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Optimizing GC/MS Performance for Lowest Detection Limits and Widest Linear Range

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Overview

Sensitivity is an important criteria used to evaluate instrument performance. The measure of sensitivity is often related to an instrument detection limit (IDL) or signal-to-noise ratio (SNR). Detector gain is one parameter used to optimize signal response. The gain can increase signal response, but can compromise the linear range. This study evaluated the detector gain settings on Single Quadrupole (SQ) and Triple Quadrupole (TQ).

Introduction

Traditionally in specifying the performance of GC/MS instruments a signal-to-noise ratio has been equated with system sensitivity. Although these terms are not directly synonymous, the SNR has served well in helping to measure how low an instrument 'can see.' With the advent of instruments with lower noise, the utility of SNR to estimate sensitivity decreases. (i.e. a system with zero measureable noise would have a SNR of infinity, which doesn't help in assessing actual instrument performance).

An alternative to using SNR is to use Method Detection Limits (MDL), a multi-injection, statistical methodology. MDL is commonly used to establish limit of detection for trace analysis in complex matrices as described by the US EPA [1] and the European Communities [2].

The Instrument Detection Limit (IDL) is determined in the same manner as MDL except that it is the injection of clean standards instead of spiked extracted samples. IDL and MDL relate the instrument detection limit to the Relative Standard Deviation (RSD) of measured areas of replicate injections, a statistical confidence factor t_a and the amount of the standard (fg) by:

$$IDL= (t_a)\ (RSD)\ (\text{amount of standard})\ /\ 100$$

The statistical factor is taken from the one-sided Student t-distribution, and for a 99 % confidence limit for 8 replicate injections is equal to 2.998 [3].

As the equation above indicates, the IDL is related to the deviation in peak area of multiple injections. This is typically most impacted by the precision of the entire instrument and by ion statistics, particularly at low levels of ion abundance. It should therefore be relatively independent of gain over the working range of the detector.

Experimental

Data was acquired on an Agilent 5977 Single Quadrupole Mass Selective Detector (SQ) and an Agilent 7000 Series Triple Quadrupole (TQ) GCMS using the following conditions.

GC Acquisition Parameters	
Column	HP-5MS UI 30m x 0.25mm x 0.25µm
Test Solution	OFN in iso-octane
Injection Volume	1 µl
Injection Port Temperature	250 °C
Injection Mode	Pulsed Splitless / Pulse Pressure 25.0 psi / Pulse Time 0.50 min / Purge Flow 50.0 ml/min / Purge Time 1.00 min
Flow Settings	Constant Flow @ 1.2 ml/min
Oven Temperature Program	Init Temp 45 °C Hold Time 1.00 min Ramp 40.00 °C/min to 190 °C Hold Time 0.00 min
Interface Temperature	250 °C
Source Temperature	230 °C
Quad Temperature	150 °C
TQ MS Acquisition Parameters	
Mode	MRM
Q1, Q2 Peak widths	Wide, Wide
Transitions (M1 : M2 : E : Dwell)	272: 222 : 20 : 100
Collision Gas	N_2 @ 1.5 ml/min
He Collision Cell Flow	2.25 ml/min
EM Setting	Gain Factor
Time Filter	0.7 sec
SQ Acquisition Parameters	
Mode	SIM
SIM Ion	272
SIM Dwell Time	100ms
EM Setting	Gain Factor
Tune	Etune
Data Analysis Parameters	
Signal Definition	Peak Height or Agile Area
Noise Definition	Auto-RMS x 1.0
Noise Window	0.25 min

References:

1) U. S. EPA - Title 40: Protection of Environment; Part 136 – Guidelines Establishing Test Procedures for the Analysis of Pollutants; Appendix B to Part 136 – Definition and Procedure for the Determination of the Method Detection Limit – Revision 1.11.

2) Official Journal of the European Communities; Commission Decision of 12 August 2002; Implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results.

3) "Why use Signal-To-Noise as a Measure of MS Performance When it is Often Meaningless?" Agilent Technologies Technical Note, publication 5990-8341EN

