

Selecting the best Q Exactive Orbitrap mass spectrometer scan mode for your application

Authors

Anton Kaufmann,
KLZH, Zürich, Switzerland

Maciej Bromirski,
Thermo Fisher Scientific,
San Jose, CA, USA

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Introduction

Thermo Scientific™ Q Exactive™ hybrid quadrupole-Orbitrap™ series mass spectrometers offer analysts a range of scan modes that provide functionality comparable to the modes provided by conventional tandem quadrupole mass spectrometers: the product ion, fragment ion, and data-dependent neutral loss trigger scan modes. Although the Q Exactive series mass spectrometers provide the analyst with a toolbox similar to that of triple quadrupole (QQQ) instruments, key differences exist between the two technologies. Most importantly, the Orbitrap analyzer of the Q Exactive series mass spectrometer is a trapping, not a scanning, device. Certain Q Exactive series mass spectrometer data acquisition modes may resemble conventional QQQ scan modes, but there are differences in their selectivity and sensitivity characteristics, as well as the number of data points acquired per unit time. This white paper describes each of the various scan modes, and the key differences between trapping and scanning devices. Method development guidance, including consideration of intrinsic dependencies such as resolution and scan speed, sensitivity, and selectivity, is also provided.¹

General principles and considerations

As shown in Figure 1, the Q Exactive series mass spectrometer includes a quadrupole mass filter (blue) for either broad or narrow mass range transmission, a C-Trap (green) for ion storage, a higher-energy collision dissociation cell (HCD) for fragmentation (red), and the Thermo Scientific™ Orbitrap™ mass analyzer (purple) for ion detection and mass analysis. The importance of each of these parts is explained briefly below. More in-depth explanation of the instrument and its hardware features is provided in the reference publications.²⁻⁶



Figure 1. Schematic of the Q Exactive series mass spectrometer.

Key parts of the instrument include the quadrupole (blue), C-Trap (green), higher-energy collision dissociation cell (HCD) (red), and the Orbitrap mass analyzer (purple).

The isolating quadrupole (Q) in front of the C-Trap is used as a mass filter for either wide (e.g. 10 to 100 Da isolation) or narrow (e.g., 0.4 to 2 Da isolation) mass range selection. High-end instruments, including the Thermo Scientific™ Q Exactive™ Plus hybrid quadrupole-Orbitrap™ mass spectrometer, Thermo Scientific™ Q Exactive™ HF hybrid quadrupole-Orbitrap™ mass spectrometer and Thermo Scientific™ Q Exactive™ HF-X hybrid quadrupole-Orbitrap™ mass spectrometer, utilize a segmented isolating quadrupole that provides sharper isolation and improved transmission compared to the Q Exactive and Thermo Scientific™ Q Exactive™ Focus hybrid quadrupole-Orbitrap™ mass spectrometers, which feature a hyperbolic quadrupole. Notably, the quadrupole is not used for scanning as it is in conventional tandem

quadrupole mass spectrometers. Instead it is used purely for isolation. Additionally, mass spectrometer selectivity is obtained with narrower isolation, and MS² selectivity is gained with enhanced fragment resolution.

The C-Trap is a radio frequency (RF)-based ion collecting and cooling device. To avoid overfilling and space-charge effects, the C-Trap is controlled by automatic gain control (AGC) and the C-Trap Charge detector (CTCD) behind the HCD cell. The C-Trap directs ions either to the higher-energy collisional dissociation cell (HCD) for ion fragmentation, or to the Orbitrap mass analyzer for detection.

The HCD cell is used to fragment ions passed through the isolation quadrupole. Fragmentation with residual nitrogen gas occurs when ions are accelerated from the C-Trap into the HCD cell. Locating the HCD cell behind the C-Trap provides unique advantages, including parallelization and multiplexing. User-defined collision energies allow spectral multiplexing for up to 10 injections, which is not possible using quadrupole-time-of-flight (Q-TOF) instruments.

The Orbitrap mass analyzer acts as both an analyzer and a detector. Ions inside the Orbitrap mass analyzer undergo an extensive number of oscillations, producing ion separation and generates a time-varying signal, referred to as a transient, from which the mass spectrum may be derived. The length of a transient affects the mass resolving power but does not influence the measurement sensitivity. With Q-TOF instruments, sensitivity is reduced with higher resolving power. High-field (HF) Orbitrap mass analyzers are deployed on both the Q Exactive HF and Q Exactive HF-X mass spectrometers, allowing scan speeds of up to 40 Hz for MS and MS/MS scans.*

*Please note, the Orbitrap mass spectrometer is not a true scanning device, but it produces HRMS spectra like that obtainable when employing a quadrupole. Hence for convenience reasons, the word “scan” is used throughout the white paper.

