
4. 2rd GC Column (polar)
   separation by polarity (fast analysis)
5. Detector (e.g.MS, FID)
6. Mass Chromatogram
   (GCMSsolution / GCsolution)
7. 2D Chromatogram
   (GCxGC Specialized Software-ChromSquare)

Figure 32. Instrumentation of 2D-GC (GC x GC)

Learn More: Refer to our in-depth fundamental guide and application handbook on 2D-GC.

GC x GC Handbook Fundamental Principles of Comprehensive 2D GC

Click here

GC x GC Handbook Application Compendium of Comprehensive 2D GC Vol.1-5

Click here

Gel Permeation Chromatography (GPC)-GCMS

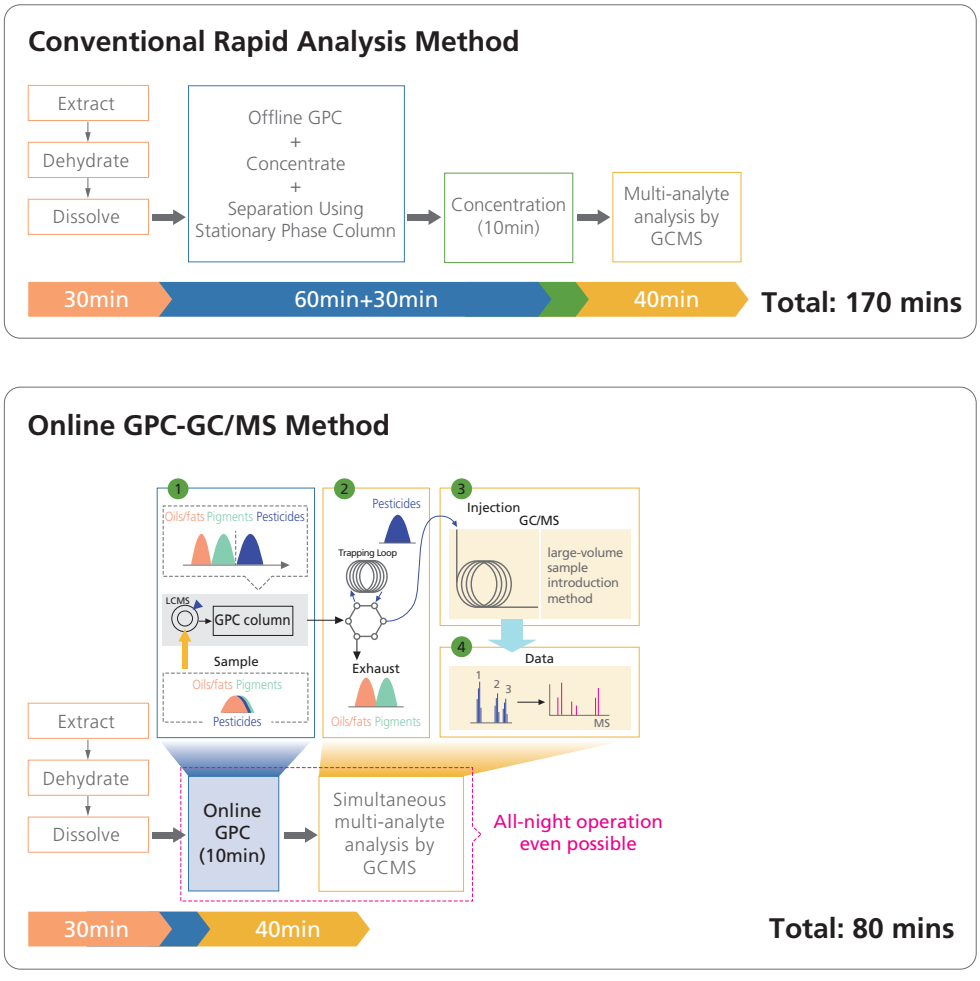


Figure 33. Instrumentation of GPC-GCMS

Find out more on Shimadzu's Prep Q System (GPC-GCMS):

It is a fast and labor-saving system for screening of residual pesticides in food. Click here for more information.

Click here

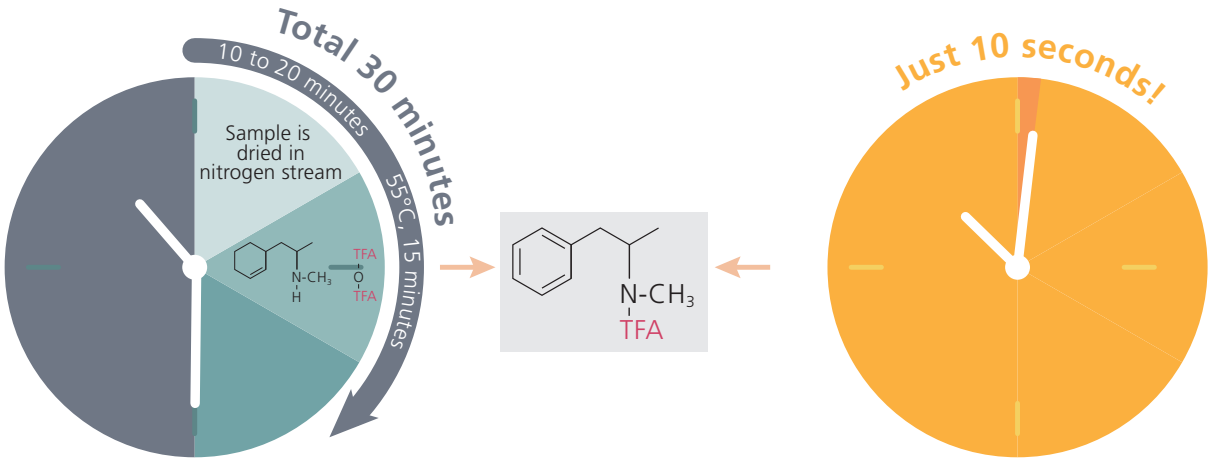
Gel Permeation Chromatography (GPC) - GCMS is an online system (Figure 33) that performs sample cleanup using GPC, followed by GCMS analysis of the pretreated samples. The online connection of the GPC and GCMS provides a fast and labor-saving method for applications such as screening of residual pesticides in food. Complex samples are first separated using a GPC column, unwanted compounds in the sample are ejected out of the system while selected target compounds are transferred and injected into the GCMS for further analysis. With this online system, GPC-GCMS provides a direct and automated workflow, from cleanup to analysis, with no need for human involvement.

