

Changing the Landscape of Mass Detection in the Chromatography Lab

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INTRODUCTION

Traditionally, mass spectrometry (MS) instruments have been marketed for use by MS experts and have not played a major role in most chromatography laboratories. However, the advent of smaller more accessible mass detectors has brought MS data within the reach of the chromatographer. This whitepaper discusses how the landscape of the chromatography laboratory is changing, how the value of mass data can be realized by the chromatographer, and how a chromatography data system (CDS) should utilize the power of mass detection and mass data in the modern chromatography laboratory.

THE MS DETECTION LANDSCAPE

Traditionally, MS has been performed by a MS specialist, on research instruments whose access was limited. Analysts would submit samples to the MS specialist who would run the samples, interpret the results and pass the data back. Access was usually limited because the MS specialist was doing research on MS itself and wasn't always amendable to running samples in a timely fashion. Most chromatographers would never actually get access to the instruments, or often times even the MS specialists themselves. Data collection and analysis was usually performed by software separate from CDS software on dedicated workstations and sometimes processed on a separate computer. Instruments were large; their footprint often took up an entire room and were very expensive as well. However, over the last couple of decades the landscape has evolved as more and more chromatographers have started to use MS detection in their laboratories.

Empower® Chromatography Data Software (or Millennium® as Empower used to be called), first integrated MS technology over 20 years ago but at that time the technology was still very much aimed at MS specialists. Since then, single quadrupole, and later triple quadrupole instruments, were added to the Empower family but were still mostly designed for use by MS experts. That all changed when a MS instrument aimed at chromatographers, the ACQUITY® QDa® Mass Detector was introduced by Waters in 2014. With its introduction, the assumption was that the person using it would be a chromatographer without any real significant experience in mass spectrometry, as opposed to a MS specialist. In 2016, with the inclusion of the SQ Detector 2 Mass Detector into Empower, Waters demonstrated for the first time that chromatographers and MS specialists could coexist, by providing a sophisticated MS instrument that could be used by chromatographers and MS specialists alike. Today there is a broad range of different instruments and uses within both the chromatography and analytical laboratory in general. There are still specialists working in research laboratories with large, costly MS systems, but there are also smaller footprint systems in use by chromatographers in development and even QC laboratories.

MS systems can place considerable demands on a CDS. Quite often a CDS is part of a network environment with centralized data storage that must allow access to many people, and being able to deal with a large amount of data also becomes more critical.

While MS instruments have become more powerful, they've also become more compact and with a smaller footprint comes a reduction in initial purchase and ownership cost. The net result is that MS detection plays a much broader role in today's laboratories.

MS DETECTION AND THE CHROMATOGRAPHER

People using MS detection have a wide range of skills, requirements and expectations. An analyst skilled in the art is going to have a very different set of requirements and expectations when compared to an analyst that interacts only occasionally with MS. Some analysts may require full, in-depth access to MS data. They expect to be able to interact with the software and to be able to access the data exactly when needed and be able to drill down into the details or "mine" the data to get the required results. Another type of

analyst may come from a background that includes frequent MS use, but is now working in a chromatography environment. This type of analyst will require a good understanding of the MS data, but in their environment it is possible that the MS data is more of a subset of a full data set because they already have a very good idea of exactly what is needed and what they need to do. There is also the occasional user that may have a reasonable understanding of what MS data is required from following existing methods, resulting in a limited data set. Finally, there is another group of analysts that view MS detection as just another tool or detector to be used in the laboratory.

MS detection can also be considered from two different perspectives based upon the MS experience level of the analyst. The ACQUITY QDa has been designed specifically as an accessible LC detector providing mass information. Analysts familiar with UV and photodiode array (PDA) detectors can adopt mass detection without extensive training as user interactions and instrument maintenance and features have been specifically implemented with them in mind, as illustrated in Figure 1.