Both the Q Exactive series mass spectrometers and QQQ instruments perform tandem MS. However, the technologies differ in how product ions are measured and, most significantly, the resulting mass resolution. Compared to QQQ technology, Q Exactive series instruments provide a much higher mass resolving power for product ion detection and full mass range scan analysis.

Another difference between technologies is that the second high-resolution mass spectrometer (HRMS) dimension does not continuously measure ions. Instead, it processes pulsed ion beams in a sequential manner. Here, the Q Exactive mass spectrometer technology is similar to Q-TOF technology in that both measure sequential ion pulses. The Q Exactive series mass spectrometer however provides a significantly greater mass resolving power (up to 280,000 (FWHM) at m/z 200 on the Q Exactive Plus mass spectrometer) and does not require spectral averaging for high-confidence data generation. The Q Exactive HF mass spectrometer can be used to monitor six data points at

a resolution setting of 60 k (FWHM) at m/z 200, or 12 at resolution setting of 30 k (FWHM) at m/z 200, which is sufficient for both screening and quantitation with ultra-high performance liquid chromatography (UHPLC). For further information, refer to Thermo Fisher Scientific Technical Note 64287.⁷

Scan modes: technical principles

Figures 2 through 10 illustrate how the scan modes function, showing the flow path of the ions within the Q Exactive series mass spectrometer, from left to right (x-axis). The y-axis shows the time sequence of individual experiments. The quadrupole is represented as a long bar (rectangle). The length of the bar represents the possible scan range. The shaded sections within the bar indicate the user-defined mass range (m/z value) of the ion that was selected or isolated by the quadrupole. The height of the bar corresponds to the typical ion injection time into the C-Trap for a particular scan mode. The height of the Orbitrap mass analyzer corresponds to the required transient measurement time for the selected mass resolution. Unfragmented ions are shown in blue



Magic triangle: Sensitivity – Selectivity – Scan Speed

and fragmented ions (e.g., fragmentation induced in the HCD cell) are shown in red. Solid arrows present the physical flow of ions, and dashed arrows indicate logical connections, such as when an accurate mass listed in an inclusion list was detected, leading to the triggering collection of a selected ion monitoring (SIM) or MS/MS spectra in the next experiment. Note that the C-Trap is shown twice in each ion flow path. Although the Q Exactive series mass spectrometer contains only one C-Trap, ions can be forwarded from the C-Trap to the HCD and back into the C-Trap. The second C-Trapping event is depicted as a dashed square in the sequence of events.

Full MS

The full MS mode uses a full MS scan without HCD fragmentation (Figure 2) and is often used for both applied and research applications.

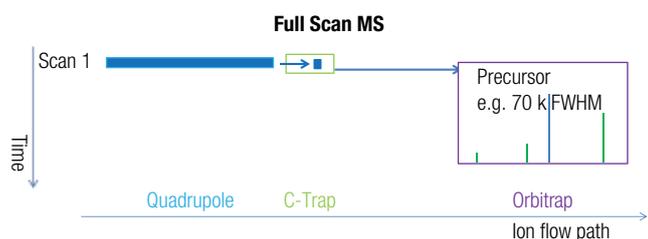


Figure 2. Full Scan MS without HCD fragmentation

A mass range can be defined that ensures the recording of all ions with an m/z value located within it with HRMS (MS1) spectral information subsequently obtained. The quadrupole in front of the Orbitrap mass analyzer is operated as a wide-pass mass filter, preventing filling the C-Trap with ions outside the defined mass range. This approach permits the detection of all compounds ionized in the electrospray (ESI) ion source with m/z values in the defined mass range. Because the full scan range is covered, the user can extract any desired m/z value after data acquisition has been completed. The Full MS mode is the most frequently used mode since it contains comprehensive information and provides good quantitative data. However, there are other modes available that provide superior sensitivity or selectivity.

Full MS/AIF

The Full MS/AIF mode uses a full MS scan (without HCD fragmentation), followed by an all ion fragmentation (AIF) scan (with a fragmentation energy applied) (Figure 3). Only ions of the second scan event enter the HCD cell; ions of the first scan event do not. This mode is most often used in small molecule applications.

