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Improving MS/MS Sensitivity using Xevo TQ MS with ScanWave

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Abstract

In this application note, ScanWave technology has allowed the peak detection of the vancomycin sample in MS/MS mode to be significantly improved.

Introduction

Tandem quadrupole mass spectrometry (MS) combined with liquid chromatography (LC) – and, in particular, UltraPerformance LC (UPLC) – has become the technology of choice for high sensitivity quantitative analyses such as bioanalysis in the pharmaceutical industry. The high selectivity and specificity of multiple reaction monitoring (MRM) analysis gives rise to excellent signal-to-noise ratios for the analysis of compounds in complex matrices. Full-scan acquisitions are also used to provide useful information for structural elucidation in MS and MS/MS modes.

Conventional tandem quadrupole MS instruments have limited sensitivity in full-scan mode due to poor duty cycle. The Waters Xevo TQ Mass Spectrometer with ScanWave functionality delivers significant duty cycle improvements that provide enhanced sensitivity in scanning acquisition modes.

ScanWave experiments are performed at up to 10,000 amu/sec, making it possible to characterize narrow chromatographic peaks better. This has become a necessity since the advent of sub-2 µm column particle technology where narrow chromatographic peaks can be 2 seconds wide or less.

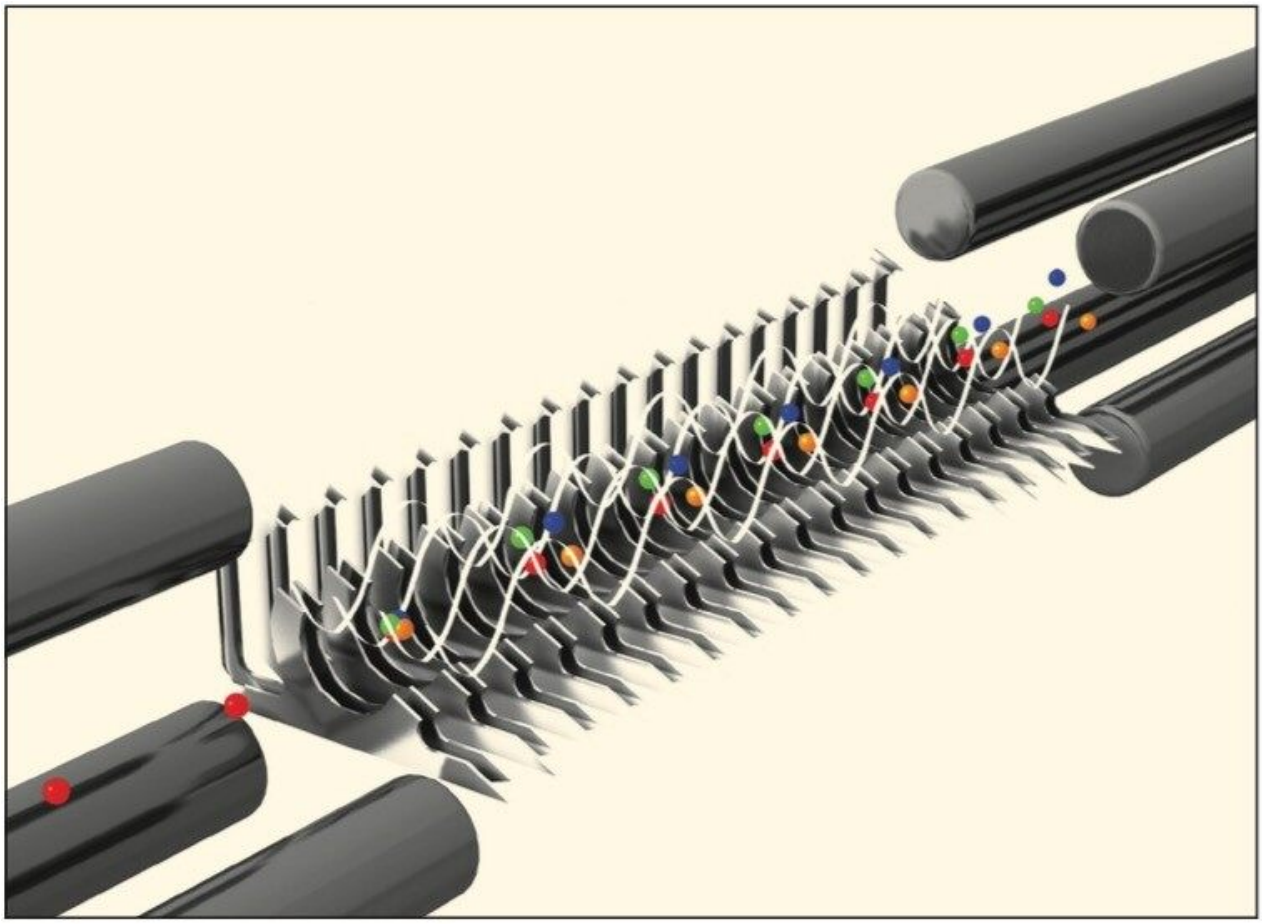

Figure 1. Unique T-Wave and ScanWave-enabled collision cell technology for the very best MS/MS data.

Results and Discussion

ScanWave Defined

The Xevo TQ MS employs a unique concept in collision cell technology. Based on a novel use of Waters' proven T-Wave[1] collision cell, the new ScanWave mode of operation enhances both MS scan and product ion data. ScanWave operation is based upon two concepts (Figure 2).

