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the Analytical Scientist

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Image of the Month

Hold the Front Page

Barmak Heshmat and his team at the MIT Media Lab have developed an imaging system incorporating terahertz time-domain spectroscopy (THz-TDS), that allows users to 'read' through multiple layers of paper. Unlike with x-ray technology, the short bursts of radiation emitted from the terahertz camera are able to distinguish between paper and ink – and in this case, the research team's prototype was able to identify letters on the first nine sheets of a stack of paper. With its potential to analyze material organized in thin layers in a non-destructive manner, the discovery has implications for pharmaceuticals and the machine industry, as well as art galleries and museums. Credit: Courtesy of Barmak Heshmat

Reference 1. A Redo-Sanchez et al, "Terahertz time-gated spectral imaging for content extraction through layered structures," Nat Commun, online (2016). DOI:10.1038/ncomms12665

Would you like your photo featured in Image of the Month? Send it to rich.whitworth@texerepublishing.com

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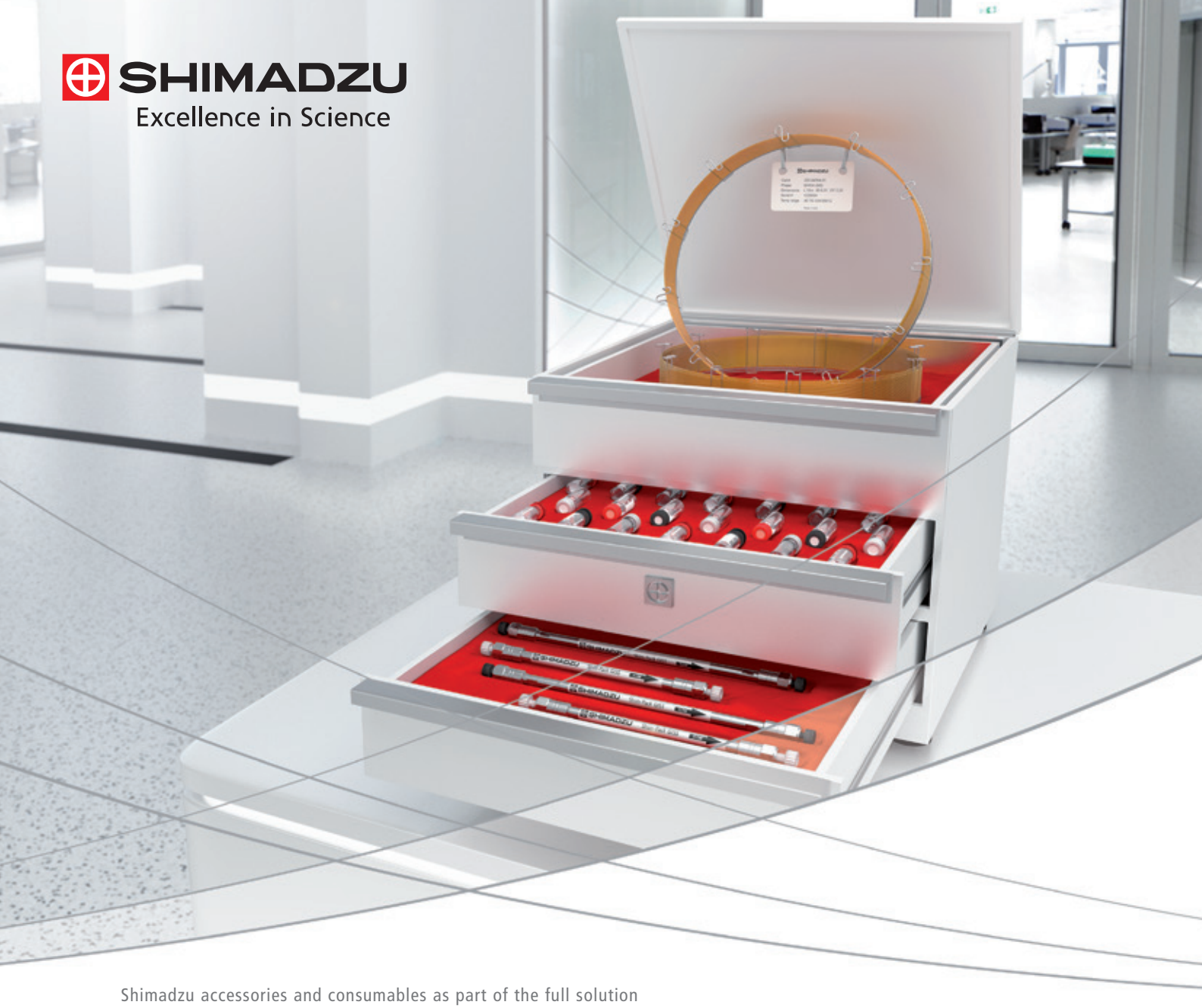

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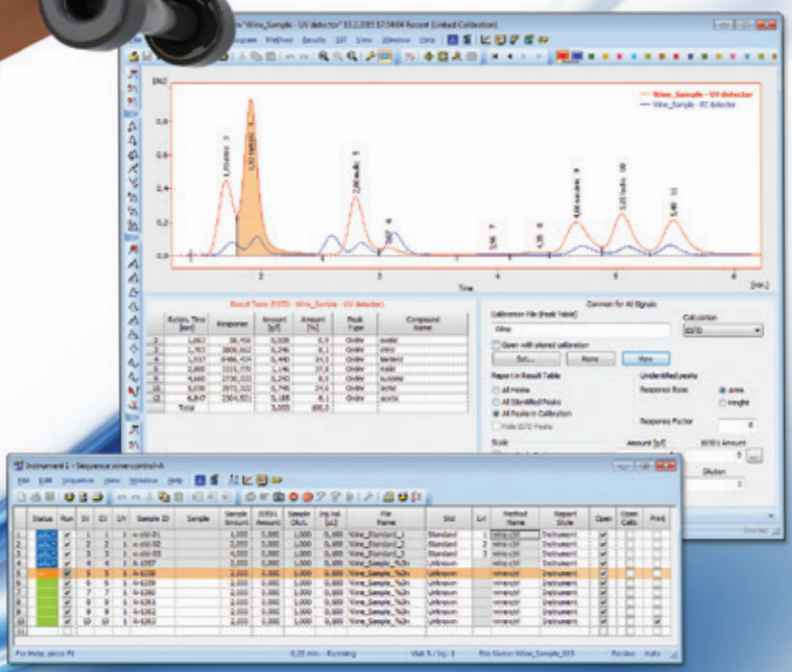

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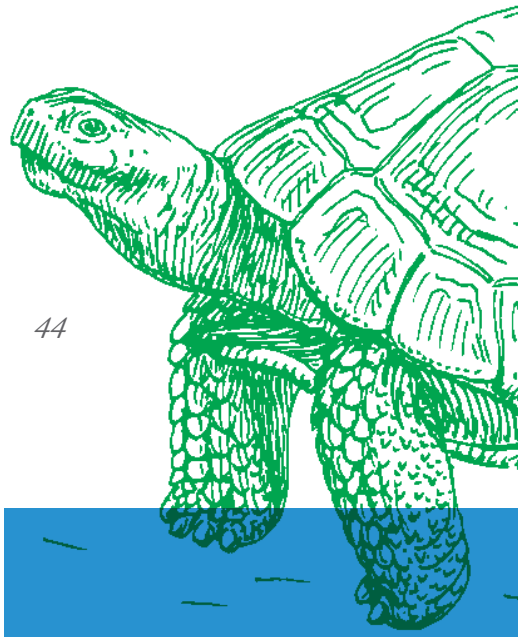

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In My View

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Don't Press Pause

Analytical scientists have achieved a great deal – but there's so much more to do.

The word 'mature' often crops up in analytical science. "Gas chromatography is a mature technique," states Hans Gerd Janssen (1). Few would actually disagree with his statement, but does it not very much depend on the definition? Do we mean:

i) having attained a final or desired state, or

ii) having achieved a low but stable growth rate?

For me, the two definitions (Merriam Webster) are worlds apart.

I've selected Hans Gerd's statement because, knowing him, I suspect there is a hint of irony; he follows his statement with, "[GC] grew from a technique that was thought to be almost perfect to a technique that performs 100 times better and is still 'only' almost perfect..." referring to several "revolutions" in GC.