On-Column Derivatization

Conventionally, derivatization is commonly performed on a laboratory bench prior to GCMS analysis. With automation and technological advancements, on-column derivatization is possible. Now, with a autoinjector syringe and an autosampler method, derivatization can be automated and performed in the GCMS directly. An example of the on-column derivatization using N-methyl-bis-trifluoroacetamide (MBTFA) is illustrated in Figure 34. This technique reduces manual laboratory work and overall sample preparation time, giving a fast analysis and simplified operation.

Sample Introduction System

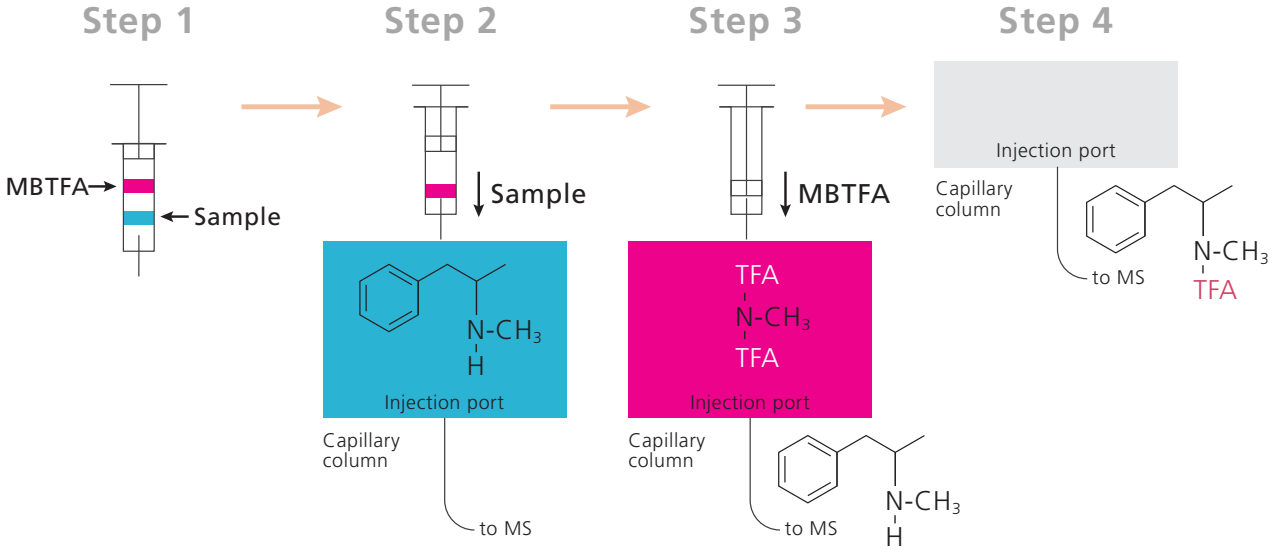
The GCMS sample introduction system allows different sample phases (i.e. solid, liquid and gas) to be separately introduced into the analytical instrument. These versatile systems have different operational procedures but ultimately, they transfer the volatile target compounds into the GC ionization source. Figure 35 describes five of these systems that simplify your workflow and reduces the manual manpower and time required for sample introduction.



Conventional derivatization

On-column derivatization

- Faster analysis
- Automated derivatization process
- Simplified operation



Step 1: Derivatizing agent (MBTFA) & sample - both taken up into syringe

Step 2: Sample injection

Step 3: Injection of derivatizing agent

Step 4: On-column derivatization then GCMS analysis

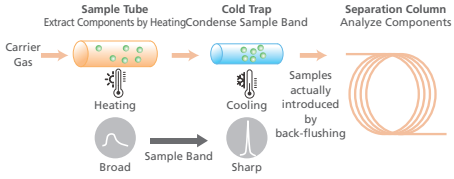
Figure 34. Illustration of how On-Column Derivatization works with a two-step autoinjector in GCMS.

Multi-functional Autosampler

- Supports 3 sample injection methords: Liquid Sample Injection, Headspace (HS) Injection and Solid Phase Micro-Extraction (SPME) injection
- Allows various forms of sample to be analyzed using a single autosampler
- Enables automatic swtching of injection methods in a continuous operation
- Automated sample preparation (e.g. addition of IS and dilution) can be performed using the same autoinjector apparatus; enhances the speed and reliability of data

Click here

Thermal Desorption System



- Optimal solution for gas and materials analysis (e.g. toxic air pollutants)
- No solvents required, user-griendly design and operation (easy-to operate and maintain)
- High-sensitivity analysis of high boiling point compounds achieved using a sample line with no cold points
- With the 'overlap' and 'interrrupt' function, efficient analysis can be performed

Click here

Pyrolysis

- Direct thermal decomposition of material at elevated temperatures in an inert environment, with no solvents required
- Versatile tool for the characterization of polymers and other samples which cannot be introduced into GC directly (e.g. insoluble and complex materials at trace levels)

Scan to learn more on Shimadzu's Py-Screener® Phthalate Ester Screening System

- Selectively detect and quantify of phthalate esters in polymers, toys and food pachaging
- Easy-to-operate, consists of all-inclusive sampling toolkit, standards and software

Click here

Purge & Trap

- Utilized for the immediate analysis of volatile compounds in water sample
- Inert gas is used to purge the samples; the targe volatile compounds are collected and concentrated on an adsorbent and are desorbed and introduced to the GC by heating.

Click to read the application news on 'Analysis of Leachate from Water Supply Equipment Using Purge and Trap GCMS'.

Click here

Also, refer to Shimadzu's Guide to keep your purge and trap system running at top performance.

Click here

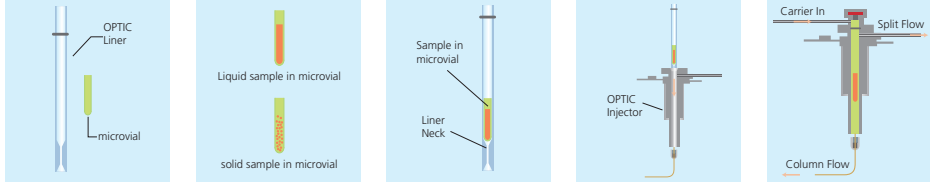
Multimode Sample Inlet (Optic 4)

- Accommodates an extensive range of injection modes, all available in a single inlet
- Equipped with ideal flow channels,avoiding cold spots; optimal for compounds with hige boiling points
- Simplifies pretreatment using 'Difficult Matrix Introduction (DMI) mode'

Click here

DMI Mode

DMI is a method of analyzing samples by placing a mocrovial containing the sample inside a liner, and then heating the liner at the inlet. By adjusting the temperature of the inlet, nonvolatile impurities can be lefe behind in the microvial, enabling GC-MS analyses with simplified pretreatment.