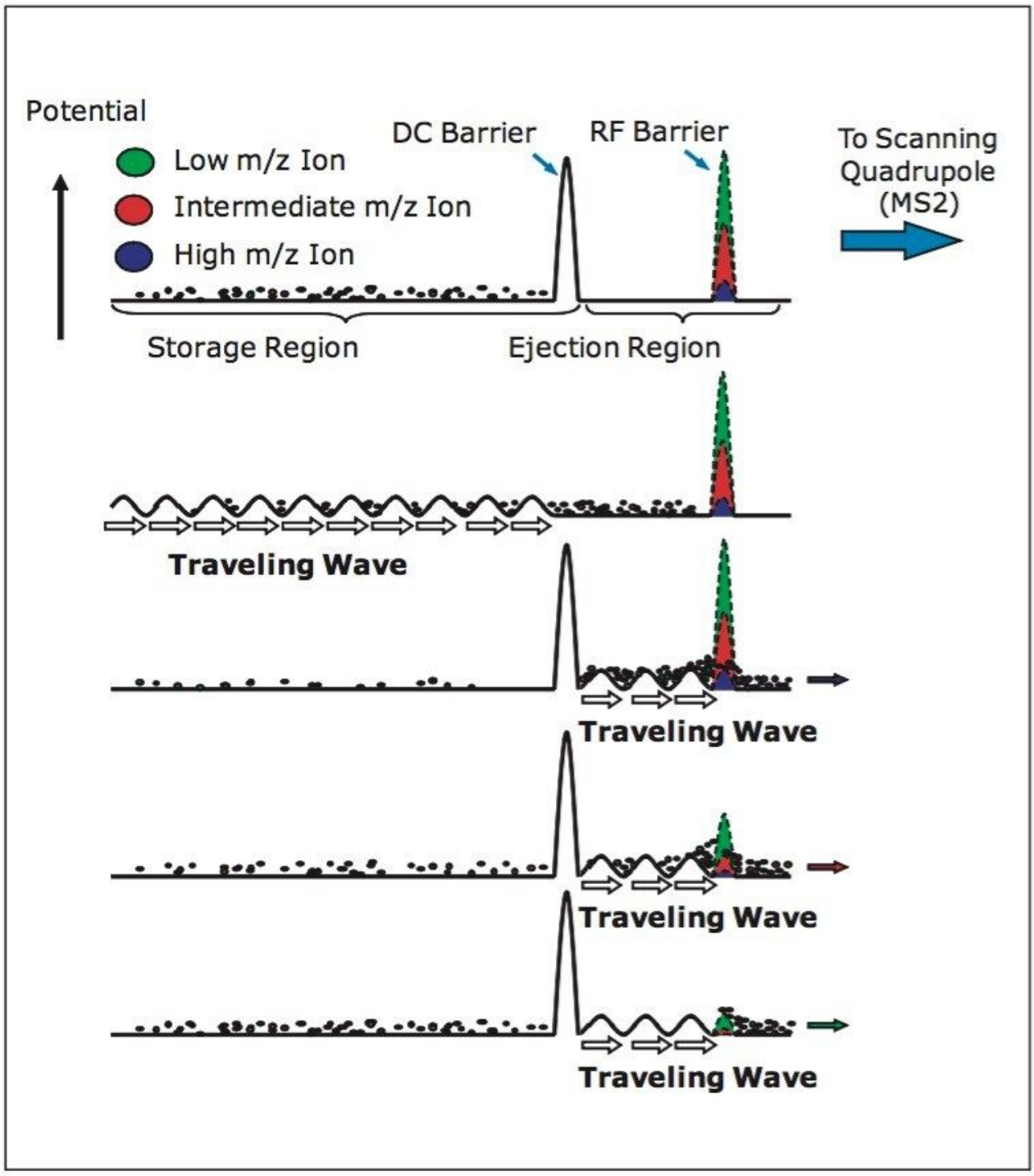

Figure 2. Schematic depicting a ScanWave experiment, where ions are accumulated before being sequentially ejected.

The first is that the front and back of the collision cell are independently controlled, which allows fragmentation and accumulation of ions to occur in the front of the gas cell while previouslyaccumulated ions

are simultaneously ejected from the back of the gas cell. This provides 100 percent sampling efficiency.

Ejection of ions from the gas cell is mass dependent, although low resolution. This low-resolution behavior allows for high space-charge capacity without degradation of performance.

The second concept behind ScanWave is that it links the low-resolution ion ejection from the gas cell with scanning of the final-resolving quadrupole (MS2). This enables an intelligent ion delivery where ions are presented to the final quadrupole when they are actually needed, rather than continuously as in traditional tandem quadrupole instruments.

This novel ion delivery technique provides significant duty cycle improvements that in turn result in enhanced signal in scanning acquisition modes. Since the scanning quadrupole (MS2) is the device performing the mass analysis, it is not necessary to perform a separate calibration. Scan rates, mass accuracy, and mass resolution are all identical to that for operation in traditional scanning acquisition modes.

Significant Increases in Sensitivity using ScanWave

