Ultra-fast Quadrupole Scanning With Improved Mass Filtering

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Introduction

The speed of chromatographic analyses continues to increase as UHPLC and high efficiency sub-2 micron columns become commonplace in many analytical laboratories. Advanced chromatography systems and ballistic gradients have reduced chromatographic peak widths to less than one second for many routine analyses. Typical quadrupole scan speeds of 5,000 m/z per sec may be insufficient to scan one second wide peaks using a broad mass range and resulting in quantitative results with unacceptable precision. Increasing scan speeds creates trade-offs in sensitivity and mass resolution as the noise increases due to unfavorable ion statistics. These issues have been addressed with advanced filtering algorithms that combine noise rejection with resolution enhancement. These advances have greatly improved data quality in fast-scanning quadrupole LC/MS instruments.

Figure 1: Agilent 1290 Infinity Binary LC and Agilent 6100 series Single Quadrupole MS

Experimental

LC conditions

Mobile phase: A = 0.1% formic acid in Water
B = 0.1% formic acid in Acetonitrile

Flow rate: 2.0 mL/min

Gradient:

Time	%B
0.00	10
0.01	19
0.30	24
0.40	60
0.48	60

Method Run Time: 0.6 min
Post Run Time: 0.5 min

Column: Agilent ZORBAX RRHD Eclipse Plus C18
2.1 x 50 mm, 1.8 µm (959757-902)

Column temperature: 50 °C
Autosampler temperature: 6 °C
Injection volume: 1 µL

MS conditions

Ionization mode: AJS-ESI (+/–)
Drying Gas: 7 L/min @ 350 °C
Nebulizer pressure: 50 Psi,
Sheath gas: 12 L/min @ 360 °C,
Capillary voltage: 2500 V (+/ –)
Nozzle voltage: 500 V (+/ –)

Ultra Fast Scan: 15 KDa/sec
Scan Range: 250–1250 *m/z*
Polarity Switching Delay: 20 msec
Fragmentor: 110V
Peak width: 0.05 min
Threshold: 200/25 (+/ –)
Step size 0.2 (fixed)
Gain 1.0

Sample Preparation

Agilent ESI-L Tuning Mix (G1969-85000) was used neat to generate profile data at 10 KDa/sec and 15 KDa/sec scan speeds.

Agilent ES LC Demo Sample (59987-20033) was diluted with 20% acetonitrile to a final concentration of 1 µg/mL each sulfamethizole, sulfamethazine, sulfachloropyridazine, and sulfadimethoxine to evaluate chromatographic performance and spectral data quality at 15 KDa/sec scan speeds.

Results and Discussion

Patented Quadrupole Fast Scanning Technology

In practice, the RF and DC control voltages to the quadrupole are both decremented over time so as to scan a sequential range of m/z ions (highest to lowest m/z). Scanning starts at a predetermined m/z and both voltages then decremented at a predetermined rate (i.e. the scanning speed) until the final predetermined m/z is achieved (i.e. the scan range). At each decrement, the RF and DC timing ratio must be carefully matched. If the DC is too high, the quadrupole will attenuate the desired m/z ions. If the DC is too low, the quadrupole will not effectively attenuate unwanted m/z ions (i.e. resolution is decreased). Thus the DC is typically matched to that of the RF (see the "Standard Response" curve in Figure 1). However at very fast scan rates, matching the RF and DC response is no longer sufficient as the ion transient time through the quadrupole becomes longer than the time between scan decrement steps.

Agilent's patented Quadrupole Fast Scan Technology provides the benefit of actually speeding up the DC response relative to the RF during the settling time of each scan step. The lower DC voltage during the settling time "opens" the quadrupole field, so ions already in transit are able to proceed through the quadrupole assembly without their abundance being severely attenuated by each succeeding scan decrement shift. At the end of the settling time, the matched RF and DC ratio is restored to preserve resolution of the mass peak.

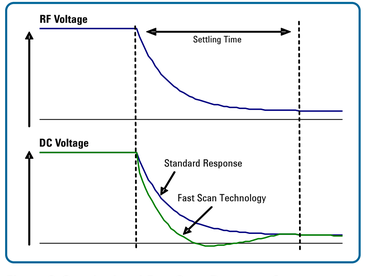


Figure 2: Standard and Fast Scan Response Curves

Unfiltered Spectral Output

At 10 KDa/sec scan speeds, data collected directly from the detector amplifier exhibits significant noise with poorly resolved isotopes. This can be seen in the oscilloscope trace in Figure 3 below. The oscilloscope trace has been transposed so that the plus one isotope is seen at the right.