Results and Discussion

Determining the Detection Limit

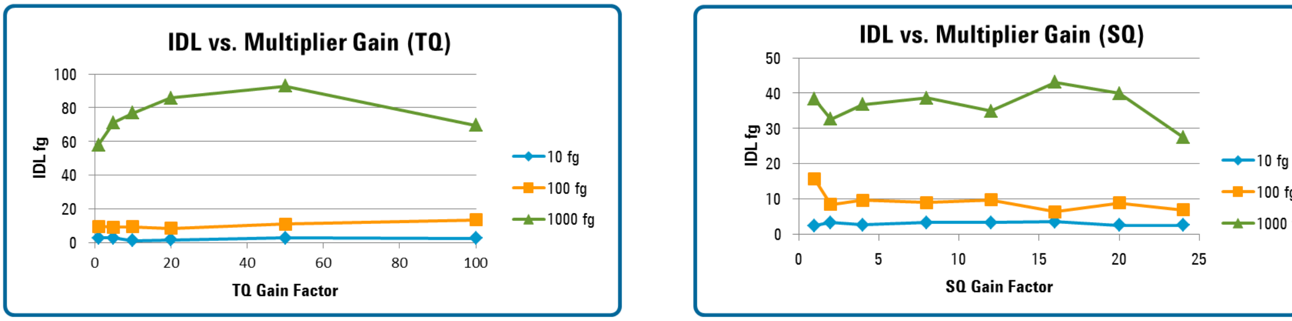

Figure 1. **IDL for varying electron multiplier gains for 8 injections using standards of 10, 100, and 1000 fg**. We observed the widest range of IDLs at the highest concentration, and the range narrows as we approach the limit of detection. On the TQ the avg. %RSD for 10 fg was 7.4%, for 100 fg was 3.3 % and 1.9 % for 1000fg. One would expect the improved %RSD is due to better ion generation and statistics[3]. The TQ IDL for 1000 fg was 58 to 83 fg, for 100 fg was 9 to 14 fg and for **10 fg was 2-3 fg**. The IDL for the SQ was 28 to 43 fg, 6 to 16 fg, and **2 to 4 fg** for the respective concentrations. There appears to be *no significant effect of gain on the determination of IDL.*

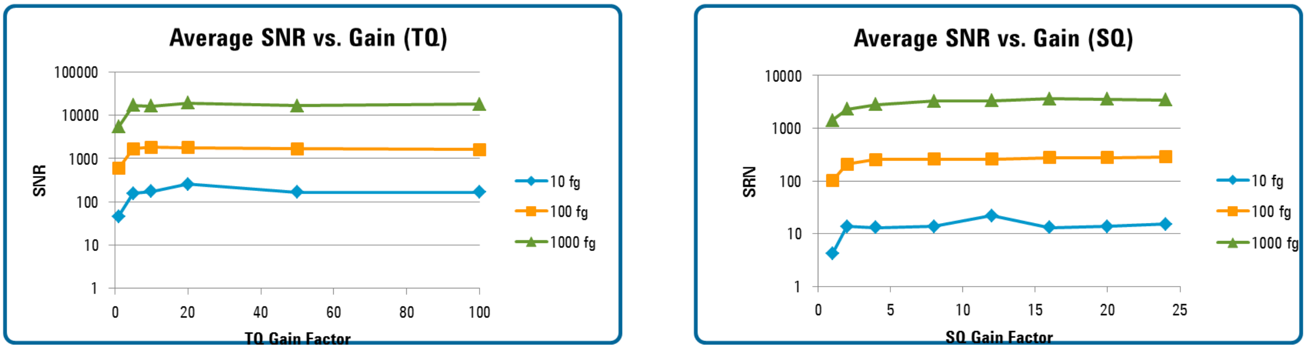

Figure 2. The TQ's best signal to noise was observed with Gain Factors of 15 to 20. For a 10 fg sample at a gain of 20, SNR was ~250, and for 100fg the SNR was ~1800. Both of these SNR results suggest one could see signal more than 3X the noise at concentrations **less than 0.2 fg** OFN. For the SQ, the SNR (>250 at 100 fg) suggest that a signal greater than 3X the noise would be achievable with less than **1.2 fg**.

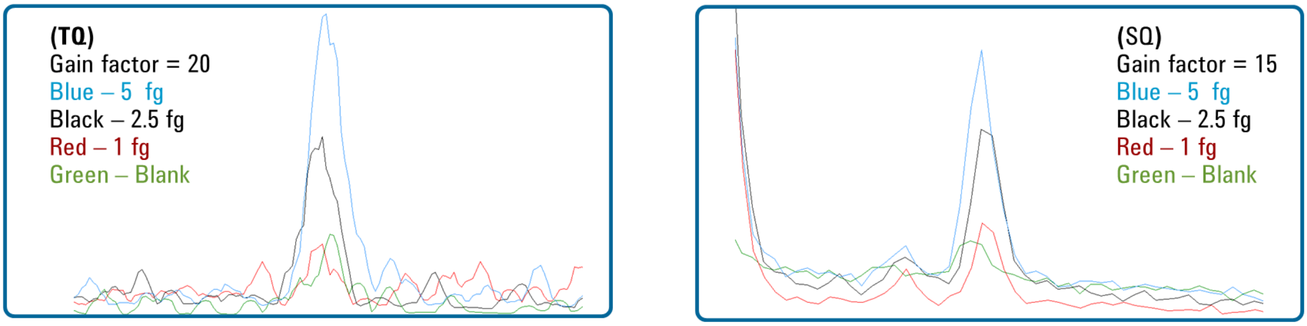

Figure 3. To test the limits of detection, we injected OFN at concentrations ranging from 0.1 fg to 5 fg. Concentrations less than 1 fg were undistinguishable from injections of blank OFN. At 2.5 fg, the OFN peak can be clearly differentiated from the noise. The IDL with a *99% Confidence Limit* for the TQ was determined to *be* **2.4 fg** and **3.5 fg** for the SQ.

