Advantages of Wide Dynamic Range on an Orthogonal Acceleration Time-of-Flight Mass Spectrometer

Technical Overview

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Introduction

A wide dynamic range is a desirable characteristic in mass spectrometers. It allows compounds of differing abundances to be analyzed at the same time. This can simplify sample preparation and facilitates "walk-up" access for researchers who are not experts in mass spectrometry. In the case of time-of-flight mass spectrometers, it also facilitates the introduction of a reference mass compound, which enhances the accuracy of mass measurements.

This technical overview reviews the concept of dynamic range. It then discusses how dynamic range is achieved in a time-of-flight mass spectrometer and how a detector using analog-to-digital converter technology can dramatically improve dynamic range compared to older detector technologies.

Dynamic Range

Every mass spectrometer has an upper limit to the magnitude of signal it can measure without saturating its detector. If the signal exceeds this limit, the signal is "clipped" and part of it is lost. Likewise, every mass spectrometer has a lower limit to the magnitude of signal that it can distinguish from electronic and chemical background noise. The ratio of the maximum signal to the minimum signal is the mass spectrometer's dynamic range.

Effect of Dynamic Range on MS

Dynamic range has a significant effect on a mass spectrometer's usability. If an instrument's dynamic range is very narrow, sample preparation becomes more critical and more difficult. It is easy to introduce the wrong amount of sample and either get a clipped signal (too much sample) or no signal (too little sample). It is then necessary to either dilute or concentrate the sample and run it again. When sample amounts are limited, this can present a serious problem.

If mixtures of chemicals are being analyzed, a narrow dynamic range means that all of the compounds in the mixture must have similar abundances. If they do not, either the signals from high-abundance compounds are clipped, affecting response linearity and making quantitation difficult, or signals from low-abundance compounds are not detected and those compounds are not identified.

In contrast, a wide dynamic range makes it much easier to use a mass spectrometer. Sample preparation and abundance becomes less critical. If mixtures are being analyzed, both high- and low-abundance compounds can be identified. Linearity is improved, making quantitation easier and more reliable.

Implications of Dynamic Range for TOF MS

For time-of-flight (TOF) mass spectrometers, a wide dynamic range has an additional benefit. To maximize mass accuracy, a reference mass compound whose mass is known to a very accurate degree is often introduced into a TOF MS for purposes of calibration. If a TOF MS has a narrow dynamic range, the reference mass compound must be introduced at an abundance nearly the same as the abundance of samples being analyzed. This can create significant chemical interferences and affect analytical results. One solution is to introduce the reference mass compound briefly, perform the calibration, and then wait for traces of the reference mass compound to dissipate. This

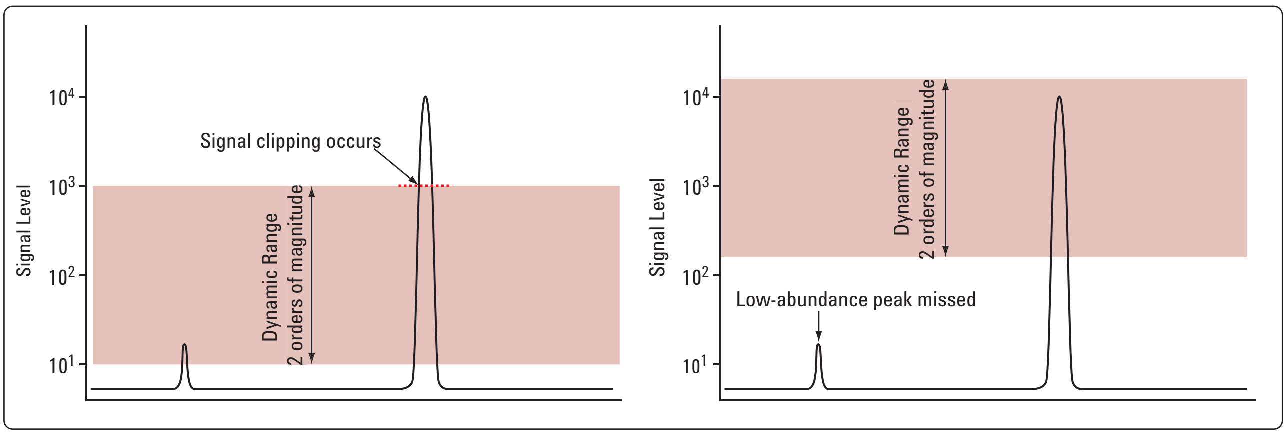

Figure 1. Consequences of narrow dynamic range

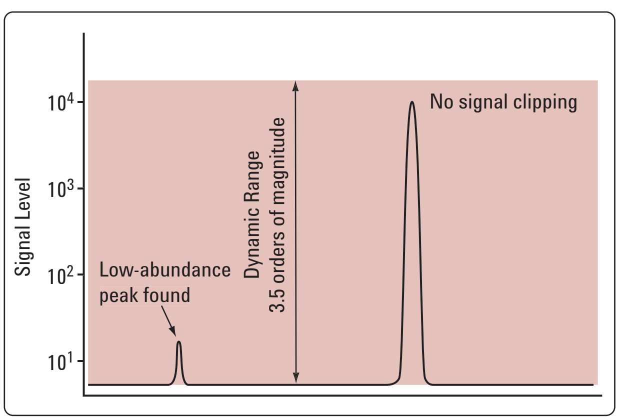

Figure 2. Advantages of wide dynamic range

wastes time and the mass accuracy of the TOF MS can drift between calibrations.