Liner and microvial

Liner or solid samples are placed in the microvial.

The microvial containing the sample is placed in the liner.

The liner is inserted in the inlet. (Automatic liner replacement is possible as an option.)

The liner is heated, and volatile and semivolatile compounds are introduced to the separation column. Nonvolatile compounds remain in the microvial.

Figure 35. GCMS sample introduction systems: (a) Multi-functional autosampler, (b) Thermal desorption, (c) Pyrolysis, (d) Purge and trap, (e) Multimode sample inlet.

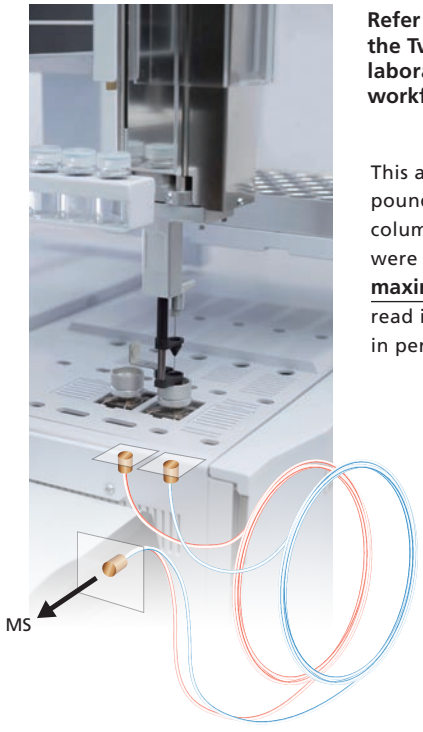
Twin Line MS

Apart from simplifying the sample pretreatment steps and automating the sample introduction procedures, Shimadzu further explored on how to make GCMS routine analysis easier and more streamlined. For this reason, the Twin Line MS System was developed; this system allows the installation of a second-column without the need to vent the MS. It increases the efficiency and reduces the downtime for users who need to run different capillary columns on a single GCMS. This setup is only possible due to Shimadzu's high-capacity vacuum system and an exceptionally accurate control of carrier gas flow through the columns. Overall, the Twin Line MS System provides automatic switching of sample introduction methods and columns during continuous analyses.

Twin Line MS System

Simultaneously install 2 capillary GC columns into single MS

Click here



*Do note that Twin Line does not support simultaneous analysis of the two lines

Refer to this application news to learn how the Twin Line MS System can simplify your laboratory operations and accelerate your workflow.

This application news describes the analysis of 59 compounds using a Twin Line GC-MS/MS method. Two columns of different polarity (i.e. weakly polar and WAX) were installed in order to **achieve less downtime and maximum selectivity** applying optimized MRM. Click to read in detail the determination of 59 potential allergens in perfumes by twin line fast GC-MS/MS.

Figure 36. Twin Line MS System.

Gain insights and learn more on the simultaneous FID and MS detection of pharmaceutical residual solvents with Shimadzu headspace GC-FID/MS detector splitting system.

Click here

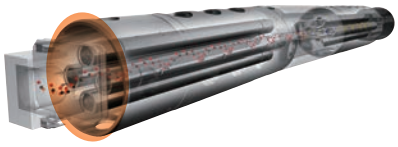
Key Developments in Shimadzu's GCMS: Ultra-Fast Mass Spectrometry (UFMS)

Extensive product research and development has been conducted to design and manufacture a GCMS instrument that not only fits your requirements but also delivers a cutting-edge technology. These advanced technologies, notably Shimadzu's Ultra-Fast Mass Spectrometry (UFMS), are developed to enhance the performance of MS-based techniques. There are several components to UFMS, for example, the hardware and software, all well-equipped with various functions. All these components and configurations are aimed to generate high-sensitivity and robust results and allow efficient use of the instrument (e.g. less down time and reduced maintenance frequency and time).

One major highlight of the UFMS is its MS hardware. It consists of five crucial components: (a) pre-rods, (b) off-axis ion optics, (c) UFsweeper collision cell, (d) overdrive lens and (e) a shielded detector. All these components are illustrated in Figure 37, which features Shimadzu's gas chromatography triple quadrupole mass spectrometer, TQ8050 NX.

(A) Pre-rods

- located ahead of quadrupole
- prevents contamination and ensure sensitivity
- can be rotated 90° for a clean surface (save maintenance cost)

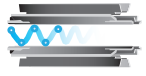


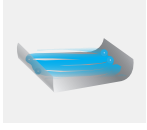
(B) OFF-Axis Ion Optics

- target ions are detected
- meta-stable & neutral ions (noise) are removed without sacrificing sensitivity
- lower detection limits achieved

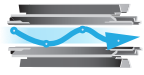
(C) UFsweeper™ Collision Cell

Conventional design
Ions lose momentum due to collision with gas





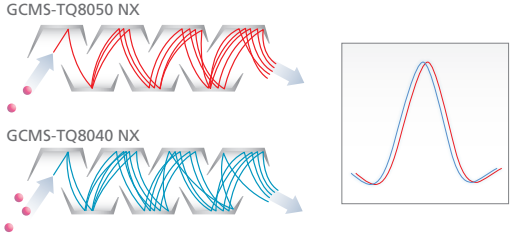
UFsweeper™
UFsweeper efficiently accelerates ions out of the collision cell without losing momentum



- accelerates ions out of collision cell by forming a pseudo-potential surface
- prevents any drop in signal or cross-talk even at fast measurement speeds
- achieve outstanding ion transfer efficiency

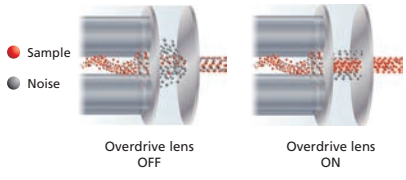
(E) Shielded Detector

- noise reduction system and brand new electron multiplier gives great sensitivity



(D) Overdrive Lens

- random noise reduced dramatically by applying optimal voltage
- focus the ions that passes through the mass filter (improves signal-to-noise ratio)



Noise reduction due to overdrive lenses

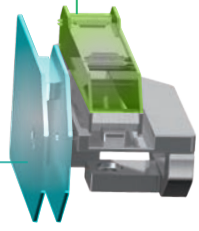


Figure 37. Ultra-Fast Mass Spectrometry (UFMS®) key hardware: (a) Pre-rods, (b) Off-axis ion optics, (c) UFsweeper® collision cell, (d) Overdrive lenses and (e) Shielded detector.

