Benefits of Equipping your Lab with a Time-of-Flight Mass Spectrometer

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Purchasing a mass spectrometer (MS) is an important investment for a laboratory. When considering instrument platforms, selection of the right mass analyzer expands lab capabilities while meeting data quality objectives, detection limits, and budget. A time-of-flight mass spectrometer (TOFMS) for gas chromatography (GC) can benefit both high throughput and research laboratories. A GC-TOFMS is the right choice for discovering new compounds in your sample, quantifying targeted compounds in complex samples (e.g. environmental, food, metabolomics, petrochemical, and botanical), and increasing throughput with fast chromatography.

Introduction

Mass spectrometers are perhaps the greatest tool available for the analytical chemist. With the ability to ionize, sort, and measure complex chemical mixtures by their mass-to-charge ratio (m/z) with femtogram (fg) to nanogram (ng) sensitivity, it is no wonder that mass spectrometers are widely used across many industries. The mass spectrometer can be divided into three main components: ionization source, mass analyzer, and detector. While the functions of the ionization source and detector are extremely important to the function of the mass spectrometer, it is the selection of the mass analyzer that can be tailored to meet data quality objectives. Sample matrix, required detection levels, target or non-target analysis, and budget all play an important role when selecting a mass analyzer. There are typically four types of mass analyzers to choose from: time-of-flight, quadrupole, ion trap and magnetic sector.

A magnetic sector is typically used for high resolution and accurate mass determination. Although expensive, it excels in targeted, low level quantification of chemical contaminants such as dioxins. An ion trap mass analyzer is particularly useful for performing tandem mass spectrometry (MS/MS) or multiple MS experiments (MS^n). Multiple MS experiments provide ionic structure information that can be used for quality control, structure elucidation, and analyte identification. A quadrupole mass analyzer is rugged, inexpensive, and great for targeted routine analyses. With its small footprint (benchtop) and relative ease-of-use, it can be found in most analytical laboratories. A time-of-flight mass analyzer acquires full mass range with fast data acquisition. It can be a great asset in any laboratory faced with challenging environmental, metabolomics, food, petrochemical, or botanical samples. TOFMS instrumentation includes benchtop models, standalone, nominal resolution, high resolution, and can be combined with quadrupoles or another TOF to perform MS/MS experiments.

A GC-TOFMS has the ability to collect a full mass range up to 500 spectra/s with a dynamic range up to 5 orders of magnitude. Equipping a laboratory with a GC-TOFMS is advantageous because it allows non-target data mining with full mass acquisition, yields high quality library matches through mass spectral deconvolution, and it supports fast gas chromatography (GC) with accurate quantitation.

Non-Target Data Mining with Full Mass Range Acquisition

The role of the mass analyzer is to select (or deselect) a specific ion's mass-to-charge ratio (m/z) and transport them to the detector. A TOFMS is considered a non-scanning mass analyzer because of its ability to separate a full range of mass-to-charge ratios simultaneously. In a TOFMS, the ions are pulsed from the ionization source, accelerated, and focused through the flight tube to the reflectron where ions are finally guided to the detector **(Figure 1)**. On the other hand, a quadrupole mass analyzer is more specifically a “mass filter” that uses DC voltage and RF potentials on four parallel rods to allow only a specific m/z to reach the detector. In order to collect a full mass range, the DC and RF potentials must be scanned so that each m/z can reach the detector[1].