"Almost perfect" sounds like we've reached definition ii) – but subsequent "revolutions" change the game and blow our previous perceptions of maturity out of the water.

Definition i) is trickier to handle. "Final" is a heavy word – and I'm not sure any analytical scientist (or any scientist for that matter) would dare suggest that no further progress can be made at all. "Desired" is closer to the truth – but sounds rather emotionally compromised. I much prefer Hans Gerd's mantra of "good enough," which is an entirely different concept and has more to do with balancing analytical need, throughput and cost.

What is my point? Declarations of maturity lull us into a false sense of security – or allow us to rest on our laurels. Have we really got to our desired state? Are we really happy with a low but steady growth rate? If not: don't press pause.

As Emily Hilder notes on page 51, "What we've been able to achieve over the last 10 or 20 years has already been phenomenal, but right now, we tend to measure what we can measure rather than what we need to."

Think about the latter part of that statement for a moment and then reconsider the notion of maturity... The reality is, there is so much more to do in so many fields that maturity shouldn't really be on the agenda.

From page 24, our Top 50 influential women in analytical science (aka The Power List) share real vision for the future, making it very clear that opportunities to make a difference abound.

I dare be so bold as to offer a "final state" in analytical science: the ability to accurately measure everything, everywhere, every time, all the time. And if that seems too extreme, Emily Hilder has thrown down a more reasonable gauntlet: real-time, in situ measurements in complex systems – who will accept the challenge?

Rich Whitworth
Editor

Reference

1. 1. http://tas.txp.to/1016/chromedia

Upfront

Reporting on research, personalities, policies and partnerships that are shaping analytical science.

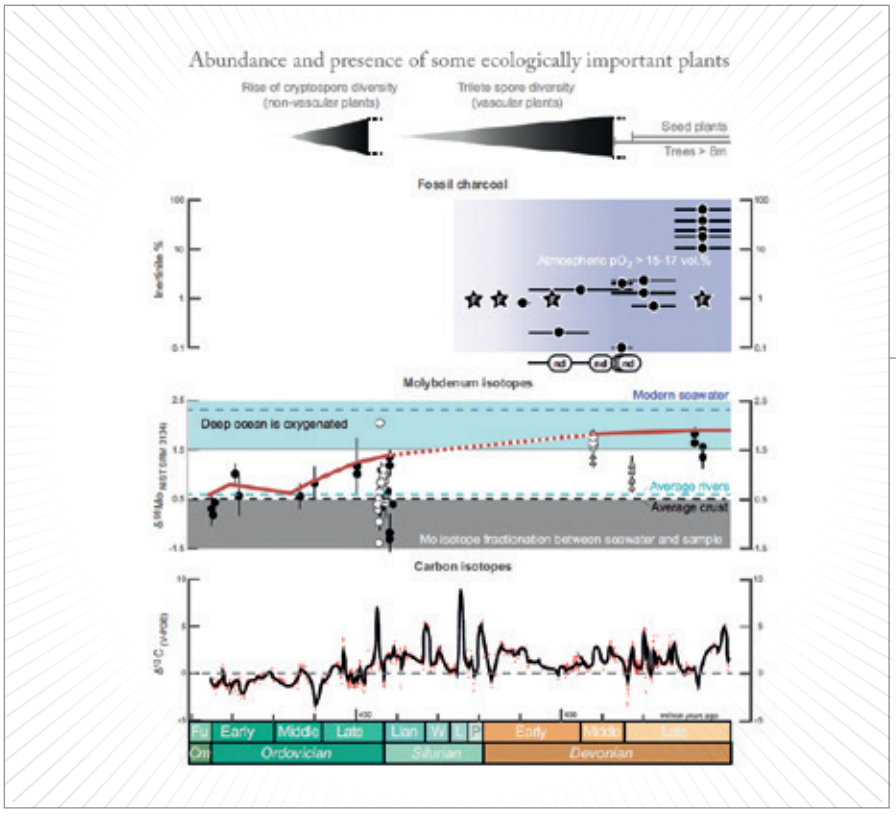
We welcome information on interesting collaborations or research that has really caught your eye, in a good or bad way. Email: rich.whitworth @texerepublishing.com

Of Moss and Men

Were Earth's earliest land plants responsible for the rise in oxygen that shaped the world as we know it?

Despite atmospheric oxygen over Earth's history having recently received a lot of airtime (pun unintended), the puzzle of when and how atmospheric oxygen reached modern levels remains unresolved. Climate change scientist Tim Lenton (Professor at the University of Exeter) was struck by how the timing corresponded with the rise of the earliest plants, and, wanting to explore it further, gathered a team. "I was working with co-author Philipp Porada on modeling of the productivity of the early plant biosphere and realized that plants could be responsible for the rise in oxygen," he says. "I brought the rest of the team together to get a better handle on the geochemical data establishing the timing and mechanism of oxygen rise, and to help develop the model for long-term controls on atmospheric oxygen."

The team used a computer simulation model built on a process-based understanding of early plant ecophysiology and long-term biogeochemical cycling. "Our predictions were then tested against geochemical data such as the isotopic composition of carbonate rocks over geologic time," says Lenton. Inductively coupled plasma mass spectrometry (ICP-MS) was used to reconstruct the carbon isotope record and proxies for ocean oxygenation state, notably molybdenum content of shales



and their molybdenum isotope composition (measured using a multi-collector ICP-MS).

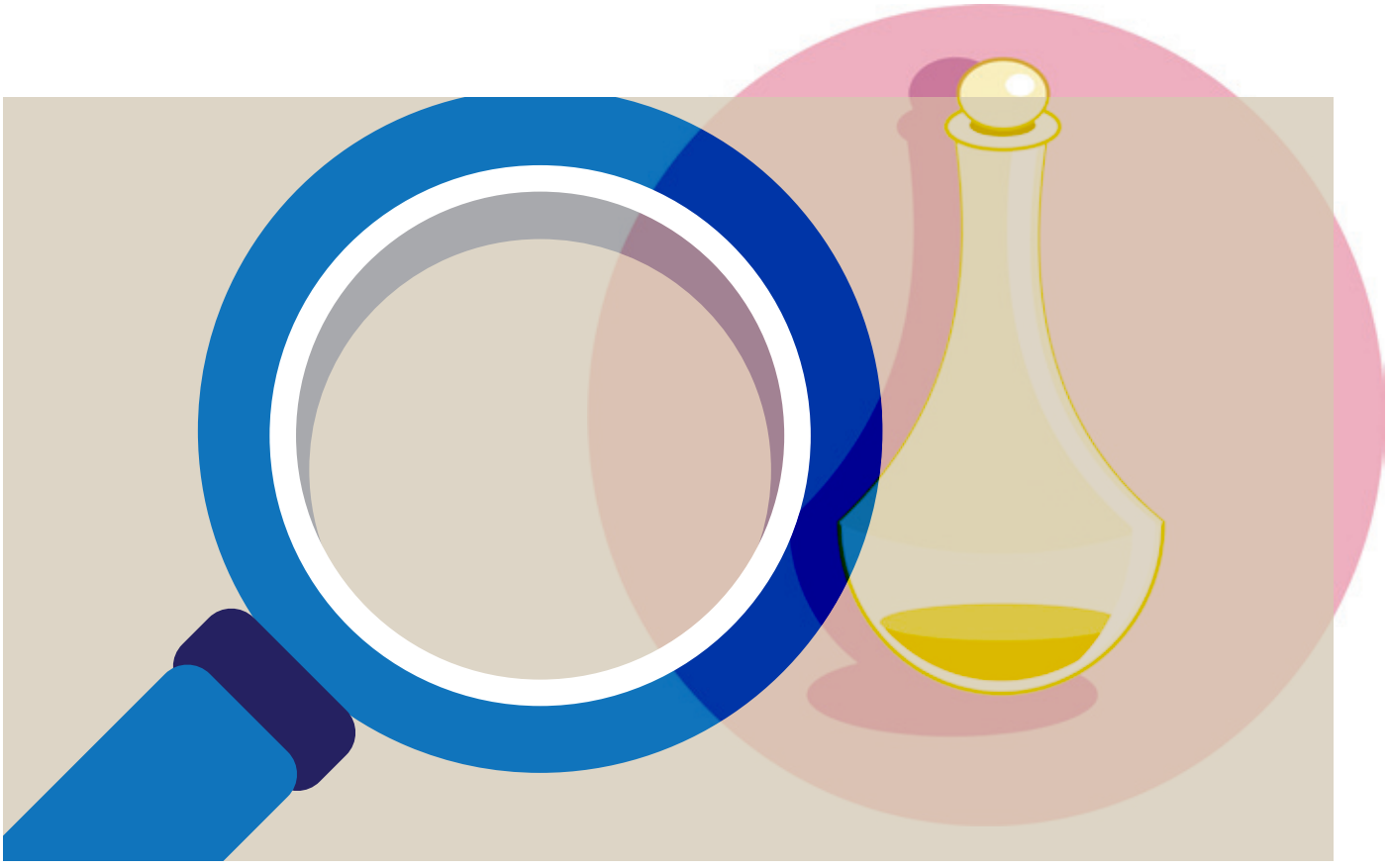
They discovered that the earliest plants could have caused a major rise in the oxygen content of the Earth's atmosphere – particularly significant for us because it shaped subsequent evolution of animals. The rise in oxygen also represented a fundamental shift in how the concentration of this life-giving gas was regulated and established over time. The fact that early "diminutive-in-stature" plants could have had such a large effect on the planet was something that surprised Lenton. "Current theories predicted that a late Paleozoic oxygen rise (<380 Ma) had to await the later evolution of trees, with other recent studies arguing for a major oxygenation event – of uncertain cause – in the Neoproterozoic Era >541 Ma," he says. "But neither of these hypotheses fit the data, which shows the key changes unfolding 445-400 Ma. Of course, our theory could also ultimately turn out to be wrong, but so far it has made several predictions that match a range of geochemical data."