Using the illustration of TQ8050 NX (Figure 37), the UFMS components are elaborated in detail. Firstly, pre-rods are located right before the quadrupole mass analyzer; it prevents the contamination of the main rods of the quadrupole. As ions enter the quadrupole, the pre-rods act as a MS protector and the first line of defense from complex samples and multiple injections. In doing so, it eliminates the need for quadrupole maintenance and allows the generation of stable and high-sensitivity peaks and accurate mass spectra.

As the ions travel from the ion source, they are focused into a beam and guided into the mass analyzer using an ion optics system. Ion optics are used to electrostatically guide the ions into the desired direction, similar to the light manipulation by optical lenses. The ion optics system, with the help of the vacuum pumps, remove interferences such as residual particles and non-ionic gas particles (e.g. meta-stable and neutral ions) from the ion beam. The key feature of Shimadzu's ion optics system is the capacity of the differential vacuum pumps and the off-axis arrangement. With the design of the off-axis ion optics (Figure 37), the residual particles are not deflected by the ion optics system and still move in a straight line. The target ions are directed to the second quadrupole and detector. Thereby, the ions are transmitted and focused as they travel to the detector, achieving high-sensitivity analysis and low detection limits.

Shimadzu has improved the design of the collision cell, UFsweeper. Now, with the new pseudo-potential surface (Figure 38), it allows ultra-fast ion sweeping where ions entering the collision cell are accelerated and their momentums are maintained upon collision. Residual ions are also efficiently swept out of the collision cell. Under these circumstances, the efficiency of the target ion transmission and collision-induced dissociation (fragmentation) is improved. With the high-sensitivity and high-efficiency collision cell, shorter dwell and pause[7] times can be used to achieve the required ion intensity. This minimizes crosstalk, enables more time for measuring other compounds and thus simultaneously achieves multi-component analysis and high-sensitivity MRM.

[7] MS and MRM measurement conditions may be switched to perform simultaneous measurements of multiple components. The time needed for this is termed as pause time. As data cannot be acquired during the pause time, it should be as short as possible.

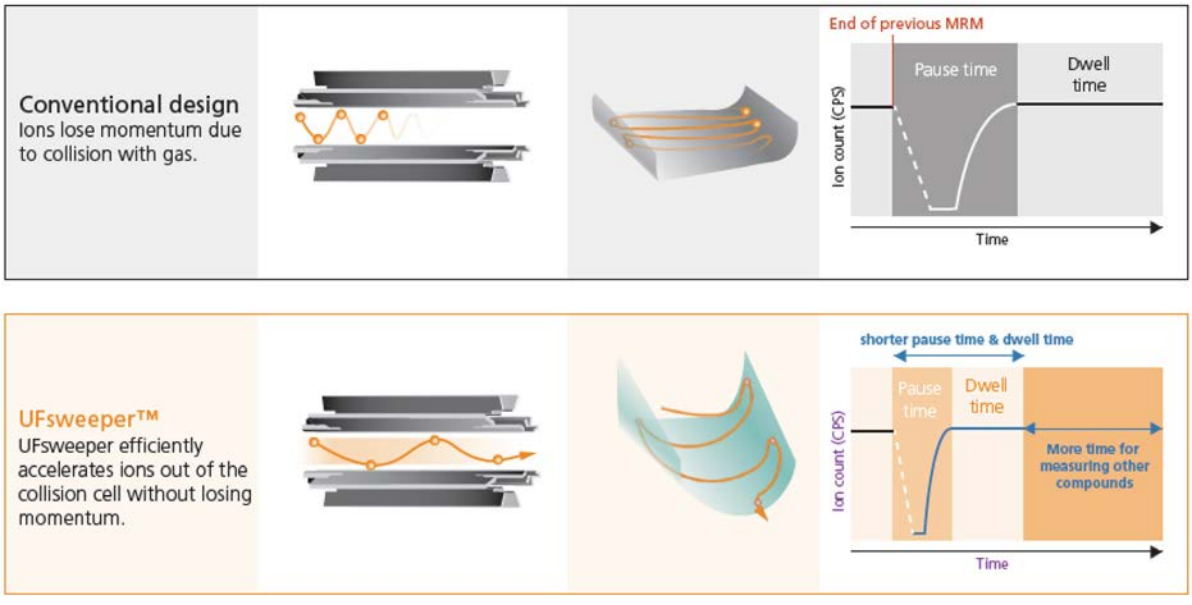


Figure 38. Comparison of a conventional collision cell and UFsweeper® collision cell.

Another factor contributing to the high-sensitivity of Shimadzu's MS is the overdrive lens (U.S. Patent No. 6737644) and the shielded detector. Two overdrive lenses, located in front of the detector, reduce random noise from Helium or Argon, focus the ions that pass through the mass filter and improve the signal to noise levels. Similarly, the shield plate right before the detector further reduce the noise. With the enhanced electron multiplier detector (Figure 39 (c)), the same signal intensity can now be achieved with lesser ions. Altogether, ultra-fast trace analysis (femtogram-level) is achievable with Shimadzu UFMS system.

With increasing attention and emphasis on user experience, and capabilities on integration and automation, Shimadzu has looked into our MS software programs and optimized the method development and data analysis process. These programs work together with the UFMS hardware to provide a convenient and user-centric software system. In addition, they allow high-speed scanning, automated retention time of adjustment, with no compromise on the sensitivity and resolution for both quantitative and qualitative analyses. The next few paragraphs describe some of these key method development systems, such as MRM Optimization Tool, Smart MRM and Smart Database.

