Technical Overview

Water Analysis

Agilent

Trusted Answers

Auto MS/MS and Identification of Unknowns in Water Samples

Authors

Imma Ferrer,
E. Michael Thurman, and
Jerry A. Zweigenbaum
University of Colorado and
Agilent Technologies, Inc.

Abstract

When looking for nontarget compounds, one of the tools available with high resolution mass spectrometry instruments is data-dependent acquisition (DDA). In this mode, a group of ions that fulfill all the experimental parameters contained in a given method are selected for MS/MS and a unique fragmentation spectrum is obtained for each. The number of selected precursor ions for MS/MS depends on the conditions and values chosen during the analysis of a sample. This Technical Overview carefully explains and optimizes all the parameters included in the DDA mode of Agilent quadrupole time-of-flight instruments, Auto MS/MS. We discuss the differences between various values, and point out the relevant parameters to be considered when analyzing complex water samples.

Introduction

Liquid chromatography quadrupole time-of-flight mass spectrometers (LC/Q-TOF MS) are heavily used for the analysis of nontarget compounds by the scientific community. Due to their high resolving power, mass accuracy, and the capability of full-spectrum measurement, almost every compound that ionizes can be detected. The amount of data gathered this way can often be overwhelming, needing accurate mass tools (that is, databases, isotope filters, and mass profiling software) to unravel the identification of small molecules in complex water samples. One of the tools that this type of MS instrument offers is the ability to do a real-time automated MS/MS analysis of the sample being analyzed. This ability enables the best fragmentation information from a selection of prominent ions to be captured. On Agilent LC/Q-TOF instruments, this mode is called Auto MS/MS. The user can optimize this mode, depending on the application to be carried out. The criteria set by the user determines which ions detected in the single MS experiment will become precursors for MS/MS, and the quality of the MS/MS spectra.

To study the differences and outcomes for the detection of small molecules (including pesticides and pharmaceuticals) in water samples, this work varies the different parameters offered by the methodology. We selected five compounds as model compounds; atenolol, atrazine, lamotrigine, trimethoprim, and venlafaxine. These compounds include chlorine isotopes, compounds that are easier and harder to fragment, and compounds with different polarities. By studying the differences obtained in their precursor selection and MS/MS fragmentation spectra, we conclude with a few recommendations for the optimization of Auto MS/MS methods.

LC/Q-TOF analysis

The separation of the analytes was carried out using an Agilent 1290 Infinity II LC consisting of a vacuum degasser, a temperature-controlled autosampler, a column compartment, and a binary pump. The HPLC system was connected to an Agilent 6545 LC/Q-TOF equipped with an Agilent Jet Stream source. Table 1 shows the operational parameters used for the experiments.

Table 1. LC/Q-TOF MS chromatographic and instrumental conditions used in this study.

LC conditions for the 1290 Infinity II LC	
Column	Agilent ZORBAX Eclipse XDB, C8, 4.6 × 150 mm, 3.5 µm (p/n 963967-906)
Column temperature	25 °C
Injection volume	10 µL
Mobile phase	A) Acetonitrile B) 0.1 % Formic acid in water
Run time	30 minutes
Flow rate	0.6 mL/min
Gradient	90 %B at time 0, hold for 5 minutes, gradient to 100 %B at 30 minutes, then 10 minutes post run time
MS conditions in positive mode	
Sheath gas temperature	350 °C
Sheath gas flow	11 L/min
Gas temperature	250 °C
Desolvation gas flow-rate	10 L/min
Nebulizer pressure	45 psi
Capillary voltage	3,500 V
Nozzle voltage	0 V
Skimmer voltage	65 V
Octopole RF	750 V
Accurate mass spectral range	50–1,000 *m/z*
Fragmentor voltage	175 V
Internal reference masses	Purine *m/z* 121.0509 and HP-921 at *m/z* 922.0098
Mass spectral range	Low (1,700 *m/z*) at 2 GHz
Resolving power	30,000 at *m/z* 1,522

Results and discussion

The operational Auto MS/MS parameters are selected using the Method Editor function of the Agilent MassHunter Acquisition software. We detail each of the tabs and various operational parameters to be optimized. Each section contains a brief explanation of what impact the different settings have in the identification and mass spectral quality of the compounds selected.

Under the Acquisition tab of the Method Editor, there are five different tabs where the various parameters for Auto MS/MS are selected. The following sections discuss each of these tabs with the diversity of values available in each one.

Spectral parameters tab

See Figure 1 for the nomenclature of the different parameters.

We chose a range from 100 to 1,000 *m/z* in single MS mode. This range was chosen to capture the calibrant masses at *m/z* 121.0509 and 922.0098 for accurate mass correction. We also chose a range from 40 to 700 *m/z* in MS/MS mode to cover most common small molecules including pharmaceuticals and pesticides. These ranges define what data are recorded even though the instrument will continue its acquisition cycle to 1,700 *m/z* as set in the Instrument State tab of the tune instance.

Since acquisition rate/time is intrinsically related to another parameter found under the Precursor Selection II tab, we want to point out that the *scan speed varied based on precursor abundance* box was not marked for this optimization.

However, if the intended goal of an experiment is to obtain MS/MS for as many precursors as possible, this option would be beneficial, as explained later.

The acquisition rate refers to the number of spectra collected per second; changing this number affects the time spent to acquire data for each spectrum and the total number of transients per spectrum. The slower the rate, the more time spent on each MS spectrum and the more transients per spectrum used. The more transients, the greater the counts per *m/z*, and the better the signal-to-noise (S/N) of the spectra. To optimize this parameter, we used many values, ranging from 1–10 spectra/s, and a combination of these two values in both MS and MS/MS modes.

To understand the time it takes to get MS and MS/MS data, the total cycle time according to Equation 1 should be accounted for.