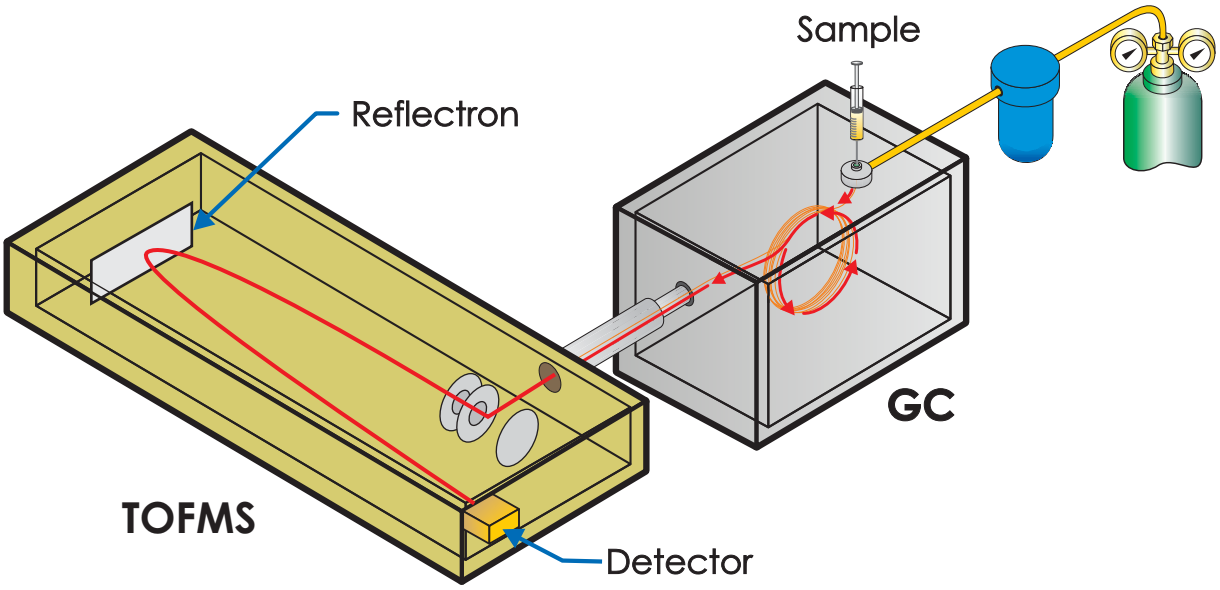


Figure 1. In the LECO GC-TOFMS system, the reflectron allows differing penetration of ions depending on their kinetic energy and reflects them back to the detector. This yields a longer flight path, increasing mass resolution, and better detectability because ions with the same m/z are reaching the detector at the same time.

The ability to collect a full mass range without sacrificing data acquisition speed or sensitivity is perfectly suited for non-targeted analyses. Using a non-targeted approach is beneficial for discovery-type work. This includes finding potential biomarkers in metabolomics, finding new or illegal chemicals in environmental or food samples, and collecting valuable information for forensic or toxicology use. Collecting a full mass range provides a historical catalog of information about a sample that can be used for future inquiries without the need to recollect any data.

A targeted analytical method also benefits from acquiring a full mass range. In a quadrupole mass spectrometer, selected ion monitoring (SIM) is used to increase sensitivity of target analytes. In SIM mode, specific m/z ions are selected for target analytes and all other ionic masses do not reach the detector. This increases target analyte detectability by increasing the signal-to-noise ratio (S/N). When collecting in SIM mode response bias is still possible from the coeluting matrix interferences. Information collected about the sample is limited to the selected m/z ions that make it to the detector. If further information about the sample is needed, or additional analytes are added to the target list, the sample must be re-acquired. Re-acquiring data is not always feasible with limited time or sample. When acquiring the full mass range in a TOFMS, however, an extracted ion chromatogram (XIC) can be used for quantitation purposes. If reduced response is observed, it is possible to view the total ion chromatogram (TIC) to pinpoint interferences that could be corrupting data quality. If analytes are added to the target list, no further data acquisition is needed, as all of the information was collected in one analytical analysis. While targeted analyte methods using a quadrupole mass spectrometer operated in SIM mode have superior sensitivity compared to a TOFMS analysis, it is possible to calibrate a TOFMS to low pigogram (pg) levels without sacrificing the information afforded with collecting a full mass range (**Figure 2**).