Lenton is now working on what stabilized atmospheric oxygen earlier in Earth's history, in the planet's middle ages – known as the Proterozoic Eon. "We know the atmosphere was oxidizing after the 'Great Oxidation' 2.4 billion years ago, and that the oxygen levels were at least an order of magnitude below today's level," he says. "No one currently knows what maintained them at such low levels... but we now have a mechanism to explain that." *JC*

Reference

1. *T Lenton et al, "Earliest land plants created modern levels of atmospheric oxygen," Proc Natl Acad Sci USA, 113, 9704-9709 (2016)*

Figure 1. Ordovician, Silurian, and Devonian periods in context. The rise of nonvascular and then vascular plants (indicated by cryptospore and trilete spore diversity, respectively) overlaps wth the first appearance of fossil charcoal. (F = fossils; black dots = inertinite in coal; nd = none detected). Molybdenum isotope data indicates oxygenation of the deep ocean, following an uncertain trajectory 440–390 Ma. Black circles indicate euxinic shales as defined by Fe speciation. White circles = euxinic shales as defined by Mo enrichment; gray triangles = ferruginous shales as defined by Fe speciation; blue area = isotope offset from oceanic input that requires a substantial Mn oxide sink in the deep oceans. The carbonate carbon isotope record (red dots, black line is a smoothed spline fit) indicates elevated organic carbon burial (13C 2‰) from 445 Ma. Cm = Cambrian; Fu = Furongian; Llan = Llandovery; L = Ludlow; P = Pridoli; W = Wenlock.



Fragrant Forensics

Perfume detection by GC-MS could have crime-fighting implications

With low conviction rates and often no witnesses, criminal cases involving close physical or sexual contact need all the help they can get. Now, a recent UCL study suggests that perfume traces could help provide another piece of the puzzle. Analysis of perfume trace materials from clothing is not commonly employed within forensic casework, but according to Simona Ghergel, lead researcher of a recently published study (1), fragrance has the potential to provide valuable intelligence as a form of trace evidence.

Unfortunately, the analysis of fragrance comes with a unique set of challenges. "Perfumes are complex mixtures that may contain up to 100 different ingredients. Also, by their nature, fragrance compounds are volatile molecules, which means they evaporate readily into air at room temperature," says Ghergel.

The team assessed the potential of gas chromatography-mass spectrometry (GC-MS) in the analysis of samples of a commercially available male perfume, as well as fragranced fabrics. The fabric used was 100 percent cotton, understood to be one of the most common garments encountered by forensic textile examiners. "GC-MS is a well-established technique, not only in the perfume industry, but also in forensic labs across the world," Ghergel says. "It has been employed for the analysis of various samples, such as drugs of abuse, fire debris and car paint – and even for the analysis of scent from human remains."

The team were pleased to see positive results. "A contact time of one minute was enough to lead to an average of 15 perfume components (out of 44 components identified in a specific male perfume) being transferred and detected on a secondary piece of fabric by GC-MS," says Ghergel. With a contact time of 30 minutes, only four additional components were detected. "This is really interesting, as it indicates that comparatively brief contact between garments may result in sufficient transfer of perfume components for detection and for aiding forensic reconstructions in the future." Ghergel adds, "I am currently carrying out experiments investigating the extraction ability of various solvents, and also the use of stir bar sorptive extraction (SBSE) and solid-phase microextraction (SPME)."

The aromatic research is part of a body of work being developed at UCL to understand the dynamics of a variety of different types of trace evidence, such as particulates, DNA and residues. "Going forward, we are keen to establish the most readily transferred perfume components, what difference certain types of clothing can make to that transfer process, and whether it is possible to identify transferred components after varying lengths of time and conditions of storage," Ghergel says. "We are also looking at how readily trace materials transfer, how long they persist and to what extent can they survive attempts to destroy the evidence. With this kind of information, we will be better able to offer evidence that can be useful in forensic reconstructions – and in assessing the significance or weight of a particular form of evidence in a case." *JC*

Reference

1. *S Ghergel et al, "Analysis of transferred fragrance and its forensic implications," Sci. Justice, [published online] 2016, http://dx.doi.org/10.1016/j.scijus.2016.08.004*

85 Years Young

An inventive mind never gets old

Last month, Herbert Knauer celebrated his 85th birthday – and nearly 55 years at Knauer. Perhaps more impressive, however, is the fact that he's still doing what he loves: working meticulously at his workbench on new inventions for the company his daughter (Alexandra) now runs. If there's a more experienced inventor out there in the world of analytical science, we'd love to know about it. In the meantime, Happy Birthday Dr Knauer!

Mass Spec on the Streets of London

Our short guide to the 2016 Mass Spectrometry and Proteomics Congress

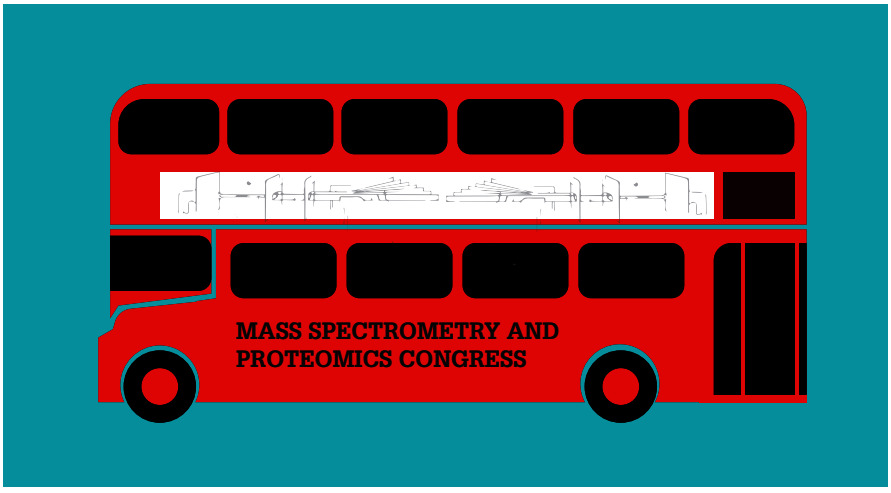
This November sees the inaugural Mass Spectrometry and Proteomics Congress in London, UK. Aiming to unite colleagues from across the field of mass spec and health sciences for the improvement of medical research, the event focuses on three major subject areas:

- Mass Spectrometry: Strategies and Technologies
- Mass Spectrometry-Related Methodologies
- Healthcare Studies and Applications

The sessions will cover the gamut of related topics, from MALDI-TOF to bioinformatics, from peptide mapping to personalized medicine, as well as poster presentations, a networking forum and interactive Q&A discussions with a number of experts including friends of The Analytical Scientist: Ian Wilson, Ron Heeren, Georgios Theodoridis, and Filip Cuyckens. We've bookmarked the key sessions below.

