Extending the Quantitative Linear Range of A Quadrupole-Time of Flight Mass Spectrometer using Digital Deadtime Correction (DDTC)

Hilary J. Major, Jose M. Castro-Perez, John Hoyes, Gary Harland

Waters Corporation

This is an Application Brief and does not contain a detailed Experimental section.

Abstract

This application brief extends the quantitative linear range of a quadrupole-time of flight mass spectrometer using digital deadtime correction (DDTC).

Benefits

- The use of a correction algorithm, based on the mathematical model for the dead time effect, has been shown to extend the linear dynamic range of oa-TOF mass spectrometers
- The application of DDTC allows accurate mass measurement and a linear response with sample concentration over a range up to four orders of magnitude

Introduction

The high resolution, full scan sensitivity and mass accuracy of time-of-flight (TOF) analysers has seen their use in qualitative analysis increase significantly in recent years.

In contrast, their ability to perform in quantitative applications has been relatively restricted. The ion counting systems employed in these oa-TOF analyzers exhibit saturation effects which at higher sample concentrations has lead to a restricted linear dynamic range. The Linear dynamic range achieved is dependant on the time allowed for acquisition of data. Where the sample is introduced via on-line HPLC the available time is limited such as to restrict the linear dynamic range to between 2 and 3 orders of magnitude.

Experimental

LC Conditions

HPLC system:	Waters 2795 Solvent Management System
Column:	Waters Symmetry C_{18}, 3.5 µm, 2.1 x 50 mm
Mobile phase:	70% water 30% acetonitrile + 0.1% formic acid, isocratic
Flow rate:	0.25 mL/min
Injection volume:	10 µL

MS Conditions

MS:	Q-Tof-micro
Ionization mode:	ESI+
Capillary voltage:	3200 V
Source temp.:	120 °C

Desolvation temp.: 350 °C

Desolvation gas: 650 L/hr

Collision gas: argon

Results and Discussion

Deadtime Correction

Ions are detected by a microchannel plate (MCP) and their arrival times stored by a time to digital converter (TDC). After the arrival of an ion the TDC takes a finite time to recover before it can register the next ion. This period is known as the deadtime of the TDC.

At high concentrations, the arrival of multiple ions at the detector results in some of the later ions being ‘missed’. At this point there is no longer a linear relationship between concentration and response.

The application of an algorithm which can compensate for this effect (digital deadtime correction; DDTC) allows the linear dynamic range to be significantly enhanced (3 to 4 orders), providing a wide working range for quantitative analyses.

In these experiments, the linearity of the Q-Tof Micro in electrospray mode was investigated using sulfamethazine. Standards of sulfamethazine were prepared over the range 0.1 pg/µL to 5000 pg/µL with sulfadimethoxine, another sulfonamide, present at 100pg/µL as an internal standard.

Triplicate injections were made of a solvent blank followed by the standards using the experimental conditions.