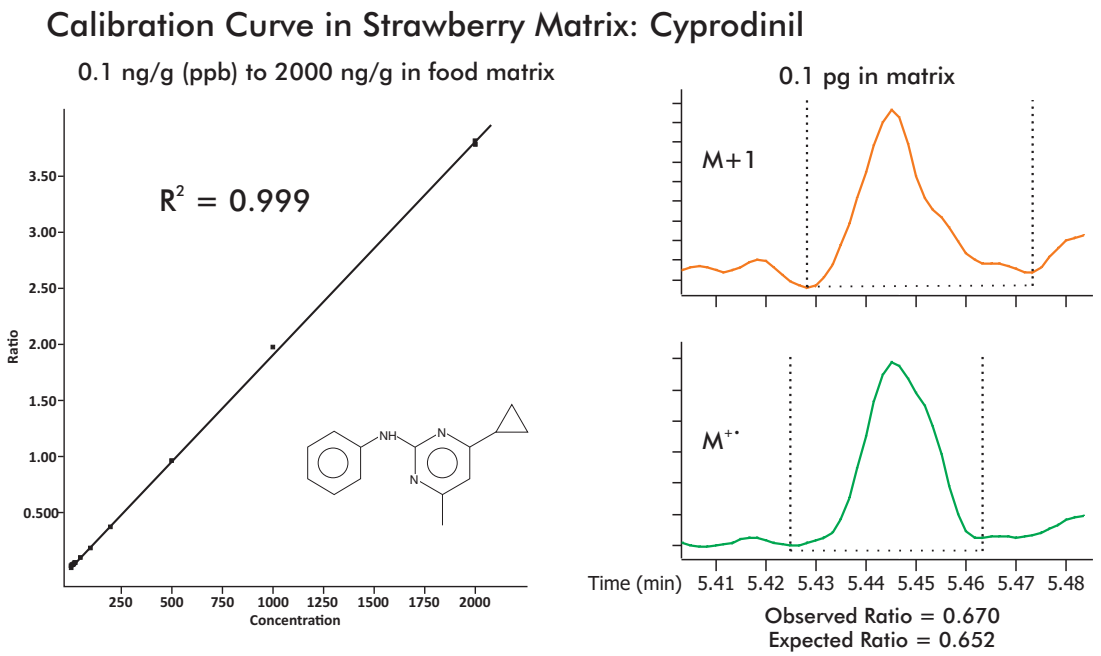


Figure 2. Calibration curve (0.1 ng/g to 2000 ng/g) of fungicide cyprodinil in strawberry matrix. The sensitivity of the LECO Pegasus® BT GC-TOFMS achieves quantitation of cyprodinil below regulated maximum residue limits (MRL). The calibration curve, in food matrix, also highlights the dynamic range of the TOFMS instrumentation.

High Quality Library Matches with Mass Spectral Deconvolution

The use of a spectral library with GC-MS is extremely useful for identifying peaks in a chromatogram. The ability to have a high-quality match of a reference spectrum to a sample spectrum allows for positive identification of an analyte. The higher the library match, the more confidence that can be placed in the identification. In a scanning mass analyzer like the quadrupole, the abundancies of m/z ions can change throughout the same peak even for a single analyte. The analyte peak is eluting while the instrument is scanning, therefore analyte concentrations are changing in the source. Multiple scans must then be averaged or summed to combat spectral skewing[2]. In a TOFMS, since the ion packets are formed and almost simultaneously analyzed, concentration changes in the source are negligible. Therefore, a mass spectrum from a TOFMS instrument has better spectral continuity across a peak than with a scanning mass analyzer **(Figure 3).**