Monday am

09.00–09.35
Translational molecular imaging mass spectrometry: from instrumentation to clinical research (Keynote Presentation) – Ron Heeren, Limburg Chair, Professor of Molecular Imaging and Director of M4I, Maastricht University, The Netherlands.



11.55–12.20
High-throughput analysis of serum (glyco)proteins by various mass spectrometry-based proteomics strategies – Yuri van der Burgt, Associate Professor, Leiden University Medical Center, The Netherlands.

Monday pm

14.15–14.40
Clinical applications of breast cancer proteomics – Peter James, Professor of Protein Technology, Lund University, Sweden.

17.15–17.40
Where next for mass spectrometry instrumentation: Mass analysers and ionisation techniques – Gareth Brenton, Professor of Mass Spectrometry, University of Swansea and Director, EPSRC National Mass Spectrometry Facility, UK.

Tuesday am

09.45–10.10
The Perseus computational platform for comprehensive analysis of (prote)omics data – Juergen Cox, Professor and Group Leader, Max Planck Institute of Biochemistry, Germany.

11.55–12.20
Mass spectrometry imaging standardisation in the Mannheim Molecular Intervention Environment (M^2OLIE) – Carsten Hopf, Professor and Head of the Research Center for Applied Biomedical Mass Spectrometry (ABIMAS), Mannheim University of Applied Sciences, Germany.

Tuesday pm

14.40–15.05
The Bottom to Top of Signaling using Mass Spectrometry - Claire Eyers, Professor of Biomolecular Mass Spectrometry and Co-Director of the Centre for Proteome Research, University of Liverpool, UK.

16.35–17.00
The use of metabolomics in the study of embryo growth and neonatology – Georgios Theodoridis, Professor of Chemistry, Aristotle University, Thessaloniki, Greece.

The Mass Spectrometry and Proteomics Congress will be held November 14–15 at London's Heathrow Marriott.
For more information, visit:
http://tas.txp.to/1016/MSLondon

TASIAs: The Next Frontier

The Analytical Scientist Innovation Awards (TASIAs) return for 2016 to showcase the new technologies, instruments and software solutions that are breaking boundaries.

The TASIAs are back! And like last year, the great minds behind the top five innovations will each have the opportunity to share the development story in a three-page Solutions article in 2016. Nominations are open – and all of these will be put to an expert panel, who will decide on the top 15 innovations of the year. You can enter by filling out the form here: http://tas.txp.to/2016TASIA The deadline is November 8.

Looking for some inspiration? Here are the Top Five innovations from 2015:

1. Full Spectrum Molecular Imaging (Waters)
   A combination of advanced MS imaging technologies, designed to deliver high quality, comprehensive, spatially resolved molecular information.
2. REIMS Research System with iKnife Sampling (Waters)
   A direct sampling ionization technique combined with high performance time-of-flight MS
3. Thermo Scientific Orbitrap Fusion Lumos Tribrid Mass Spectrometer (Thermo Fisher Scientific)
   A high-performance mass spectrometer with enhanced sensitivity
4. Dual-needle Technology for LC-autosamplers (Agilent Technologies)
   Two independent flow paths within a single LC-autosampler module
5. MS-PECD (MassSpecpecD)
   Direct mass spectrometric detection of chiral molecules without any prior enantiomeric separation.

You can also nominate an innovation by emailing rich.whitworth@texerepublishing.com (Subject line: 2016 TASIAs).

Please include:

- name of innovation
- launch date
- brief description (~10 words)
- detailed description (50-150 words)
- the potential impact (50-150 words)
- one image (if applicable).

Sorcerers, SONAR and Standards for Cannabis

What's new in business?

In our regular column, we partner with www.mass-spec-capital.com to let you know what's going on in the business world of analytical science. This month sees some interesting collaborations and organizational developments, as well as product launches with positive implications for the omics.

The new M Lab Collaboration Center in Korea

Products

- Bruker releases wine-profiling Module 3.1 for NMR FoodScreener, the Tracer 5i Handheld XRF Elemental Analyzer System and a complete AFM-based SECM solution.
- Sage-N Research launches a cloud-based Sorcerer for proteomics.
- Advion sells its 500th compact mass spec system.
- Waters presents the SONAR MS data acquisition mode at HUPO.
- Thermo Scientific launches the KingFisher Presto sample purification system.
- Genedata Expressionist version 10.5 extends support of MAM for biotherapeutics characterization.
- Agilent introduces the 4210 Microwave Plasma AES system.
- 908 Devices announces feature upgrades for its M908 HPMS product.

Collaborations

- Agilent and Burning Rock partner in molecular diagnostics.
- Bruker and 3M expand FFPE tissue handling license for MALDI-MS.
- Northeastern University to use VUV Analytics' detector.
- Brazilian SENAI outfits new tribology lab with Bruker UMT Systems.
- Sciex and CW Analytical to develop cannabis-testing standards.

People

- Microsaic: Chairman Colin Nicholl to retire on January 31, 2017.
- Analytik Jena: Ulrich Krauss to succeed Klaus Berka as CEO.

Investments & Acquisitions

- Tecan completes acquisition of SPEware Corporation.
- Thermo Fisher completes acquisition of FEI Company.
- Microsaic general meeting approves conditional £5.4m placing.

Organizations

- Merck unveils New M Lab Collaboration Center in Korea.
- Eurofins opens new food testing laboratory in Singapore.
- Thermo Fisher opens new global headquarters in Waltham, MA

For links to original press releases and more business news, visit the online version of this article at: tas.txp.to/1016/BUSINESS

Exploring Pesticides Without Bugbears

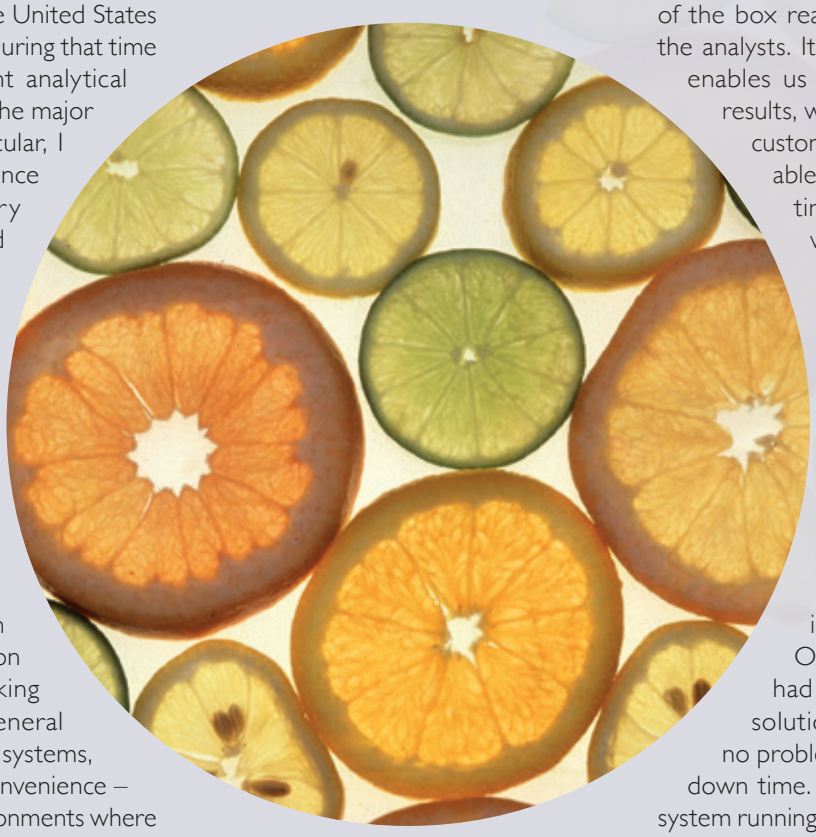
Then & Now, with Mohamed Hamad, Director, Food Chemistry & Nutrition, Microbac Laboratories, Pennsylvania, USA.

