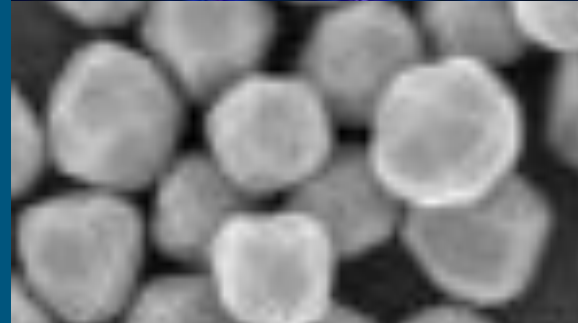


# Total flexibility and unrivalled control of interferences in reaction mode by ICP-MS/MS technique

Presenter:  
Andrea Carcano

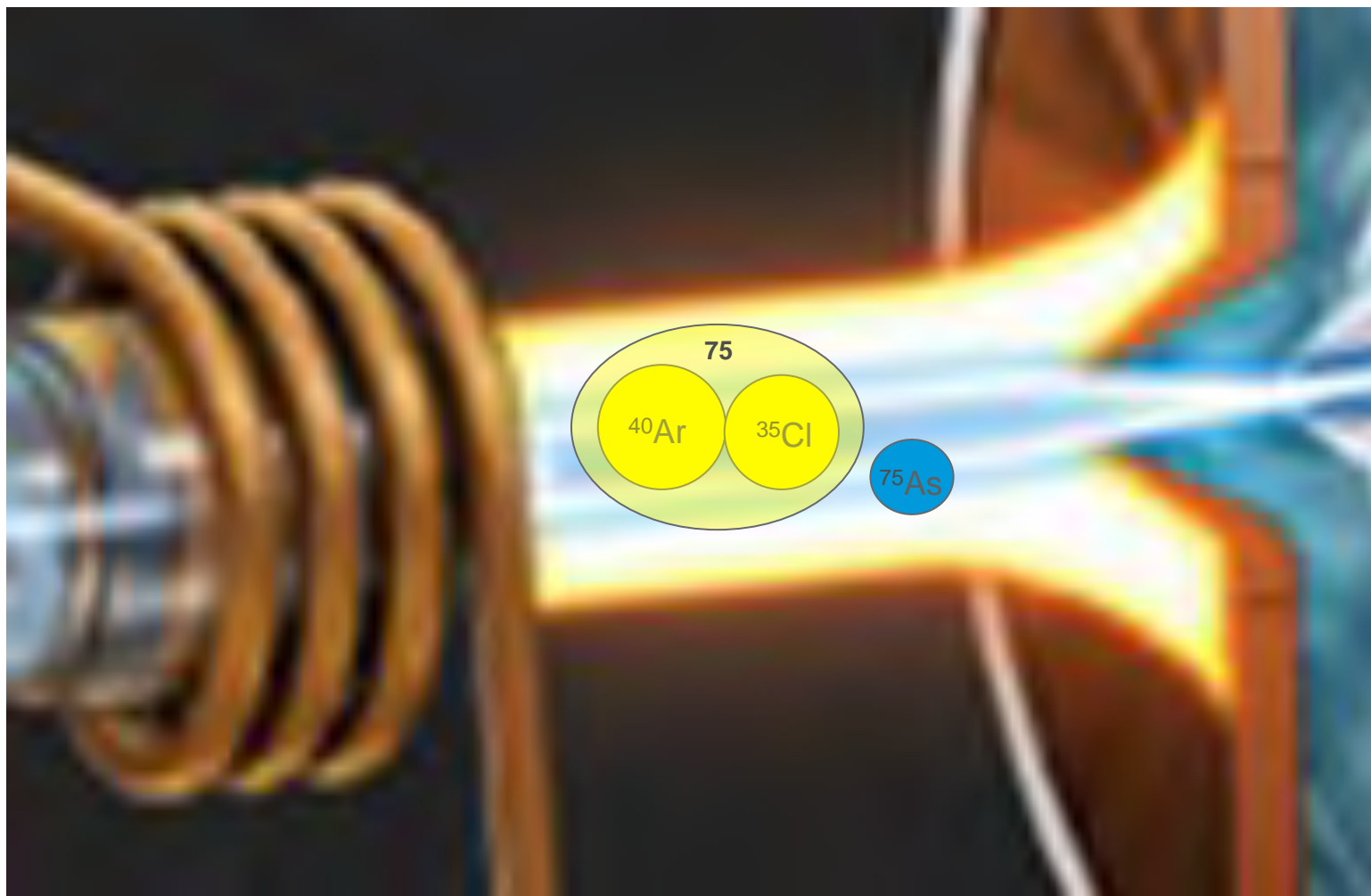
Agilent Technologies



# General ICP-MS Components/Technology

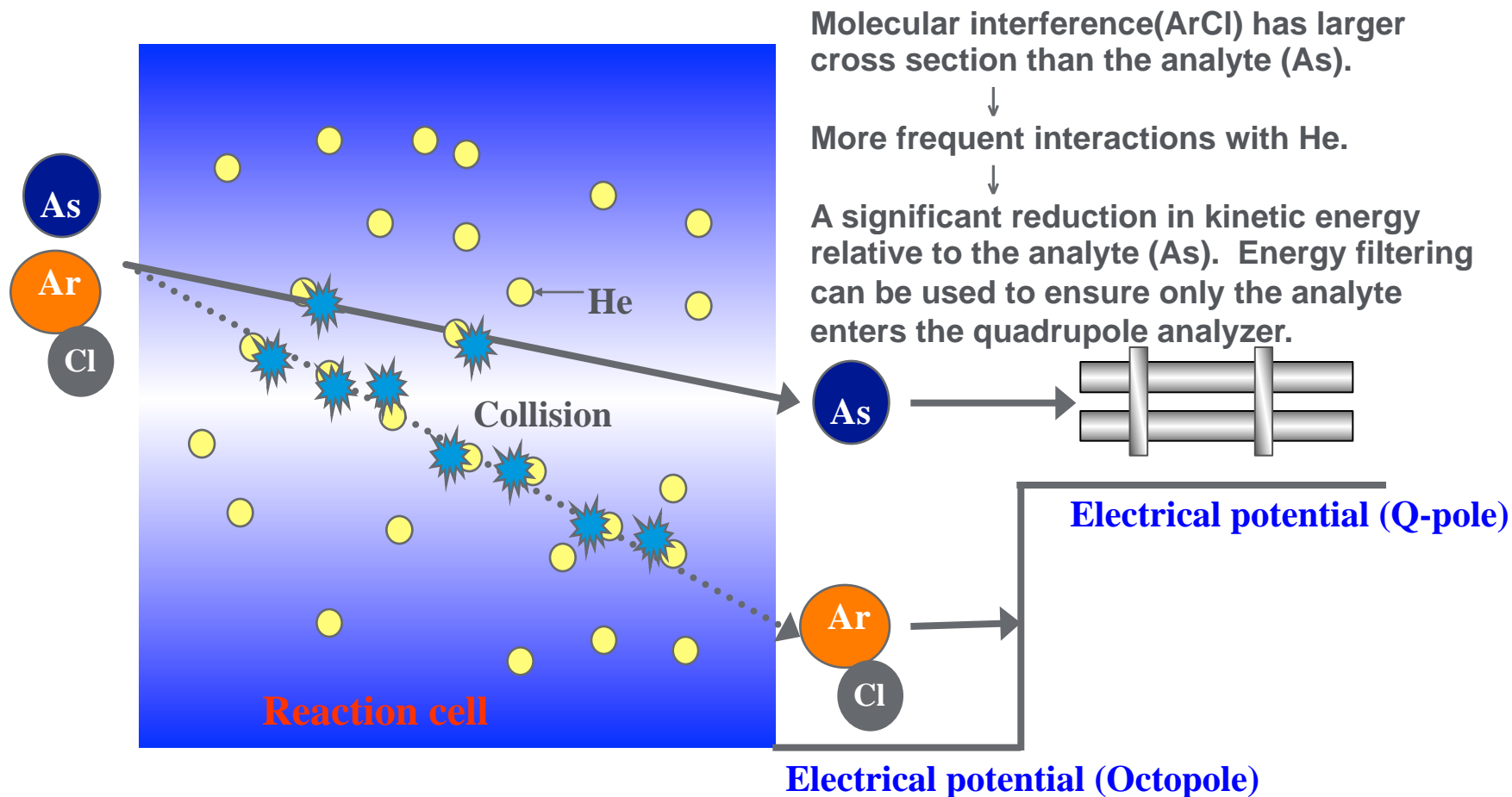


# Polyatomic Interference Formation



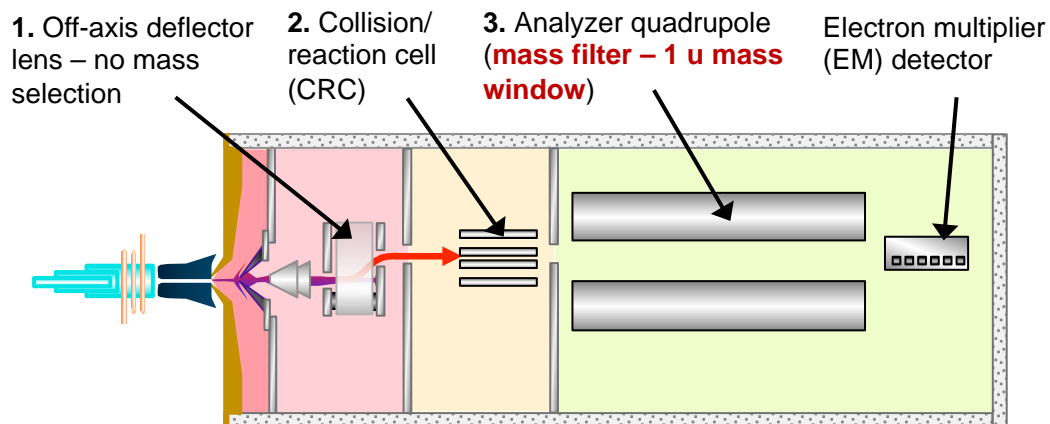
# Helium interactions in an Octopole Reaction Cell

## Collision: Energy discrimination



# Conventional (Single) Quadrupole ICP-MS

Simplest, lowest-cost solution for typical applications



The industry-standard ICP-MS layout:

1. Off-axis deflector lens to separate the ions from photons & neutrals
2. Collision/reaction cell (CRC)\*, and