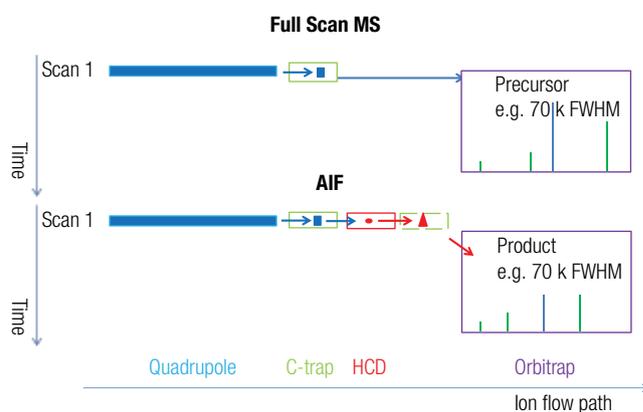


Figure 3. Full Scan MS followed by an AIF scan

In the Full MS/AIF mode, the instrument continuously acquires two different full MS scans. The ions intended for the first full MS scan are directly injected from the C-Trap into the Orbitrap mass analyzer central electrode. The ions intended for the second AIF scan are transferred as a whole into the HCD cell, where they are fragmented. All resulting product ions and remaining precursor ions are returned to the C-Trap, and then injected into the Orbitrap mass analyzer central electrode. The first scan consists of precursor ions, while the second scan contains non-precursor selected product ions that are the result of all the incoming precursor ions (AIF). Alternatively, the user can induce fragmentation within the ESI source interface instead of the HCD cell.

Targeted-SIM (t-SIM)

The t-SIM mode acquires SIM scans based on the specified inclusion list (Figure 4), which is mandatory and always activated. This mode provides ultimate sensitivity and is often used in small molecule applications.

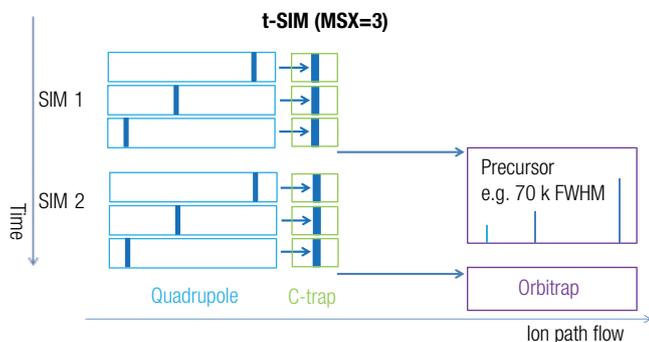


Figure 4. t-SIM with multiplexed SIM (MSX = 3)

The SIM mode monitors a narrow user-defined mass range (as narrow as 0.4 Da). Figure 4 also shows multiplexed SIM. Mass isolation is performed by the quadrupole, where its geometry permits very sharp mass cut offs. The Orbitrap mass analyzer central electrode resolves ions located within the narrow mass range specified. t-SIM is not more selective than full MS, but it does provide enhanced detection sensitivity. Detection sensitivity is affected by the number of ions (charges) injected into the Orbitrap mass analyzer central electrode. The number of ions is limited by the capacity of the C-Trap, which currently accommodates a maximum of 3,000,000 charges. However, the ESI interface produces many more ions than can normally be accommodated during a single measurement cycle. Therefore, usually only a small fraction (time segment) of the continuously entering ion beam is actually sampled by the C-Trap. Compared to the Full MS mode, using the quadrupole as a mass isolation device (SIM mode) greatly reduces the number of ions transmitted. Accordingly, a much longer segment of the continuously entering ion beam can be collected (long injection time) within the C-Trap before the target capacity (i.e., 3,000,000 charge) is exceeded. This concept is represented by the increased height of the quadrupole rectangles shown in Figure 4. The higher number of target ions sent to the Orbitrap mass analyzer central electrode results in significantly higher sensitivity.

PRM or Targeted-MS² (t-MS²)

The Parallel Reaction Monitoring (PRM) mode acquires MS/MS scans based on the specified inclusion list (Figure 5). The mandatory inclusion list is processed from the first to the last row without automated sorting. This mode is most often used for small molecule applications involving analyses of complex sample matrices when ultimate selectivity is required.