Then: 2009

I've worked in several fields over the years, first as a professor, then in the petrochemical and pharmaceutical industries – and even the United States Equestrian Federation. During that time I've used many different analytical platforms from most of the major manufacturers. In particular, I have extensive experience in mass spectrometry and know what I need (and want) in a system – and what I don't. One bugbear of mine has always been the cleaning of the ion transfer tube. It typically used to take several hours and resulted in the instrument being down for most of a day. I'd rather not think too much about the time wasted on this menial task! Looking back, down time in general has plagued certain MS systems, which is a significant inconvenience – especially in routine environments where meeting deadlines is key.

In 2014, I joined Microbac Laboratories, which runs one of the world's most diversified commercial laboratory networks, serving a client base of thousands. Essentially, we're responsible for delivering information that businesses need to survive, so dependable results are a cornerstone of our company. Just after I joined, we experienced a significant expansion to the business and needed to increase our LC-MS capability for a range of analyses – including routine pesticide screening – and started looking for the best solutions available.

The big challenge in pesticide residue analysis is setting up a good, robust method, which includes setting up the right transitions for all the compounds to minimize interferences. We wanted a system that we could get up and running as soon as possible – preferably a total solution.



Now: 2016

In 2015, we made the decision to purchase the standard quantitation solution from the Thermo Scientific™ Pesticide Explorer Collection. Our particular kit includes the Thermo Scientific TSQ Endura™ Triple Quadrupole MS and the Thermo Scientific Vanquish™ UHPLC. We've been using the system for about a year now, so we've had enough time to assess various aspects. And I can honestly say I am impressed.

First of all, you get a lot of value for money, which is a consideration that doesn't always get discussed. The competitive price belies the fact that you walk away with a complete workflow – everything you need from sample preparation to data analysis for quantitation of nearly 300 pesticides (we use the short method). And having a method ready to roll straight out of the box really makes life easier for the analysts. It's a real workhorse that enables us to reduce our time to results, which is also good for our customers – in fact, we've been able to halve our turnaround time. Equally importantly, we have confidence in those results.

Another key point for us is the absence of carry over, which can be challenging with certain systems. The low levels of maintenance required in general (and the ease with which maintenance can be conducted) result in additional cost savings. Over the year we've had our Pesticide Explorer solution, we've experienced no problems that have resulted in down time. Given that we have the system running 24/7, that's not just good – it's surprising!

But what do I really love about the Endura? The fact that you can take out the ion transfer tube, clean it, and put it back in 10 minutes – all without breaking the vacuum. My bugbear has finally been vanquished!

In My View

In this opinion section, experts from across the world share a single strongly-held view or key idea.

Submissions are welcome. Articles should be short, focused, personal and passionate, and may deal with any aspect of analytical science. They can be up to 600 words in length and written in the first person.

Contact the editors at edit@texerepublishing.com

The Analytical Needs of Neuroscience

What's the best route to quantifying picomolar levels of neuropeptides in biological samples?

By Ann Van Eeckhaut, Assistant Professor, Department of Pharmaceutical Chemistry & Drug Analysis, Research Group Experimental Pharmacology, Center for Neurosciences (C4N), Vrije Universiteit Brussel, Belgium.

Seventy million people suffer from epilepsy worldwide, and with current drugs only controlling the symptoms (seizures) rather than curing the disease – and with more than 30 percent of patients resistant to current therapies – there is a clear need for more effective and better-tolerated options (1). To that end, we study neuropeptides (and their receptors), which are highly attractive in drug discovery because of their enormous diversity in functions and their involvement in almost every essential physiological process. Moreover, neuropeptides are preferentially released and exert their main actions when the nervous system is stressed, challenged or affected by disease. And because of their high receptor affinity and modulatory effect on neuronal communication, drugs interfering with peptidergic mechanisms are expected to be more potent and to give rise to less pronounced side effects compared with most currently available small-molecule therapeutics (2, 3).

Although progress has been made in the elucidation of the mechanisms of neuropeptide synthesis and the identification of neuropeptide receptors, physiological roles and mechanisms of release often remain elusive. To gain insight into central peptidergic effects, we can monitor the concentration changes of neuropeptides in the brain as a function of time; in such neurochemical studies, microdialysis is an established in vivo sampling technique that allows collection at basal extracellular levels as well as under pathological conditions. However, bioanalysis of the sampled neuropeptides is challenging because of the low concentration of these analytes in the brain (picomolar levels), the large number of potential interferences, and the limited sample volume (4). Although immunoassays are able to facilitate ultra-sensitive analyses, they suffer from a lack of standardization and a limited dynamic range and there can be large selectivity issues.

I believe that the high sensitivity and selectivity of nano (75-150 µm ID columns) UHPLC–ESI-MS/MS makes it the method of choice for the quantification of individual neuropeptides in brain dialysates. Over the years, nanoLC systems have become more robust, precise and user-friendly, but extracolumn peak broadening and long run times caused by significant gradient delays remain drawbacks. In my opinion, the availability of chip-based LC systems is a major step forward. Integrating all chromatographic components on a chip, including the electrospray emitter for MS detection, eliminates the need for fluidic connections. Consequently, delay and dead volumes as well as the post-separation volume are minimized, leading to a reduced total analysis time and decreased band broadening (5).

Independent of the analysis technique used, there are several challenges that should be taken into account when quantifying peptides, including analyte stability, the purity of the peptide standard, and solubility and related adsorption issues. Moreover, the behavior of neuropeptides under various sample preparation and

chromatographic conditions is not well understood. In my experience, to obtain a method with maximal sensitivity, a tailored optimization – from peptide dissolution through to detection – should be performed for every peptide of interest. Indeed, because of the great diversity in peptide physicochemical properties, there really is no general approach. Fortunately, we can at least follow strategies based on design of experiments that can result in faster optimization of each method (6, 7).

As we want to quantify very low concentrations of peptides (low picomolar concentrations that represent attomole levels on column), the difficulties and challenges of analyzing peptides are even more pronounced; the adsorption of peptides is clearly more detrimental at this low level compared with micro- or nanomolar levels. In fact, aspecific binding of the peptides can occur at all steps of the method, from microdialysis sampling through to chromatographic analysis (7, 8).

Although improvements in MS technology are an important step forward for quantification of low concentrations of endogenous peptides, there is an additional challenge for analytical chemists: low sensitivity caused by the peptide ion current being divided amongst the multiple charged states that are commonly observed in ESI-MS. I believe in the capability of superchargers that can minimize the charge state distribution and thus maximize the relative abundance of one precursor ion, but more research is needed to assess their true potential.

The difficulty in quantifying endogenously released neuropeptides in vivo is evident in the low number of papers published. And it is even more difficult to find methods that were properly validated for the purpose. On many occasions I notice – to my regret – that analytical method validation is not always so well established in biomedical research labs. Whatever the field, we must remember that reliability of the generated data is the fundamental basis of scientific research.

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All-at-Once MS

Two-dimensional Fourier-transform ion cyclotron resonance mass spectrometry (2D-FT-ICR MS) is able to provide both molecular mass and fragmentation information in complex samples in a single run and without chromatographic separation – but does it have as much potential as 2D NMR did in the 1980s?

By Christian Rolando, CNRS Senior Scientist, Miniaturization for Synthesis, Analysis & Proteomics Research Unit, University of Lille, France

In recent years, fantastic technological advances in mass spectrometry (MS) have driven the emergence of fields such as

proteomics and metabolomics. MS also plays a pivotal role in pharmacology, environment and forensic sciences by providing two kinds of information: molecular mass and structure (through fragmentation). Whereas masses of molecules can be obtained in a single spectrum, structures are painfully obtained one by one, after selection (either manually or automatically) of each component of interest in the mixture.