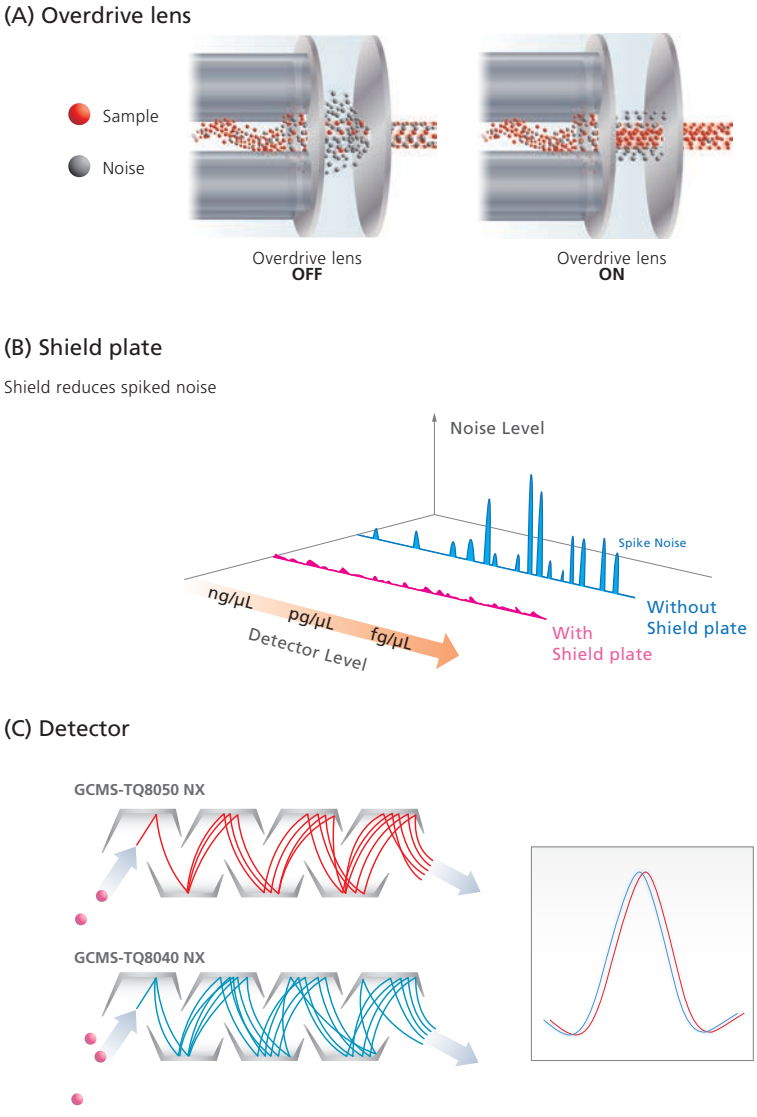


Figure 39. Shimadzu UFMS system: (a) Overdrive lens, (b) Shield plate and (c) Detector.

The entire method development process, from creating methods for product ion scans to configuring product ions and collision energies, can be fully automated with the use of MRM Optimization Tool. This tool allows MRM transitions and their collision energies to be quickly and accurately optimized. The program can also define up to ten potential precursor ions for each compound (a feature only unique to MRM Optimization Tool), thereby able to generate different precursor ions for the optimized target and reference transitions. With the automated MRM Optimization Tool, it saves precious time and labor for method development and gives accurate optimized transitions.

Smart MRM/SIM technology creates MRM/SIM methods that can analyze more than 400 components in a single run. This is only possible as this technology automatically optimizes and allocates the dwell time for each transition in a method, thereby efficiently acquiring data only during the elution time of the target compounds. This not only improves sensitivity and peak shape but also increases the number of compounds that can be analyzed in a single run. GCMS acquisition methods are easily created using the Smart MRM/SIM system and the Automatic Adjustment of Retention Time (AART) function in the system estimates retention time with high accuracy. Consequently, with the use of Smart MRM/SIM, the time required for method development and analysis is reduced.