Equation 1.

$$\textit{Total cycle time} = (\textit{time spent on MS}) + (\textit{number of precursors per cycle}) \times (\textit{number of collision energies}) \times (\textit{time spent on each MS/MS})$$

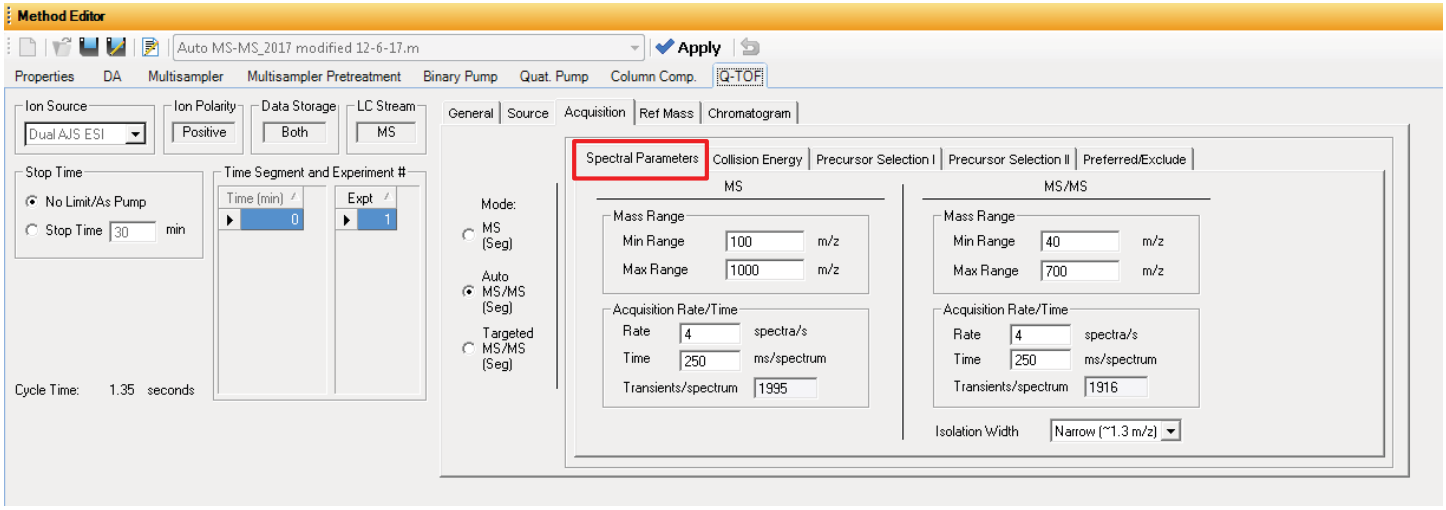

Figure 1. The Spectral Parameters tab of the Method Editor in the MassHunter LC/Q-TOF MS software.

We chose a rate of four spectra/s. The time spent on MS and on each precursor was 0.25 seconds. If only one precursor and one collision energy was chosen, the total time would be 0.50 seconds. For two precursors and two collision energies, the total time would be approximately 1.25 seconds, due to minor turnover times. We also noticed that using lower acquisition rates allowed for higher intensity spectral counts and better-quality MS/MS spectra. This is because the S/N is enhanced by collecting more transients, as the standard deviation of the signal decreases by the square root of the number of transients. Using higher acquisition rates will not only provide lower S/N, but also lower absolute counts. Therefore, for less abundant peaks, a static threshold must be lowered to detect less abundant compounds. Faster acquisition rates allow for more coeluting precursors to be detected if the thresholds are set appropriately. Thus, the analyst must compromise the quality of spectra with number of precursors selected for MS/MS. If several higher abundance compounds coelute, then faster acquisition with more precursors per cycle would be appropriate for maximum identification. In contrast, if there are better-separated lower-abundance compounds present, then slower acquisition rates would detect these compounds with higher-quality MS/MS.

One advantage of a higher fragmentor voltage is that in-source fragmentation can be intentionally induced. Fragments created in the source can then be selected as precursors during Auto MS/MS, and an extra MS/MS spectrum can be obtained, imitating pseudo MS^3 conditions. However, too high a fragmentor voltage may produce no pseudomolecular ion, and its MS/MS would be missed. A true MS^3 would require isolation of the fragment ions and further fragmentation, but by knowing the fragmentation pattern, one can mimic those conditions. Figures 2A and 2B depict examples of this. These experimental conditions would meet the goal of getting as much structural information on a particular precursor as possible. However, if the goal is to obtain MS/MS on as many precursors as possible in a complex data file, the in-source fragmentation should be limited by a low fragmentor voltage setting (for example, 100 V), as shown in this experiment.

These data are consistent with the fragmentation pattern of atenolol, as shown in Figure 3. It is a powerful approach as it combines the use of accurate mass for each individual ion and fragmentation pattern using MS/MS conditions for the precursor ion as well. This approach is useful in the determination of the structure of a true unknown, a compound not found in a database. It would be augmented with both a good response for the unknown and specific settings in Auto MS/MS (for example, active exclusion turned on, otherwise the decision process for Auto MS/MS would continually take the MS/MS of the most abundant ion in the single MS experiment whether it is a fragment or the protonated molecule).

For our experiments, we found that a rate of four spectra/s was a good compromise to get the most of our precursors and maintain good spectral quality. Furthermore, peak shape was better at four spectra/s than at two spectra/s, as more data points were acquired from the reduced cycle time.

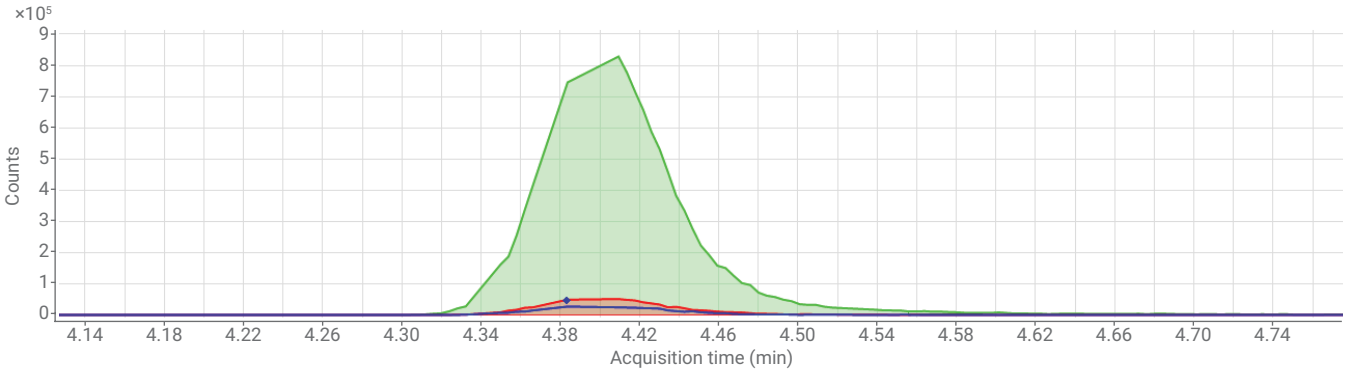

Figure 2A. Extracted ion chromatogram of m/z 267 (atenolol) in green, m/z 225 (fragment ion) in red, and m/z 190 (fragment ion) in blue.