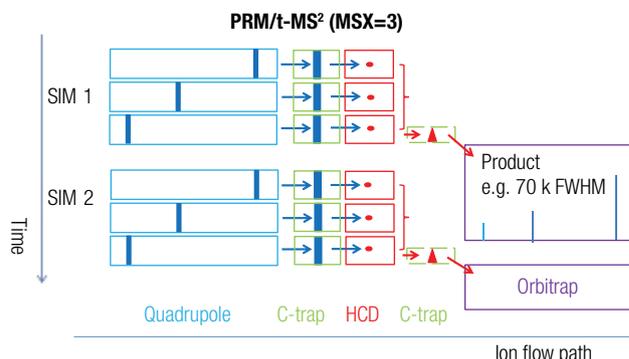


Figure 5. Parallel Reaction Monitoring (PRM) scan or t-MS² (targeted MS/MS) mode with use of multiplexed t-MS² (MSX = 3)

In this mode, the quadrupole is used as a mass filter to isolate precursor ions. Only ions belonging to a narrow user-defined mass range (e.g., 1 Da) enter the C-Trap. The ions are then transmitted to the HCD cell, fragmented, and returned to the C-Trap, where they are subsequently injected into the Orbitrap mass analyzer. The PRM mode corresponds to a QQQ instrument product ion scan. However, unlike QQQ-based product ion scans, a PRM scan produces significantly higher selectivity and sensitivity. Precursor selection combined with high-resolution product ion scanning provides enhanced selectivity. High sensitivity results from the long ion injection times (represented by the increased height of the quadrupole rectangles shown in Figure 5). Operating the quadrupole in SIM mode reduces the ion beam abundance. As a result, the ion beam can be collected for a much longer period without causing trap overfilling. However, the instrument only collects spectral information related to one particular precursor m/z value from the user-defined target list. Figure 5 also illustrates multiplexed PRM.

Full MS/dd-MS² (Top N)

The Full MS/dd-MS² mode acquires a full MS scan (without HCD fragmentation) followed by a set of data-dependent (dd) scans with fragmentation energy applied (Figure 6). Ions of the second scan event enter the HCD collision cell; ions of the first do not. This mode is most often used in proteomic applications for peptide and protein identification.

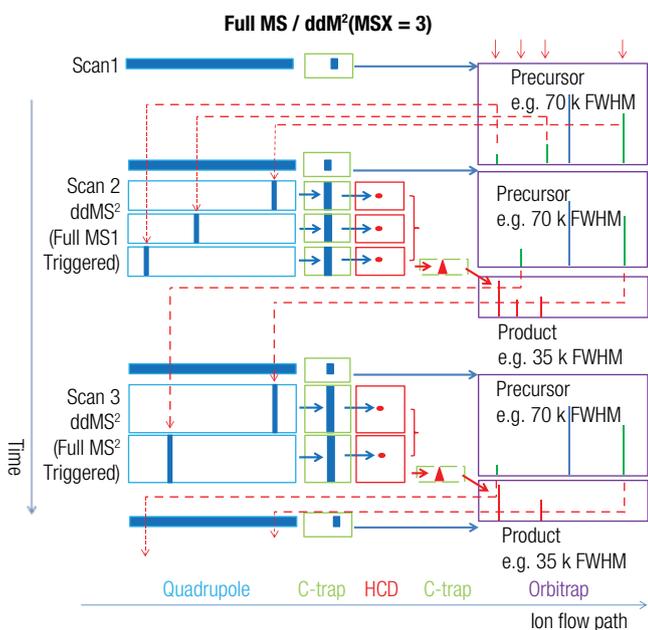


Figure 6. Full MS/dd-MS²: data-dependent acquisition based on survey scans. MSX = 3 multiplexing permits collection of three triggered precursor ions. Please see page 8 (Combining different scan modes) to better understand this figure.

In this mode, the instrument measures one full MS scan (known as a survey scan) and then analyzes the HRMS spectral information obtained based on the user-defined target list. Upon finding the presence of a mass peak corresponding to the accurate mass in the target list, precursor isolation is initiated in the quadrupole. Masses of the target ions are shown as small vertical arrows on the top right of Figure 6. Shown by the dashed arrows, collection of ions corresponding to these masses is triggered. The unit-mass resolved ions are precursor ions selected by the quadrupole and then later fragmented in the HCD cell. The resulting product ions are injected into the Orbitrap mass analyzer central electrode, where they are measured. A variety of parameters (e.g., mass window, ion abundance required for triggering, and maximum number of events) can be defined to control the number of triggering events. The inclusion and exclusion lists can contain a large number of potential

target and non-target ions, respectively. However, triggering initiates precursor selection in a sequential mode, which in turn determines the total cycle time. The time interval between the two full scans will be prolonged when several consecutive triggering events are initiated. The selection of ions to trigger is based on the observed ion abundance, and the user can define the maximum number of ions to trigger after one survey scan. This parameter is called “Top N.” Multiplexing permits the collection of more than one targeted precursor ion species in one dd-MS² experiment (Figure 6).

