



# Principles of ICP Tandem Mass Spectrometry (ICP-MS/MS)

Agilent ICP-MS technology brief

## Origin of ICP tandem mass spectrometry:

Tandem mass spectrometry—or MS/MS—is a well-known and widely used technique in organic mass spectrometry, where it is used to study the structure of organic molecules. Various MS/MS configurations exist, of which triple quadrupole MS (QQQ, or TQ) is the most relevant to ICP-MS.

According to IUPAC (1), the term “triple quadrupole” refers to any tandem mass spectrometer that includes two quadrupole mass filters separated by a collision/reaction cell containing a multipole ion guide. In an organic QQQ MS, the first quadrupole, Q1, selects the mass of the precursor ion of interest, which passes through to a collision cell for fragmentation. The resulting fragments are then selected by a second mass analyzer, Q2 (or Q3, if a quadrupole ion guide is also used in the cell) and passed to the detector.

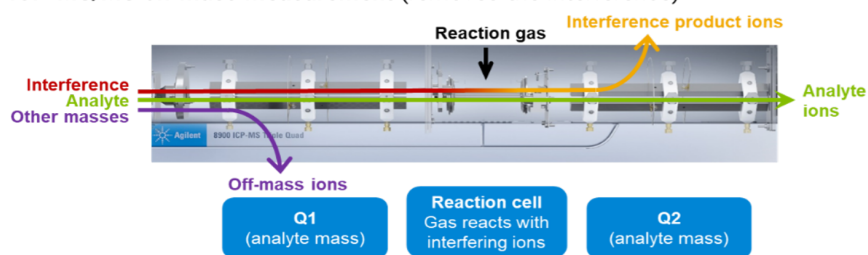
First commercialized by Agilent in 2012, ICP-QQQ measures elemental ions, so the analyte (precursor) ions are not fragmented. Instead, the cell of an ICP-QQQ is typically filled with a reactive gas, and ion-molecule reactions are used to separate the analyte ions from any on-mass spectral overlaps. ICP-MS/MS uses the differences in the reactivities of the analyte ions and the interfering ions, with the chosen reaction gas.

## ICP-MS/MS principles of operation

An ICP-QQQ can be used with Q1 operating as an ion guide, i.e., “Single Quad” mode. Under these conditions, the ICP-QQQ works like a conventional single quadrupole ICP-MS, which can be useful for labs that perform a mix of routine and more advanced ICP-QQQ applications.

But the main benefit of the QQQ configuration is that both quadrupoles can be operated as 1u mass filters (MS/MS mode). In MS/MS mode, Q1 selects the specific mass of ions that can pass to the reaction cell, so the ion-molecule reactions are independent of the sample composition (2). This eliminates the uncertainty and variability seen with reactive cell gases on single quadrupole (or bandpass) ICP-MS systems. ICP-MS/MS resolves interferences using either on-mass measurement or mass shift measurement, both shown in Figure 1.

### ICP-MS/MS on-mass measurement (removes the interference)



### ICP-MS/MS mass-shift measurement (avoids the interference)

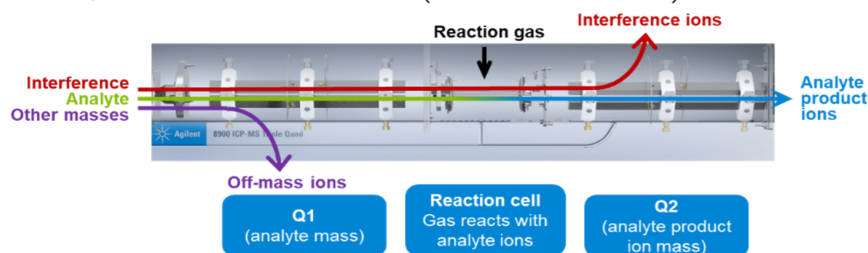


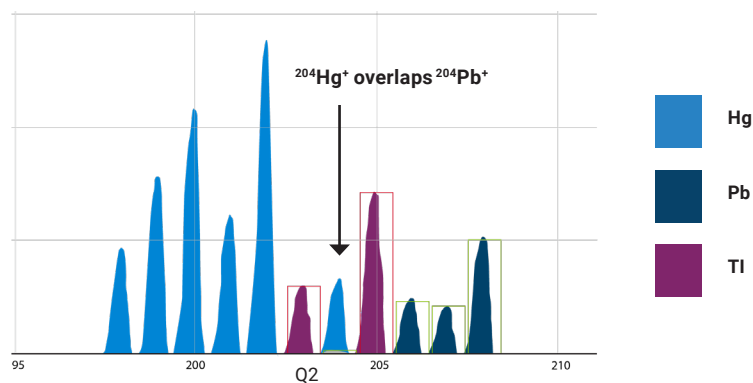
Figure 1. ICP-MS/MS measurement modes. Top: On-mass; Bottom: Mass-shift.

