

Expedited Troubleshooting Article

Determination of Quadrupole Charging in MS/MS Instruments

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Ion Optics

The ion optics of a MS/MS detector can be referred to as the lens and quadrupoles that compose the ion path that guide and focus the ionized molecules from the first quadrupole to the electron multiplier

Introduction

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS) has rapidly become the analytical technique of choice for the quantification of drugs in biological fluids. Its lower limits of quantification and the high selectivity compared with UV or fluorescence detection have made it an obvious choice. However, along with its utilization, the problems related to MS/MS detection are much more complicated. Among these, loss of sensitivity over time is one of the most frequent. The intensive use of the instrument, the lack of sample preparation and the inadequate system utilization are not unfamiliar to this problem. These reasons are frequently due to interface and ion optics contamination over time and as a result the instrument is less optimal and can require maintenance. Occasional and sometime misinterpreted as interface contamination, charging issue can be the source of the problem. Indeed, the importance of being able to identify and distinguish both problems is important to adequately troubleshoot and clean the instrument accordingly.

Over time particulates that enter the mass spectrometer may start to settle somewhere on a quadrupole and accumulate a charge affecting the efficacy of the ion optics. The ions of interests that go through the detector will be diminished since more ions will collide with the charged lens/rods of the quadrupole resulting in a loss of system sensitivity.

To demonstrate the problem, the MS/MS signal of internal standard was plotted over time in Figure 1. The figure clearly illustrates the pattern variation of a contaminated ion optic. In this example, the signal decrease by approximately 4-fold (from 3.4E4 to 8.0E3) during a batch injection of 100 samples. Since

interface contamination and charging can manifest such a loss of sensitivity over time, and over a short period of time, it became important to define the root cause of this sensitivity issue prior to cleaning the instrument.

Identifying Charging vs. Interface Contamination

As shown in Figure 1, if a constant sample (reference) is injected, the first symptom of contamination is a loss of signal over time. Nonetheless, the main approach to identify and locate charging in a mass spectrometer is to change the polarity of the method. The inversion of the polarity can remove ions that accumulate onto the ion optic and restore the original sensitivity for a short period of time. For example if the method uses a positive mode, infuse or inject a reference sample in negative mode and then return to the original mode. You should, at this point, get back most of the sensitivity lost during injection. Indeed, if a particulate accumulates a charge over time in positive mode, it is likely to get rid of that same charge in negative mode. Therefore it should be easy to locate and identify charging in the detector. If no modification in signal intensity is observed, chances are that you have interface contamination (contamination found before the first quadrupole, i.e. orifice, focusing ring, and skimmer). Interface contamination may also be confirmed with standard calibration solution.

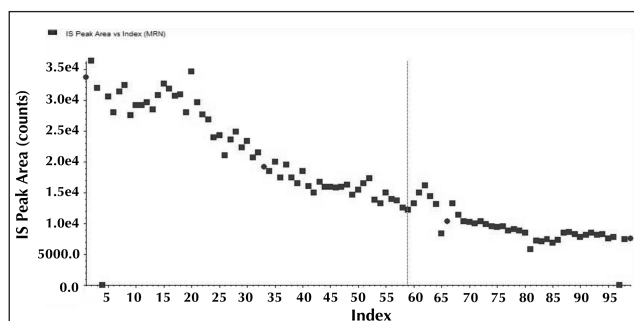


Figure 1. Drop in IS response, reaching plateau after 100 injections (4 min runtime). Very serious case, as the sensitivity loss occurs over 5 hours.

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Below is a step-by-step troubleshooting procedure created for an API3000™, manufactured by AB/Sciex™. Also note that the same logic and testing can be applied to a different configuration or type of MS instrument.

- Create a Q1 positive calibration method, and infuse the appropriate standard solution related to your instrument (e.g. PPG solution for AB/Sciex™).
- Start scanning for at least 10 minutes, monitoring the total ion count for your selected mass. (Mass 906 amu is usually used with an AB/Sciex™ instrument). If charging occurs, you should notice a decline in sensitivity over time (5 to 10 min).
- Change the polarity to negative mode and start scanning for a minute or so.
- Reopen the Q1 positive calibration method; start scanning for at least 10 minutes. The total ion count should start high, and decreases with approximately the same pattern as previously observe in the first Q1 scan. This indicates charging.
- Do the same test with the Q3 positive calibration method.
- If charging occurs for both Q1 and Q3, it is very likely that the charging is coming from the interface or the Q0
- If charging occurs only for Q1 and not for Q3, then is the region the charging is most likely occurring.

It's very unlikely to find charging in the Q3 region, since the quadrupole is very far from the sample introduction source and does not require cleaning as often (if at all). With this troubleshooting method, you should be able to confirm the charging diagnosis, and direct your efforts toward the affected area.

Cleaning Technique

The cleaning technique will of course depend on the source and the nature of the contamination. In the case of charging, some will clean the Q0 rod directly on the instrument; for a more serious case where Q1 and/or Q3 might be affected, disassembly of the ion optic is necessary. This is not an easy task, and should be left to well trained/qualified personnel only.

The first step prior to cleaning is to break the vacuum of the instrument in order to clean the instrument. That being said, a general approach should include at least a successive cleaning of the parts with solvents of different polarities. You can either clean them with gentle materials (e.g. Kim wipes) or immerse them completely in the solvents below (note that the use of ultrasonic bath may also help the cleaning procedure):

1. Hexane 100%
2. Acetonitrile–water 50:50 (% v/v) with 0.1% formic acid
3. MeOH–water 50:50 (% v/v)
4. MeOH or isopropanol

Finally, prior to re-installation, thoroughly dry the part with a flow of clean, ultra-pure gas (nitrogen or air). The detector should be allowed to pump down overnight to ensure that no residual solvent from the cleaning is present. Following this period, a system calibration is essential before using the instrument again since some of the electronic components may have been affected during disassembly and reassembly of the optic rail. Those changes can result in inadequate mass assignment or bad peak width.

In case of contamination, the cleaning is usually limited to the interface. Depending on your level of expertise you can remove the entire interface to get a nice cleaning of the back of the orifice, focusing ring and the skimmer; the Q0 rods can also be wiped with methanol at this point. Again make sure all your parts are dry before reassembly and let the system pump down for a few hours before you verify the sensitivity with you usual calibration standard.

Conclusion

As discussed, the key to troubleshooting the loss of sensitivity is to have the right knowledge in diagnosing the problem at hand. We have summarized how to diagnose the problem between interface contamination and quadrupole charging, and how to test your system and then how to use the most efficient cleaning technique in these situations. These are only two of many reasons (e.g. a defective ion source, bad source position etc.) why an instrument can lose sensitivity over time, but keep in mind that good instrument maintenance and proper use are the best tools to keep your system sensitive, reliable and optimal.

Acknowledgements

The authors would like to thank Milton Furtado, Jean-Nicholas Mess and Natasha Savoie for their help and valuable advice during the review of this manuscript.

Financial and Disclosure Competing Interests

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matters or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending or royalties. No writing assistance was utilized in the production of this manuscript.

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