In contrast, two-dimensional (2D) techniques allow the simultaneous acquisition of both mass and structural information, whatever the number of molecules, opening up a completely new way to work with complex samples – and without reliance on prior separation by chromatography. 2D Fourier transform techniques have revolutionized nuclear magnetic resonance (NMR) since their introduction by Ernst in 1974, paving the way for the analysis of complex samples, such as isolated proteins but also blood or urine. No surprise that they have also been awarded two Nobel prizes. Among mass analyzers, the Fourier-transform ion cyclotron resonance (FT-ICR) spectrometer has the best capability to separate individual molecules, reaching a resolution of ten thousand (distinguishing one electron at 20,000 Dalton) and a mass precision of 0.1 ppb. The principle of 2D FT-ICR was established in the late eighties by the joint efforts of two groups at the École Polytechnique Fédérale de Lausanne (Switzerland) – the Geoffrey Bodenhausen NMR team and later Tino Gäumann's FT-ICR team. Unfortunately, 2D FT-ICR did not follow in the footsteps of 2D NMR as the initial version suffered from three main drawbacks: loss of resolution caused by in-cell fragmentation by collision induced dissociation, difficulty in data treatment at full resolution, and intense scintillation noise.

From 2010 onwards, we revisited 2D FT-ICR with two NMR groups – Geoffrey Bodenhausen (who had moved to the Ecole Normale Supérieure in Paris) and Marc-André Delsuc (University of Strasbourg) and introduced solutions to those problems by using gas-free fragmentation modes like IRMPD and ECD, developing data treatment to handle files of several gigabytes, developing improved pulse sequences and by introducing an innovative algorithm based on mathematical sparsity theory for noise reduction (1). Currently, a 2D acquisition takes approximately the same time as an LC-MS run to obtain a 2D spectrum with unit mass resolution for precursor ions and FT-ICR ion resolution for fragments. With these new tools, our group and that of Peter O'Connor's at the University of Warwick (UK) demonstrated that 2D FT-ICR is now able to analyze complex mixtures of peptides starting from the classic Cytochrome C digestion mixture containing a dozen peptides and up to a very complex digest of a cell line, also allowing detection of polar peptides that were lost in nanoLC separations. Moreover, whatever the sample complexity, 2D FT-ICR is a completely 'data independent analysis' – acquisition from the full mixture takes place without chromatography separation and without triggered MS/MS acquisition.

However, the resolution of precursor ions in 2D FT-ICR is limited by the number of scans acquired in one experiment: currently 2048 (2k) to 8192 (8k) or 0.5 to 4 hour acquisition times, respectively. For many applications, especially in the field of environmental or petroleum analysis, high resolution of precursors is highly desirable but requires at least 128k points. The standard solution used for accelerating acquisition in 2D techniques based on Fourier Transform is non-uniform sampling (NUS). NUS consists of skipping points in the dimension with the higher cost in term of acquisition time, which, in 2D FT-ICR, is the first dimension (precursors). In order to obtain the desired structural information, missing points have to be reconstructed through data treatment – in NMR, data is processed using a maximum entropy algorithm. Unfortunately, the time dependence of this algorithm precludes its use in mass spectrometry. We recently reported the development of NUS acquisition in 2D FT-ICR MS and data reconstruction based on a denoising algorithm we published in 2014 (2). We were able to acquire "square" 2D FT-ICR spectrum with the same resolution on precursors and fragments using 32k points at NUS 4 for precursors and 128k for fragments, which exhibits resolution over 20 000 at m/z 400 in both dimensions (4). We are currently applying our NUS protocol to various samples: complex digests of proteins, lipid mixtures that are not easily separated by chromatography, and beverage flavors.

Much remains to be done in 2D FT-ICR MS to join the performance level of 2D NMR: design of new pulse sequences for MS3 and MSn experiments, including the development of new algorithms for speeding up data treatment and expansion into new applications. But 2D FT-ICR MS, which relies only on pulse sequence and so works on all commercial FT-ICR mass spectrometers, is already a powerful tool. Indeed, through data-independent acquisition it can provide a full MS/MS map at high resolution for fragments and precursors of complex mixtures without chromatographic separation, solving a challenge in mass spectrometry.

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Unlocking the Sample Prep Black Box

It's time to get vocal and excited about the "simplest" analytical step – especially as we have so much to learn.

By Elia Psillakis, Professor, School of Environmental Engineering, Technical University of Crete, Greece.

Academic researchers working on sample preparation are not communication champions, apparently. Research in the area has been outstandingly successful, but still fails to excite outsiders. Regarded more as if it has reached a plateau where there is a lack of fundamental challenges, many believe that the focus can only be on the novel application of what is already known. Clearly, the discipline has not been effective enough at projecting its advances and has acquired the image of a slow-paced discipline in a 'big bang' era of analytical instrumentation.

One of the underlying causes for this communication failure stems from presenting sample preparation advances in the context of "applications" and "simplicity" while overlooking the potentially complex science and engineering efforts behind them. As a result, sample preparation is seen as a sequence of activities: samples are exposed to (small) amounts of an extractant phase, and then something happens and the analytes are pre-concentrated in/on the extractant phase. In other words, sample prep is a 'black box' with inputs and outputs – and little knowledge of internal workings.

Our own eagerness to present ultimate black-box simplicity led to an associated misconception: "sample prep is simple and there is no theory to it". Well, there must be some theory, and chemical equilibrium is not the only candidate.

A few years ago, Brian Arthur, a leading economist and complexity thinker, described technology as "exploiting a phenomenon for useful purposes". Sample preparation techniques can be viewed as bodies of technology built around discoveries of phenomena like diffusion, sorption or evaporation, to name a few. If we want to fully exploit these phenomena, we first need to understand them, and this is not always an easy task.

To start with, analytes have to "cross" interface(s); the effect of different experimental parameters on this interphase analyte transfer can be complicated or nearly impossible to describe – especially given that several basic interfacial properties (like the intrinsic acidity of the water interface and its charge) are still under vigorous debate. Even the very simple step of sample agitation is a subject of intensive research in many engineering disciplines and, as surprising as it may sound, our ability to predict the performance of turbulent mixing in multiphase systems is severely limited.

I believe that the fundamental challenges underlying sample prep are too exciting to ignore. We work with microextraction, a sub-discipline of sample prep that has the unique feature of simulating processes found in natural and engineered systems on a small scale. Just like in any other discipline, we have to face a number of fundamental challenges (or 'brain teasers' as we enjoy calling them) every time we unlock the black box. Our studies on the effect of reduced pressure on headspace SPME is a prime example, proving that there are still fundamental challenges underlying even well established microextraction techniques. Solving this 'brain teaser' required us to work effectively across disciplinary boundaries. We had to import engineering models and approaches previously applied to natural bodies, which brought new insights on SPME and helped us better understand, control and eventually exploit headspace SPME.

"Our own eagerness to present ultimate black-box simplicity led to an associated misconception."

Looking at the bigger picture, the small-scale simulation feature of microextraction could be considered a platform that can be used to tackle problems in other disciplines. For example, microextraction technologies played the leading role in previous bioavailability and photodegradation simulation studies. But to deploy such platforms, we must take the risk of asking unconventional questions and interacting with creative scientists from other disciplines. Thinking big can be a talent, but it can also be a skill that can be developed by exposing ourselves to other disciplines.

In short, sample preparation needs to get the attention it deserves in academia. One way of doing this is by communicating a systems-thinking approach, where analyte extraction is the emergent property of an interrelated whole. We have to continue developing knowledge of other fields and embrace fresh perspectives on the phenomena we are exploiting. Our commitment to unlocking the black box may only go a short way to addressing the under-recognition of sample prep – but it's a good start.

Cutting Single Cell Analysis Down to Size

How do we best accomplish analysis of extremely low volume samples?

By Takayuki Kawai, Special Postdoctoral Researcher, Quantitative Biology Center, RIKEN, and PRESTO Researcher, Japan Science and Technology Agency, Japan

Single cell analysis has gained huge attention because cellular heterogeneity is important when it comes to understanding the complexity of life – but it remains a tough analytical challenge. Quantifying large numbers of chemical compounds tagged with spatial and temporal information is key, but in no way easy.