The data shown in Figure 3A are chromatograms for the conventional product ion scan, DS, and for the enhanced product ion scan, using ScanWave DS, produced from the UPLC-MS/MS analysis of vancomycin, a glycopeptide antibiotic, with *m/z* 725 for the $[M+2H]^{2+}$ in positive ion electrospray mode. The chromatograms have been superimposed and the vertical axes are displayed on the same scale.

A factor of 6X signal enhancement is observed for the largest chromatographic peak, number 5, when ScanWave DS is used.

In the conventional product ion scan mode, peaks 1, 2, 4, and 5 are detected. When the same sample is analyzed using ScanWave DS, the resulting signal enhancement improved the level of sensitivity and the total number of peaks detected. In addition to the peaks that were found in this sample using the conventional product ion scan, spectra can be obtained for peaks 3, 6, 7, and 8.

Modern high resolution chromatography using sub-2 µm column particles produces peaks with widths of 1 to 3 seconds at the base. To accurately define these peaks, a high duty cycle/scan speed mass spectrometer is required.

Figure 3B shows the same chromatogram plotted with scan number as the x-axis. The scan speed of both the ScanWave DS and the conventional product ion scan experiments was 5000 amu/sec. This allowed more than 10 data points for the mass range 90 to 1455 amu to be collected across chromatographic peaks which were 3 seconds wide.