Targeted SIM/dd-MS²

The Targeted SIM/dd-MS² mode acquires SIM scans based on the inclusion list, which is mandatory and always activated (Figure 7). This mode is most often used for small molecule applications.

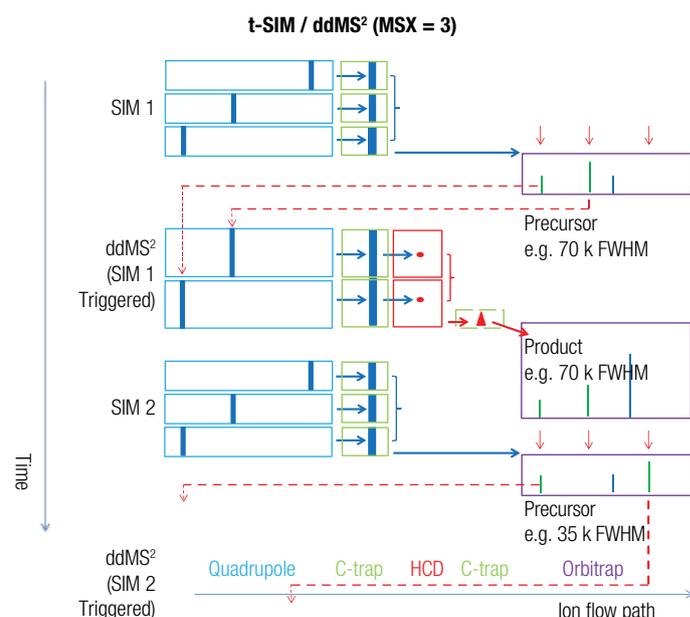


Figure 7. t-SIM/dd-MS²: data-dependent acquisition based on a survey SIM. The MSX = 3 multiplexing mode permits the collection of two triggered precursor ions.

The Targeted SIM/dd-MS² mode is closely related to the full MS/dd-MS² mode. However, in the Targeted SIM/dd-MS² mode, the quadrupole is operated in the SIM mode (survey scan), allowing only a narrow mass range to enter the C-Trap. A SIM scan, instead of a full scan, serves as the survey scan. The resulting reduction of ion abundances permits use of long ion collection times. Triggering of product ion spectra is obtained at lower analyte concentrations. Furthermore, the spectra

observed show high ion abundances. Because the t-MS² mode usually provides more comprehensive information, the Targeted SIM/dd-MS² mode has limited application. Figure 7 shows operation of the instrument in the multiplexing mode (MSX=3), where it simultaneously looks for the presence of the three different analytes.

Full MS/AIF NL/dd-MS²

The Full MS/AIF NL/dd-MS² mode acquires a full MS scan followed by an AIF-scan (Figure 8). When the Q Exactive series mass spectrometer recognizes the user-defined *m/z* loss between two signals in the scan events, it automatically performs a data-dependent MS/MS scan on the precursor ion. This mode is predominantly used in research applications.

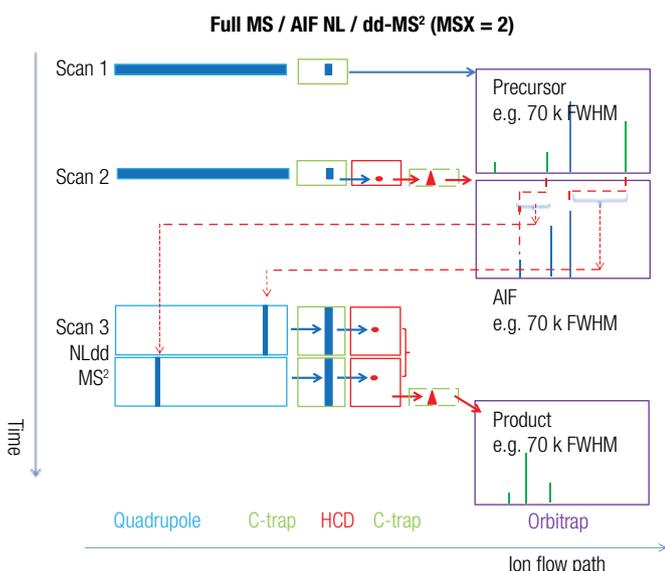


Figure 8. Full MS/AIF NL/dd-MS²: neutral loss scan based on two survey scans trigger an MS² scan as soon as a user-defined neutral loss is observed. MSX = 2 multiplexing permits collection of two triggered precursor ions.