If, on the other hand, a TOF MS has a wide dynamic range, a reference mass compound can be introduced at an abundance much lower than the abundances of typical samples. This eliminates, or at least minimizes, interferences. Thus, a reference mass compound can be introduced continuously and the mass accuracy of the TOF MS never has a chance to drift, ensuring maximum mass accuracy.

TOF MS Design and Dynamic Range

The dynamic range of a TOF MS is determined by many aspects of the instrument design. One of the most influential is the detector and its electronics. The detector senses ions as they impact it and generates a signal based on those impacts. The signal is converted to digital form so that it can be processed.

A time-of-flight mass spectrometer, as its name implies, determines ion masses based on the time it takes them to "fly" from a starting point to an ending point. TOF is a pulsed technique, with each electrical pulse starting a group of ions on their flight to the detector. For each pulse, the detector records a corresponding spectrum, called a transient. Many transients are summed to create a mass spectrum.

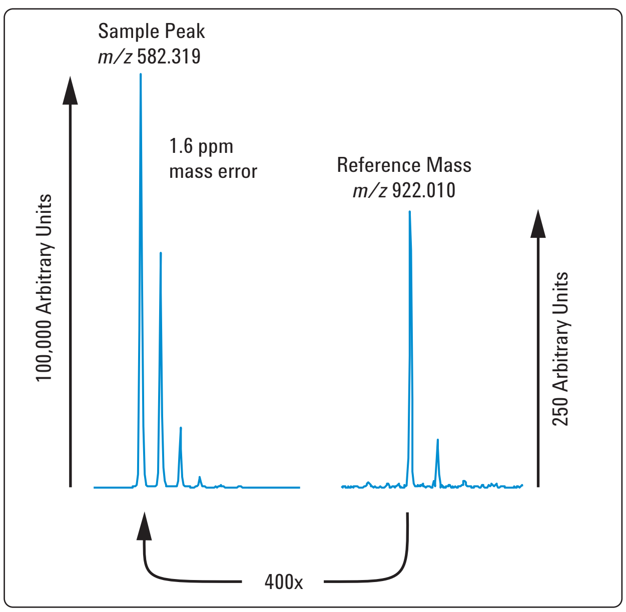

Figure 3. Wide dynamic range enables continuous introduction of reference mass compound at a low level, providing maximum mass accuracy with minimum interference

Time-to-digital signal conversion

Traditionally, TOF mass spectrometers have used a detector with a time-to-digital converter (TDC). A TDC records a precise arrival time for each mass within a transient. Because a TDC records the arrival time based on the arrival of the first ion of a given mass, it cannot tell the difference between one ion at a given mass arriving in a transient and several ions with the same mass arriving in a transient (see Figure 4).

This was acceptable in previous generations of TOF mass spectrometers, when inefficient ion sources and ion optics made it unlikely that more than one ion of a given mass would be present in a single transient. However, with the improved efficiency of modern ion sources and ion optics, there is a good chance that a transient will include multiple ions at a given mass. The TDC's inability to determine how many ions are arriving severely limits the instrument's dynamic range. TOF mass spectrometers using TDC detectors often have dynamic ranges of only one or two orders of magnitude. Sample abundance must be

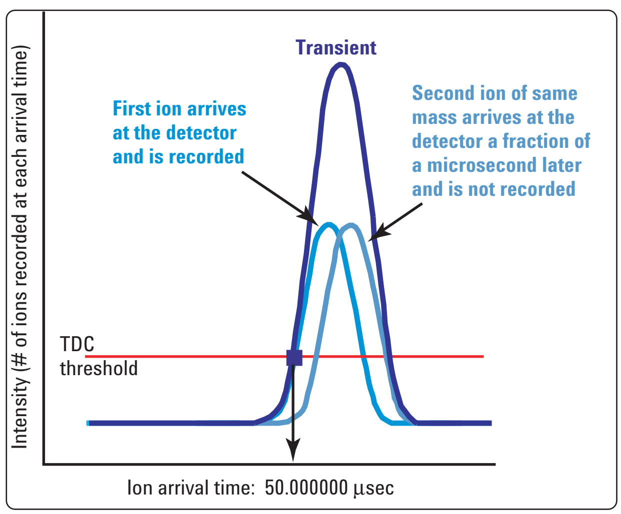

Figure 4. Limitations of TDC performance

adjusted to match the instrument's range; often this entails a time-consuming trial-and-error, dilute-and-reshoot process.