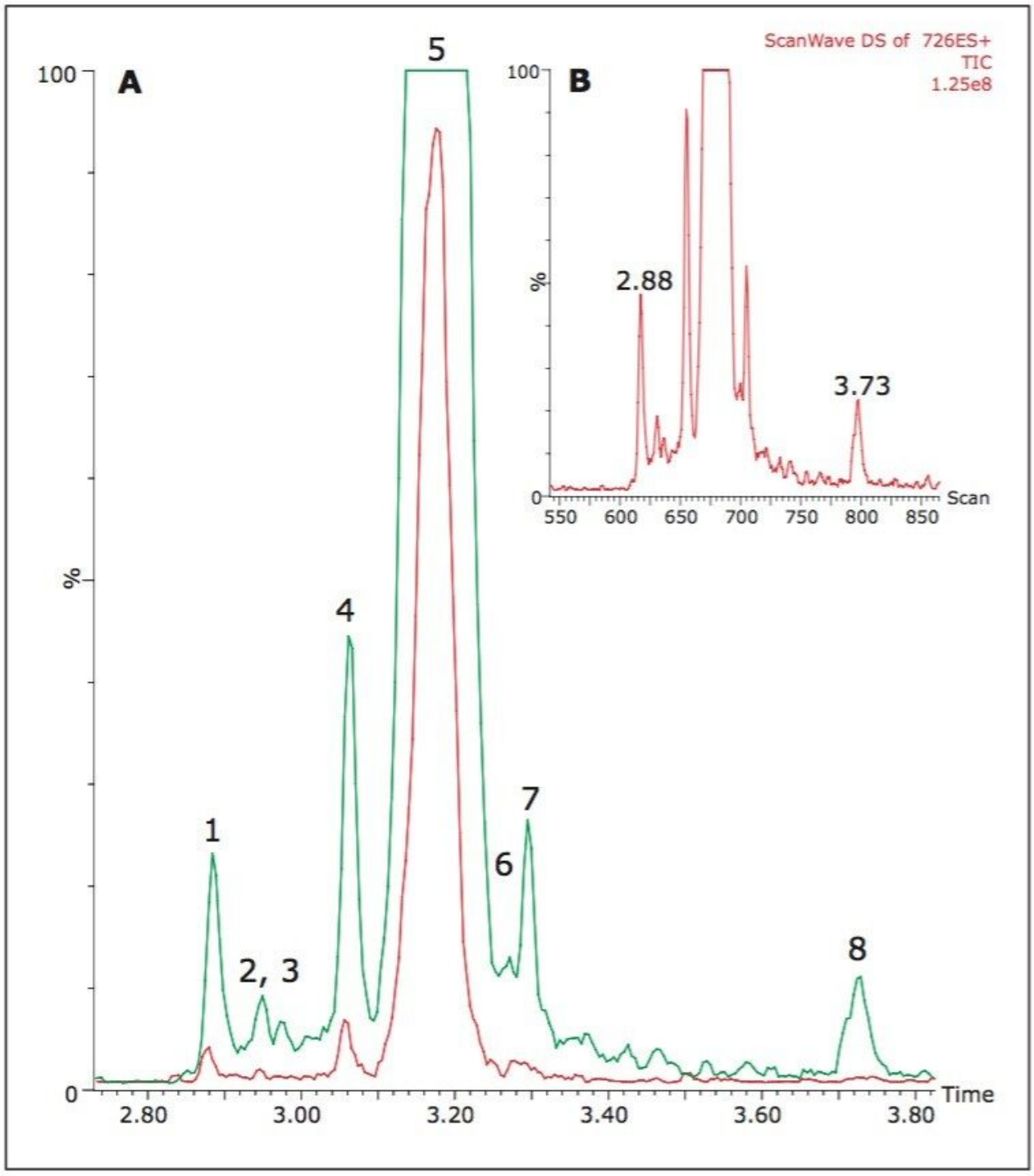

Figure 3. Chromatogram A shows ScanWave product ion scan (ScanWave DS, green trace) versus the regular product ion scan (DS, red trace) of vancomycin, $[M+2H]^{2+}$ m/z 725. In B, the ScanWave DS chromatogram is shown with the x-axis plotted in scan number.

Figure 4 shows a mass spectrum of the largest chromatographic peak (number 5) shown in Figure 3A.

ScanWave DS of the doubly-charged ion *m/z* 725 resulted in the major singly-charged fragments *m/z* 100, *m/z* 144, and *m/z* 1306.

