Emerging Trends in Liquid Chromatography and Mass Spectrometry Instrumentation for Analytical & Bioanalytical Techniques

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With recent advancement in instrumentation from a variety of researchers and manufactures the use of liquid chromatography (LC) and mass spectrometry (MS) has become a powerful twodimensional (2D) hyphenated technology for the use in a wide assortment of analytical and bioanalytical techniques for the analysis of nucleic acids, amino acids, peptides, proteins, carbohydrates, lipids, and etcetera [1-3] and/or in the main classification of omics fields such as genomics, proteomics, metabolomics, lipidomics, and etcetera [4-7]. This advancement in LCMS was originally and still is fueled by the need for more powerful analytical and bioanalytical techniques that can accurately and precisely discriminate target analytes from high complexity mixtures in a sensitive and selective way. With this in mind, this review will briefly attempt to focus on the most current classifications and emerging trends in LC-MS instrumentation and their respective contributions to the field of analytical and bioanalytical techniques.

Two primary classifications in the use of LC-MS come to mind in the form of discovery and directed analysis of complex samples. With discovery LC-MS taking the form of qualitative types of assays employing ultra performance liquid chromatography (UPLC) coupled to a variety of mass spectrometers that include for example time-of-flight, quadrupole-ion trap, linear-ion trap, Fourier transform ion cyclotron resonance, and orbi-ion trap mass spectrometers (i.e., TOFMS, QITMS, LTITMS, FT-ICRMS, Orbi-ITMS respectively) [8-10], and directed LC-MS taking the form of quantitative types of assays that employ UPLC coupled to mass spectrometers that typically utilize time-of-flight, single quadrupole, and triple quadrupole mass spectrometers (i.e., TOFMS, QMS, QqQMS) [11-13]. These two distinct classifications have now recently become blurred with the emergence of a new hybrid class of LC-MS instrumentation that has the unique ability to do both routine qualitative discovery as well as routine quantitative directed analysis of high complexity mixtures. This hybrid class of LC-MS instrumentation typically takes the form of an UPLC separation system interfaced to two or more mass spectrometers that are placed in series such as a UPLC-QMS/TOFMS, UPLC-QITMS/TOFMS, UPLC QqQMS/TOFMS, or UPLC-QqQMS/LITMS system [9,10,14,15].

The combination of this hybrid class of LC-MS to do both routine qualitative discovery and quantitative directed analysis of complex mixtures is perhaps one of the most significant combinations of developments in separations and mass spectrometry detection science for analytical & bioanalytical techniques in the past decade. Take for example traditional low pressure (e.g., 400 bar) long length column (e.g. 10-25 cm) high performance liquid chromatography (HPLC) in comparison to higher pressure (e.g., 1200 bar) shorter length column (e.g., 1.0 - 1.2 cm) UPLC separations which now allows for rapid injection cycles, a 10-20 times reduction in delay volumes, decreased sample broadening, increased sample throughput, and reduced carryover. This in turn translates into increased resolution of larger peak capacities that will enhance mass spectrometry sensitivity while still extending the dynamic range of mass spectrometry to yield faster and more consistent results. Thus, giving the researcher an increased level of robustness and reliability out of their LC systems and improved detection capabilities when paired with a MS system [16,17].

Thus, when paring for example a hybrid MS system (i.e., QqQMS/TOFMS), with that of an UPLC system as discussed above, the serial stacking of two typically independent MS instruments provides a uniquely integrated qualitative discovery and quantitative directed analysis workflow into a single platform that truly helps to define the whole as being more than the sum of its parts. Here the front ends of this example hybrid MS employs a QqQMS that enables comprehensive quantitative precursor to product ion transitions for most components in high complexity mixtures. With sensitivity and precision that is now becoming almost comparable to that of traditional high-performance standalone QqQMS systems. The back end of this example hybrid MS employs a TOFMS that delivers rapid acquisition speeds up to 100 spectra per second, a high level of sample peak resolution of up to 40,000 FWHM, and a high level of sensitivity with a mass accuracy of ≤ 2 ppm for both precursor and product ion scan modes. These TOFMS attributes, with emphasis on accurate mass determinations, allows for the effective qualitative analysis of high complexity mixtures. To that end, when the combination of the QqQMS with that of a TOFMS takes place to form a QqQMS/TOFMS instrument current researchers are able to utilize one of the most rapid, sensitive, high-resolution hybrid MS currently available to do both qualitative discovery and quantitative directed analysis at the same time [9,18].

In closing, as we look to the future of LC-MS instrumentation for the analysis of high complexity samples for analytical & bioanalytical techniques we feel confident this new hybrid class of LC-MS instrumentation that has the unique ability to do both routine qualitative discovery and routine quantitative directed analysis of high complexity samples may well in fact phase out the traditional class of standalone LC-MS instrumentation that is typically found in present laboratories today. The ability to combine discovery and directed analysis into one instrument alone is not just the cost effective replacement of two standalone instruments with one, but rather the multiplying effect of the amount of qualitative and quantitative information obtained by the researcher in a single temporal window. Meaning, high speed UPLC QqQMS/TOFMS types of hybrid LC-MS instrumentation enables researchers to rapidly acquire qualitative accurate mass precursor and...
product ion information while simultaneously obtaining quantitative profiles for most of the detectable components in a single sample at the same time with the same instrument. This will become especially important and advantageous to researchers wishing to data-mine samples that were previously analyzed. For example, quality assurance managers looking to find underlying trends in failed specimens samples, high throughput operations with large numbers of samples being assayed but data review is not conducted in real-time, or any other situation where the correct analyte or species to monitor was not evident before injection. Overall, this emerging trend in LC-MS instrumentation may just be the next paradigm shift offering multi-dimensional, temporally resolved, information in a single LC-MS instrument.

Conflict of Interest

The views expressed in this manuscript are those of the author(s) and do not reflect the official policy or position of the Department of Army, Department of Defense, or the U.S. Government.

References