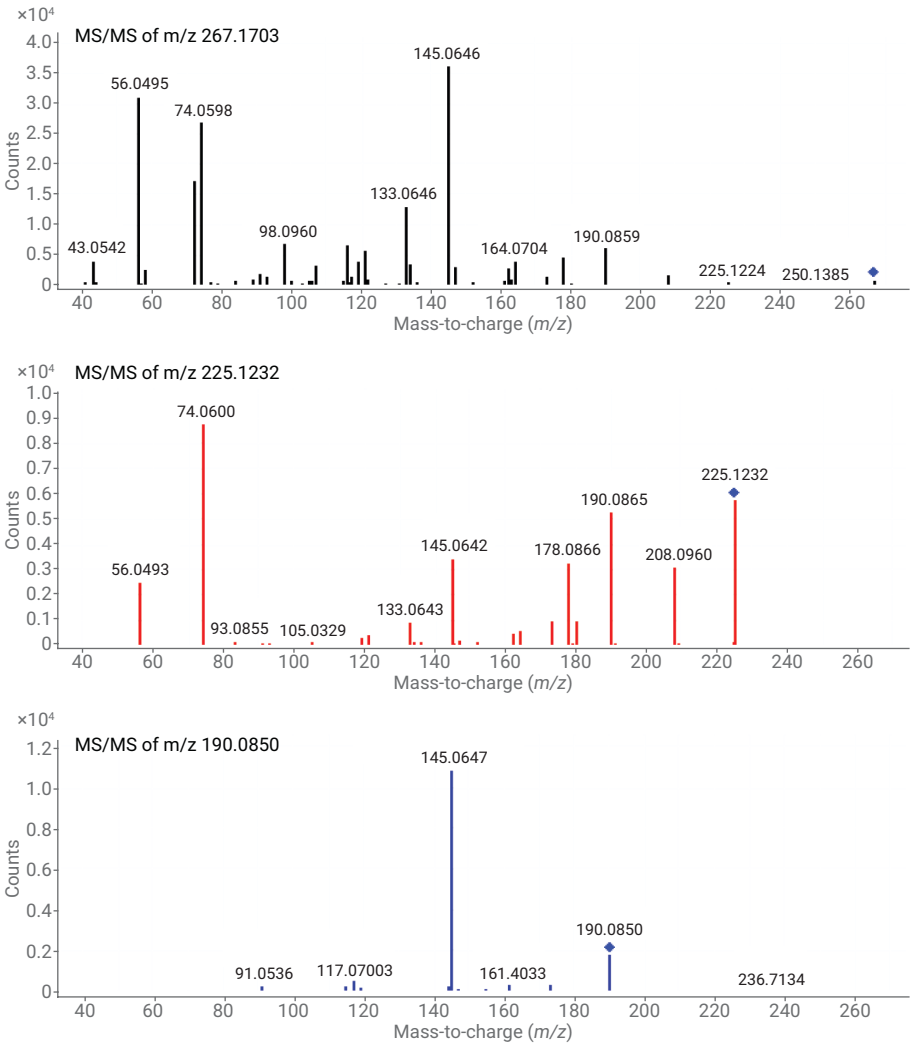

Figure 2B. MS/MS spectra of selected ions by auto MS/MS.

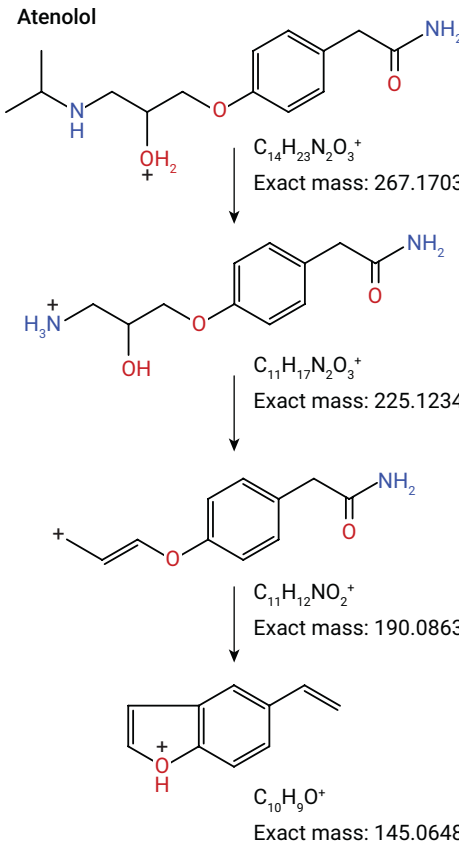

Figure 3. Fragmentation pattern of atenolol by accurate mass.

Under the Spectral Parameters tab, there is another important parameter to consider: isolation width of the precursor selection window. This refers to the quadrupole mass window used during MS/MS precursor isolation. For narrow isolation widths, the isolation window is centered on the mono-isotopic peak of a cluster, and the ion is isolated within a 1.3 *m/z* window (0.65 to the left and right of mono-isotopic peak). For medium and wide isolation widths, the range is not evenly applied. The charge state of the ion is determined first so that the mono-isotopic ion can be determined. For medium width, having an isolation window of 4.0 *m/z*, once the mono-isotopic ion is determined, 0.3 *m/z* is subtracted from that mass. This is the beginning of the isolation window. Then, 2 *m/z* is added to the now-determined subtracted mass, and this *m/z* is used as the center point of the isolation window (with 2 *m/z* on either side of the center point). For the precursor in Figure 4, the charge state was calculated as z = 1, as the isotopes are spaced 1 *m/z* apart, and the mono-isotopic mass was determined at 216.1008. The isolation window for medium was 215.8008 to 219.8008.

This window offset was calculated to accommodate both singly and multiply charged ions and their isotope clusters; additionally, the chlorine isotope can be seen in the fragment cluster of *m/z* 174.0534. Note that for most small molecules of environmental concern, the selected charge state would be 1 or unknown (see the Precursor Selection II tab section).

We found that a medium isolation window of 4 *m/z* is a good match for pesticides and pharmaceuticals. This window is highly useful for compounds that have chlorine, bromine, or sulfur atoms in their chemical structures.