The Full MS/AIF NL/dd-MS² mode resembles the constant neutral loss scan capability of QQQ technology. However, neutral losses are mathematically calculated, rather than physically detected and resolved. Q Exactive series instruments operate in the full MS/AIF mode and constantly check for an ion pair with the mass difference (neutral loss) corresponding to the user-defined neutral loss list. Triggering product of ion spectra is initiated when an observed precursor ion in the full MS scan and another observed product ion in the AIF scan (within the same cycle) differ by an *m/z* value in the user-defined neutral loss mass list.

Data independent acquisition (DIA)

The data-independent acquisition (DIA) mode covers the scan range using targeted HCD events (Figure 9). The inclusion list specifies the centred *m/z* value and the static isolation window determines the isolation precursor *m/z* range. The mandatory inclusion list is processed from the first to the last row without automated sorting. This mode is used in both applied and research applications.

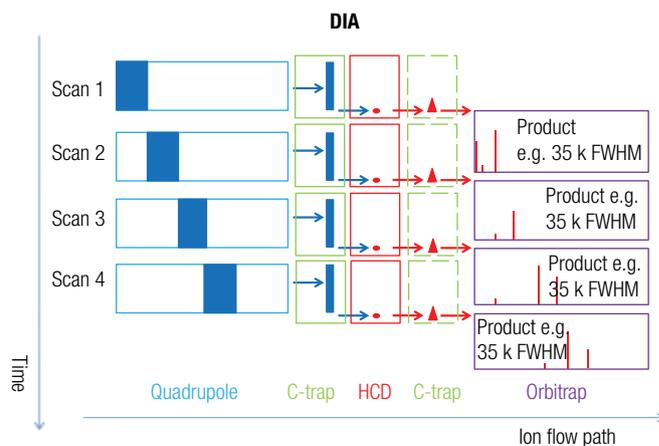


Figure 9. DIA (data independent acquisition). The entire scan range is sliced into consecutive sub-scans. After fragmentation, MS² results are recorded.

In DIA mode, the user enables a selective and sensitive method for a global view of MS² data for the user-defined mass range. The quadrupole isolates a relatively narrow mass range (e.g., 20 Da), which is advanced to the collision cell where an all ion fragmentation is performed. The entire ion cloud is injected into the Orbitrap mass analyzer central electrode, which monitors the entire MS² mass range. In the following scan, the quadrupole shifts the isolation mass range upwards (e.g., by 20 Da). All isolated ions are again fragmented and analyzed by the Orbitrap mass analyzer. Continuous upward shifting of the isolation mass range continues until the entire selected mass range is covered. The fragment ion spectra obtained are from a wider user-defined mass range, instead of isolated unit mass precursors.

Combining different scan modes

By cycling modes (loop count), users can define the number of repetitions of the corresponding scan event before continuing to the next scan event or experiment cycle. This is most often used for MS² acquisition in research applications.

All the modes described here can be combined and processed in sequence. Care must be taken to obtain sufficient data points across fast eluting chromatographic peaks when combining experiments. The general rule is to have five or more scans across an LC peak for screening, and 10 or more scans for quantitation. Simply adding the individual Orbitrap mass analyzer measurement times may result in a slightly longer observed cycle rate than calculated. There are various reasons for this. One is the need for the AGC of the Orbitrap mass analyzer to produce a periodic “pre-scan.” The pre-scan is required to evaluate current ion abundance. There are also minor time variations related to the scan range chosen. In addition, a data-dependent scan can only be triggered after a survey scan has been measured, undergone Fourier Transformation, and interpreted by the software. Thus, the detection of an ion in a survey scan cannot directly lead to the triggering of a t-MS² scan. A “positive” survey scan is followed by another survey scan, and only then by the t-MS² scan.

Multiplexing (MSX)

In spectral multiplexing, multiple preselected precursors are collected in the C-Trap, with the option of fragmentation, followed by simultaneous detection in the Orbitrap mass analyzer (Figure 10). This capability increases the duty cycle and shortens the analysis.