3. **One quadrupole mass analyzer (a mass filter with a 1 u mass window)**

\* Since 1999 CRCs have been used to control spectral interferences in ICP-MS:

- Collision mode is well-established and widely used for typical analytes and applications
- Reaction mode is efficient and attractive, but can give errors due to unwanted reactions with other analytes and matrix elements

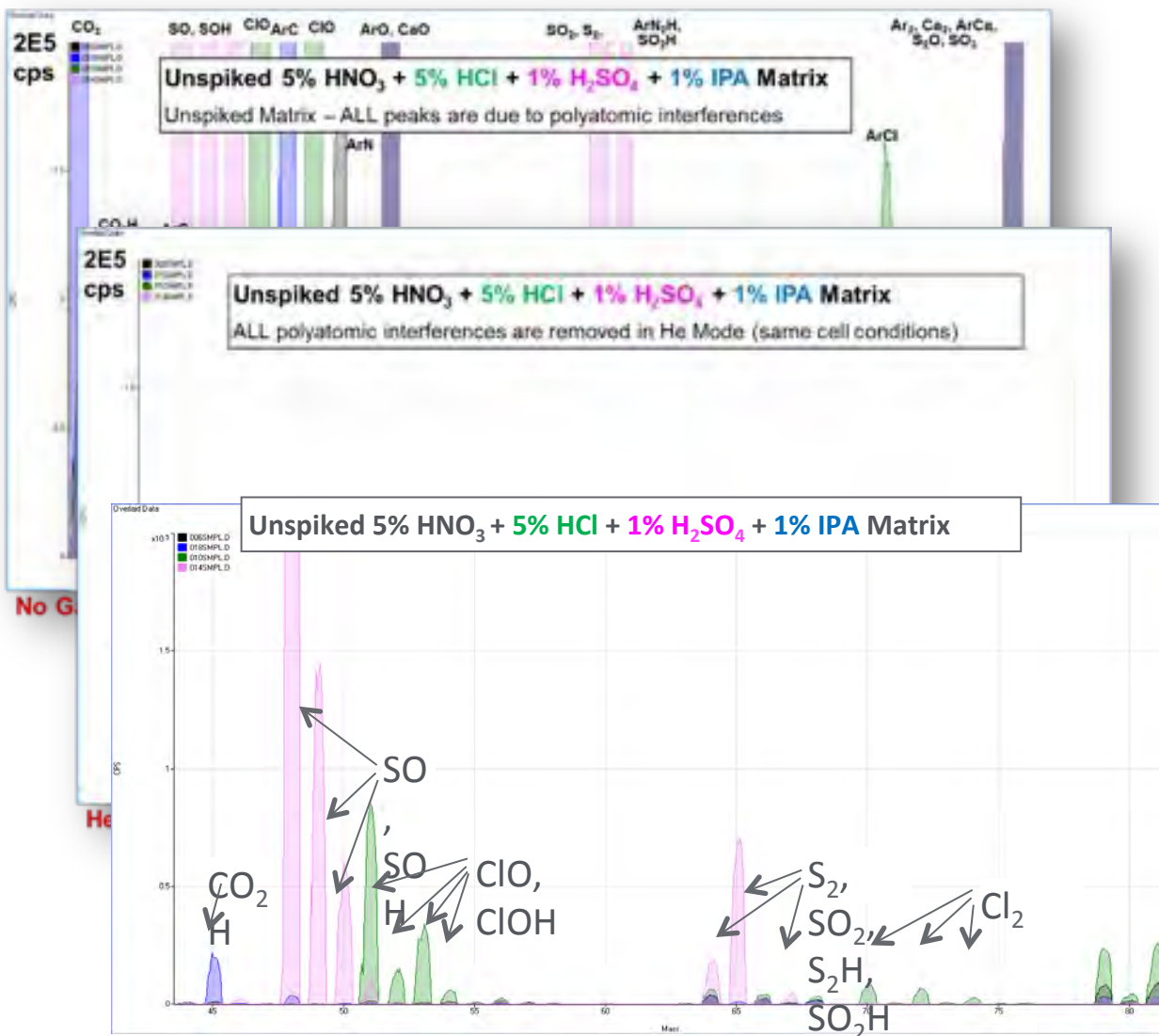
# Uses Helium Mode or Hydrogen mode



**He mode** is effective against **all common polyatomic interferences** – even from unknown or variable matrices.

He mode **simplifies method development**, by allowing a **single set of cell conditions** to be used for all analytes in all typical matrices.