Results and Discussion

Effect of Gain on Working Linear Range

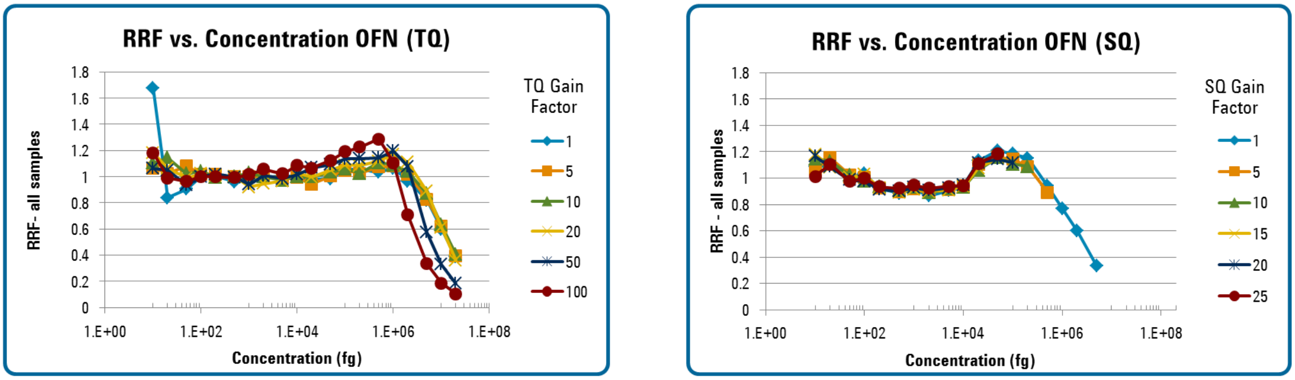

Figure 4. Determination of working linear range (WLR) with varying Gain Factors. The WLR definition used is < 15% RSD of the relative response factor (RRF). Gains at both high and low extremes show the most deviation. The widest WLR for the TQ was obtained with Gain Factors between 5 and 20. The SQ saturated the detector at all gains other than gain factor = 1. Deviation of the RRFs at the highest concentrations maybe due to GC conditions which were optimized for the trace analysis. The concentration axis is a logarithmic scale.

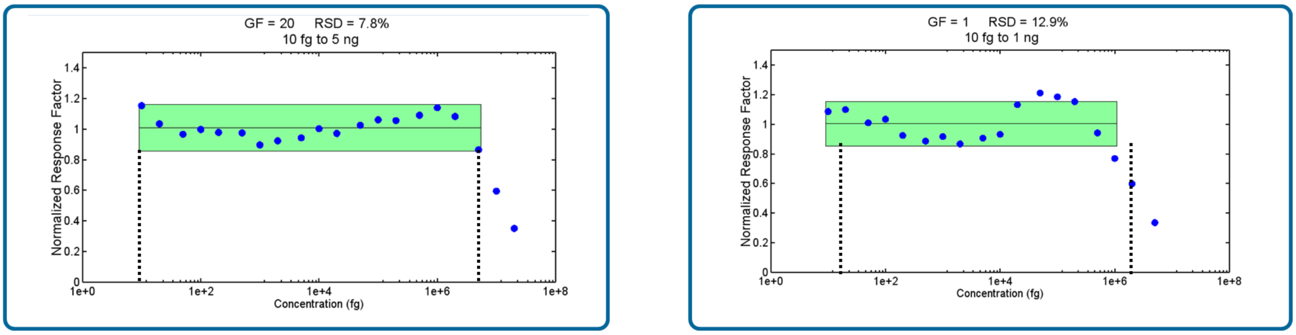

Figure 5. Plots of the RRF at concentrations ranging from 10 fg to 20 ng show the region of WLR (< 15% RSD of the RRF). The green area represents +/- 15% of the normalized RRF. The TQ demonstrated a WLR of 10 fg to 5 ng with a RSD of 7.8% and the SQ demonstrated a WLR of 10 fg to 1 ng with a RSD of 12.9% under these conditions.

Conclusions

- The low level of noise (RMS calculation) gives unrealistic values of system's detection limits when using the SNR approach.
- The IDL is not dependent on electron multiplier gain but on ion generation and statistics at low sample concentrations
- Linearity is best for mid-range gain values. Using high gains will decrease linear range, shorten Electron Multiplier lifetimes and provides no benefit for routine analysis
- The multi-injection approach of IDL is a more reliable tool than SNR for estimating the performance of GC/MS instruments.