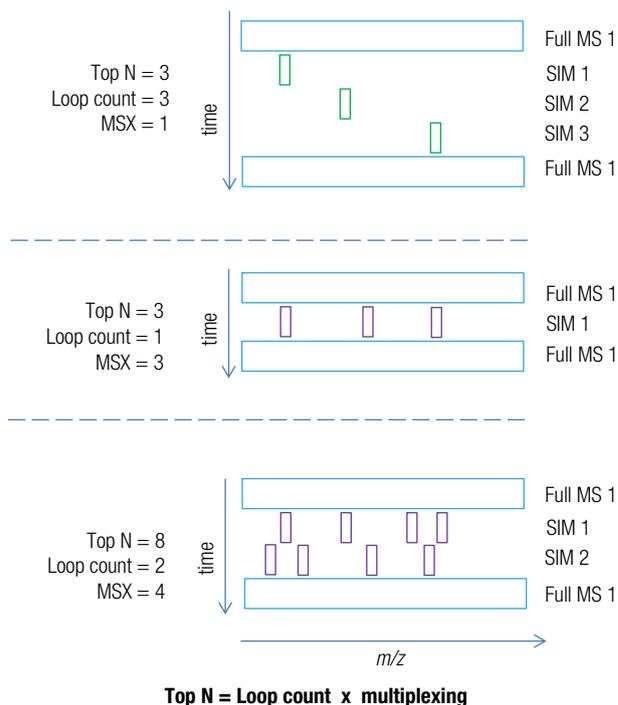


Figure 10. Time sequence of sequential (Top N) and “parallel” MSX or multiplexed measurements. The width of the boxes indicates the quadrupole selected mass range(s).

Targeted-MS² or targeted-SIM can be processed in sequence. The quadrupole isolates a particular precursor ion mass, sends the unit mass-resolved m/z ion package to the C-Trap, and from there it is accelerated into the HCD cell. Fragmentation at a given collision energy occurs when ions enter the HCD (t-MS² mode). The resulting ions are stored in the HCD cell, and a second set of precursor-selected ions are isolated in the quadrupole, accelerated, fragmented at another user-defined collision energy, and then transferred into the HCD cell. This process can be repeated for up to 10 different m/z values (multiple fills with targeted compounds). All the fragmented ions derived from the various precursors are stored in the HCD cell. After completion of the collection of all the precursor fragments, they are returned in a single ion cloud into the C-Trap. The C-Trap then focuses and injects the entire set of ions into the Orbitrap mass analyzer.

The user can define a different collision energy for every selected precursor ion, ensuring that the optimum collision energy is applied to each analyte. The resulting product ion spectrum consists of all the product ions derived from all the unit-mass-isolated precursor ions. Though a particular product ion cannot be directly linked to a specific precursor ion, this mode of operation has several advantages. Unit mass isolation of precursor ions reduces the ion abundance, thus permitting longer ion injection times without overloading the C-Trap and ultimately higher sensitivity. Some selectivity is lost by accumulating different precursor ions into one product ion scan, yet this loss of selectivity is more than compensated for by the high resolution of the product ion scan. Analytes that produce identical product ions should not be placed into the same MSX function. The following formula links Top N, loop count and MSX:

$$\text{Top } N = \text{loop count} \times \text{MSX}$$

Positive/negative switching

Positive/negative switching toggles between positive and negative ion polarity for maximum compound coverage in a single injection. This feature is frequently used in applied markets.

Q Exactive series mass spectrometers allow continuous positive/negative switching with a resolution of 35,000 FWHM within 1 s. Unlike some Q-TOF instruments, Q Exactive series mass spectrometers do not lose mass calibration during polarity switching and switching can be performed on the LC time scale.

Method development recommendations

To facilitate the development of analytical methods that take full advantage of the various scan modes described here, the authors provide the following recommendations. These recommendations apply to analytical methods intended to detect, quantify, and confirm analytes in complex matrices. Generally, QQQ instruments provide the best results (sensitivity and selectivity) when operated in selected reaction monitoring (SRM) mode, while Q Exactive series instruments provide the most comprehensive data, in terms of ions and compounds monitored, when operated in full MS mode. Therefore,

with Q Exactive series mass spectrometers, method development typically employs the full MS mode, and, in many cases, there is no reason to use any other mode. QQQ-trained users should avoid the impulse to look for MS transitions (targeted mode) when using Q Exactive series instruments. Instead they should give their instrument the chance to detect and quantify the unfragmented analyte with sufficient sensitivity and selectivity in full MS mode.