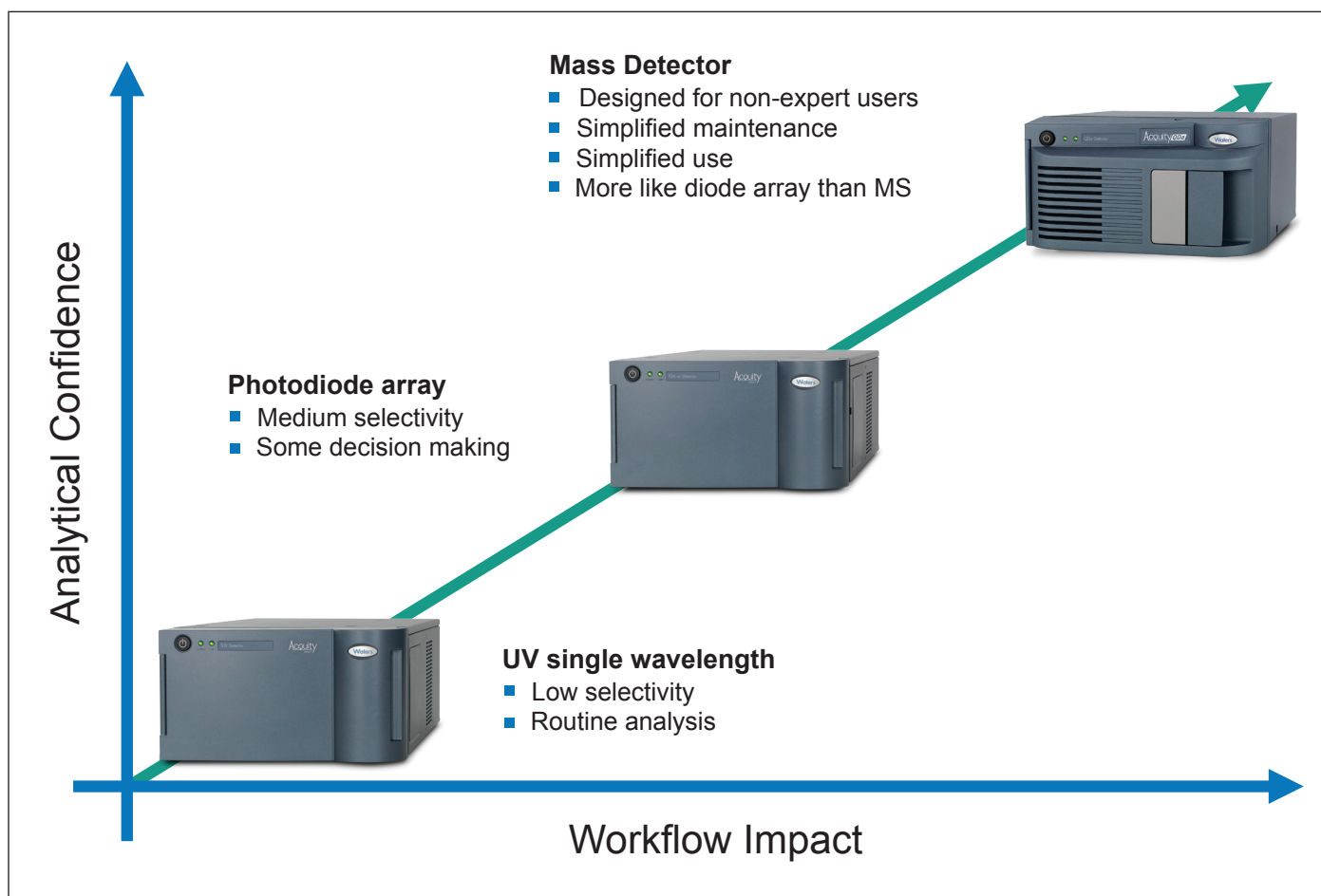


Figure 1. Non-MS user.