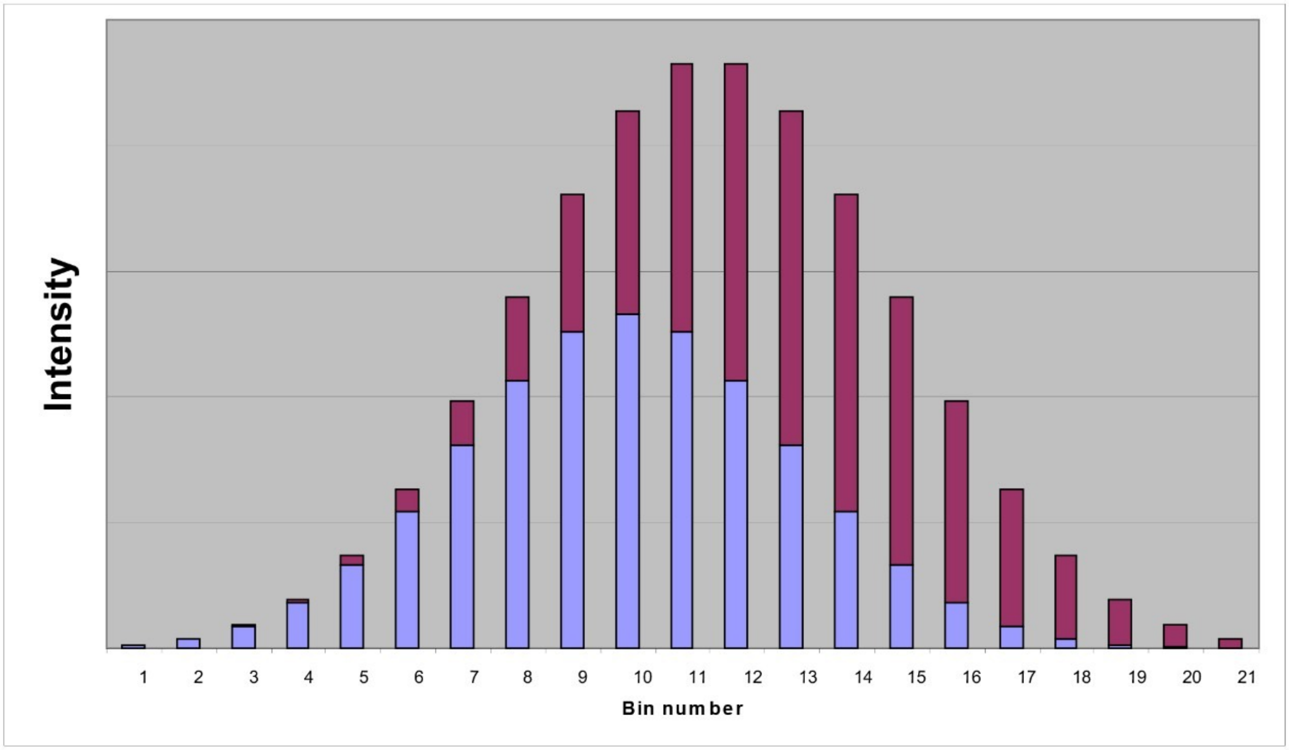
