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Practical determination and validation of instrument detection limit of Thermo Scientific ISQ 7000 single quadrupole GC-MS with ExtractaBrite EI ionization source

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Introduction

Signal-to-noise ratio (S/N) has been used for decades to convey the detection limit of an instrument. Technological innovation has driven instruments to exhibit lower noise and greater sensitivity; while advancements in gas separation technology mean lower bleed columns and sharper peaks, again, leading to significant improvements in S/N values obtained. Moreover, S/N calculations are also typically performed on a single injection, not demonstrating the repeatability of the instrument in question. S/N measurements usually always rely on some form of operator involvement, such as selecting the start and end of the peak being measured and more importantly choosing the noise range. Figures 1 and 2 show the differences in S/N value for the *m/z* 284 fragment ion of hexachlorobenzene when the selected noise range differs by only 0.05 minutes. On many GC triple quadrupole instruments the added selectivity leads to much lower baseline noise, rendering the use of S/N as an accurate measure of instrument detection limit inadequate. Therefore, a more accurate or statistically significant method of calculating the detection limit of an instrument is required.

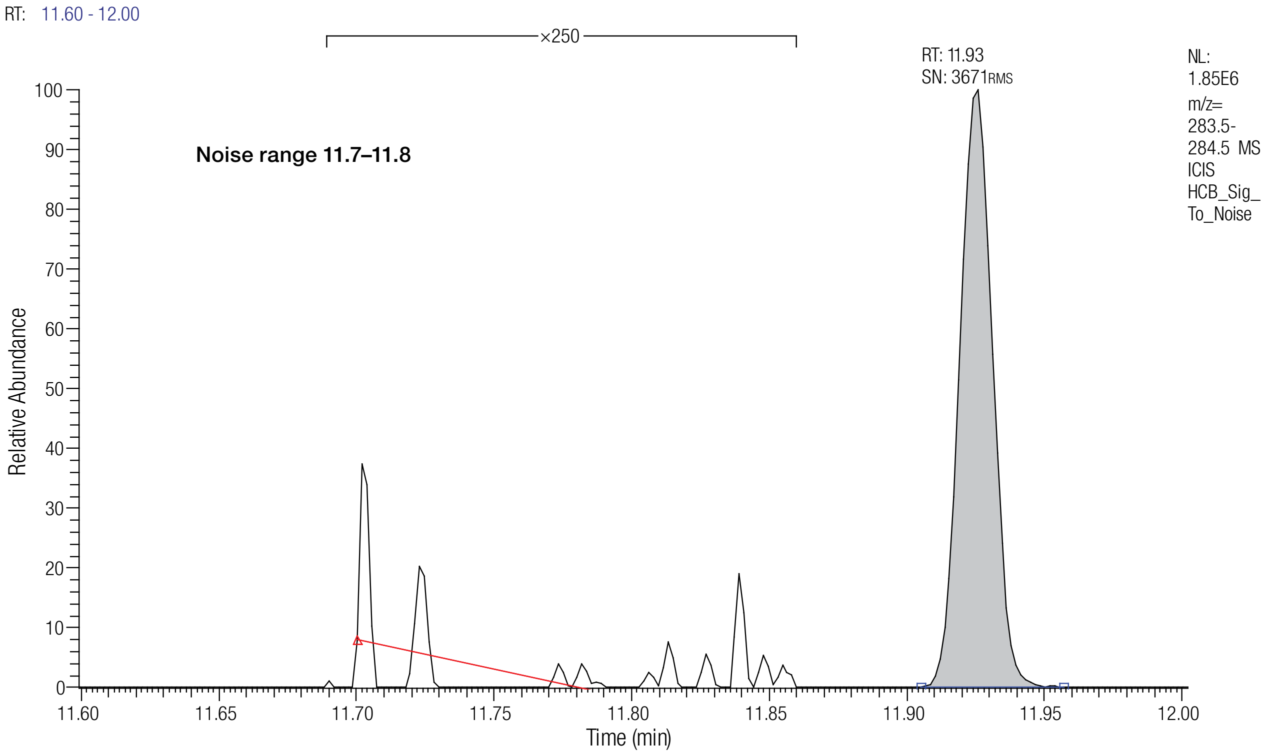

Figure 1. Chromatogram showing the effect of noise range selection on S/N value calculated.