**Saves time and cost**



# Controlling Interferences in ICP-MS

## Collision Mode or Reaction Mode

### (Helium) Collision Mode

- Employed successfully by Agilent ICP-QMS users since 2001 to control polyatomic interferences in complex sample matrices
- Filters out polyatomic ions using kinetic energy discrimination (KED);
- Ensures accurate analysis of most common analytes in typical samples
- BUT, He mode is not effective for doubly-charged or isobaric overlaps, and is not suitable for ultra-low level (semicon) analysis

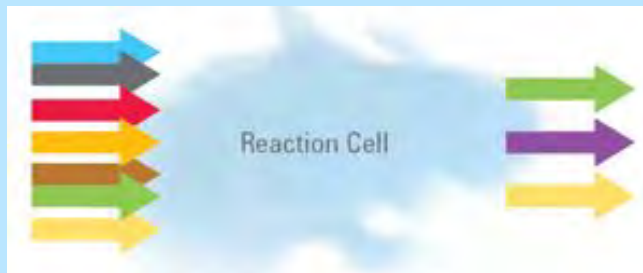
### Reaction Mode

- Can be effective for doubly-charged and isobaric overlaps, and to remove very intense polyatomics
- BUT, reaction chemistry depends on ions in the cell, so results vary if sample composition changes
- Reaction mode on ICP-QMS is often not reliable, and gives errors in variable samples
- **HOW CAN WE MAKE REACTION CHEMISTRY MORE RELIABLE?**

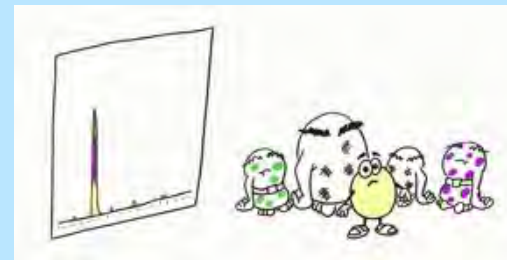
# The Answer: ICP-MS/MS

Quadrupole ICP-MS (ICP-QMS). Single mass filter, after the cell

**No mass selection before cell; ALL ions enter cell and can react**



All ions can pass through cell or react to form new product ions



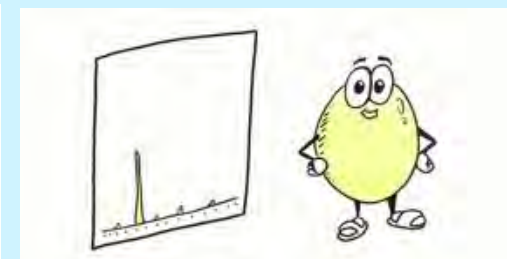
Many different ions can contribute to the measured signal

Triple Quadrupole ICP-MS (ICP-QQQ). Double mass filter, before/after cell

**Mass selection before cell; Q1 rejects all masses except target ion  $m/z$ . ONLY target analyte and on-mass interferences enter cell. Overlaps at product ion mass are eliminated**



Analyte and on-mass interference separated by reaction chemistry



Only the target analyte ions contribute to the measured signal



# The Solution to Controlling Reaction Chemistry in the CRC?

## Triple Quadrupole ICP-MS (ICP-QQQ or TQ):

- Uses an additional mass filter **before** the CRC in a “tandem” mass spec configuration (MS/MS)
- First quadrupole (Q1) selects the specific mass of the ions that can enter the cell. Ensures that reaction chemistry is predictable and reliable
- MS/MS allows reaction gas methods to be applied to normal applications and variable, real-world samples, with confidence in the results

MS/MS requires two fully functioning mass filters. Each mass spectrometer must be able to select individual mass to charge values ( $m/z$ )

**IUPAC definition of Mass spectrometer** (Term 318 from the 2013 Recommendations): *“Instrument that measures the  $m/z$  values... of gas-phase ions”*

First commercial ICP-QQQ instrument (Agilent 8800) in 2012. Superseded by the Agilent 8900 (below) in 2016



**MS/MS releases  
the full potential  
of reaction mode**

# Additional Mass Filter (Q1) in ICP-QQQ

ICP (plasma) and Interface: Forms and extracts ions from the sample

**Q1 extra mass filter enables MS/MS**



**Q1 – selects ions that enter the cell**

- Consistent reactions even if sample composition changes

**Collision/reaction cell gas added**

- Ions react and are neutralized or moved
- Product ions are formed

**Q2 – selects target analyte mass**

- Interference-free analyte ions (or product ions) passed to EM



**EM (detector):** Measures the ions that pass through Q2

ICP-QQQ (ICP-MS/MS) provides superior performance to single quad ICP-MS because of its **double mass selection** (one mass filter before the collision/reaction cell and one after the cell). Without double mass selection, reaction chemistry is not controlled – like on single quad

# What is ICP-QQQ?



# When is Triple Quadrupole ICP-MS Needed?

For interferences **that can't be resolved adequately** using single quad methods

## Lower analyte concentrations

- Ever-lower DLs required for “emerging” trace element contaminants (REEs, PGEs, Pu, Np...) and unusual applications (speciation, nanomaterials...)

## Higher/more complex matrices

- Contaminant analysis in high-purity chemicals and complex materials (alloys, ceramics, REEs, liquid crystal...)

## “Unusual” elements/isotopes

- Increasing interest in trace level and/or isotopic analysis of “non-ICP-MS” elements (Si, P, S, Cl, F...) – often affected by intense interferences O<sub>2</sub>, N<sub>2</sub>, ArH...

## Overlaps not from polyatomic ions

- Isobaric & doubly charged interferences and peak tail overlaps that can't be addressed using helium (collision) mode and kinetic energy discrimination

**Reaction gas methods** enable (or improve) the targeted removal of these types of interferences

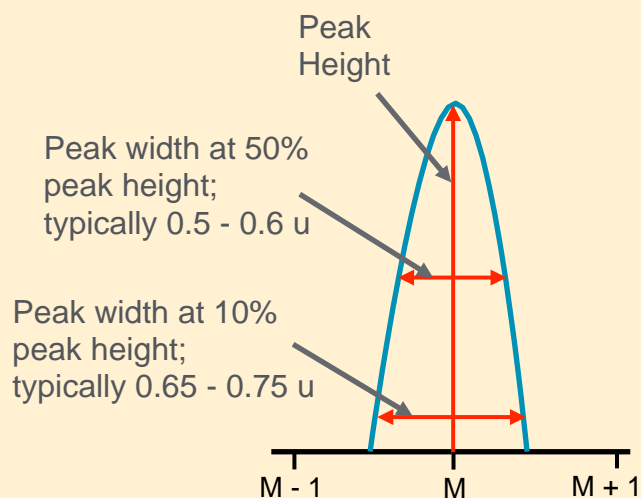
# Abundance Sensitivity (AS) in ICP-MS and ICP-MS/MS

Why having two functioning mass filters improves your analytical results

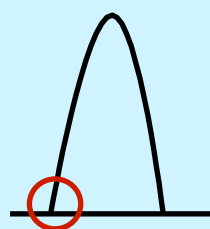
Abundance sensitivity is a measure of peak tailing – the contribution a peak at mass M makes to the adjacent masses at M-1 and M+1.