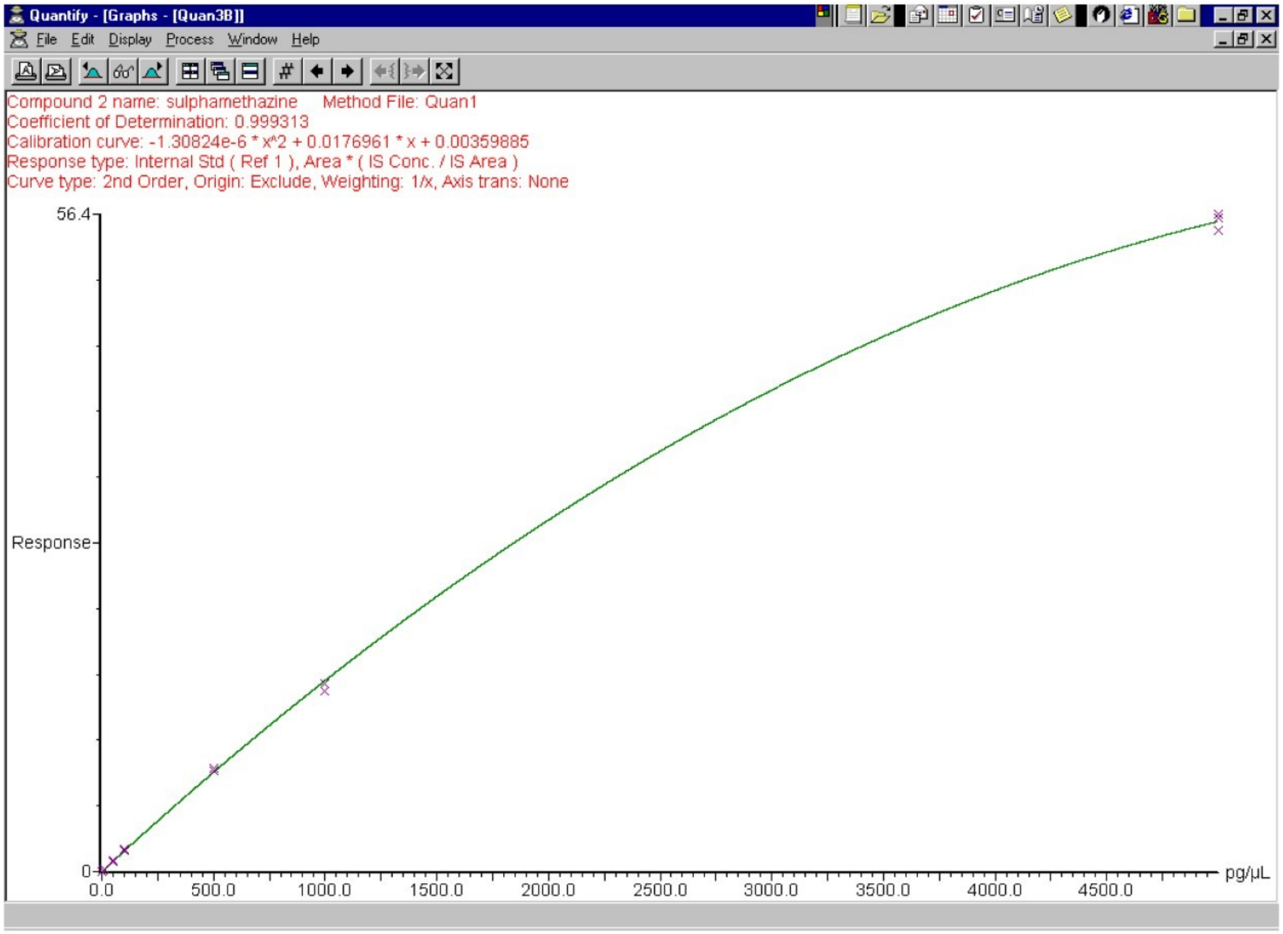