When developing methods, selection of mass range is important. A narrow mass range increases sensitivity because lower ion abundances allow longer ion injection times. In our laboratory, the quadrupole is used more frequently as a wide pass filter to exclude ions resulting from the mobile phase and column bleed than as a mass isolation device that captures precursor ions. Single-stage Orbitrap mass analyzers are not designed to perform this function (the octapole is for ion transmission, not the quadrupole). Consequently, single-stage Orbitrap mass analyzer systems, like the Thermo Scientific™ Exactive™ Plus Orbitrap mass spectrometer, are not equally suited to applications involving very complex matrices. It is a good habit to look at the ion injection time across the entire chromatographic time range where the analytes of interest elute. Sections with very short ion injection times are not ideal due to low sensitivity in the matrix and may require definition of a narrower scan range or targeted experiments.

When the application requires unequivocal confirmation of a tentatively found residue in addition to screening and quantification, data-dependent modes of operation (e.g., full MS/dd-MS²) are recommended. However, unequivocal confirmation may also be achieved by monitoring an AIF trace.⁸ Quantification should be based on the full-scan trace. Using data-dependent techniques requires optimization to set the appropriate triggering levels. It is beyond the scope of this white paper to discuss this optimization process in detail. Nonetheless, standard settings are for protein and peptide applications and they need to be turned off when using data-dependent techniques for small molecule applications. If the user has access to suitable quantification software, such as Thermo Scientific™ TraceFinder™ data processing software, DIA methods present an attractive solution.

There may be situations where sensitivity or selectivity for some analytes is insufficient. Often, it is only one or a small set, of analytes that cause sensitivity problems. In this case, it may be helpful to quantify the “non-problem” analytes using the full MS mode and then add additional experiments to address the problematic compounds. If a lack of sensitivity is a concern, using a SIM experiment may be the answer. If sensitivity and selectivity must be improved, the authors recommend using the PRM mode. The PRM mode generally provides sensitivity rivaling high-end QQQ instruments operating in the SRM mode. Furthermore, the PRM mode provides selectivity surpassing that of a unit-mass-resolving QQQ instrument. If a number of problematic compounds must be analyzed, retention time-dependent experiments can help.

For all modes, it is recommended that the user optimize the precursor RF entrance lens in front of Q1, because in-source fragmentation might occur, particularly for fragile compounds.

Multiplexing is a way to combine the best modes to address an application, and can reduce cycle time, while still providing reliable confirmatory data.

Table 1 summarizes the scan modes available on each of the Q Exactive series mass spectrometers.

Conclusion

The scan modes available on Q Exactive series mass spectrometers permit transfer of almost any QQQ- or Q-TOF-based method to an Orbitrap mass analyzer environment, with comparable, or even enhanced sensitivity, selectivity, and dynamic range. Depending on the particular problem presented by an analytical method, different scan functions and experiments can be used. For best results, methods should be migrated in a way that fully utilizes the capabilities of Orbitrap mass analyzer technology. In particular, the quadrupole is best used as either a wide-mass-range cut-off filter or a unit-mass-isolation device.

The Full Scan MS mode is always a good starting point for most applications. The SIM and PRM modes are best deployed when ultimate sensitivity and selectivity are required, respectively. Top N methods often are used for proteomics applications. DIA has the advantage of being able to fragment “everything” for both applied and research applications.

Real-world examples of use of Q Exactive series mass spectrometers for small and large molecule quantitation and confirmation by full MS, PRM, and SIM, are available in AI-64645, a summary of over 50 peer-reviewed publications in the fields of food safety testing, environmental contaminants, clinical research, pharmaceutical discovery, and omics.⁹

Table 1. Availability of scan modes provided by each of the Q Exactive series mass spectrometers models

Scan Function per Instrument	Full MS	Full MS/AIF	Targeted-SIM	PRM	Full MS/dd-MS ² (Top N)	Targeted SIM/dd-MS ²	Full MS/AIF NL/dd-MS ²	DIA	Multiplexing (MSX)
Q Exactive Focus	Yes	Yes	Yes	Yes	Yes (Top 3)	No	No	Yes (vDIA)*	Yes (SIM only)
Q Exactive	Yes	Yes	Yes	Yes	Yes (Top 10)	Yes	Yes	Yes	Yes (SIM & PRM)
Q Exactive Plus	Yes	Yes	Yes	Yes	Yes (Top 10)	Yes	Yes	Yes	Yes (SIM & PRM)
Q Exactive HF	Yes	Yes	Yes	Yes	Yes (Top 20)	Yes	Yes	Yes	Yes (SIM & PRM)
Q Exactive HF-X	Yes	Yes	Yes	Yes	Yes (Top 40)	Yes	Yes	Yes	Yes (SIM & PRM)

*vDIA method is not available in the United States of America

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