## MS/MS reaction mode application examples

**On-mass** mode uses a reaction gas to separate unreactive analyte ions from reactive interfering ions. Both Q1 and Q2 are set to the mass of the analyte (precursor) ion. Examples of on-mass measurement include using  $\text{NH}_3$  cell gas to separate  $\text{V}^+$  from the intense  $\text{ClO}^+$  interference in high purity HCl (3).  $\text{NH}_3$  cell gas can also separate  $\text{Cr}^+$  from the intense  $\text{ArC}^+$  polyatomic in high purity solvents. In both cases, the interfering ions react by charge transfer with the  $\text{NH}_3$  cell gas. MS/MS controls the reaction chemistry to allow the analytes to be measured at single or sub-ng/L (ppt) levels.

MS/MS on-mass mode with  $\text{NH}_3$  cell gas can also be used to resolve the Hg-204 contribution on Pb-204, as required in some geochronology applications. Figure 2 shows the comparison of the spectra with and without  $\text{NH}_3$  cell gas.

### ICP-MS; no reaction gas



### ICP-MS/MS; $\text{NH}_3$ reaction gas

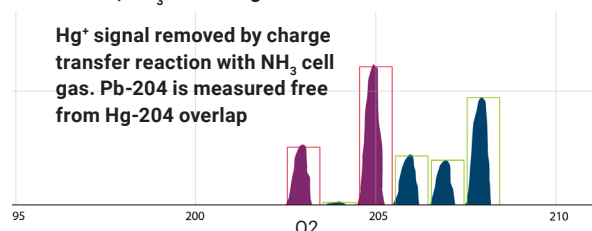


Figure 2. MS/MS on-mass mode resolves Pb-204 from the Hg-204 overlap.

**Mass shift** mode uses a cell gas that reacts with the analyte ions to form new reaction product ions at a different mass. Q1 is set to the mass of the analyte (precursor) ion and Q2 is set to the mass of the analyte reaction product ion. Mass shift mode avoids the interference as the interfering ions are unreactive, so they remain at their original mass and are rejected by Q2.

Examples include using  $\text{O}_2$  cell gas to avoid the intense polyatomic ion overlaps on P and S, allowing trace-level analysis of these previously difficult analytes. The main interference on S-32 is  $^{16}\text{O}_2$ , formed from the oxygen in aqueous solutions and air that enters the plasma.  $^{32}\text{S}^+$  ions react with the  $\text{O}_2$  cell gas to form  $\text{SO}^+$  product ions at mass 48, avoiding the  $\text{O}_2^+$  interference.  $\text{SO}^+$  can be measured by single quadrupole ICP-MS, but existing ions at mass 48 cause errors. Using MS/MS, these existing ions are rejected by Q1 (set to mass 32), allowing  $\text{SO}^+$  to be measured without overlap, as shown in Figure 3.

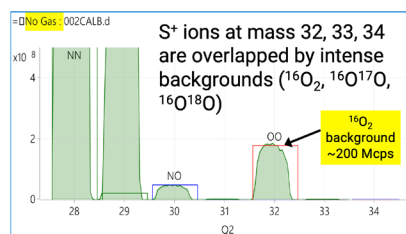
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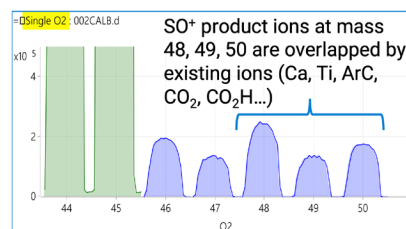
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### ICP-MS: $\text{S}^+$ cannot be measured at mass 32



### ICP-MS: $\text{SO}^+$ cannot be measured at mass 48



**ICP-MS/MS: S** can be measured at low level as  $\text{SO}^+$  product ions (mass 48, 49, and 50). Interfering ions (Ca, Ti, ArC,  $\text{CO}_2$ ,  $\text{CO}_2\text{H}$ ...) are removed by Q1, set to  $\text{S}^+$  precursor ion mass (32, 33, 34).

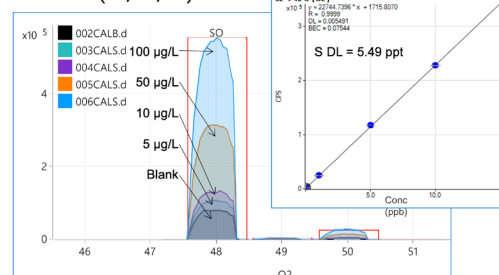


Figure 3. Top: Single quadrupole ICP-MS cannot resolve interferences on S. Bottom: MS/MS mass shift with  $\text{O}_2$  cell gas enables reliable trace level S analysis.

## Conclusion

ICP-MS/MS enables the full capability of reactive cell gas methods to be realized. Using an appropriate cell gas and on-mass or mass-shift measurement, novel applications can be addressed, and previously problematic interferences can be resolved reliably.

## References

1. Pure Appl. Chem., Vol. 85, No. 7, pp. 1515-1609 (2013)
2. Handbook of ICP-QQQ Applications using the Agilent 8800 and 8900, 5th Edition, 2022, Agilent publication [5991-2802EN](#)
3. Agilent ICP-MS Journal issue 84, [5994-3239EN](#)