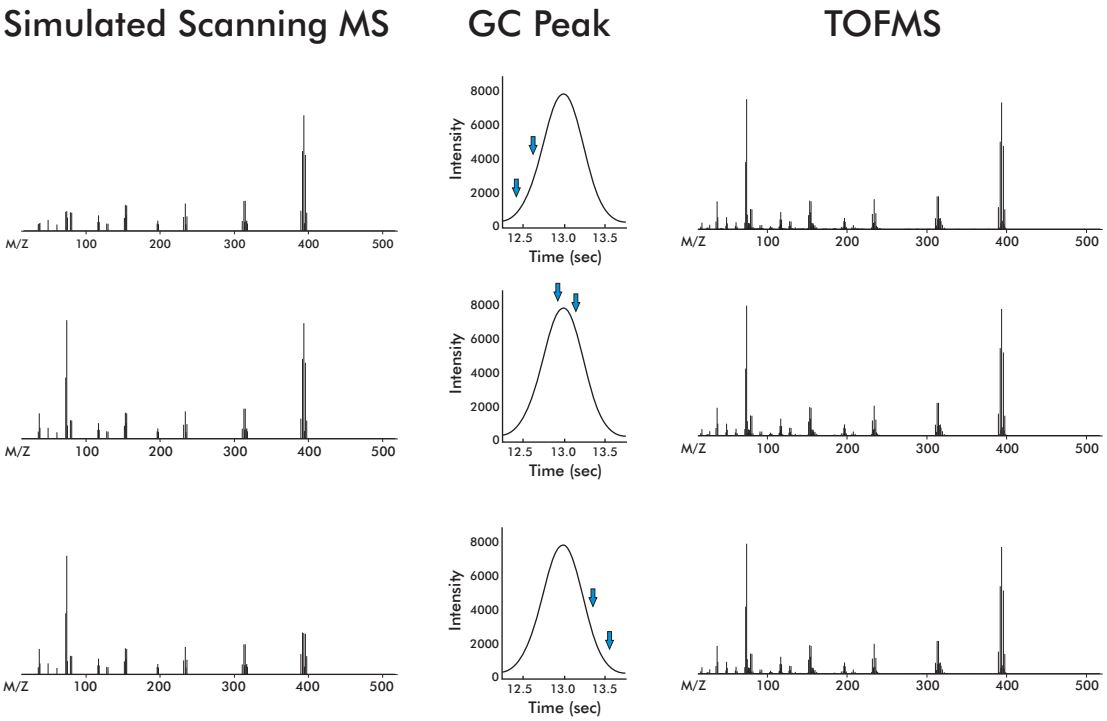


Figure 3: Spectral continuity of TOFMS vs Simulated Scanning MS across a GC peak

Spectral continuity is important for maximizing the performance of mass spectral deconvolution algorithms. Mass spectral deconvolution algorithms extract analyte mass spectra from overlapping compounds in order to get a more “pure” mass spectrum. These algorithms mathematically differentiate a coeluting peak's spectrum so that each peak can be identified through library matches. High library match factors are difficult without deconvolution in complex environmental, metabolomics, food, petrochemical, and botanical samples. Matrix compounds can interfere with important analytes corrupting the analyte mass spectrum. With deconvolution algorithms, target analytes overloaded with matrix interferences will still produce a high library match factor **(Figure 4)**.