Mass spectrometry (MS) is an essential tool for biological research because of its ability to identify numerous compounds with high sensitivity. Indeed, MS has the potential to provide zeptomole sensitivity – sufficient for single-cell metabolome, lipidome or peptidome analyses – and can be combined with direct sampling from a single cell ahead of electrospray ionization (1). However, MS often suffers from ionization suppression in ESI that results in unreliable quantitation. To avoid ion suppression, MS can be coupled with separation techniques, such as liquid chromatography (LC) and capillary electrophoresis (CE). And though LC-MS is currently the most frequently employed method for quantitative omics research, flow rates in LC are typically higher than 100 nL/min even with narrow capillary columns, which is still too high to obtain the highest sensitivity in ESI-MS detection. In contrast, CE provides high resolution and rapid analysis time as well as extremely low flow rates in the order of 10 nL/min, which is more suitable for sensitive ESI-MS detection. By using CE-MS, single cell metabolome and lipidome analyses have been partially realized, but detection of all compounds has not been possible because sensitivity is still too low (2). With the exception of extremely large cells, single cell proteome analyses have been almost impossible because sample loss by surface adsorption is inevitable during difficult sample pretreatment.

A clear analytical challenge is the development of well-organized protocols for tiny samples, including sample pretreatment, injection, separation and detection. Microfluidics is expected to step up to the task at some point, but currently lacks maturity when it comes to accomplishing the flexible flow control necessary to complete complicated analytical protocols with tens of steps. How can we design robust step-by-step methods for analyzing tiny-volume samples successfully with currently available techniques?

One solution is the combination of conventional pretreatment and in-capillary preconcentration in CE. To this end, I have developed a new analytical protocol called nano-dilution/preconcentration, which consists of:

i. dilution of single cell (nL-pL volume) to μL order,
ii. flexible pretreatment by conventional micropipette-based method,
iii. large-volume injection to capillary (~2 μL),
iv. in-capillary preconcentration to focus the band at nL scale, and
v. separation and detection by CE-MS or fluorescence detection.

By using this method, both flexible sample pretreatment and sensitive detection were simultaneously obtained.

Another solution is to enhance sensitivity by improving ESI technology. Although sheathless CE-MS, using the so-called "CESI" emitter (originally developed by Moini, 3), is considered to be highly sensitive because of its low flow rate (~10 nL/min), it is typically only compatible with MS systems designed uniquely for CESI use. From my experiments, the internal diameter (ID) of the emitter tip should be less than 20 μm – otherwise, an unstable ESI signal is often obtained. As the ID of the capillary is decreased, however, injectable sample volumes in the capillary also decreased, resulting in low concentration sensitivity. To overcome that hurdle, I developed a 'nanoCESI' emitter, which has a 50 μm ID separation column and a ~10 μm ID emitter tip with a porous glass wall of less than 10-μm thickness. The emitter allowed both high injection volume (from few nL to 2 μL) and high sensitivity; in a typical nanoCESI-MS analysis of peptides we were able to achieve sub-nM (corresponding to a few amol) detection limits.

In my view, though basic MS-related technology is quite mature, systematic protocols that enable the analysis of tiny but complicated biological samples in terms of spatial, temporal, physical, and chemical aspects are deeply needed.

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Cheers to IC!

Art Fitchett recounts his early days in ion chromatography and highlights how a string of innovations have made it a beverage analysis workhorse.

It was while I was at the DuPont Experiment Station as an analytical chemist in the biochemicals department that I was first exposed to ion chromatography (IC). I read the first article in Analytical Chemistry with great enthusiasm and told my management how useful the technology could be in a number of different challenging areas. Their response was, "Go build one!" I ignored that remark and went to a seminar by Dionex. Having seen a system in operation, I went back to my managers with a letter of justification that included 10 specific problem areas.

In 1976, I was allowed to buy my first ion chromatograph (the first ever commercial instrument was sold in October 1975, so I was a real early adopter). I started working on my new IC system and within a week I'd solved all 10 application problems. Within another few days, I'd solved another challenge in the business and they wanted my IC system for that project, so I had to buy another. So in just a month or two, we had purchased two ICs at DuPont and I had become the unwitting IC guru. I was asked to present IC technology to other operating departments and to see how applicable it was to solving their problems, so I developed a training seminar and wrote courses on methods development.

Teaching Dionex a thing or two about IC

Dionex found about what I was doing and asked me to share what I had learned with them. I put on a three-day workshop about IC for Dionex and at the end of the month, I was invited to join the company. I started in November 1977. To cut a long story short, I was heavily involved in the creation of US Environmental Protection Agency Method 300.0 (Determination of Inorganic Anions by Ion Chromatography), which put IC into routine use – and the rest is history!

The development of hydroxide-selective anion-exchange columns was a game changer for IC and opened up a number of new markets, including food and beverages. The ability to generate high-purity eluent (in this case hydroxide) electrolytically was also key; not only did it increase sensitivity, it also allowed us to run gradient separations with an isocratic pump, which meant we could analyze both the inorganic species but also the bulk of organic acids that we find in food and beverages. Another major step for beverage analysis using IC was the introduction of pulsed amperometric detection, which facilitated the analysis of carbohydrates. More recently, the introduction of 4-µm particle size packing materials has allowed us to really ramp up separation efficiency – today's IC peaks look like they've come off a GC system!

The marriage of IC and mass spectrometry is another significant but natural step forward. IC systems are now even being connected to our top-end Thermo Scientific™ Orbitrap Fusion™ Tribrid™ Mass Spectrometers, which pushes the technique into another new application area: metabolomics. Meanwhile, hyphenation with inductively coupled plasma (ICP)-MS opens the door to arsenic speciation, which is another interesting application area in food and beverage analysis.

Looking back over nearly 40 years, it's surprising to see just how much innovation has gone into modern IC systems, such as the Thermo Scientific™ Dionex™ ICS-5000+.

From water to wine

It's fair to say we're working with all the major manufacturers of beverages when it comes to the application of IC. To offer just a few examples, we can start with the measurement of bromate in bottled water; IC is the only real way of conducting such an analysis, so it's an important application that links nicely back to IC's strong history in environmental applications.

Having the potential to analyze all the inorganics and the majority of the organic acids in a single run means that it's easy to visualize the difference when a process goes awry, or if a beverage product has spoiled. I often share the example of fresh and spoiled orange juice; when we overlay the chromatograms, we can clearly see how peaks have changed and how new peaks have appeared through spoilage, so it can be used as a profiling tool.

Coffee manufacturers like to assess organic acids and carbohydrates in extracts to assess whether the roasting process is robust, and microbreweries might do the same to monitor the fermentation of IPAs that are popular because of their complex flavor profiles.

Sports drinks – where electrolytes, carbohydrates and amino acids may all be of interest – also lend themselves to IC analysis, which can offer a full profile in a single run.

On the cation side, we can take a look at biogenic amines, such as histamine, cadaverine and putrescine in wine. Histamine is regulated in some regions because it is considered an early indicator of decomposition (or poor winemaking) – the same can be said of other biogenic amines, and winemakers are naturally concerned about the negative sensory impact they could have on wine.

And the list goes on...

Back in the mid-1970s, all we had was ion chromatography with conductivity detection. I couldn't have imagined all of the applications of today – and we've not done innovating yet. IC has given me a long, successful and varied career, so I can say in earnest, "Cheers to IC!"

50 XX

the Analytical Scientist

Power List

2016

With three somewhat provocative Power Lists behind us (but certainly not forgotten), we once again forge ahead with our mission: to prove just how impactful and diverse our field is by sharing the passions, pivotal moments and predictions of brilliant scientists who continue to shape our future. Welcome to the 2016 Power List and the Top 50 most influential women in the analytical sciences.

NANCY ALLBRITTON

KENAN DISTINGUISHED PROFESSOR, CHEMISTRY, UNIVERSITY OF NORTH CAROLINA, USA

ALISON ASHCROFT

PROFESSOR OF BIOMOLECULAR MASS SPECTROMETRY, ASTBURY CENTRE FOR STRUCTURAL MOLECULAR BIOLOGY, FACULTY OF BIOLOGICAL SCIENCES, UNIVERSITY OF LEEDS, UK

Passion: Using mass spectrometry to solve biochemical enigmas and to try to better understand protein-related diseases.

Pivotal moment: My first job in mass spectrometry. When I realized how versatile the technique is and how widely it can be applied, I was hooked!

Prediction: Increased sensitivity, further options for separation techniques to be coupled to mass spectrometry.