Figure 4 shows how useful information can be obtained from both the precursor ions and fragment ions of atrazine (a chlorinated pesticide). Widening this window also allows other potential interfering ions to enter the collision cell, thus lowering the possible purity of the MS/MS spectra. These settings are made based on the goal of the experiments. If the goal is only to compare the MS/MS spectra collected in the sample to a library spectrum, for small molecules, a narrow isolation window (1.3 *m/z*) can provide the cleanest MS/MS spectra.

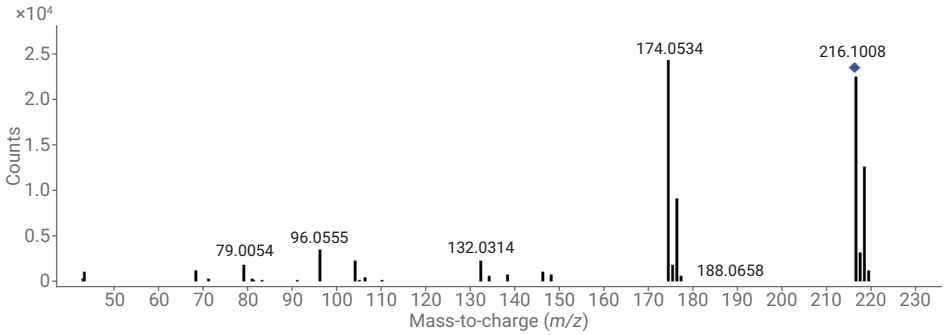

Figure 4. MS/MS spectrum of atrazine, showing the chlorine isotope signature for both the precursor and fragment ion, showing which fragments contain the chlorine and which ones do not.

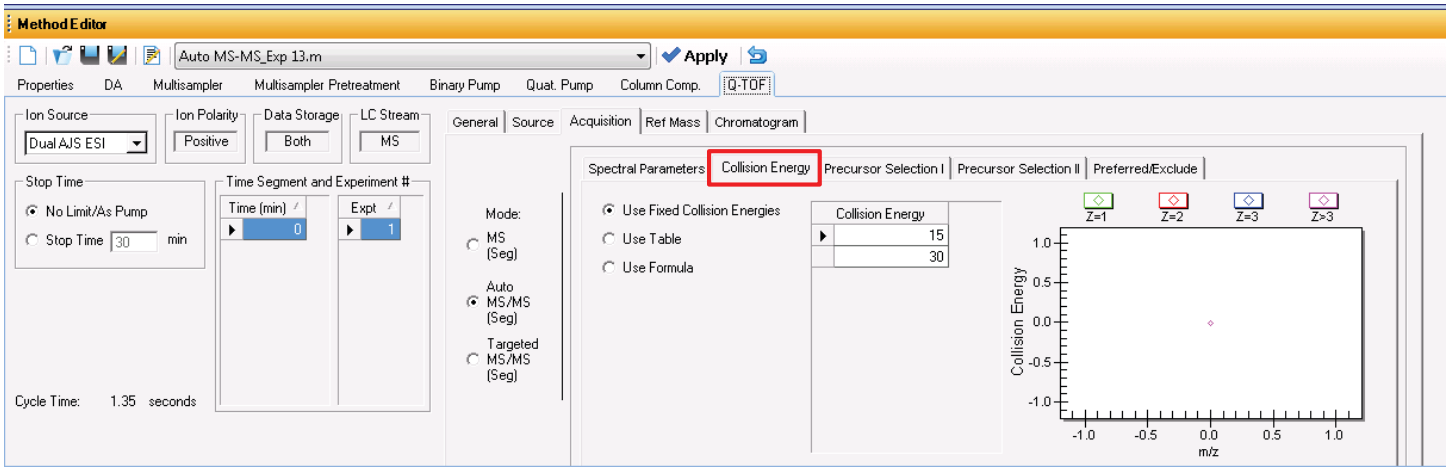

Figure 5. The Collision Energy tab under Method Editor of the MassHunter LC/Q-TOF MS software.

Collision Energy tab

Figure 5 shows the nomenclature of the different parameters.

The Collision Energy tab allows set collision voltages to be applied during MS/MS experiments. There are three options:

- The first option uses fixed collision energies, in which as many different collision energies as needed can be chosen. We used two collision energies for this experiment, which is the preferred option based on the fragmentation of small molecules. Usually voltages ranging from 10 to 40 V allow for detailed inspection of the fragmentation spectra. Occasionally, a voltage of 30 V has been found to be optimal for molecules that are harder to fragment. We used values of 15 and 30 V. The more collision energies used, the more time it takes to perform one cycle, and this limits the number of precursors that can be isolated for MS/MS. As shown in Equation 1, the estimated cycle time can be calculated for the settings made. At an MS/MS acquisition rate of 0.25 s/spectrum, four precursors per cycle, two collision energies per spectrum, and 0.25 seconds for the single MS, approximately 2.25 seconds is required to complete one cycle. If a third collision energy is selected, it would require another second to complete a cycle, and at these settings, abundant precursors coeluting in a complex sample may be missed.
- The second option uses a table, which can be built based on previous knowledge of fragmentation patterns based on *m/z* values. The table allows specification of different linear interpolations for different charge states by entering a mass and a collision energy in volts. For each charge state, a linear interpolation through the values specified in the table is performed. This option is recommended for different charge states, and is useful in peptide and protein analysis. This experiment dealt with singly charged molecules; thus, this option was not explored here.
- The third option uses a formula that calculates which voltage to use depending on the *m/z* value chosen by the Auto MS/MS experiment. The formula determines the collision energy by linear interpolation, calculated according to the following equation:

Collision energy = (slope × *m/z* of precursor mass)/100 + Offset.

For example, an *m/z* of 200 would set a collision energy of 15 V using a slope of 5 and an offset of 5 (200 × 5/100 + 5). This is useful because the ions to be fragmented generally require more energy the larger the molecule. In our case, we found it sufficient to use two fixed collision energies (one low and one higher), as this gave us enough fragmentation information from a precursor. It must be considered that selecting two or more collision energies will also affect the total sampling rate, according to Equation 1.

Precursor Selection I tab

Figure 6 shows the nomenclature of the different parameters.