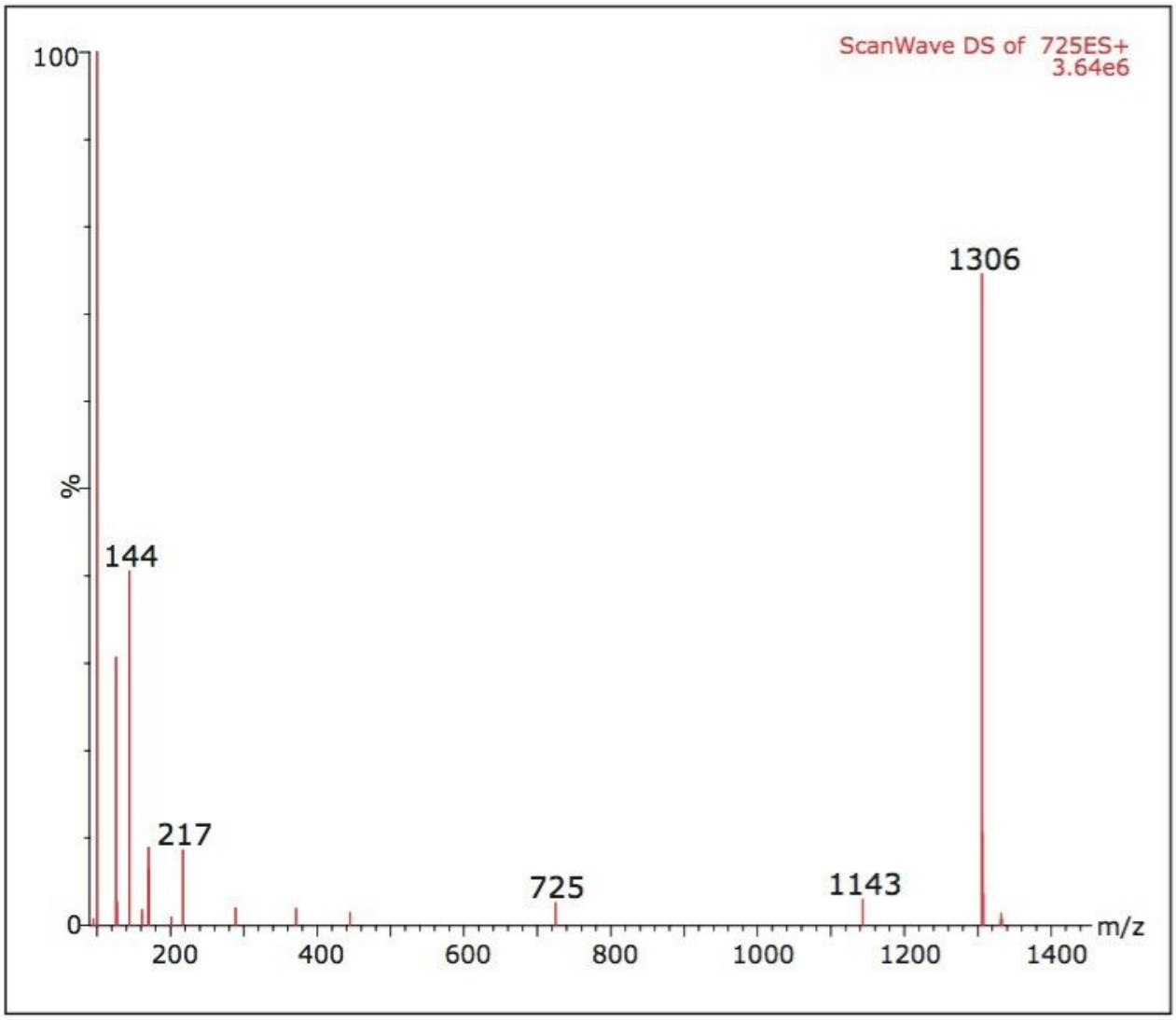

Figure 4. ScanWave DS spectrum for vancomycin, $[M+2H]^{2+}$ m/z 725.

The data illustrates that the Xevo TQ MS is capable of acquiring high-quality spectral data while operating at the high scan speeds required to characterize narrow UPLC peaks.

Conclusion

The enhanced sensitivity of the Xevo TQ MS in ScanWave mode allows users to better characterize low-level components in their samples.

ScanWave technology allows ions to be accumulated, separated, and ejected according to their *m/z*. The final quadrupole scanning is synchronized with ion ejection from the collision cell such that the ions of a given mass-to-charge ratio are delivered to the quadrupole when it is ready to scan this *m/z* value. This results in a more efficient instrument duty cycle and better sensitivity in scanning acquisitions.

In this application note, ScanWave technology has allowed the peak detection of the vancomycin sample in MS/MS mode to be significantly improved. When ScanWave DS mode was used, spectra could be obtained for chromatographic peaks that were previously not detected by the conventional product ion scan.

References

1. The traveling wave device described here is similar to that described by Kirchner in U.S. Patent 5,206,506 (1993).

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