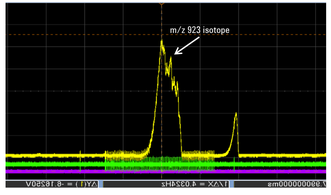


Figure 3: Oscilloscope trace of m/z 922 collected from detector amplifier while scanning at 10 KDa/sec

Linear Phase Finite Impulse Response Filter

To improve the data quality at scan speeds of 10 KDa/sec and above, a proprietary linear phase finite impulse response (FIR) filter was developed by matching the filter coefficients with the impulse response characteristics of the mass peaks to reduce spurious noise transients while enhancing spectral resolution.

An FIR filter has the general form:

$$y(n) = \sum_{k=0}^{M-1} h(k)\, x(n-k)$$

where:

- y(n) is the output signal
- x(n) is the input signal (finite impulse)
- h(k) are the filter coefficients
- M is the filter order

In this case, an odd number of taps was used for the filter order and the symmetrical filter coefficients were selected for a step interval of 0.2 Da to create a low pass, linear phase FIR filter. This new FIR filter was then compared with standard Gaussian filtering to compare its effectiveness at 15 KDa/sec scan speeds.

Results and Discussion

Ultra-fast Scan Speed Performance

When profile data was collected at 15 KDa/sec scan speeds with the Gaussian filter, isotopes could not be resolved, and full width at half maximum (FWHM) for the peaks ranged from 0.77 to 0.92 (Figure 4a).

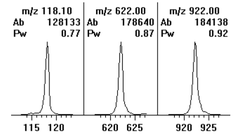


Figure 4a: Gaussian filtering at 15 KDa/sec

Profile data was then collected at 15 KDa/sec scan speeds using the proprietary FIR filter (Figure 4b). The FIR filter exhibited comparable noise attenuation, significantly better resolution, and improved profile abundances.

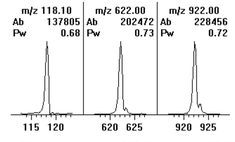


Figure 4b: Linear Phase FIR filtering at 15 KDa/sec

Agilent's quadrupole fast scan technology and the new FIR filter were then combined with fast polarity switching for the UHPLC analysis of four sulfonamide drugs in under thirty seconds. The mass spectrometer was able to acquire ten positive and ten negative scans across sub-1 second peaks from m/z 250 to 1,250 at 15 KDa/s (Figure 5).

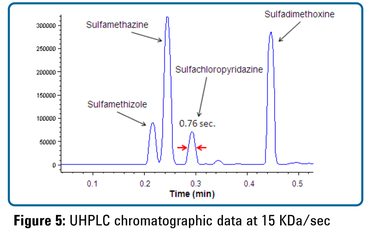
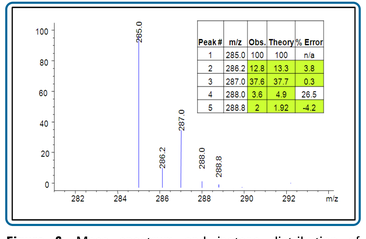


Figure 5: UHPLC chromatographic data at 15 KDa/sec

Isotopic Fidelity at Ultra-fast Scan Speeds

The five most abundant isotopes of sulfachloropyridazine (SCP) were detected at 15 KDa/sec speeds with polarity switching using the UPHLC separation shown in Figure 5. The observed isotope distribution demonstrated excellent agreement with theoretical values (Figure 6).



Peak #	m/z	Obs.	Theory	% Error
1	285.0	100	100	n/a
2	286.2	12.8	13.3	3.8
3	287.0	37.6	37.7	0.3
4	288.0	3.6	4.9	26.5
5	288.8	2	1.92	-4.2

Figure 6: Mass spectrum and isotope distribution of sulfachloropyridazine collected at 15 KDa/sec.

Conclusions

- Patented Agilent quadrupole fast scan technology improves ion transmission at scan speeds up to 15K Da/sec.
- A new proprietary linear phase FIR filter demonstrated improved signal quality and resolution when compared with a Gaussian filter at 15K Da/sec scan speeds.
- Isotopic resolution was maintained at ultra-fast scan speeds with UHPLC chromatographic data using quadrupole fast scan technology with the new linear phase FIR filter.
- The observed isotope distribution for sulfachloropyridazine obtained from UHPLC chromatographic data at ultra-fast scan speeds with fast polarity switching demonstrated excellent agreement with theoretical values.
- Ultra-fast scanning with fast polarity switching enabled the collection of ten positive and ten negative scans from m/z 250 to 1250 across FWHM chromatographic peaks of less than 1 second.