In the Precursor Selection I tab, the maximum precursors per cycle can be selected. In real environmental samples, many compounds coelute, and this setting allows the Auto MS/MS function to capture more than one precursor ion corresponding to different compounds. Some of the precursors selected when a certain peak (or compound) is eluting will coincide with the fragments of that specific compound. This allows investigation of the fragmentation spectra obtained as if it were MS^2 or

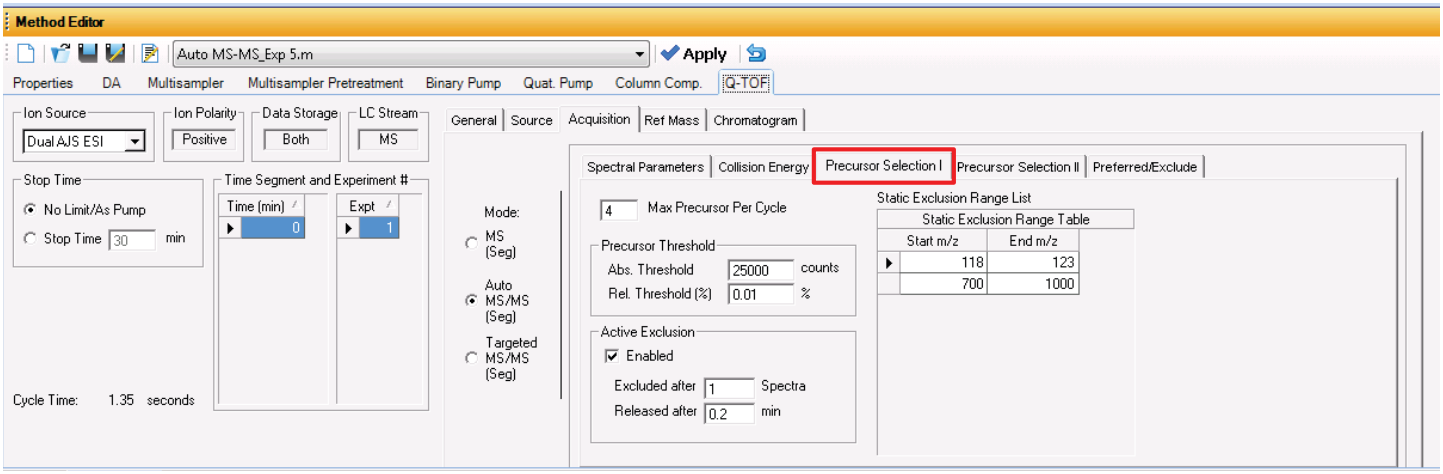

Figure 6. The Precursor Selection I Tab under Method Editor of the MassHunter LC/Q-TOF MS software.

MS^3, which proves to be useful for elucidation purposes. The value of the fragmentor voltage also plays an important role, since fragments will have more prominent peaks at higher fragmentor voltages, thus these will be considered for MS/MS fragmentation. One must consider whether the goal of the experiment is to capture as many precursors for MS/MS or for structure elucidation of the more prominently ionized compounds. An ion with very strong intensity may be ionized well and not necessarily at a very high concentration. We set this value to four precursors per cycle.

The precursor threshold values determine whether to consider an ion as a precursor. An ion is considered only if both the absolute and relative threshold values are satisfied. It must be taken into account that the relative and absolute threshold depends on the acquisition rate, which determines the number of transients collected for each spectrum. Also, the relative threshold value is based on the base peak in a spectrum. The values to choose are determined by the type of water sample analyzed, the concentration of the precursors to be selected, and the acquisition rate chosen. As expected, lowering the absolute threshold value to 5,000 would result in numerous precursors being selected and MS/MS performed, whereas a higher value gets only those precursors that are relevant in the samples. For our work, we found that a value of 25,000 works well as a compromise between getting all the relevant compounds in the samples and minimizing the background interferences. The relative threshold value is calculated from the base peak in that spectrum. For example, if the base peak is 10^5 and the relative threshold is set at 1 %, then other precursors would need to be above 10^3 counts of intensity to be selected. This relative threshold value had no effect on the number of precursors selected because it always produced an intensity less than the absolute threshold value. The threshold value can also be used to obtain MS/MS spectra near the apex of lower intensity ions. See Figure 7 for an example of where in the peak elution the MS/MS spectra are collected. Note that thresholding is used so that Auto MS/MS does not select noise as precursors. The analyst must determine whether dynamic thresholds (selecting a % of the base peak of an MS spectrum) or static thresholds (a value based on the counts determined to be non-noise for the acquisition rate used) will provide the most useful results for their datasets.

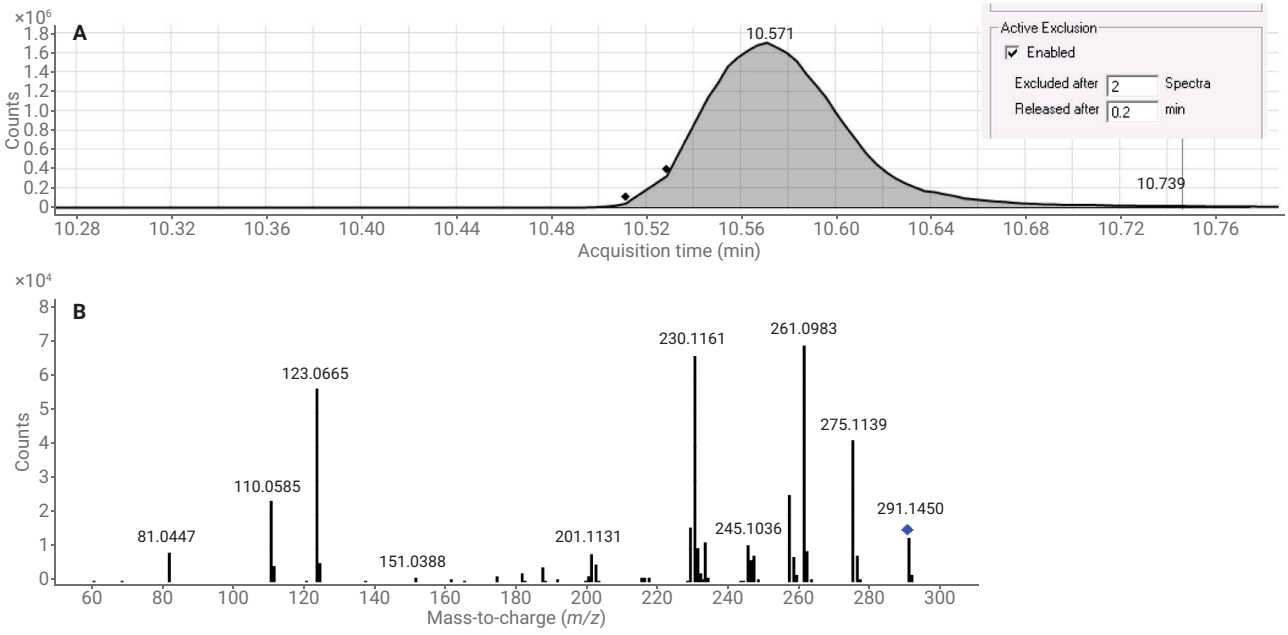

Figure 7. Auto MS/MS spectra for trimethoprim when using the active exclusion window after two spectra. A) shows where the auto MS/MS were taken (diamonds).