The ACQUITY QDa plugs into existing workflows and is seamlessly integrated into the system making adoption far easier for chromatographers to use as a complimentary detector. In much the same way that the PDA increased confidence in UV data the mass detector adds complimentary data to bring confidence to another level. For analysts with

an MS back ground there are occasions where their skills and expertise can be incorporated into methods by transferring them to a mass detector for use in a routine lab, benefiting non-MS users by making the data more accessible and more affordable for routine work, as highlighted in Figure 2.

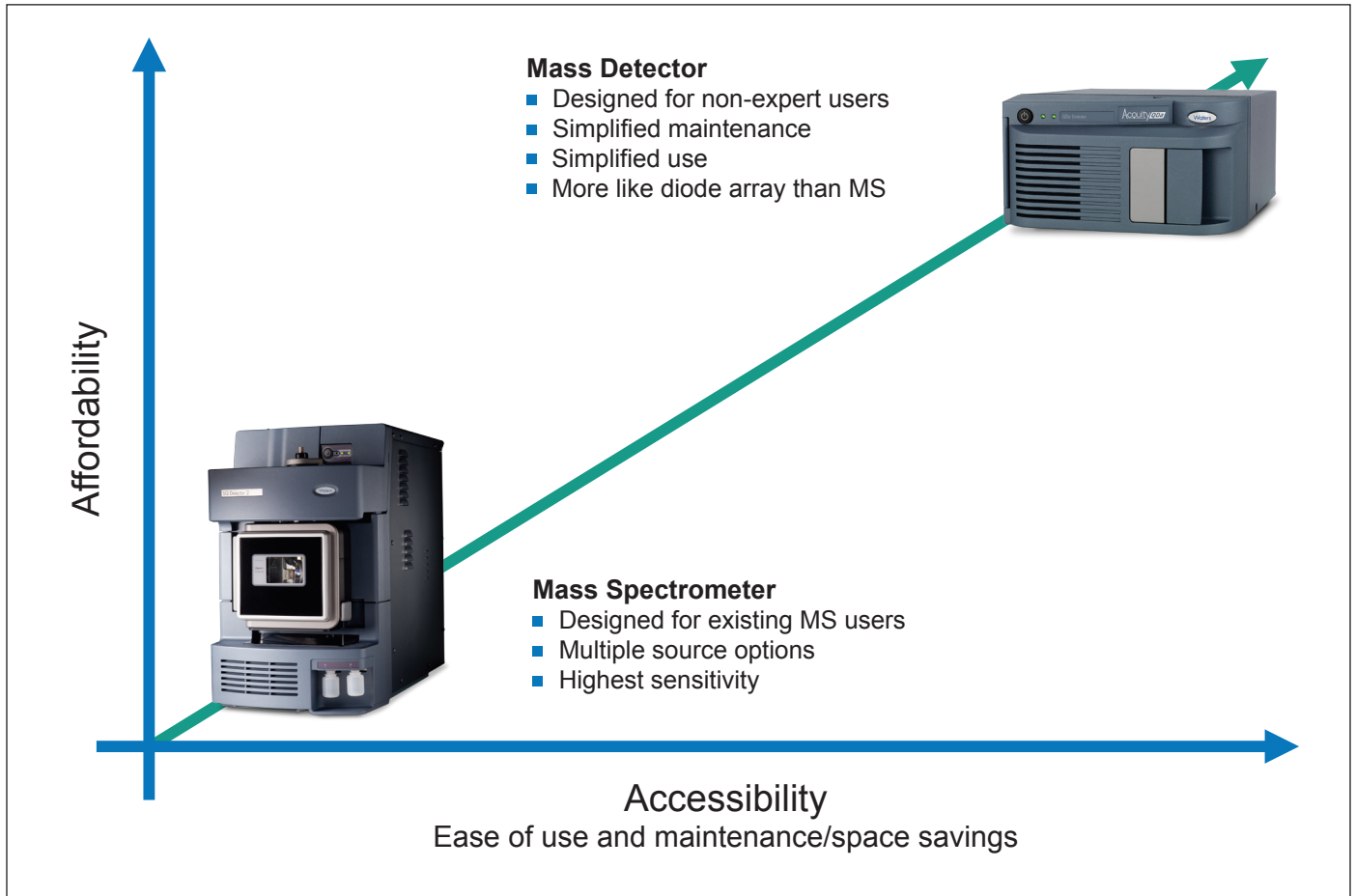


Figure 2. MS users.