Related to resolution, but applies to tailing below the 10% peak height where resolution is measured

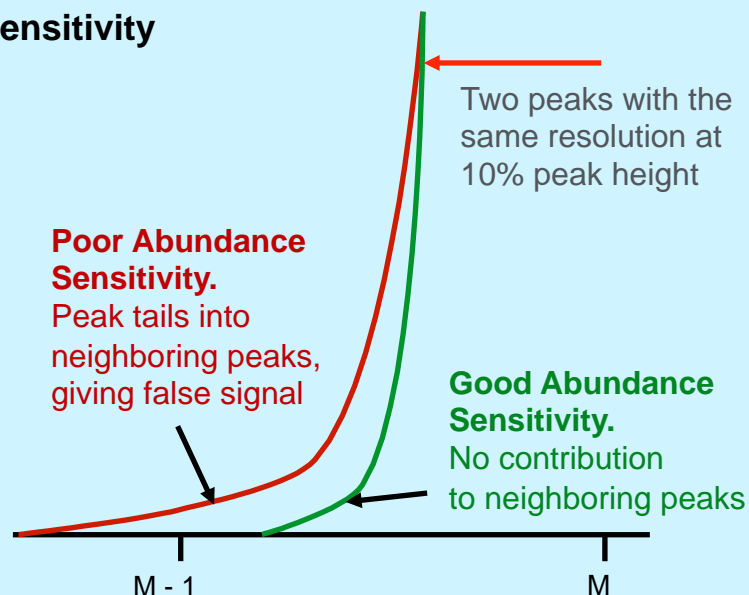
## Resolution



## Abundance Sensitivity



**Poor Abundance Sensitivity.**  
Peak tails into neighboring peaks, giving false signal

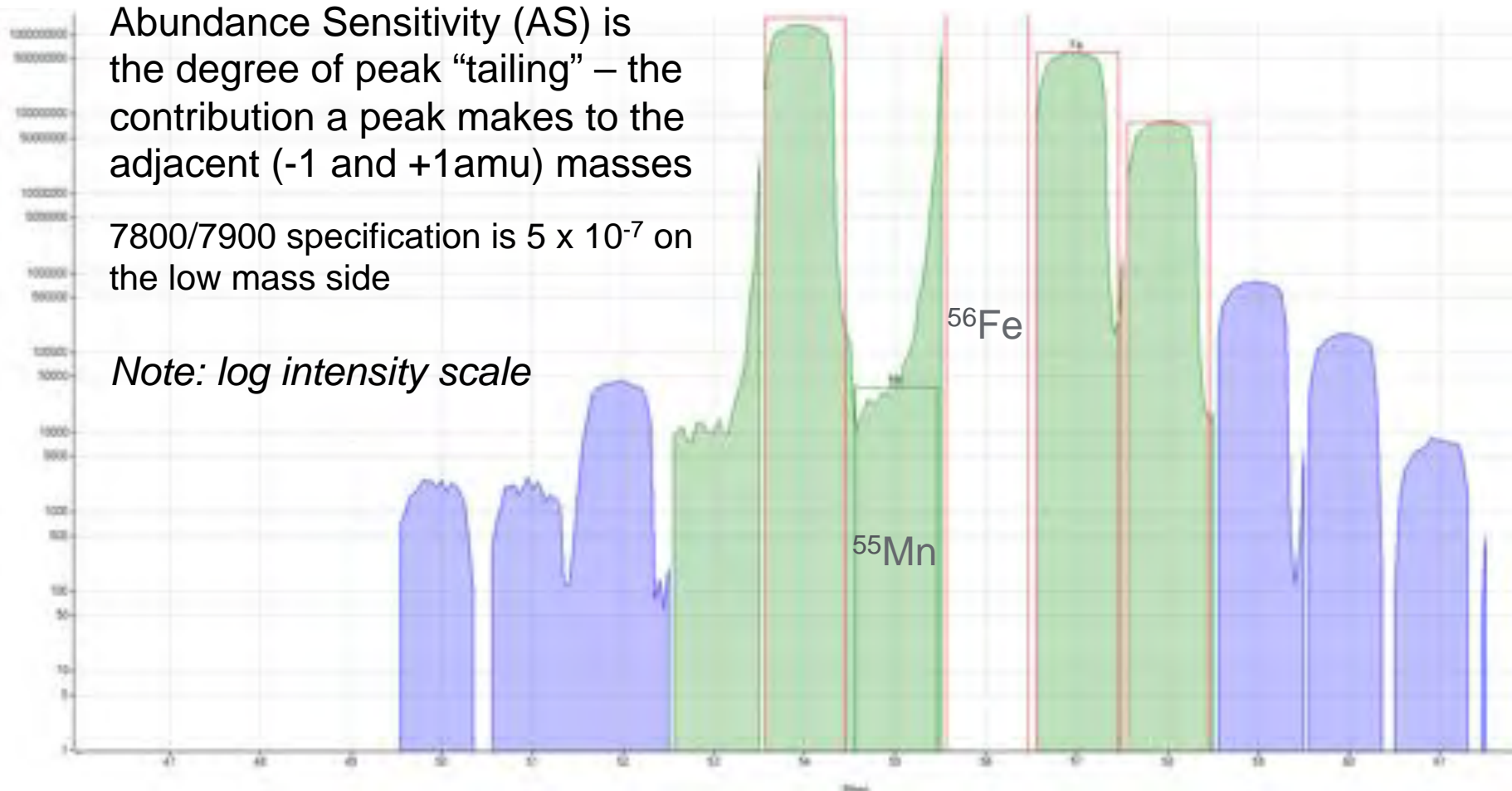


# Why ICP-QQQ? Further Benefit of MS/MS Abundance Sensitivity

Abundance Sensitivity (AS) is the degree of peak “tailing” – the contribution a peak makes to the adjacent (-1 and +1amu) masses