Smart MRM

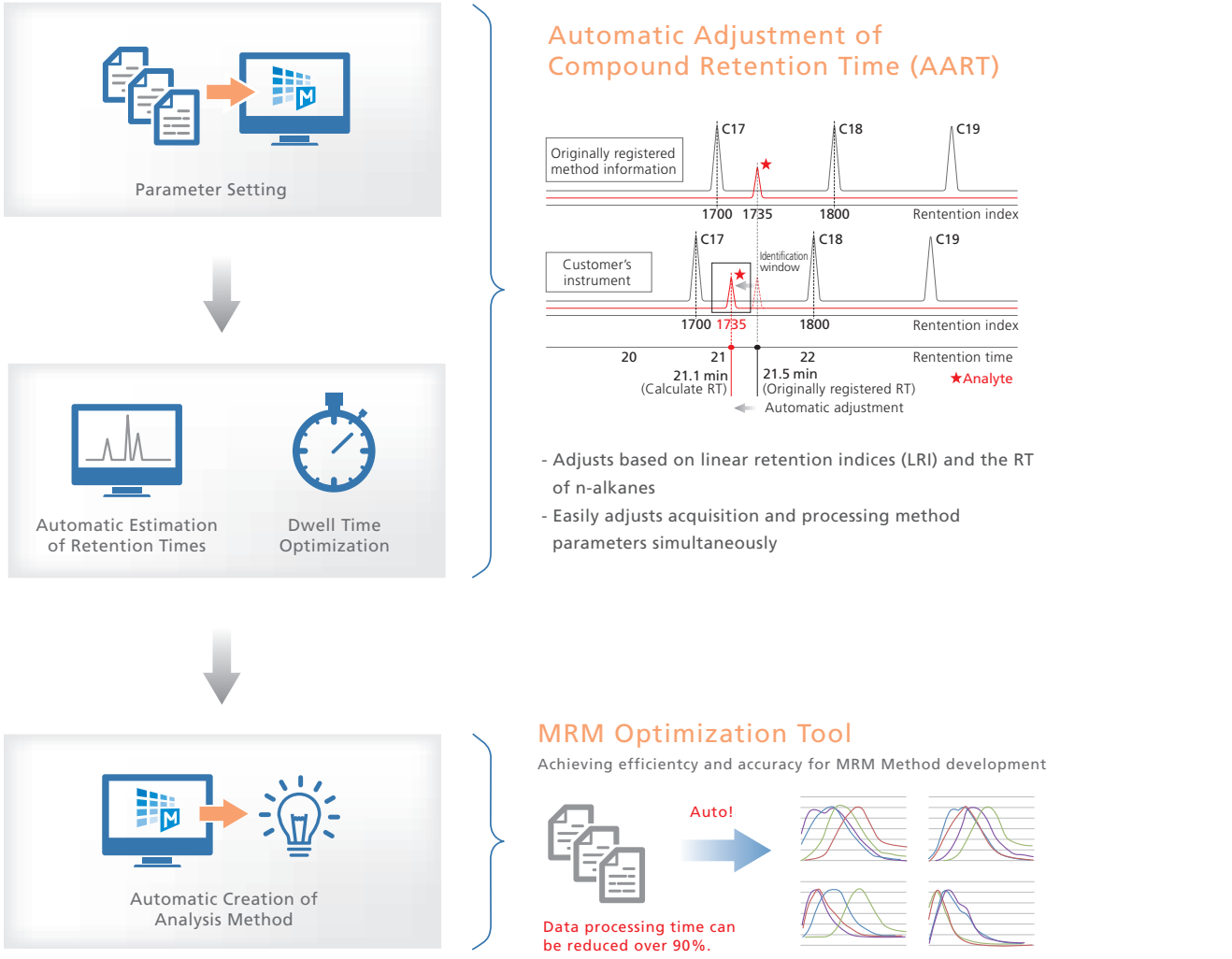
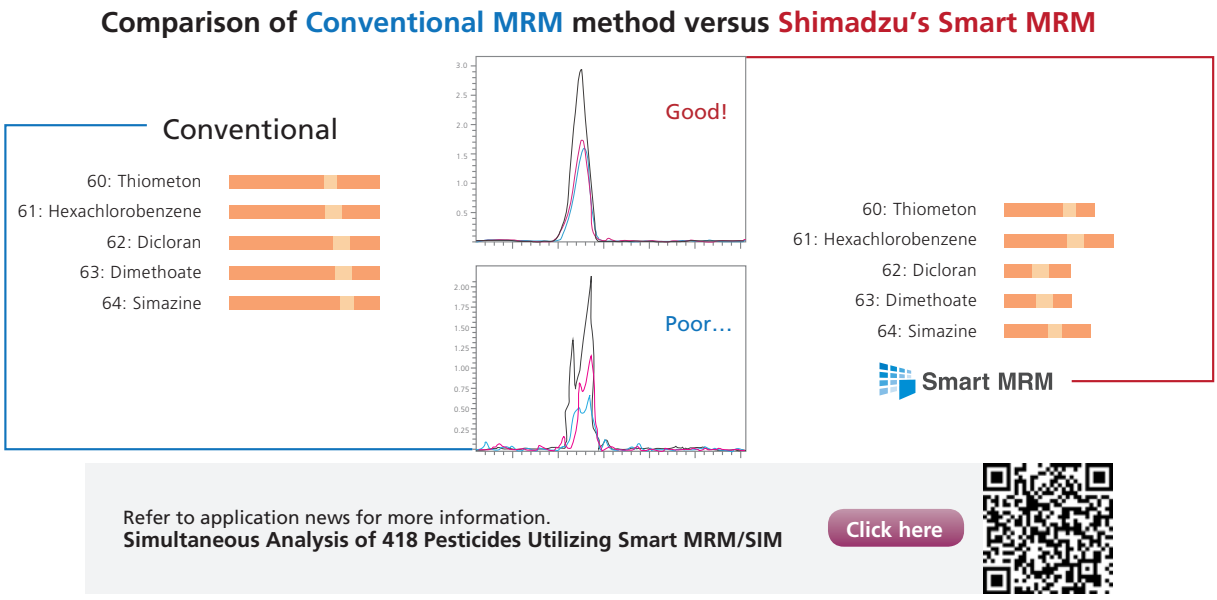
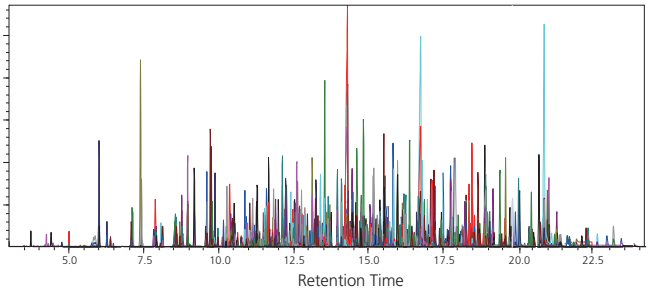
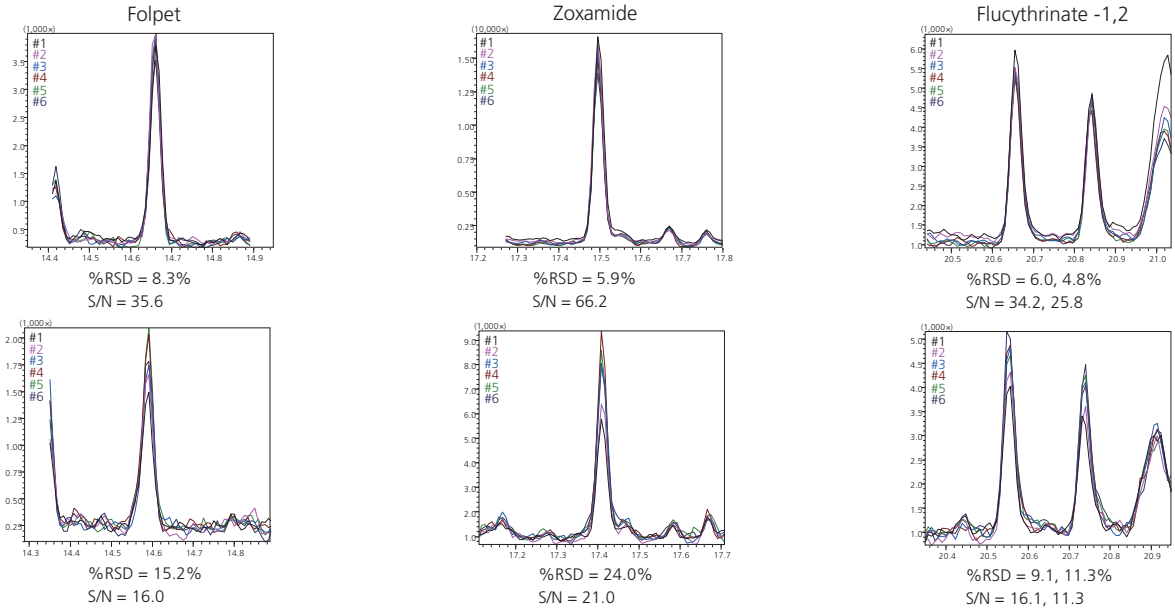


Figure 40. MRM Optimization Tool: achieving efficiency and accuracy for MRM method development.





SIM Chromatogram for a 100 ng/mL for a pesticides standard mixed solution



SIM chromatograms, %RSD and average S/N ratio (n = 6) for 2ng/mL sample

Figure 41. Comparison of conventional MRM method versus Shimadzu's Smart MRM®/SIM.

All the optimized MRM transitions and its associated collision energies, and retention indices can be preregistered and managed using Smart Database; even the optimal GC columns used for separation can be determined with Shimadzu's Smart Database. Shimadzu have a variety of database suited for screening and/or quantitative analysis, such as Smart Environmental Database, Smart Forensic Database and Smart Pesticides Database.