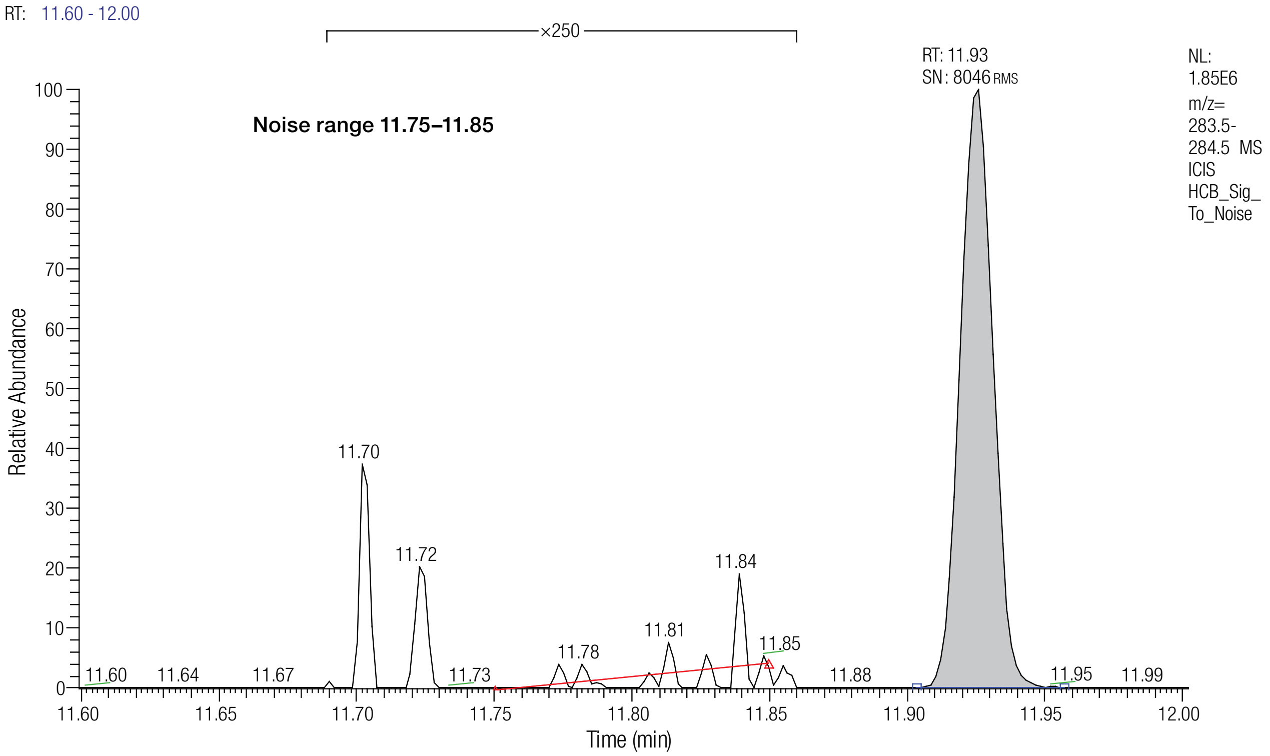

Figure 2. Chromatogram showing the effect of noise range selection on S/N value calculated.

Instrument detection limit (IDL)

One way of determining the instrumental limit of detection (LOD) is by using the standard deviation of the response of an analyte of choice at a concentration close to the estimated detection limit. This approach gives much more reliable LOD values as it takes into account not only the signal intensity, but also the consistency of the response. Method detection limits (MDL) are firmly established with many regulatory bodies and can be defined in many ways. According to the most recent U.S. Code of Federal Regulations[1], MDL is defined as: “the minimum concentration of a substance that can be measured and reported with 99% confidence that the analyte concentration is greater than zero and is determined from analysis of a sample in a given matrix containing the analyte.” This methodology can be seamlessly transferred when calculating IDL.

Unlike MDL, the IDL uses solvent-based standards containing the test chemical at concentrations that give a consistent response over several repeat injection (ex: %RSD <5). Therefore, the IDL is a statistically rigorous method that uses the precision of a measurement at low analyte levels and accurately reflects the true detection limit of an instrument, ultimately defining how sensitive an analytical system is. Simply, the IDL can be determined by using the following equation[2]:

$$\mathrm{IDL} = t \times \mathrm{Amount} \times \%\mathrm{RSD}$$

Where,

t = student t-value for one-tailed distribution:
for n = 8 injections; $t = 2.998$

Amount = amount of analyte (on-column)

%RSD = relative standard deviation of the response

During this study, the consistency in IDL for octafluronapthalene (OFN), a commonly used reference compound in GC-MS, was determined on three separate Thermo Scientific™ ISQ™ 7000 single quadrupole GC-MS systems equipped with the Thermo Scientific™ ExtractaBrite™ ionization source operating in EI mode.