7800/7900 specification is  $5 \times 10^{-7}$  on the low mass side

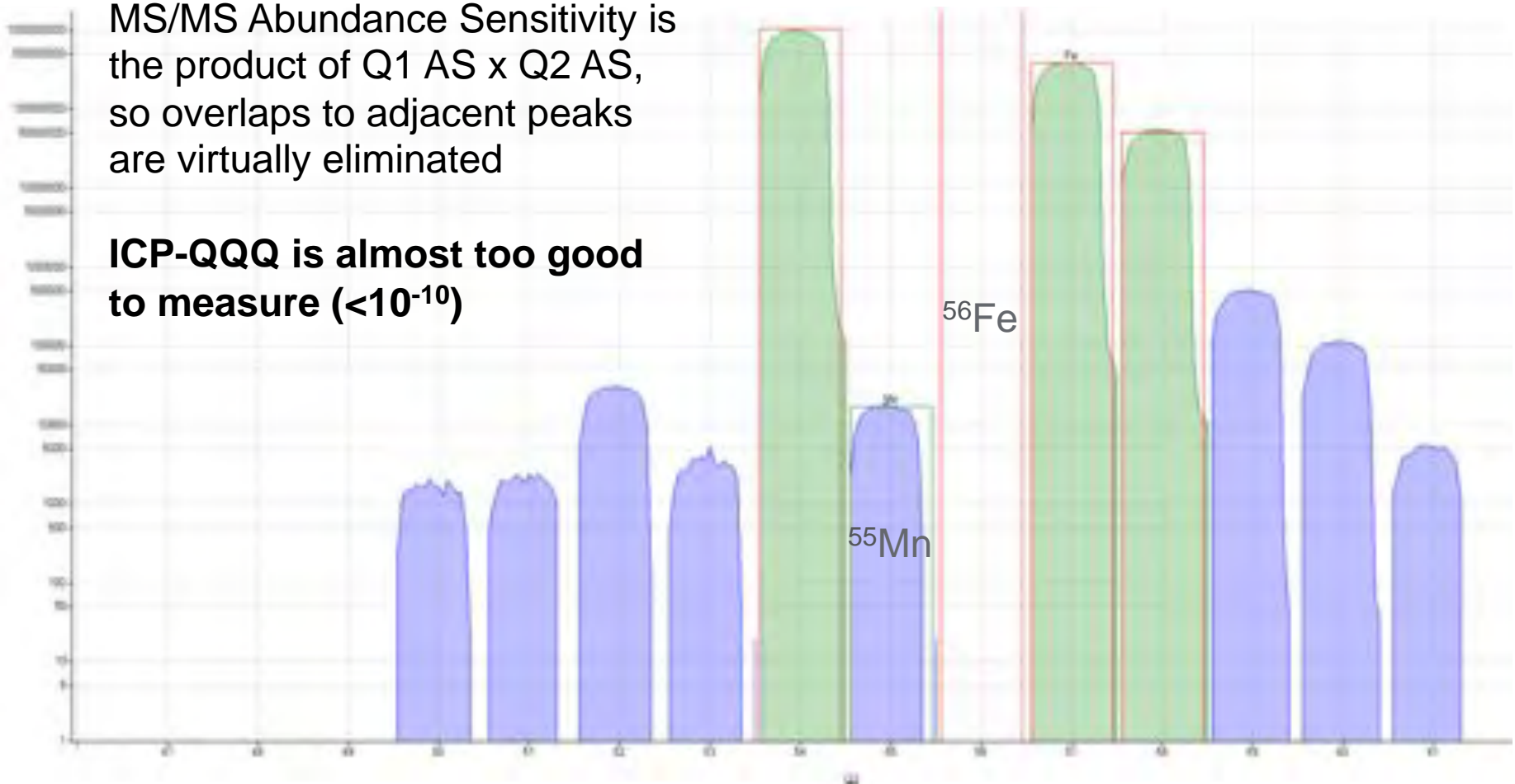
*Note: log intensity scale*



# MS/MS for Improved Peak Separation Dramatically Better Abundance Sensitivity

MS/MS Abundance Sensitivity is the product of Q1 AS x Q2 AS, so overlaps to adjacent peaks are virtually eliminated

**ICP-QQQ is almost too good to measure ( $<10^{-10}$ )**



# Abundance Sensitivity (AS) in ICP-MS and ICP-MS/MS

The AS of a typical single quadrupole ICP-MS is  $\sim 10^{-7}$ . It means a peak of  $10^7$  cps would contribute 1 cps to the neighboring peaks

Overall AS of **tandem MS** is the product of the AS of the two mass filters – **Q1 AS x Q2 AS**

- On the Agilent 8900 ICP-**QQQ** with two 1 u mass filters, this is  $10^{-7} \times 10^{-7} = 10^{-14}$
- This means a peak of  $10^{14}$  cps contributes **ONLY** 1 cps to the masses either side
- ICP-MS/MS is easily able to measure a trace analyte adjacent to a major element peak

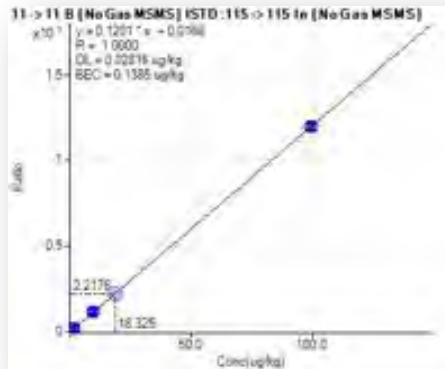




# Practical Benefits of Superior AS of ICP-MS/MS

Example applications where the better abundance sensitivity of MS/MS allows interferences to be resolved that cannot be done by SQ (or Bandpass):

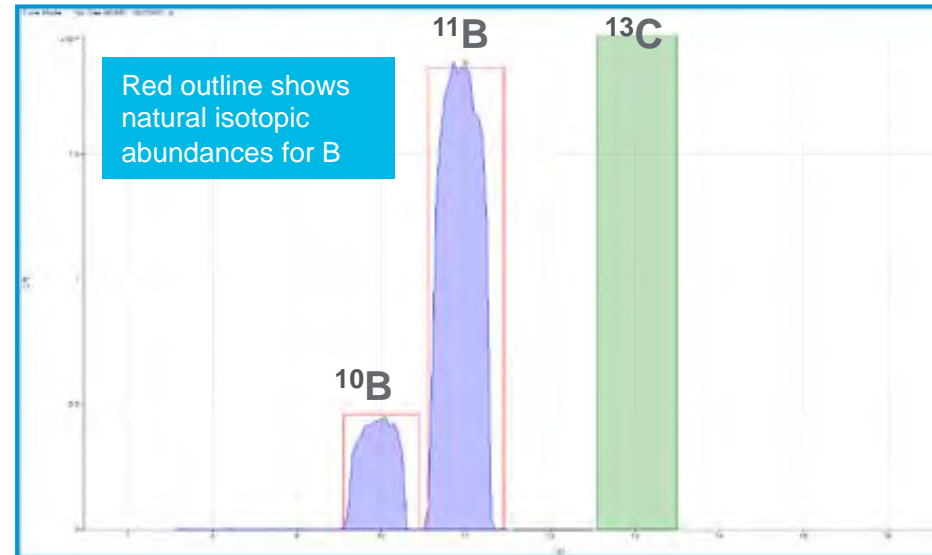
- Mn in high Fe matrix (iron, alloys, whole blood)
- $^{237}\text{Np}$  in U matrix
- B in organics ( $^{11}\text{B}$  is the major isotope, but is overlapped by the tail from the  $^{12}\text{C}$  peak)



Low ppt DL for B (left) & perfect isotope fit for B isotopes (right) in xylene using MS/MS on the Agilent 8900

Example of benefit of improved AS with MS/MS: Resolution of B isotopes from C in organic solvents (xylene)