The active exclusion window allows the automatic exclusion of a precursor from selection after specified criteria are met. So if the box is checked, ions that were selected as precursors can be excluded if the following two conditions are met:

- After a certain number of spectra, which is the minimum number of times that the precursor undergoes MS/MS before it becomes active again for re-examination
- How many minutes the precursor is ignored after the MS/MS before it becomes active again for re-examination

We found that a value of two spectra provided better MS/MS accuracy than a value of only one spectrum. This happens because, generally when a peak elutes, the Auto MS/MS engine chooses that precursor when it meets the threshold value set, but usually too early in the chromatographic peak to get enough spectral accuracy. A value of two spectra allowed the engine to retake the MS/MS at a later retention time and get much better spectral quality. Figure 7 shows an example in which the MS/MS spectrum obtained for trimethoprim is the average of two scans instead of one. The accuracies for all the fragment ions are well below 0.5 ppm.

Another way to get good spectral quality is to change the time to 0.1 minutes for the exclusion. This change allows the instrument to get fragment ions before it re-evaluates the precursor, and still get two spectra for the same precursor (Figure 8). Depending on chromatography and peak width, one can adjust this value to allow more spectra during MS/MS. One can also calculate the release time to catch the top of the peak, which in this case would be 0.05 minutes. The goal is whether to balance obtaining more MS/MS for coeluting precursor ions including fragments or to get more intense spectra with possibly higher-quality MS/MS.

The static exclusion range list allows users to specify ranges to exclude from consideration as precursors. In our experiments, we excluded the masses between *m/z* 118 and *m/z* 123 to exclude one of the calibrant masses at *m/z* 121. Similarly, we excluded a window between 700 and 1,000 *m/z* to exclude the second calibrant mass at *m/z* 922 and all molecules larger than *m/z* 700.

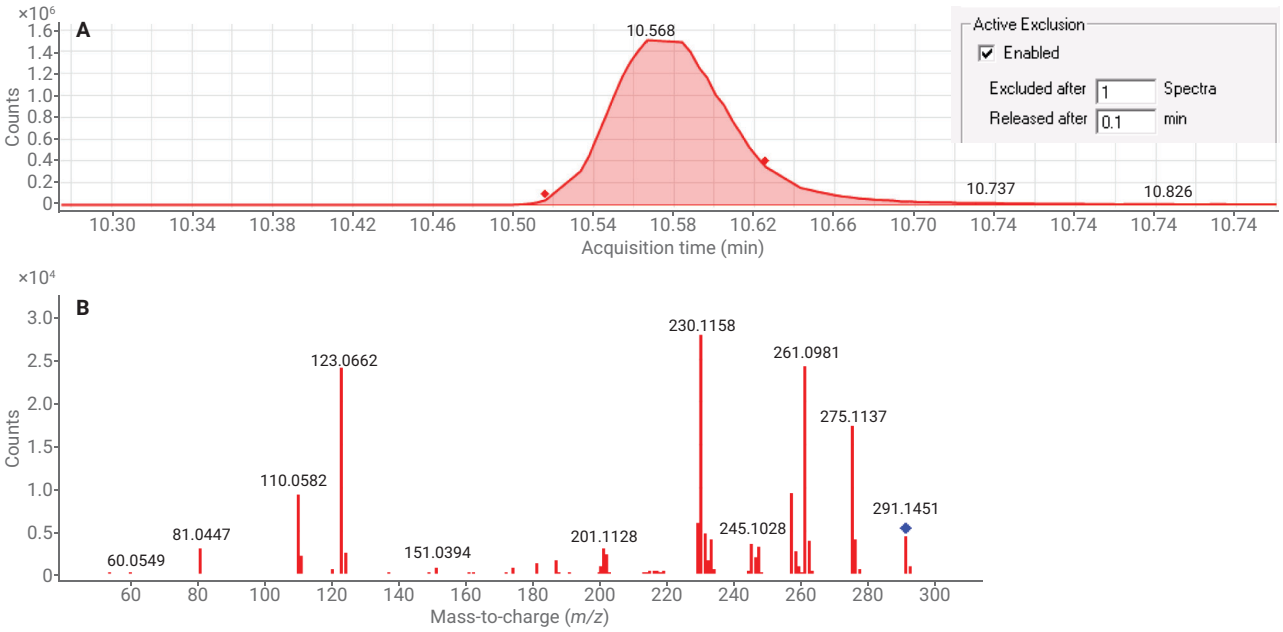

Figure 8. Auto MS/MS spectra for trimethoprim when using the active exclusion window after 0.1 minutes. A) Diamonds show where the Auto MS/MS were taken.

Precursor Selection II tab

Figure 9 shows the nomenclature of the different parameters.

The isotope model is used to accept or reject precursor isotope groups. For our application, we chose **Common Organic Molecules**; the engine looks for clusters where the ratio of the A+1 and A+2 peak is consistent with the most common elements present in small organic molecules. Since most of the small organic molecules we looked for were singly charged, we chose the **Sort Precursors by Abundance Only** option. Therefore, the decision engine selected ions based on their abundance. However, by selecting only singly charged ions as active, those ions with multiple charges, determined by the spacing of the isotopes, will not be selected as precursors. Also, by not selecting the **Unknown** option, where the decision engine cannot determine the charge, low intensity ions without distinguishable isotopes will not be selected, nor will ions that are more intense. Thus, their isotopes, now with improper spacing, will not allow for the charge determination. If the threshold from the previous tab is set low enough for low intensity ion selection as precursor or it is needed to obtain MS/MS of intense ions as precursor, the **Unknown** should be set to active.