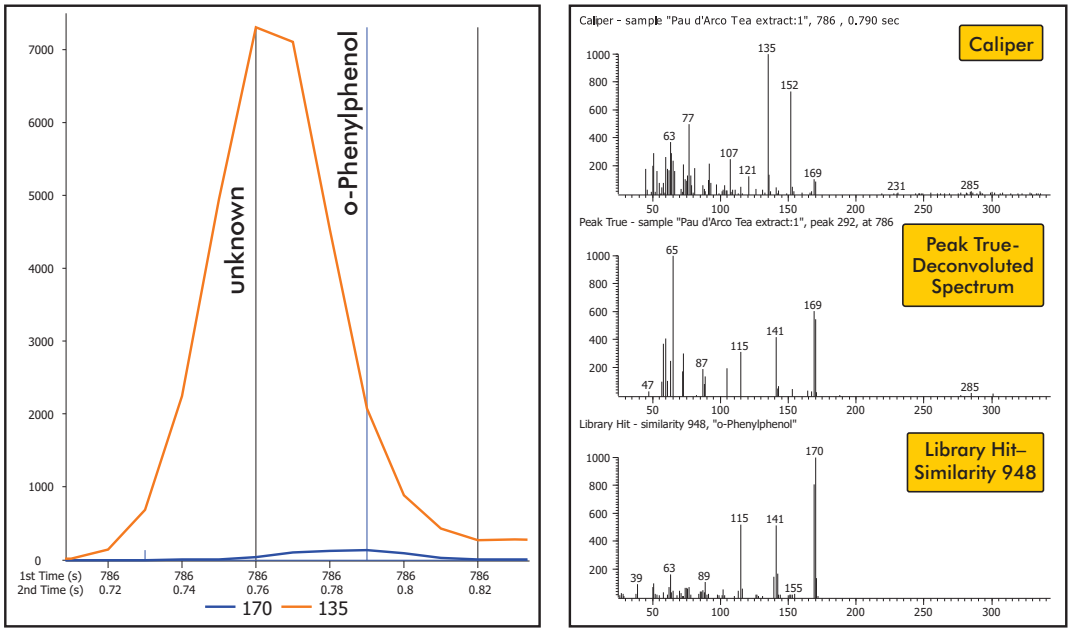


Figure 4: Analysis of pesticides in herbal tea. High library match (948) for o-phenylphenol with spectral deconvolution. Caliper spectrum shows large interference of unknown coeluting matrix peak (m/z 135). The spectral deconvolution algorithms in LECO’s ChromaTOF®-brand software removed bias from the coeluting peak yielding a quality library hit for o-phenylphenol.

The performance of deconvolution also relies on acquiring the data with enough points across a peak so that each peak's apex can be precisely defined. In complex samples with numerous coelutions, the fast data acquisition speeds of the TOFMS easily support the requirements for maximizing the performance of mass spectral deconvolution **(Figure 5)**.