$^{12}\text{C}$  peak is over-range



# Some Basics – Operational Modes

## Single Quad

- Q1 opens allowing all ions into ORS

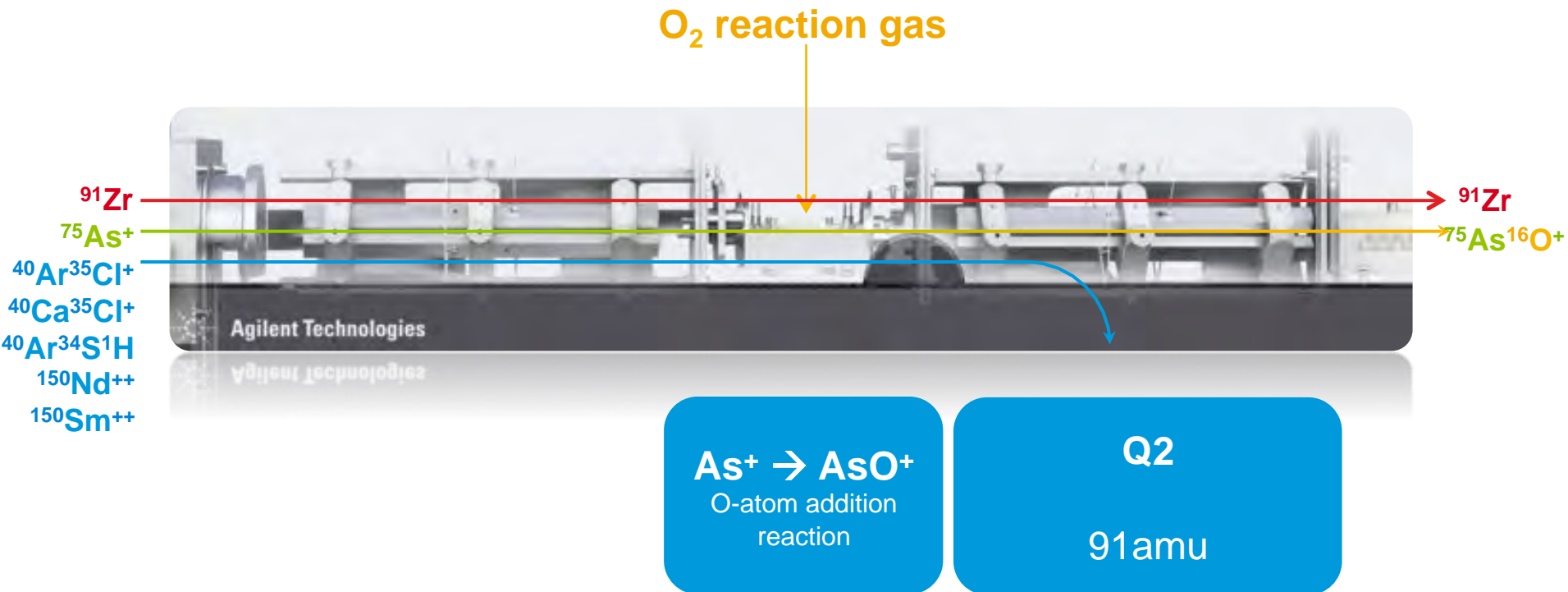
## MS/MS – On Mass

- Both Q1 and Q2 set to same mass

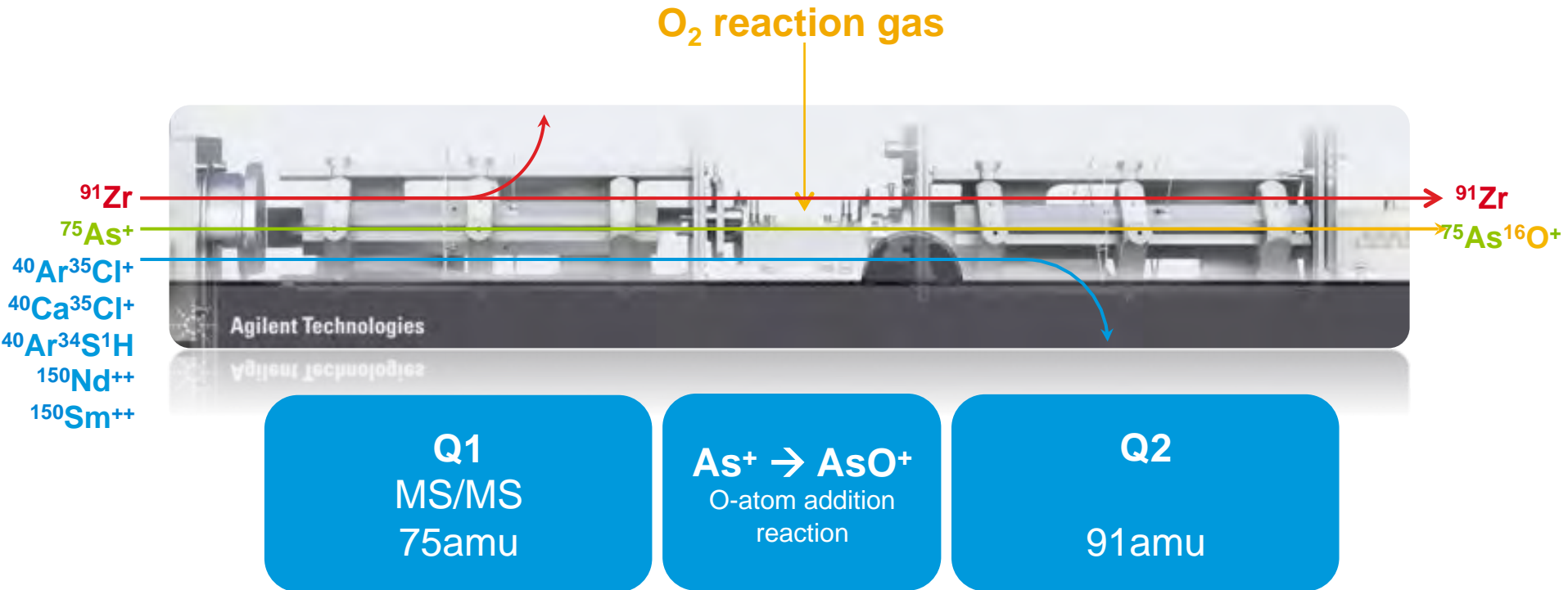
## MS/MS – Mass Shift

- Q1 and Q2 set to different masses

# Mass Shift Mode: Arsenic determination with ICP-QQQ



# Mass Shift Mode: Arsenic determination with ICP-QQQ



Q1 eliminates all off-mass species before they can enter the CRC  
This eliminates any reaction by-products before they form

## Application Example: Sulfur Analysis

Previously difficult element for quadrupole ICP-MS

Sulfur analysis is of interest in many research and commercial laboratories

- Pharma and biopharma (sulfur-containing drugs)
- Life sciences research (protein/peptide quantification)
- Petroleum (fuels) and petrochemicals industry
- Environment (soil, plants, water, air quality)
- Food (preservatives, flavor/fragrance)

**Reaction process is O-atom addition: S measured as  $\text{SO}^+$  product ions, i.e.  $^{32}\text{S}$  measured as  $^{32}\text{S}^{16}\text{O}^+$  at m/z 48**

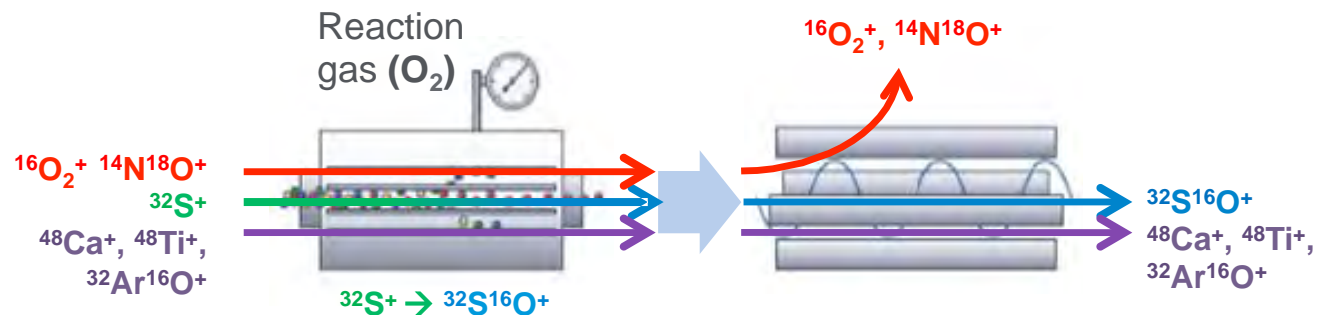
# Application Example: Analysis of Sulfur by ICP-QMS Mass-Shift with O<sub>2</sub> Reaction Gas

*Sulfur is measured as SO<sup>+</sup> using oxygen (O<sub>2</sub>) cell gas with ICP-QMS.*

*O<sub>2</sub> reaction mode can avoid <sup>16</sup>O<sub>2</sub><sup>+</sup> and <sup>14</sup>N<sup>18</sup>O<sup>+</sup> overlaps on <sup>32</sup>S<sup>+</sup>:*