A comprehensive MS technology would also consider the users' needs and include features that supports low-maintenance and easy servicing. Shimadzu MS instruments are designed in a way that contamination in the MS is avoided, maintenance frequency is reduced, and results generated are highly accurate and sensitive. Key examples are the pre-rods and ion source in Shimadzu GCMS. The GCMS instrument is also equipped with parts that are simple and quick to assemble/disassemble (e.g. One Touch, Easy sTop, ClickTek, Figure 42 (b)) and easy-to-follow practical troubleshooting guide (MS Navigator and Easy sTop, Figure 42) that ensures smooth and effortless maintenance.

Together with the use of our durable hardware such as oil-free pump, long-life detector, high-performance quadrupole mass filter, and a highly stable and sensitive ion source, these features reduce the maintenance frequency and operational costs. Along with the differential vacuum system and Twin Line MS system that are unique to Shimadzu MS, UFMS and these developments serve as a key MS instrument well-suited for your GCMS applications.

Everything you need to know about Shimadzu's GCMS.

Click to watch the short videos on the specific functions of UFMS® and learn more on the various user-centric features of Shimadzu's GCMS.

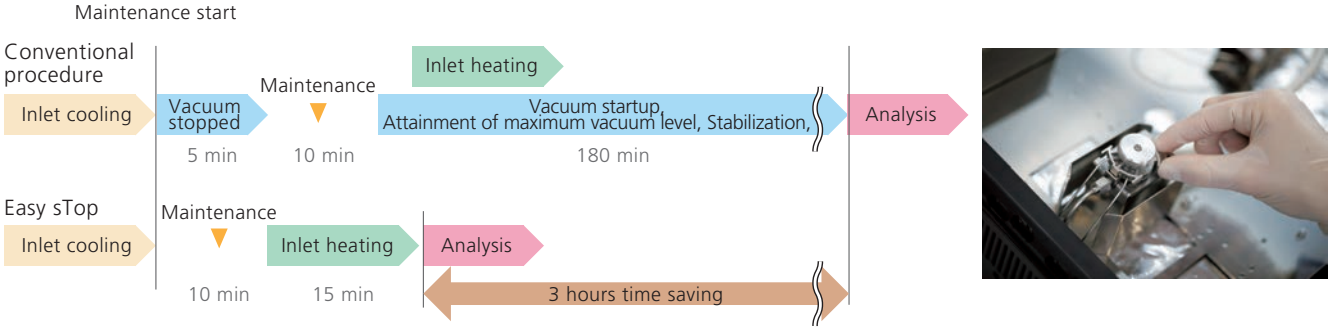
Click here

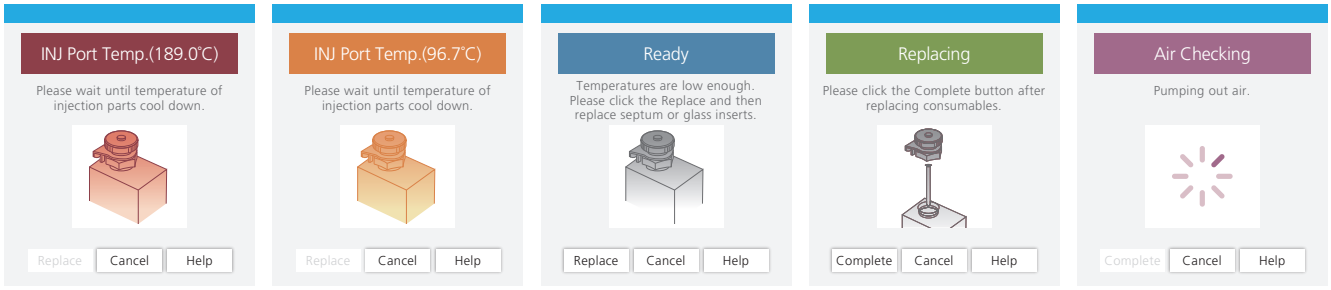
MS Navigator®, included in the GCMS software, provides easy step-by-step instructions for the most common user-maintenance procedures. User can now perform these routine maintenances by themselves easily and safely.

Easy sTop is specially designed to reduce the time required for routine maintenance of the injection port. The replacement of the septum and glass inserts can be performed without stopping the MS vacuum system. A step-by-step instruction is provided too. Click or Scan the QR Code to watch the video and learn how it works.

Click here

ClickTek makes routine analysis and maintenance more convenient. Simply sliding the ClickTek lever, the injection port can be opened/closed without tools. Columns can also be installed, ensuring leak-free connection every time.





The East sTop navigator assist in taking the appropriate steps.

Figure 42. MS Navigator®, ClickTek and Easy sTop: supporting maintenance procedures and reduces maintenance times.

Future Trends of GCMS

Although there are several ongoing efforts and developments on GCMS, there is still more to be explored to fully unleash the capacity and potential of this instrument. Future developments of GCMS are expected to focus on a variety of chromatography and mass spectrometry features that possibly expands the scope of GCMS.

Recently, applications such as toxic smell investigations, indoor air analysis and hazardous pollutants have heighted the needs for compact or on-the-go GC and GCMS. These miniaturized and field-portable systems support onsite real-time monitoring and analyses. There are a few of such systems out in the market currently and these systems work relatively well for an immediate estimation of compounds in the sample. These compact and/or portable systems are expected to increase in demand due to growing usage from industrial and environmental applications. Industries would be looking at getting a comprehensive and economical solution for these onsite real-time applications. Therefore, one of the trends is expected to head towards developing easier and more convenient onsite sample collection and preparation, and a portable, high-speed and good performance GCMS system. With the growing attention on environmental issues, another possible direction for GCMS is to go eco-friendly. Taken together, these demands suggest a GCMS instrument that is compact, portable and with low environmental footprint (consume less gases and power, also cost-saving) while still maintaining high speed, performance and robustness.

For laboratory GCMS instrument, difficulties do sometimes arise when implementing the actual GCMS workflow (e.g. sample preparation, sample analysis and data processing). Automation and optimization of workflow is increasingly recognized as a core solution and the development on this area continues to be a key trend for GCMS. The objective is to achieve more while doing less, attaining high efficiency and high throughput. One such example is to move towards minimal sample preparation or even automated the process from start till end. Moreover, research and development are ongoing to establish more intelligent data processing systems for faster screening and positive identification. With the development for more automated systems and versatile functions, high throughput and more reliable data can be achieved.