WORKFLOW ADVANTAGES

For chromatographers, it is a natural extension to use a mass detector in routine work. However, for mass spectroscopists, the SQ Detector 2 extension to the Waters mass detection product line was a welcome addition by providing access to multiple sources, increased sensitivity, and an increased mass range. For any user, regardless of skill level or experience, MS detection can provide significant workflow advantages. During method development, MS peak tracking, as chromatographic selectivity is manipulated becomes more robust compared to PDA spectra, and allows the analyst to be more confident in their data leading to better methods. When developing a method, as the conditions change the

chromatograms change: peaks can move, change shape, height and area, and even their UV spectra can change. Having an assigned mass and being able to track the peaks using the assigned mass, as shown in Figure 3 allows for better and faster method development. In the stability testing laboratory, being able to observe and identify trace-level peak responses to compare data across different time points and storage conditions can lead to a better understanding of degradation pathways and more accurate shelf-life predictions. Figure 4 demonstrates how adding MS detection to the evaluation of an impurity profile can help to identify even small peaks, like that on the left of the chromatogram.

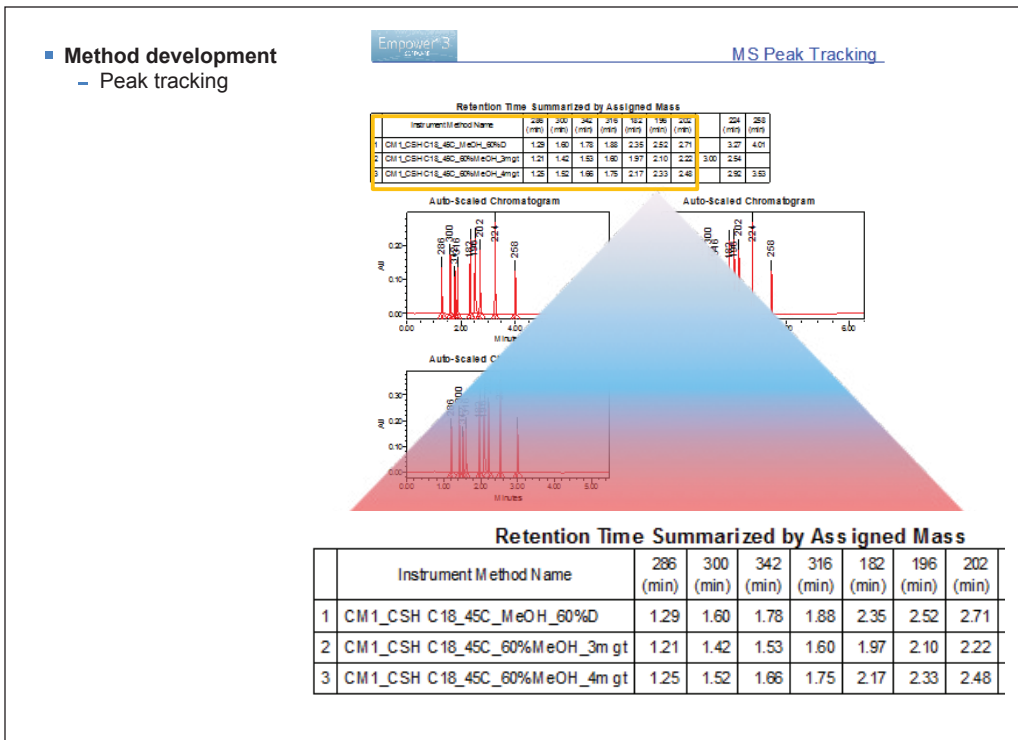


Figure 3. Method development.