Figure 1. Depiction of the ion distribution on a micro-channel plate detector/TDC combination in 'deadtime'. Blue indicates the raw data, while red indicates the DDTC corrected distribution

Data were acquired in MS-MS mode and a chromatogram trace generated which was the sum of the most intense ions in the MS-MS product ion spectrum. For the analyte, sulfamethazine, the chromatogram generated was a sum of the product ions at *m/z* 156+186+279 while for the internal standard, sulfadimethoxine, only *m/z* 156 was monitored.

The data were acquired in continuum mode and subsequently processed, without the use of the dead time correction algorithm. Using a second order fit and a 1/x weighting a coefficient of determination of 0.9993 was obtained over the range 0.5pg/µL, the limit of detection, to 5000 pg/µL (Figure 2). By excluding the top two calibration points (1000 and 5000 pg/µL) a linear calibration fit could be obtained with a coefficient of determination of 0.9989.



```
Compound 2 name: sulphamethazine     Method File: Quan1
Coefficient of Determination: 0.999313
Calibration curve: -1.30824e-6 * x^2 + 0.0176961 * x + 0.00359885
Response type: Internal Std ( Ref 1 ), Area * ( IS Conc. / IS Area )
Curve type: 2nd Order, Origin: Exclude, Weighting: 1/x, Axis trans: None
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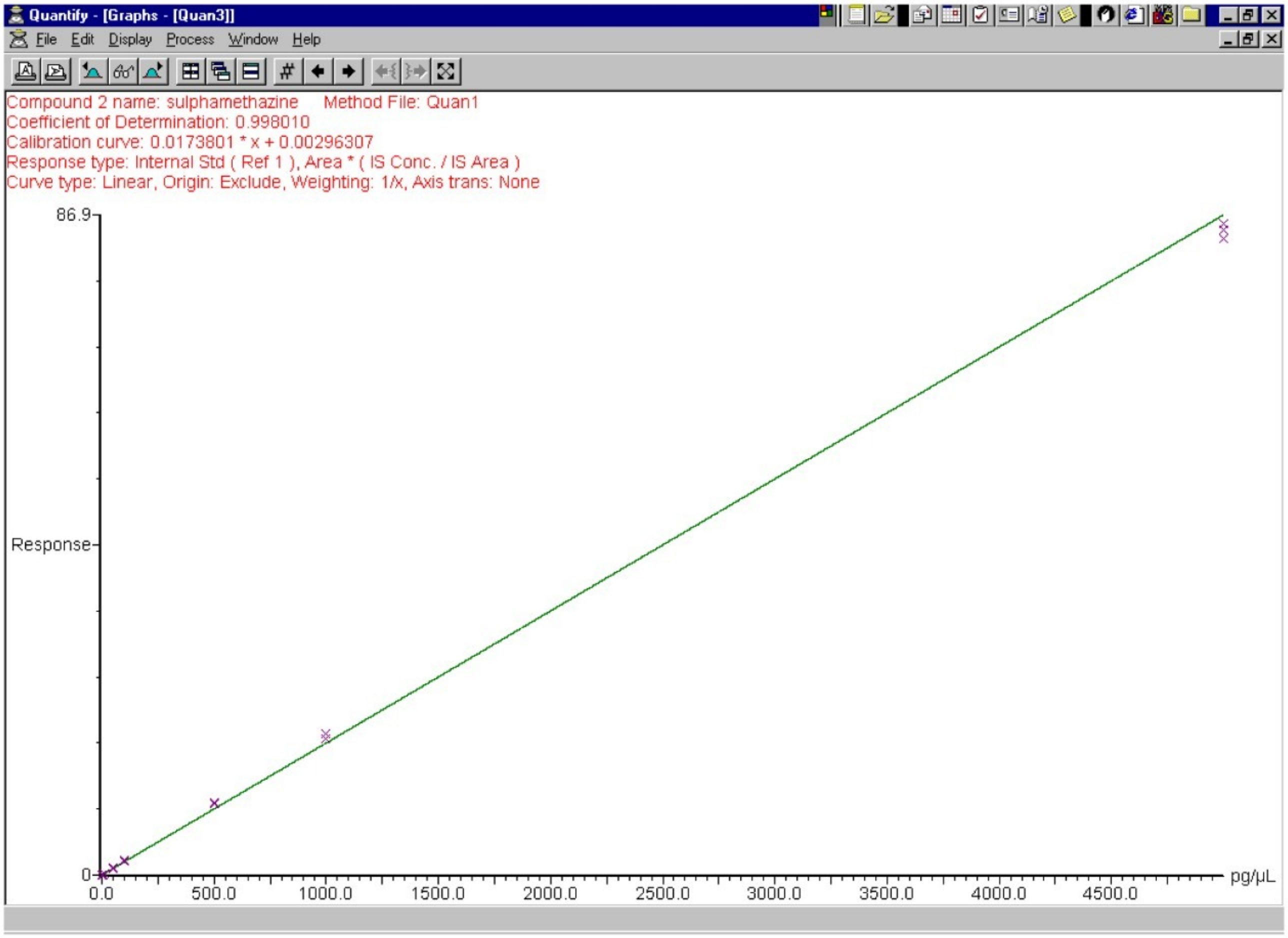
Figure 2. Calibration curve for sulfamethazine over the concentration range 0.5–5000 pg/µ L illustrating decay of response as the MCP detector enters 'deadtime'.

Application of DDTC

The same raw data was reprocessed with the digital deadtime correction algorithm enabled. In this case, plotting a calibration curve resulted in a linear response being obtained from 0.5 pg/µL to 5000 pg/µL with a coefficient of determination of 0.9980. This indicates that the linear dynamic range of the instrument can be extended to between three and four orders of magnitude with the use of DDTC (Figure 3).



Compound 2 name: sulphamethazine   Method File: Quan1
Coefficient of Determination: 0.998010
Calibration curve: 0.0173801 * x + 0.00296307
Response type: Internal Std (Ref 1), Area * (IS Conc. / IS Area)
Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None

Figure 3. Calibration curve for sulfamethazine over the concentration range 0.5–5000 pg/µ L illustrating linearity of response over > 3 orders of magnitude with DDTC applied.

Conclusion

The use of a correction algorithm, based on the mathematical model for the dead time effect, has been shown to extend the linear dynamic range of oa-TOF mass spectrometers.

The application of DDTC allows accurate mass measurement and a linear response with sample concentration over a range up to four orders of magnitude.

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