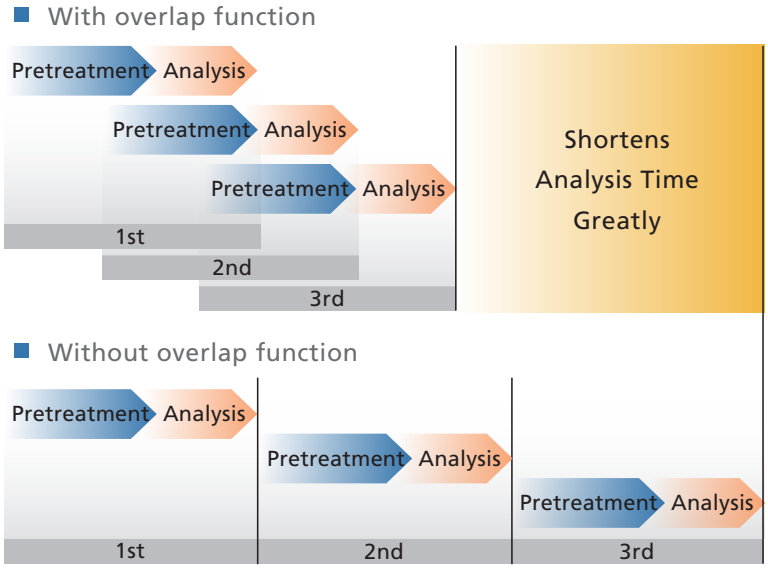
Strategies to enhance GCMS instruments and analysis involve further developments in the gas chromatographic separation and detection. Currently, the selectively of the GC stationary phases and the resulting separation resolution may be limited, especially for multi-component analyses and structurally-similar compounds. Multi-dimensional gas chromatography (MDGC) is one such solution to this issue. Another would be to revisit the principles of gas chromatography and develop new stationary phases and modes of separation. Developments are in progress and these future advancements would speed up multi-component and/or trace analysis and greatly increase the scope of GCMS. Recently, industries and GCMS users have also expressed interest in the field of dual detection involving mass spectrometry and spectroscopic techniques. This dual detection technology would be an alternative for co-eluting compounds as it merges the strengths of both detectors.

All in all, Shimadzu has made great strides in addressing current challenges and targeting future trends of GCMS. Given its capability and relevance to the industry, GCMS is expected to become an essential and routine analytical instrument for many applications. The Fundamental Guide to GCMS covers the basics of GC, key concepts and principles of GCMS and describe the various configurations and technologies of GCMS. We hope that the contents provide you with a comprehensive overview and help in your GCMS analyses. Driven by our policy of contributing to society through science and technology. Shimadzu strive to further improve our analytical technologies, create unique solutions and innovative breakthroughs with a diverse product range to protect and restore the environment, and to deliver better health and lifestyles to people.

1. Continuous overlap function heightens analysis efficiency

Accommodates ITEX, SPME arrow and other GCMS sample introduction methods (e.g. liquid, headspace, SPME)

Continuous Analysis Flow



2. Automated pre-treatment enables highly reliable quantitation

Automatic addition of solutions provides greater convenience and enhances the reliability of data

Method Creation → Automatic Dilution and Preparation

Figure 43. Shimadzu's automation capabilities and software functions for GCMS sample pretreatment and analysis.

Shimadzu's Comprehensive GC and GCMS Solutions

GAS CHROMATOGRAPH: THE NEXT INDUSTRY STANDARD

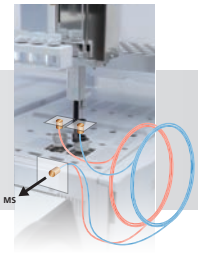
Designed with the user in mind, Shimadzu's GC systems, with exceptional performance and high-throughput capabilities, meet user requirements in every market and applications.

ULTRA-FAST MASS SPECTROMETRY (UFMS™)

Shimadzu's UFMS™ technologies not only provides high-speed analysis and high-sensitivity performance but also superior data quality for all MS-related applications.

AUTOMATED AND VERSATILE CONFIGURATIONS FOR SAMPLE INTRODUCTION

With our promise in innovation, Shimadzu constantly develops new methods and products in automation and integration to expand your productivity and simplify your workflow.

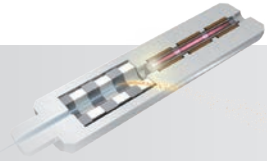


DATA MANAGEMENT AND GCMS SOFTWARE

Shimadzu's software and smart technology (Smart MRM® and Smart Database®) allows the easy creation of MRM methods, makes data analysis easier and boosts routine analytical work.

APPLICATION SUPPORT, LIBRARIES AND DATABASE

Our extensive range of mass spectral libraries, databases, application notes and method development packages are specifically developed to support all your GCMS analyses.



HIGH-PERFORMANCE GC DETECTORS

Shimadzu develops the Barrier Discharge Ionization Detector (BID) and provides a variety of other high-sensitivity detectors available for coupling with gas chromatography.

FULL RANGE OF CONSUMABLES AND PRODUCTS FOR EFFORTLESS GCMS ANALYSIS

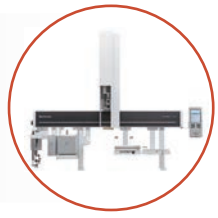
We offer a wide range of GC columns and sample preparation products. Our GCMS is equipped with an easy-to-follow guide and a one-touch lever that ensures smooth and effortless analysis and maintenance.

Pioneering New Frontiers in GCMS
Shimadzu GCMS TQ-8050 NX

Click here

Automated & Versatile Sample Introduction

- A range of system configurations that accommodates various sample forms
- Able to perform automated pretreatment which enhance reliability of data

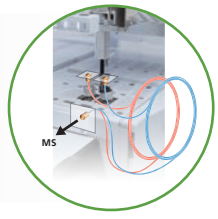


Ultra-Fast Mass Spectrometry (UFMS™)

- Pre-rods and quadrupole mass filter
- Ufsweeper™ collision cell
- Off-axis ion optics, overdrive lens & shielded detector
  Not only provides ultra-fast and high ion transmission but also minimal and easy maintenance
  Resulting in high-speed and high-sensitivity GCMS analysis

Twin Line MS System

- High throughput: reduced hassle of changing columns
- Seamless automation of routine tasks that greatly reduces cost



Differential Vacuum System

- Incomparably offers high evacuation efficiency and enables highly-accurate trace analysis

Advanced Flow Controller (AFC)

- Gives precise control of carrier gas flow, achieves exceptional reproducibility & stability
- Allows optimum resolution & method transferability between GC and GCMS

Intuitive Interface & Convenient Controls

- Touch-screen graphical user interface
- Tool-free column installation and routine inlet maintenance with ClickTek
  Equipped with an easy-to-follow guide
- For smooth and effortless analysis and maintenance

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