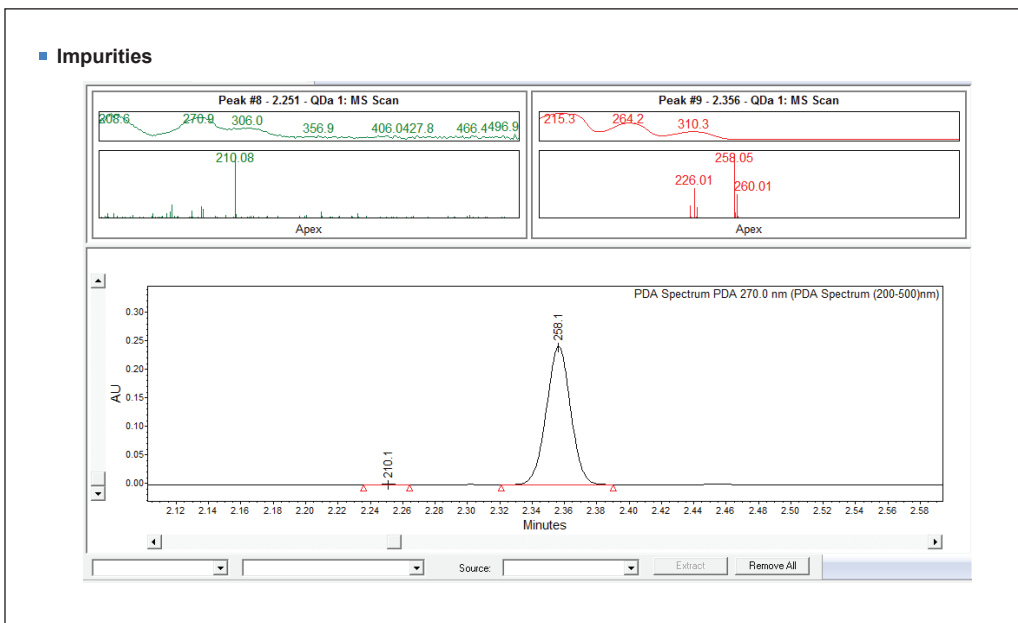


Figure 4. Impurities.

Using the Empower CDS, MS, and UV spectra can both be reported for any peak, further aiding identification. In addition to identification, by looking at spectra collected on the leading, apex, and tailing portions of any peak, co-elutions can be detected.

THE ROLE OF SOFTWARE IN MS DETECTION

Software provides an interface with the instrument for data acquisition. At the most basic level, software must be capable

of carrying out normal functions such as instrument control and data acquisition and it must be able to process and report the data. In many cases it must also be able to meet various compliance and regulatory requirements. But how do analysts know that they have the data they need when they need it, and in the proper form? The answer lies in tailoring the solution, often depending upon whether the analyst is a frequent or occasional user, as each user type will have different data and processing requirements.

It is the role of the software to provide the right level of data at the right time while streamlining the workflow allowing the chromatographer to be as efficient as possible. All while providing the right amount of data dependent upon the users' needs at any point in time, which can vary significantly.

CONCLUSION: THE FUTURE OF MS DETECTION

In many ways, the future of MS detection will follow in the footsteps created by the adoption of PDA detection, as analysts become more confident in the data obtained on a regular basis. In the last few years, MS detection has changed from being a tool for a mass spectroscopist in a chromatography lab to being just another detector for the chromatographer. That trend will only continue as the technology continues to evolve. The result of this evolution is that MS is going to become far more accessible to a lot more people. But it must be made accessible in a way that corresponds to expectations according to use and skill levels, and how the system will use the resulting knowledge and present that data. The challenge is to make sure that each user gets what they require out of the system exactly when they need it.

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