Themed issue on 'emerging technologies in mass spectrometry'

J Larry Campbell^{*,1} & Robert Plumb²

¹SCIEX, 71 Four Valley Drive, Concord, Ontario L4K 4V8, Canada

²Waters Corporation, 34 Maple Street, Milford, MA 01757, USA

* Author for correspondence: Larry.Campbell@sciex.com

First draft submitted: 21 August 2017; Accepted for publication: 14 September 2017; Published online: TBC

Keywords: acoustic droplet dispensing • high-throughput • immunocapture • LC–MS • mass spectrometry • metabolomics • miniaturization • open-port sampling probe • sample handling • supercritical fluid chromatography

In this themed issue of *Bioanalysis*, we share with you several emerging technologies in mass spectrometry (MS) that could, in the near future, provide dramatic changes to what is considered conventional bioanalysis. These articles outline new avenues of research that differ from what would have been considered 'emerging areas' only a few years ago. Where once there might have been more focus on areas such as reducing sample size and providing more sensitive detection, we are now turning our attention to the next phase in the bioanalysis revolution, with simpler and faster sample handling, and focused data analysis. Overall, the list of authors in this issue – who are well-respected leaders in their respective areas of expertise – should make this edition of *Bioanalysis* a very special and inspiring one.

Among the technologies highlighted in this issue is miniature MS, which is driving toward faster and simpler workflows to provide more seamless bioanalysis of drug molecules, such as in the pharmacokinetics study presented here. Prof Zheng Ouyang, from Tsinghua University (Beijing, China), and co-workers describe a preclinical pharmacokinetics study wherein on-site drug quantitation was accomplished using a miniature MS system coupled to an automatic blood sampler [1]. By using this minute MS system and slug-flow microextraction to replace an in-lab sample preparation method, blood samples acquired at preprogramed time points obtained concentrations of the drugs, which were subsequently used to calculate the drugs' pharmacokinetic properties.

In addition, this issue also provides critical insights into revolutionary sample handling technologies. Alternative methodologies for sample handling include the acoustic dispensing of nano- and even picolitres of solutions. In his opinion paper, Dr Hui Zhang (Pfizer) discusses how this technology, which has been widely adopted within pharmaceutical companies for the fast and reliable delivery of drug solution aliquots in microtiter plate format, is now being combined with MS [2]. Given the sampling rates that are presently being achieved by early iterations of these acoustic dispensing/MS combinations, Zhang foresees the 'sampling throughput bottleneck' becoming a problem of the past, bringing high-throughput screening workflows to an entirely new level of speed and precision.

Also presented in this themed issue of *Bioanalysis*, Dr Gary Van Berkel (Oak Ridge National Labs) and his team are striving to streamline sample delivery to the MS by combining their open port sampling interface (OPSI) with immediate drop on demand technology (I-DOT) – thereby eliminating analytical mainstays such as autosamplers and the vast majority of a liquid chromatography stack [3]. I-DOT uses bursts of air pressure to pulse droplets from the bottom of a microtiter plate without any contact, dispensing these droplets into an OPSI. This unique hybrid sampling device/ionization probe carries I-DOT dispensed droplets to an electrospray plume, producing ions for these analytes using low nanoliter volumes of nanomolar analyte solutions for quantitation or qualitative analysis of either small molecules or larger biological species (i.e., proteins). In addition, this I-DOT/OPSI workflow could achieve analysis times of approximately 8 min for a single 96-well microtiter plate, displaying a combination of simplicity, sensitivity and speed.

Another approach for improving high-throughput screening by LC–MS is described by John Janiszewski (Pfizer) and co-workers, who employed a highly streamlined microflow LC system – with benefits such as low solvent consumption, small required sample volumes and lower operating costs [4]. However, the challenges overcome to

achieve these ideals included elimination of postcolumn volume for good sample throughput (120 s/injection) with baseline separation of nine analytes at low flow (13 $\mu\text{L}/\text{min}$), as well as post-assay pooling to maximize overall throughput. All of these optimizations provided an high-throughput screening (HTS) method capable of 15 s/injection/analyte with $150\times$ lower solvent consumption compared with existing methods.

Also in this issue, Helvecio Menezes from the Federal University of Minas Gerais (Brazil) outlines a method for the use of novel carbon allotropes in a bioanalytical workflow, here for the extraction of cocaine and benzoylecgonine in breast milk [5]. Overall, the optimized method is ‘simple, fast, efficient and uses minimal amounts of organic solvents’ and provides ‘good sensitivity and suitability to determine analytes at typical levels found in breast milk’.

In addition to these highlighted articles, other offerings that round off this themed issue of *Bioanalysis* include an editorial by Prof Jiangjiang (Chris) Zhu’s (Miami University, OH, USA) on the topic of modern MS-based metabolomics and its promise of identifying biomarkers for the early detection and intervention of metabolic syndrome [6]. Prof Qin Ji (Bristol-Myers Squibb) also outlines the future of immunoaffinity capture – capillary electrophoresis (CE) MS [7] – a combination of the specificity of IC with the unique separation accommodated by CE. This workflow ‘significantly reduces the interference in the bioanalysis of biofluids and improves the performance of CE separation and HRMS detection’, especially for biotherapeutic proteins.

All of these emerging technologies strive to address important problems facing bioanalytical scientists today in achieving necessary limits of quantitation from the most complex of samples and matrices. We hope you find this glimpse into the future of bioanalytical MS insightful and even inspiring, and we (and the articles’ authors) would appreciate any feedback, comments or questions you would like to share.

Financial & competing interests disclosure

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 matter 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.

References

- 1 Pu F, Zhang W, Bateman KP, Liu Y, Helmy R, Ouyang Z. Using miniature MS system with automatic blood sampler for preclinical pharmacokinetics study. *Bioanalysis* 9(21), 1633–1641 (2017).
- 2 Zhang H. Acoustic dispensing-mass spectrometry: the next high throughput bioanalytical platform for early drug discovery. *Bioanalysis* 9(21), 1619–1621 (2017).
- 3 Van Berkel G, Kertesz V, Boeltz H. Immediate drop on demand technology coupled with mass spectrometry via an open port sampling interface. *Bioanalysis* 9(21), 1667–1679 (2017).
- 4 Kapinos B, Liu J, Piotrowski M *et al.* Development of a high-performance, enterprise-level, multi-mode LC/MS/MS autosampler for drug discovery. *Bioanalysis* 9(21), 1643–1654 (2017).
- 5 dos Santos R, Nunes Paiva MJ, Veloso JC, Serp P, de Lourdes Cardeal Z, Menezes HC. Efficient extraction method using mCNT to analyze cocaine and benzoylecgonine in breast milk by GC/MS. *Bioanalysis* 9(21), 1655–1666 (2017).
- 6 Sallese A, Zhu J. Mass spectrometry based metabolomics: a novel analytical technique for detecting metabolic syndrome? *Bioanalysis* 9(21), 1623–1626 (2017).
- 7 Wang L, Dodge RW, Ji QC. The future of immunocapture–capillary electrophoresis–high resolution mass spectrometry. *Bioanalysis* 9(21), 1627–1631 (2017).