*but SO<sup>+</sup> product ion at m/z 48 can be overlapped by <sup>48</sup>Ca<sup>+</sup>, <sup>48</sup>Ti<sup>+</sup>, <sup>36</sup>Ar<sup>12</sup>C<sup>+</sup>*



No Q1 - all ions  
enter the cell

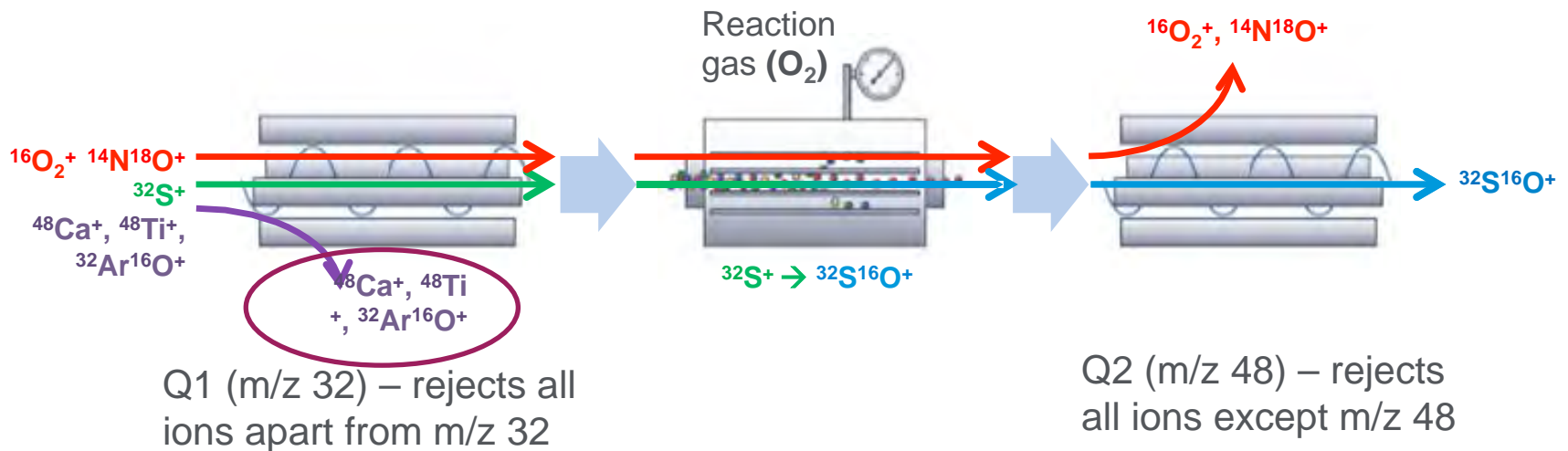
Conventional ICP-QMS has no mass filter before the cell, so cannot reject existing interferences that overlap cell-formed analyte reaction product ions

# Application Example: Analysis of Sulfur by ICP-QQQ MS/MS Mass-Shift with O<sub>2</sub> Reaction Gas

Same reaction with O<sub>2</sub> cell gas for S on 8900 ICP-QQQ with MS/MS:



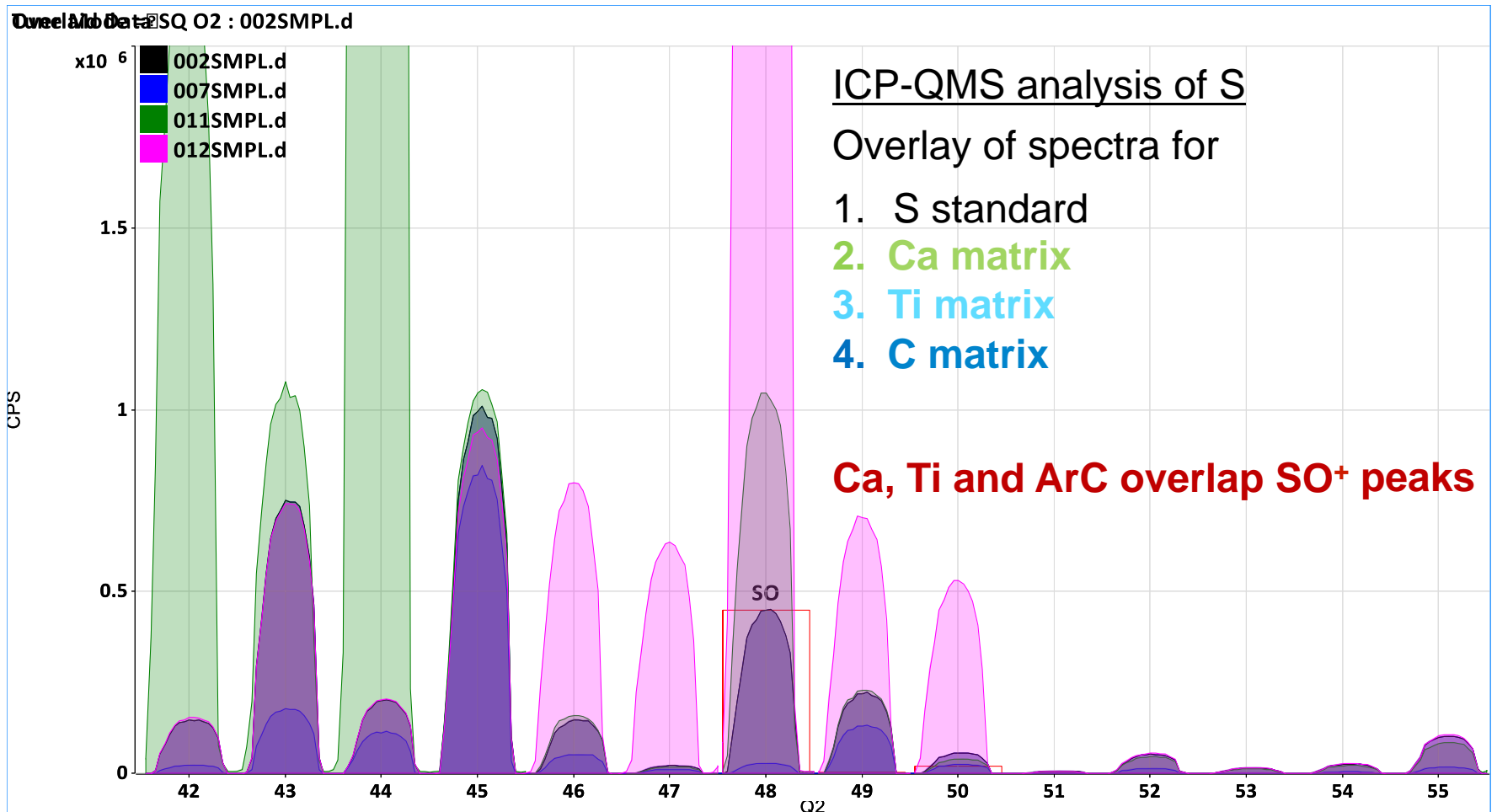
**BUT** Q1 of 8900 rejects any ions (Ca<sup>+</sup>, Ti<sup>+</sup>, ArC<sup>+</sup>) that could overlap SO<sup>+</sup> product ion at mass 48



Allows measurement of SO<sup>+</sup> at product ion mass, after removal of original O<sub>2</sub><sup>+</sup>/NO<sup>+</sup> interference, and existing ions at SO<sup>+</sup> product ion mass