Experimental

ISQ 7000 single quadrupole GC-MS systems featuring a 300 L/s turbo pump and equipped with the ExtractaBrite ion source were used in all of the experiments, with an AS 1310 Liquid Autosampler (two experiments) and a Thermo Scientific™ TriPlus™ RSH™ Autosampler (one experiment). Choosing different robotic arms on ISQs used for this test adds to the rigorosity of the experimental setup and the reduction of any potential autosampler bias. See Table 1 for detailed conditions. All experiments were performed using a 1 µL injection solution containing 10 fg/µL octafluoronaphthalene (OFN) in iso-octane. The IDL was calculated from n = 8 sequential replicate injections.

Results and discussion

Three different ISQ 7000 single quadrupole GC-MS systems were evaluated using eight sequential replicate injections of a 10 fg/µL octafluoronaphthalene standard in iso-octane. The results from each instrument, along with calculated relative standard deviations from which the IDL is derived, are summarized in Table 2.

The instruments used in the experiment are based in three different laboratories around the world and have been deployed in environments running routine applications, in instrument engineering settings, and as training instruments for a number of years (Figure 3). Three separate operators were responsible for setting up the systems, using three different standard preparations and utilizing two different autosampler types. Even with these variations, all three instruments demonstrated peak area repeatability with %RSD <4% and displayed outstandingly consistent IDL values, regardless of their age and typical usage. The combination of the ISQs off-axis ion source and unique s-shaped ion-guide creates a curved path allowing chemical and neutral noise to be kept to a minimum, enabling lower detection limits, while the Thermo Scientific™ DynaMax™ XR detection system provides the sensitivity to detect and amplify the low number of transmitted ions needed at this challenging analyte concentration.

Table 1. Experimental conditions.

GC Conditions	
Instrument:	Thermo Scientific™ TRACE™ 1310 GC system, Thermo Scientific™ ISQ™ 7000 single quadrupole GC-MS system with 300 L/s turbo pump
Column:	Thermo Scientific™ TraceGOLD™ SQC GC Column (p/n: 26070-1300)
Column dimensions:	15 m × 0.25 mm × 0.25 µm
Injection volume:	1 µL
Inlet temperature:	220 °C
Injection liner:	Thermo Scientific™ LinerGOLD™ Splitless Liner single taper with wool, 4 mm ID, 78.5 mm length (p/n: 453A0924)
Injection mode:	Splitless
Split flow rate/ Splitless time:	50 mL/min at 0.8 minutes
Septum purge flow:	5 mL/min (constant)
Carrier mode:	Constant flow
Carrier gas:	Helium
Carrier flow:	1.2 mL/min
Temp. gradient:	40 °C (hold for 1.0 min); ramp 30 °C/min to 150 °C; ramp 100 °C/min to 250 °C; (hold for 5 min)
Total run time:	10.67 min

MS Conditions	
Ionization source:	ExtractaBrite
Ionization mode:	EI, 70 eV
Emission current:	50 µA
MS transfer line temperature:	250 °C
Ion source temperature:	200 °C
Acquisition mode:	Selective Ion Monitoring (SIM) *m/z* 272
Software (CDS):	Thermo Scientific™ Chromeleon™ 7.2 Chromatography Data System

Conclusion

The ISQ 7000 single quadrupole GC-MS system with the ExtractaBrite ion source exhibits outstandingly low instrument detection limits ensuring confidence in your analysis.

The use of a statistical method to determine the IDL demonstrates the consistent and sensitive detection that can be achieved at this challenging analyte concentration.

The instrument-to-instrument detection limits using a 10 fg on-column amount have been shown to be highly reproducible and consistent in a variety of settings, regardless of age and use.

The exceptionally sensitive DynaMax XR detection system, complemented by the innovative s-shaped ion guide, effectively reduces noise while maintaining maximum sensitivity leading to IDLs significantly below 1.5 fg on column.

Table 2. Results from each instrument.

