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

Barbara Bolton, Brian Hom, Jim Oppenheimer
Agilent Technologies, Santa Clara, CA
Optimizing GC/MS Performance for Lowest Detection Limits and Widest Linear Range

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:

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

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:** N₂ @ 1.5 ml/min
- **He Collision Cell Flow:** 2.25 ml/min
- **EM Setting:** Gain Factor 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:
3) “Why use Signal-To-Noise as a Measure of MS Performance When it is Often Meaningless?” Agilent Technologies Technical Note, publication 5990-8341EN
Optimizing GC/MS Performance for Lowest Detection Limits and Widest Linear Range

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

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.