# Measurement of Sulfur by ICP-QMS

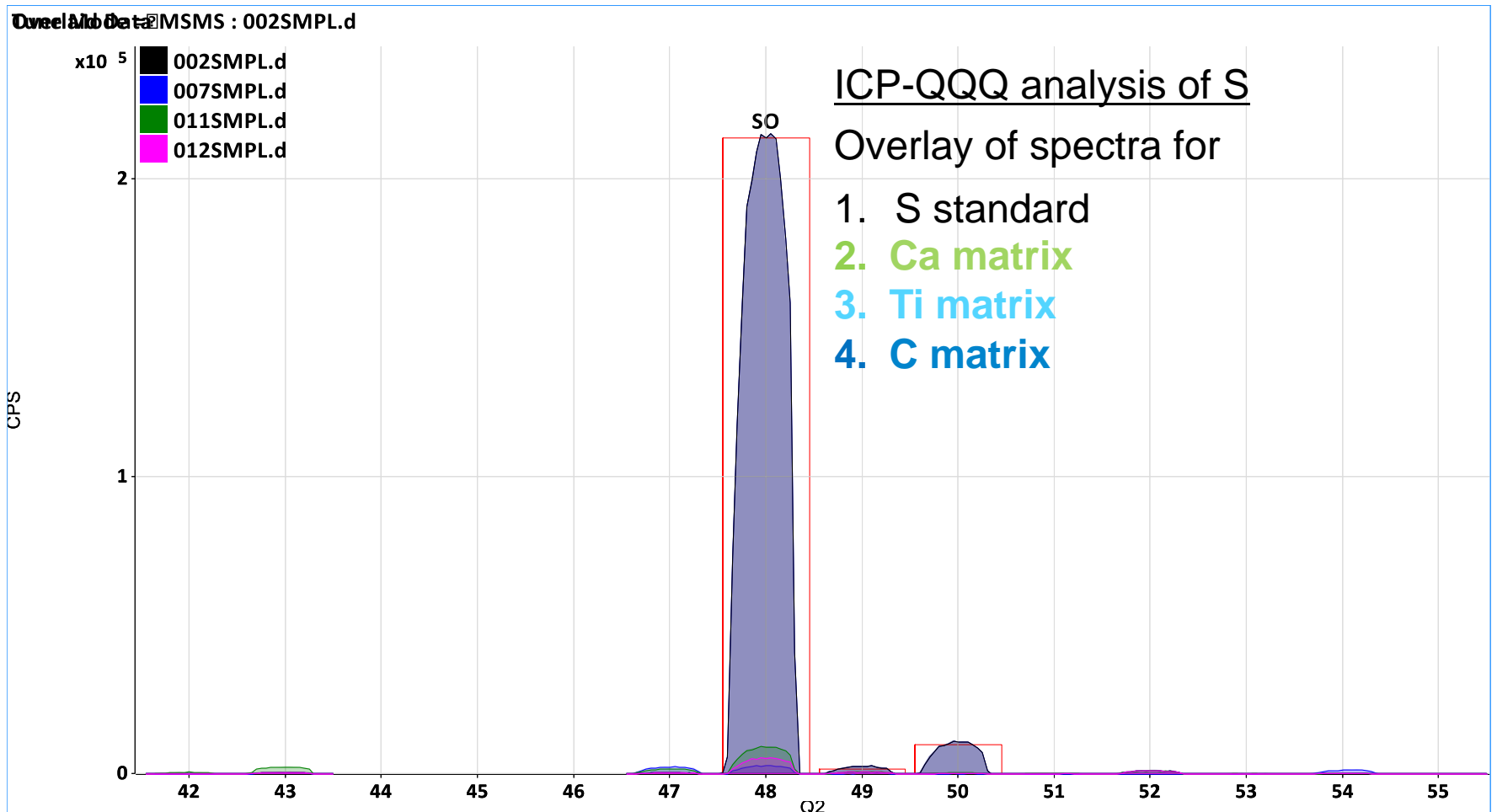
## S standard overlaid with Ca, Ti and C matrix





# Measurement of Sulfur by ICP-QQQ

## S standard overlaid with Ca, Ti and C matrix



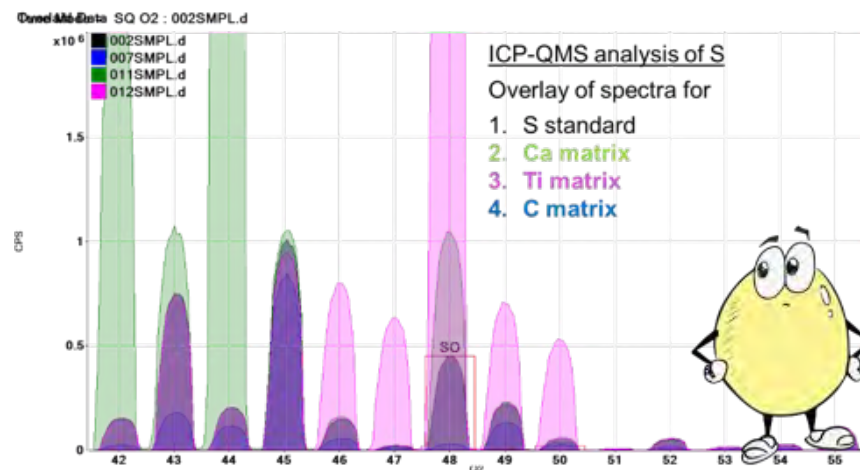
# ICP-QQQ; The Benefit of MS/MS is Clear

Sulfur measured as  $^{32/33/34}\text{S}^{16}\text{O}^+$  (Q2 set to Q1 + 16 amu)

## Top – “Single-Quad” Bandpass Mode

All masses between ~ 15 amu and 65 amu enter the cell, so other ions ( $\text{Ca}^+$ ,  $\text{Ti}^+$ ,  $\text{ArC}^+$ ) contribute to signal at  $\text{SO}^+$  isotope masses.

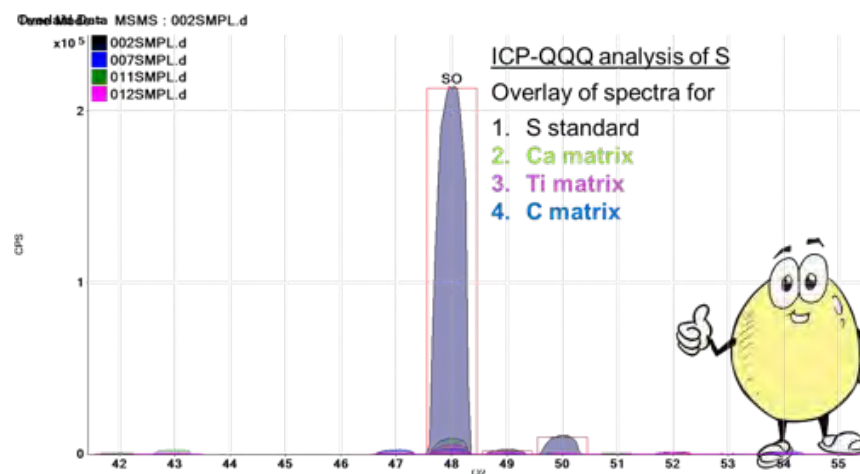
Results are unreliable; ALL S isotopes are interfered, and the interferences on the different S isotopes are matrix-dependent



## Bottom – Agilent ICP-QQQ in MS/MS Mode

$\text{SO}^+$  peaks match the theoretical isotope abundance template in all samples.

All S isotopes are interference-free; secondary isotopes can be used for confirmation, or for isotopic analysis (isotope ratio or isotope dilution)



# ICP-QQQ – Typical Applicative Markets