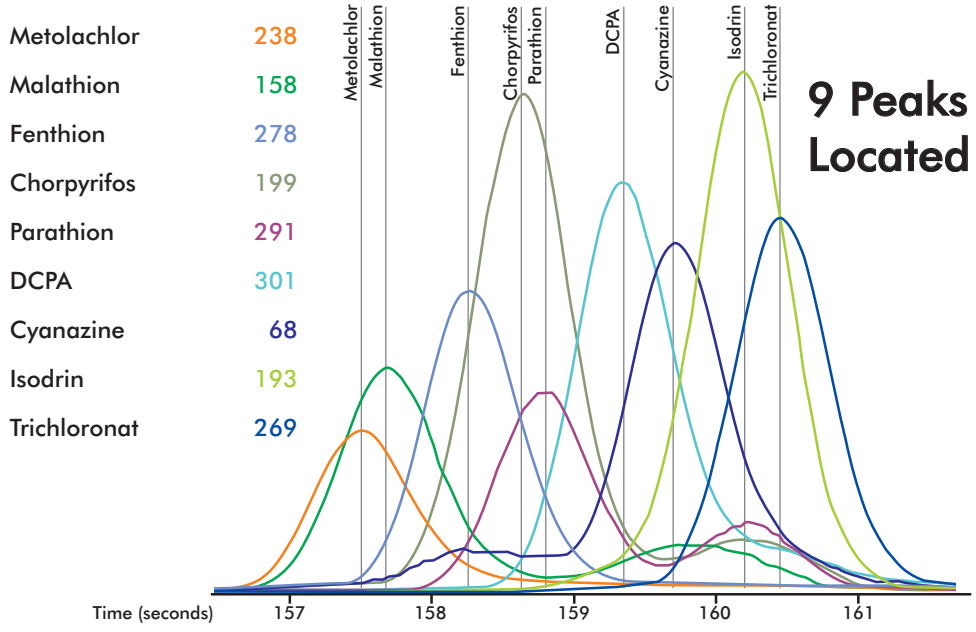
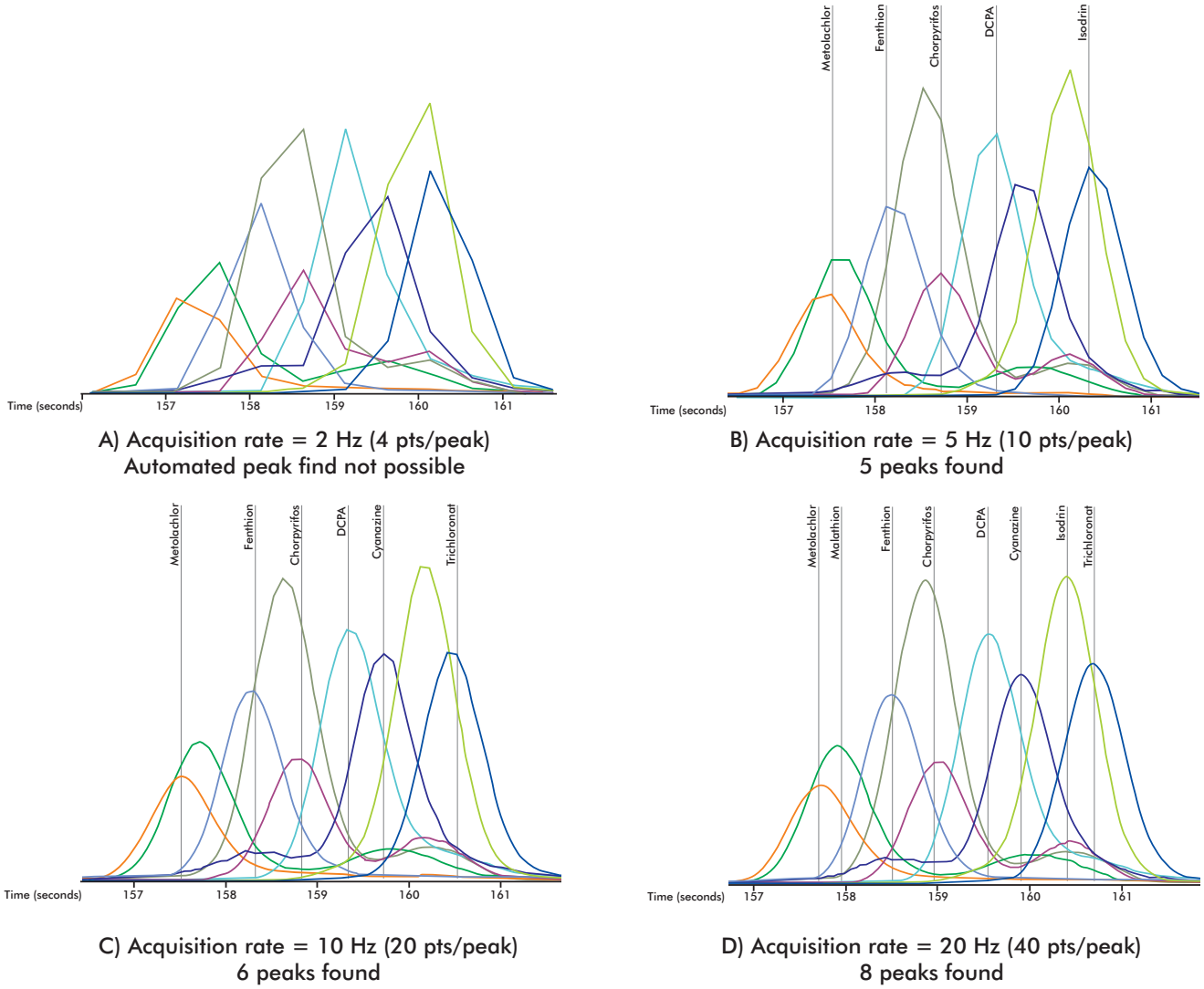


Figure 5: Spectral deconvolution with library matching allows software algorithms to perform automated peak find. The automated peak finding feature of ChromaTOF, made possible with spectral deconvolution and fast data acquisition, short-cuts the laborious process of analyte identification for both target and non-target analyses. Increasing the acquisition rate to 40 spectra/sec with spectral deconvolution resulted in the identification of 9 pesticides. *See acknowledgment.*