The abundance-dependent accumulation adjusts the MS/MS accumulation rate depending on the precursor abundance. If the precursor has an elevated abundance in the sample, the MS/MS is acquired at a fast acquisition rate (fewer transients per spectrum). Conversely, if the precursor has a low abundance, a slower acquisition rate is applied, and more time is allowed for MS/MS accumulation (more transients per spectrum). If this box is not checked, the acquisition rate is the one specified in the Spectral Parameters tab (see the Spectral Parameters tab section). If the box is checked, one has to specify the target value in counts/spectrum. This value is the sum of all peak heights in the resulting MS/MS spectrum—it is not the precursor abundance value. The decision engine will sum the transients until the target count is reached. For proteomics/peptide work, a default value of 25,000 is usually chosen because it works well for the more common use of Auto MS/MS. We examined values ranging from 10,000 to 75,000 and found that a value of 50,000 gives an appropriate balance between MS/MS spectral quality and acquisition rate for

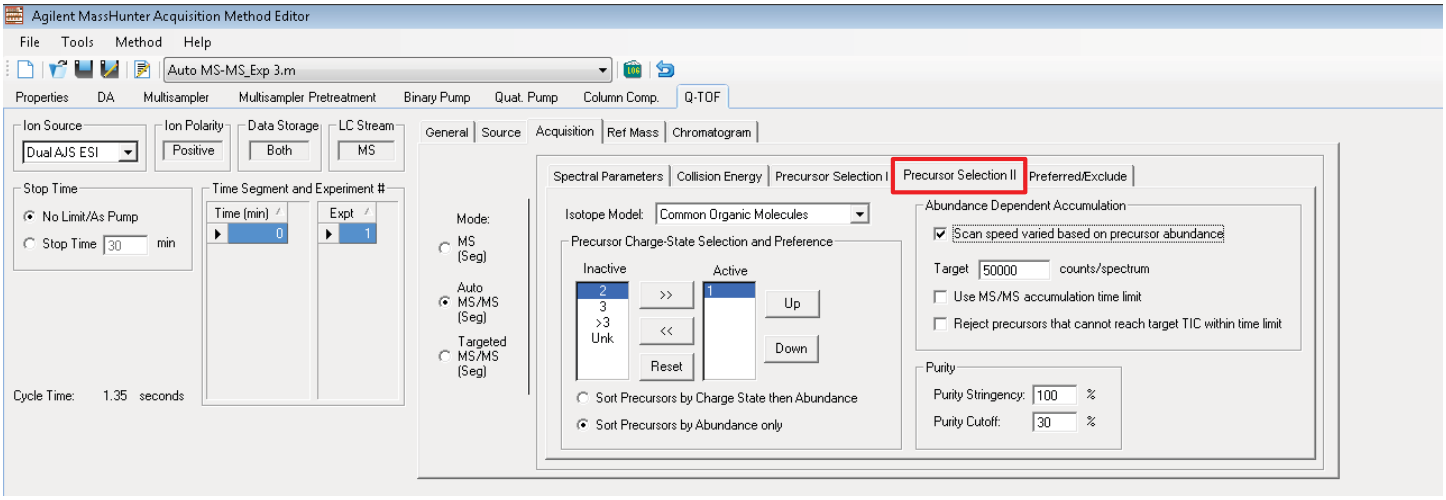

Figure 9. The Precursor Selection II Tab under Method Editor of the MassHunter LC/Q-TOF MS software.

this particular experiment with small molecules. Figure 10 shows an example for lamotrigine, a pharmaceutical that is hard to fragment. When the target value was 10,000 counts, the spectral quality was much lower than when a target value of 50,000 was chosen. For a value of 10,000 counts, the base peak is 1,800 counts, and there are more than 17 other fragments ranging from 50 to 400 counts. It takes fewer transients and less time to reach this sum, but the spectral quality suffers. At 50,000 counts, the base peak is 10,000 counts, and there are more than 36 other fragments in the spectrum. It takes more time to reach this sum, but the spectral quality is much higher. The analyst must balance spectral quality with the number of precursors selected for MS/MS. If **Use MS/MS accumulation time limit** is checked, MS/MS acquisition for a selected precursor will stop even if the target is not reached and go on to the next precursor. If it is not checked, the accumulation time will continue until the target is reached, giving a greater possibility of obtaining high-quality spectra for each precursor selected with a limit of 16,383 transients. However, this runs the risk of missing other precursors that are coeluting. Checking the last box, **Reject precursors that cannot reach target TIC within time limit**, allows the decision engine to not collect MS/MS spectra on a precursor that it determines will not reach the set value in the accumulation time set in the acquisition tab. This setting limits poor MS/MS spectra quality and maximizes the selection of precursors that will provide good spectral quality. These settings need to be selected based on the goals of the experiment.

Purity is the S/N calculation of the selected precursor. It is the ratio of the total precursor abundance (including isotope peaks) divided by the total abundance within the selected isolation window. When this value is set at 100 %, high purity precursors move higher on the precursor ranking. When set to 0 % purity ranking is disabled. The purity cutoff is the minimum purity threshold below which a precursor candidate will be rejected. We did not observe any differences by varying this value on our experiments. However, if there are other ions within the window that are not isotopes of the selected precursor, this setting will have an effect.