One partial solution to TDC dynamic range limitations is beam-splitting or defocusing. The number of ions transmitted to the TDC detector is adjusted from scan to scan to keep the signal in the proper range. While this helps prevent detector saturation, it also results in a large portion of the ions being discarded. This can reduce sensitivity and cause low-abundance components of a sample to be lost entirely. It also does nothing to improve dynamic range within a single scan (in-scan dynamic range).

Analog-to-digital signal conversion

In contrast, the Agilent LC/MSD TOF mass spectrometer uses a different approach, a detector with an analog-to-digital converter (ADC). The ADC does not try to record arrival times for individual ions. Instead, it records the total signal strength the detector is outputting at fixed, and very frequent, intervals—as often as a billion times per second. The ADC records differing signal levels, so it can tell the difference between one ion of a given mass or many ions of a given mass arriving in a single transient. The result of this is that the LC/MSD TOF, with its ADC detector, has a dynamic range of three to four orders of magnitude.

As noted previously, because the LC/MSD TOF has a wide dynamic range, it has a number of advantages over older TOF MS designs. The LC/MSD TOF features continuous introduction of reference mass compound at a very low abundance. This greatly enhances the mass accuracy of the LC/MSD TOF (better than 3 ppm) while minimizing interference with actual samples.

The wide dynamic range also enables the LC/MSD to detect less-abundant compounds in the presence of significantly more abundant compounds, even within a single scan (see Figure 5). This can be of great benefit when trying to identify minor impurities in the products of synthetic chemistry and purification, or when looking for post-translationally modified proteins in the presence of native proteins.

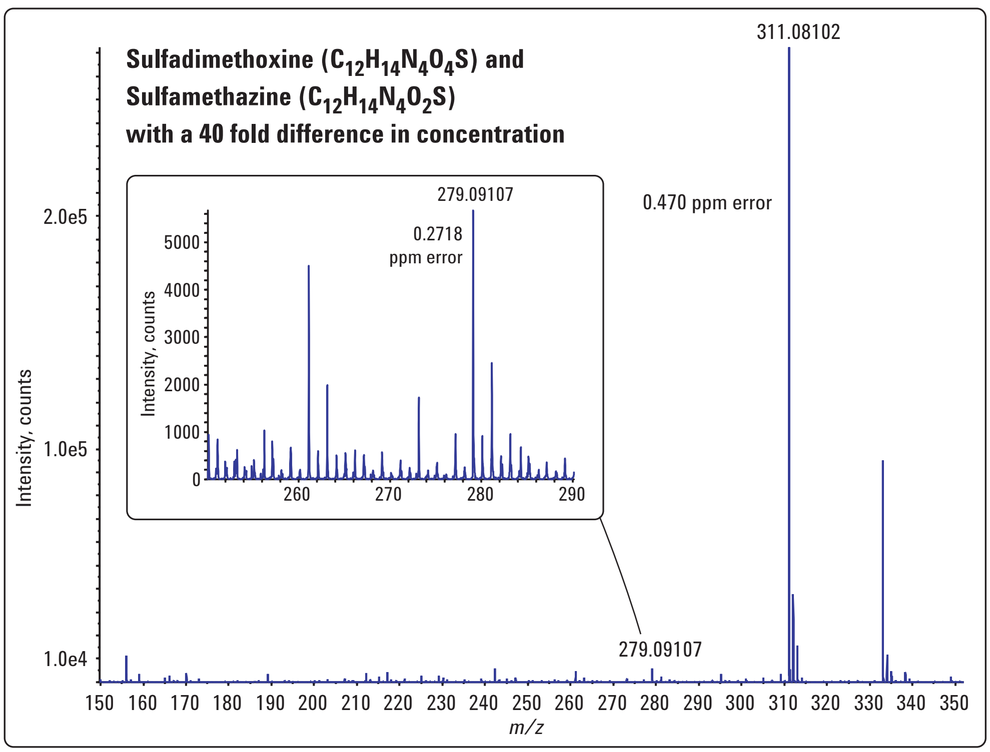

Figure 5. Wide dynamic range makes it easier to detect lower-abundance compounds in the presence of higher-abundance compounds

Conclusion

A wide dynamic range provides significant benefits for mass spectrometers, facilitating the detection of lower-abundance compounds in the presence of higher-abundance compounds. For time-of-flight mass spectrometers, this allows the continuous introduction of reference mass compounds that greatly enhance mass accuracy. The Agilent LC/MSD TOF features a detector with analog-to-digital signal conversion that greatly enhances its dynamic ranges compared to older TOF designs that rely on time-to-digital signal conversion.

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