Fast Chromatography with Accurate Quantitation

Data acquisition speeds are not only important for mass spectral deconvolution, but also accurate quantitation. To accurately define a peak, data must be acquired at a minimum of 10 points across a baseline resolved peak. This minimum is increased to 15-25 points with any added complexity to the sample (e.g. coelutions). If enough data points are not collected the peak apex might be missed, causing variation in retention times. Reproducibility of peak area also suffers when a peak is not properly defined causing relative standard deviations (RSDs) to increase. Fast gas chromatography (GC) uses combinations of narrow bore columns, different carrier gases and carrier gas flow, and fast oven programing. In a high throughput laboratory, lab profitability can be increased by decreasing analysis times. In fast GC, the demands of data acquisition are increased, peaks are narrowed, and coelutions are more prevalent. To increase sample throughput without sacrificing data quality, acquisition speeds must be tailored to accurately define more narrow peaks in a shorter time window. With fast chromatography, GC peaks can be 0.5-2 seconds wide **(Figure 6)**.



A) Acquisition rate = 2 Hz (4 pts/peak)
Automated peak find not possible

B) Acquisition rate = 5 Hz (10 pts/peak)
5 peaks found

C) Acquisition rate = 10 Hz (20 pts/peak)
6 peaks found

D) Acquisition rate = 20 Hz (40 pts/peak)
8 peaks found

Figure 6: A fast GC analysis of pesticides resulted in 2 second wide peaks. (A) At a typical scanning instrument rate, i.e. 2 Hz, automated peak find is not possible with *ChromaTOF*. (B) Increasing the acquisition rate to 5 Hz achieves the minimum 10 pts/peak. However, only 5 of the 9 total peaks are automatically found. (C,D) Acquiring data at 10 Hz and 20 Hz better defines the narrow GC peak, enhancing the benefits of the automated peak find. *See acknowledgment.*

A GC-TOFMS is beneficial in high throughput laboratories who want to employ fast gas chromatography. Routine and time-sensitive data can be accurately quantified with the fast data acquisition of a TOFMS. Complex samples analyzed by comprehensive two-dimensional gas chromatography (GCxGC) require faster acquisition speeds. Peaks produced from a GCxGC analysis are 50-200 ms wide, requiring acquisition speeds in excess of 200 Hz (Table I). The data acquisition rate of a quadrupole mass spectrometer is limited depending on the desired mass range. Data quality can suffer when narrow peaks of a fast GC analysis are under acquired.

Peak Widths (s)	Acquisition Rate (Hz)	Points/Peak
20	0.5	10
20	1.25	25
10	1	10
10	2.5	25
5	2	10
5	5	25
2.5	4	10
2.5	10	25
1	10	10
1	25	25
0.5	20	10
0.5	50	25
0.2	50	10
0.2	125	25
0.1	100	10
0.1	250	25
* Highlighted cells corresponds to acquisition rates that typically cannot be achieved by quadrupole mass analyzers (50-550 m/z)		

Table I: Acquisition rates needed to achieve desired sampling frequency (10 or 25 pts/peak).

Conclusion

A mass spectrometer is a great tool for any analytical laboratory, but selecting the right mass analyzer for your applications can improve data quality, increase lab capability, and meet budget requirements. The time-of-flight mass spectrometer is a great choice for complex samples, non-target analysis, and fast GC or GCxGC. Both accurate and quantitative, the TOFMS can be used for research and high-throughput laboratories with environmental, metabolomics, petroleum, food, and botanical samples. Full mass acquisition is perfectly suited for non-target analysis, mass spectral deconvolution makes library matching easier for complex samples, and fast data acquisition speeds support fast GC and GCxGC.

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Michelle Misselwitz is an experienced analytical chemist with expertise in gas chromatography (GC), comprehensive two-dimensional gas chromatography (GCxGC), mass spectrometry (MS) and sample preparation. As an applications chemist, she developed hot topic applications for environmental, food safety, environmental forensics, and botanical markets. Misselwitz has successfully combined her scientific and communication skills to present and write technical papers and training seminars for customers worldwide. With a decade of experience at Restek, a chromatography consumables company, and a B.S. in Chemistry from The Pennsylvania State University, Michelle is currently an independent consultant specializing in technical writing, presentations, and GC method optimization.