Injection	Peak area (counts per second)		
	Instrument 1 Singapore AI/AS 1310 ISQ 7000	Instrument 2 Italy AI/AS 1310 ISQ 7000	Instrument 3 UK TriPlus RSH ISQ 7000
1	415.02	315.48	249.12
2	417.78	326.94	244.68
3	402.36	304.92	245.52
4	393.48	289.2	266.34
5	412.26	301.92	253.32
6	403.26	308.22	260.88
7	372.12	307.98	266.16
8	388.68	319.8	257.28
Average	400.62	309.31	255.41
SD	15.37	11.59	8.66
%RSD	3.80%	3.70%	3.40%
IDL (fg)	**1.2**	**1.1**	**1**

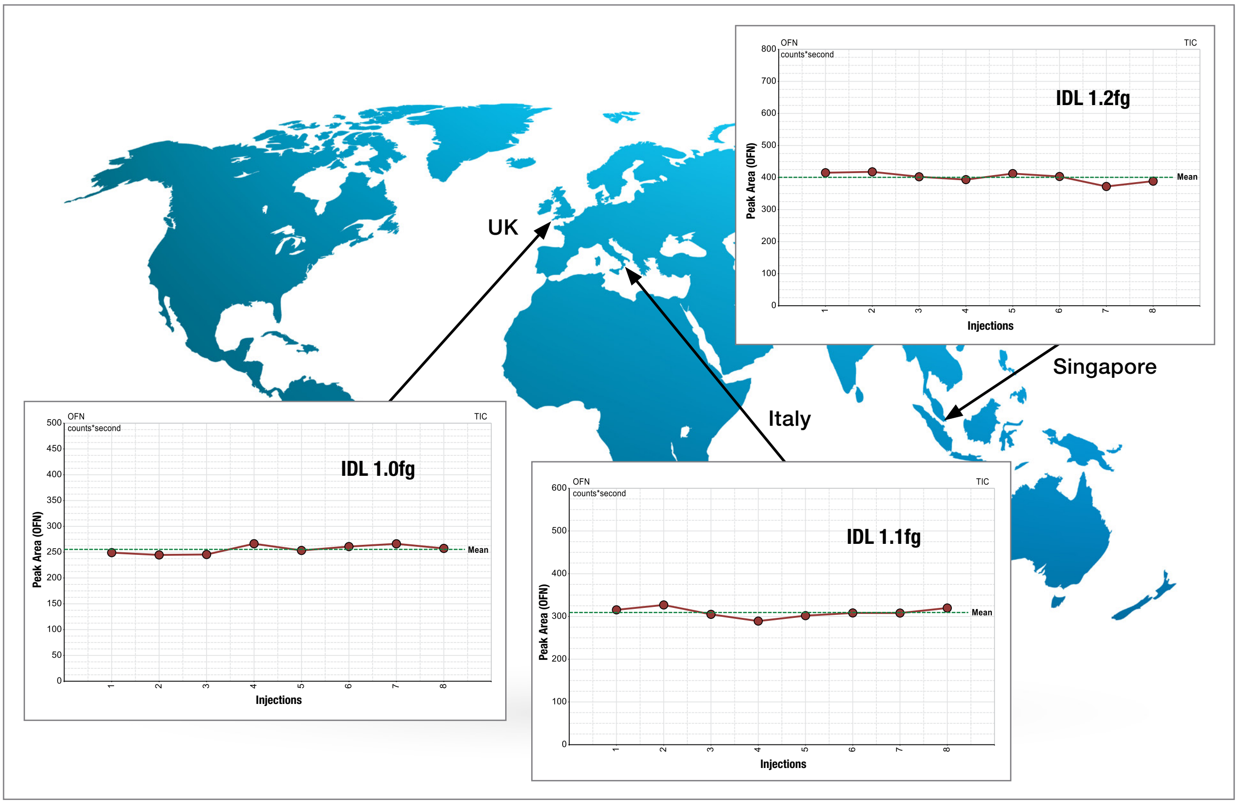

Figure 3. Locations of instruments and peak area repeatability for each.

References

1. U.S. Code of Federal Regulations, 49 FR 43430, (Oct. 26, 1984); 50 FR 694, 696 (Jan. 4, 1985), as amended at 51 FR 23703 (June 30, 1986), http://www.ecfr.gov/cgi-bin/text-idx?SID=efe93db42854f88dffcf66ba8de737e6&mc=true&node=ap40.23.136_17.b&rgn=div9
2. International Union of Pure and Applied Chemists (IUPAC), http://media.iupac.org/publications/analytical_compendium/Cha18sec437.pdf

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