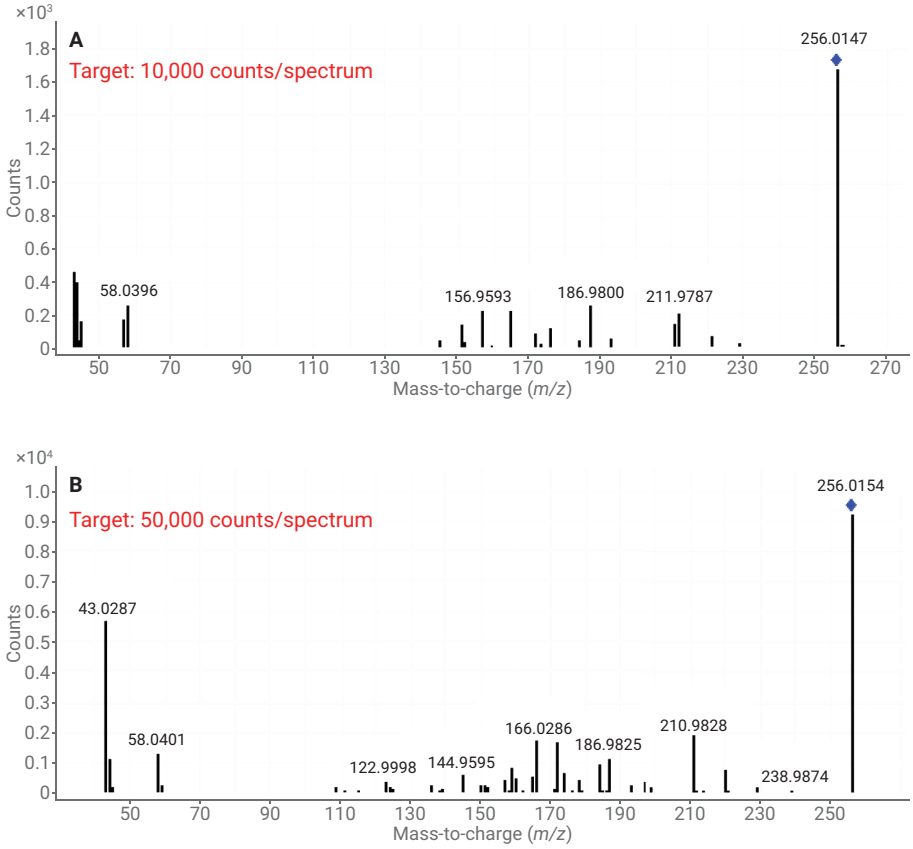

Figure 10. A) A spectrum obtained with a target of 10,000 counts/spectrum. B) A chromatogram obtained with a target of 50,000 counts/spectrum.

Preferred/Exclude tab

This tab allows the specification of precursors to include or exclude for Auto MS/MS. We found this option useful to include one of our internal standards (carbamazepine d-10) that is added to all our samples, for quality control purposes (Figure 11).

This option would be useful to exclude peaks that always appear in blanks, or to exclude peaks of compounds that are not of interest. Another option is to include peaks from a specific target list or from a specific personal compound data library (PCDL) screening search. Furthermore, a targeted list of compounds that had too much overlap in the targeted MS/MS mode could be included.

Because targeted MS/MS collects MS/MS continually within the selected retention time window, too many overlapping ions creates too long a cycle time, and important coeluting precursors are missed. Using the active exclusion in Auto MS/MS, the cycle time can greatly be improved, and good quality MS/MS spectra can be collected in one run. If **Use Preferred ion list only** is checked, this becomes a targeted MS/MS using the decision engine criteria selected in all the previous tabs. In addition, single MS data from samples can be evaluated in the Qualitative Analysis Workflow by searching a personal compound database (PCD). The hits obtained can be exported as an inclusion list, and imported into this tab. A compound list for export as an inclusion list can also be generated using the Molecular Feature Extraction (MFE) algorithm in Qualitative Analysis. Likewise, an exclusion list can be generated using MFE. In experiments that use statistical analysis using Mass Profiler (two groups) or Mass Profiler Professional (multiple groups with multivariate statistics), lists of entities that are statistically important based on the experimental design can be imported into this tab as an inclusion list, and will appear as preferred. Checking **Use Preferred ion list only** depends on the goals of the experiment.

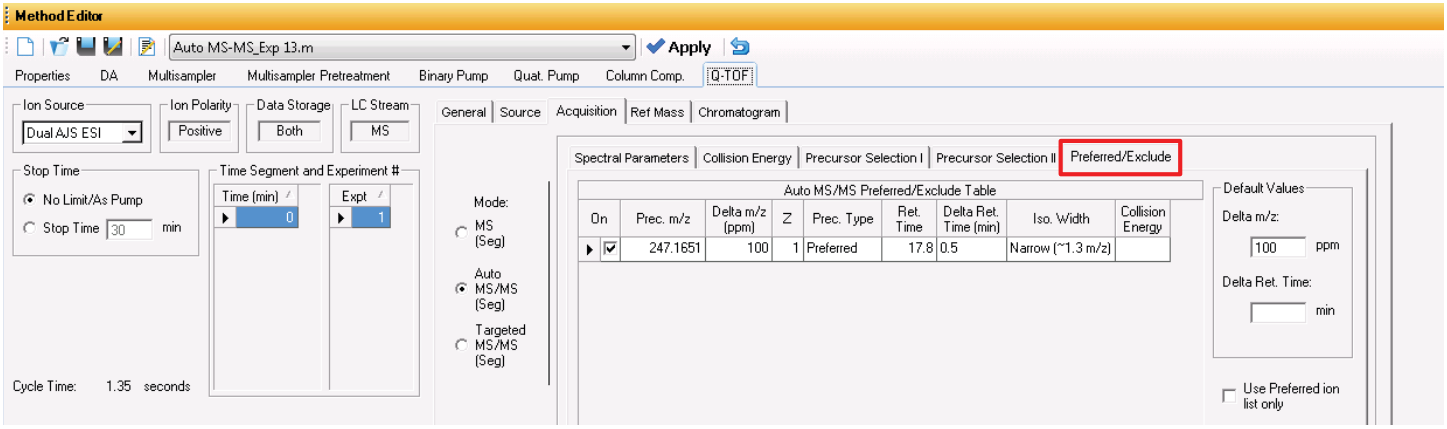

Figure 11. The Preferred/Exclude tab under Method Editor of the MassHunter LC/Q-TOF MS software.

Conclusions

Auto MS/MS is a powerful data-dependent acquisition mode that allows the analyst to collect high-quality MS/MS spectra of both simple and complex samples in targeted and nontargeted experiments. This mode provides the ability to:

- Perform nontargeted screening with the goal of obtaining good-quality MS/MS spectra of as many compounds as possible
- Perform nontargeted screening using a PCDL where the MS/MS spectra are compared to MS/MS spectra in a library*
- Obtain MS/MS spectra of both protonated molecules (or pseudomolecular ions) and fragments for structure elucidation of unknowns
- Obtain MS/MS of lists of entities (compounds) determined to be statistically significant for identification and annotation (marker compounds or emerging contaminants)

* Even with the most appropriate settings for Auto MS/MS, significant compounds with low intensity signals in regions of high chromatographic coelution may be missed. This type of analysis might be better accomplished using the All Ions MS/MS mode of acquisition. Selection of the appropriate mode of acquisition should be based on the goals of the analysis.

We showed with examples the effects of the parameters that must be set to obtain high-quality data. This Technical Overview demonstrates that although this mode is powerful, it is also complex and requires an understanding of all the possible settings and their impact on the outcome of an experiment. Selected settings must be fit for the purpose of the experiment. Specifically, the analyst must first determine the goals of the experiment, then select the appropriate settings. These settings will also depend on the type of data obtained from the samples being analyzed. For example, drinking water analyzed at part-per-billion levels will require different settings than the same sample concentrated to obtain part-per-trillion levels of detection.

www.agilent.com/chem

Printed in the USA, October 15, 2018
5994-0322EN

Agilent
Trusted Answers