PERDITA BARRAN

PROFESSOR OF MASS SPECTROMETRY, THE MICHAEL BARBER CENTRE FOR COLLABORATIVE MASS SPECTROMETRY, THE UNIVERSITY OF MANCHESTER, UK

Passion: I am most passionate about translating basic research on the conformation and flexibility of molecules to benefit humanity. Science is a global pursuit and I am constantly delighted and grateful that, as a scientist, I get to mentor, interact with and be inspired by bright minds from all over the world.

Pivotal moment: The pivotal moment in my career was in 1999 when I went to a meeting in Les Houches France, which had been set up by Jean-Pierre Shermann, John Simons and a few other brave souls to get together the emerging group of researchers working on biomolecular structure in the gas phase. I felt honored to be asked to give a hot topic talk amongst many great scientists and, whilst I described work I had performed with Tony Stace on solvated metals ions, I was for the first time able to see how even very simple systems could help the understanding of biology. Many of the attendees have now become my peers and I am a little less in awe of them than I was then. At that meeting, I was offered a post-doc by Mike Bowers, which led to my first forays of work into model biological systems, giving me the confidence to build on my track record and start an independent career. So all in all, an important meeting!

Prediction: There are many game changing technologies in biotechnology, and it would be wrong not to mention the fantastic developments in next-gen sequencing and in CRISPR-Cas9 gene editing. However, I am an analytical chemist and for me the most exciting developments will be the miniaturization of analytical devices for point-of-care use, and the first commercial mass spectrometer that can provide an IR spectrum of a mass selected ion.

CORAL ARRIBAS BARBAS

FULL PROFESSOR IN ANALYTICAL CHEMISTRY AND DIRECTOR FOR THE CENTRE OF METABOLOMICS AND BIOANALYSIS (CEMBIO), DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY, FACULTY OF PHARMACY, UNIVERSIDAD SAN PABLO CEU, MADRID, SPAIN

Passion: We are living through a change in research paradigms and analytical chemistry is playing a main role in this change. From a reductionist approach based on hypothesis testing, we have moved in the 21st century to a holistic approach through "omics" technologies, where we try to catch everything and then interpret the results, trying to find answers to our research questions. The opportunities to discover things that nobody thought about are incredible. In that process, many rules in analytical work are changing, but... as the person responsible for the information obtained, you must be very careful. Now the challenge is proposing new workflows and validation strategies that ensure the results.

Now, more than ever, analytical chemistry is the "central science" and research is multidisciplinary, with collaborations among physicians, biochemists, biostatisticians, pharmacists and chemists the only way to approach the difficult problems that are still unsolved. That opens an exciting world of opportunities to learn not only in science, but also in human relationships.

Pivotal moment: Coming from the tight pharmaceutical analysis world, I always thought that analytical chemistry had more value to add than just producing a method with 100 percent recovery and <1 percent RSD; even more so when we consider the increasing capabilities of new technologies. I applied for a Marie Curie fellowship and I thought that it should be to do something really new. I heard about the last tool in the omics toolbox – metabolomics, which was quite new at that time – and spent a year being introduced to the methodology. Once back to my lab, we only had very simple instrumentation, and our group started to do metabolomics with capillary electrophoresis and UV detection – 'where there's a will there's a way!' We had the proof of concept of the capabilities and thanks to a fantastic team of committed, enthusiastic and hard-working people and the support of different entities and people – to whom I am really grateful – we succeeded in having a state-of-the-art metabolomics lab.

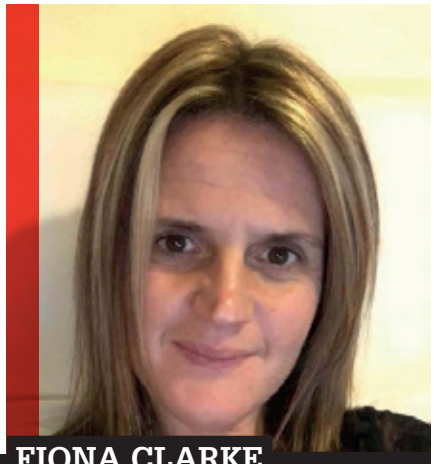
JENNIFER BRODBELT

PROFESSOR, DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TEXAS AT AUSTIN, USA

Passion: Integrating the latest and greatest light sources with mass spectrometers.

Pivotal moment: Integrating a laser with a mass spectrometer and seeing new fragment ions for the first time.

Prediction: Routine achievement of high mass accuracy and high resolution at ultra-high mass (in the field of mass spectrometry, of course).



FIONA CLARKE

DIRECTOR MATERIALS CHARACTERIZATION, PFIZER, UK

LUTGARDE BUYDENS

PROFESSOR AND DEAN OF THE FACULTY OF SCIENCE, RADBOUD UNIVERSITY, THE NETHERLANDS

Passion: During the last few years in our field, analytical chemistry has caused a paradigm change in sciences. Thanks to analytical research, analysis has become so efficient, time-wise as money-wise, while maintaining good quality. As a result, a so-called 'data-driven' research approach emerged as a new and powerful fourth science paradigm. Due to the ever-increasing production of complex data by a large variety of (analytical) technologies, data management and data mining techniques have become crucial scientific methods in modern science. This change has actually put analytical sciences and chemometrics in the driving seat of science. We need to be aware of this and exploit this opportunity.

Pivotal moment: As a young postdoc, I participated in one of the first European projects (The ESPRIT project, Expert Systems for Chromatographic Analysis – ESCA). Participating in such a multidisciplinary project with partners from many different countries and cultures not only drastically shaped and determined my scientific attitude, it also made me a better world citizen.

Prediction: Advances in "noninvasive measuring", together with miniaturization will allow the development of smart sensors, for quality control – as we are used to in analytical chemistry. I think this will boost the field of citizen science and make it evidence based. This, in my opinion, will be the fifth science paradigm.

CATHERINE COSTELLO

DIRECTOR, CENTER FOR BIOMEDICAL MASS SPECTROMETRY, BOSTON UNIVERSITY, MASSACHUSETTS, USA

DEIRDRE CABOOTER

ASSOCIATE PROFESSOR, DEPARTMENT OF PHARMACEUTICAL AND PHARMACOLOGICAL SCIENCES, UNIVERSITY OF LEUVEN, LEUVEN, BELGIUM

Passion: Trying to unravel the mechanisms behind mass transfer in liquid chromatography by developing novel procedures. Developing new hardware and software solutions for specific applications in different fields of analysis (pharmaceutical, food, environmental, bio-analysis).

Pivotal moment: I am very lucky to have been surrounded by some amazing people, such as Gert Desmet, Pat Sandra, Frederic Lynen (and many more), from an early stage. They have always supported me, believed in me and stimulated me. Their support has had a large influence on the research direction I have taken. More specifically, being given the opportunity to start up my own research group at the University of Leuven has given me the confidence to pursue my own research ideas. In this respect, I'm very grateful for the support and trust I have received from my colleagues in the department.

Prediction: The increasing number of complex samples that are emerging in different fields of research, such as environmental monitoring, biomarker research and drug design is going to drive the development of new column packing structures and packing arrangements to boost the performance of our columns. I also foresee innovative approaches to combine existing separation techniques to expand the capabilities of chromatography as we know it.

CHIARA CORDERO

ASSOCIATE PROFESSOR OF FOOD CHEMISTRY, DIPARTIMENTO DI SCIENZA E TECNOLOGIA DEL FARMACO, UNIVERSITÀ DEGLI STUDI DI TORINO, TURIN, ITALY

Passion: As a food chemist, I like to contribute to revealing the "magic" and the "logic" beneath food preferences, hedonic value and nutritional impact. The ultimate aim of our work is to understand the intriguing – and rather complex – crossroads between what we eat and why, and what we are. 'What we eat' relates to the need to understand food composition in (chemical) detail to differentiate high quality from mass-produced products, enable its authentication or assist technologists during industrial processing with a view to defining a quality benchmark. 'What we are' relates mainly to the interaction of food components within our body. It goes beyond the nutrition domain and includes the effect of non-nutrients and bioactive compounds that may promote health and wellness (nutraceuticals). Sensory pleasure drives food choice, which is fundamental for industry competitiveness and production chain sustainability. Quality food improves our health and wellness, which is crucial for our society.

Pivotal moment: I began my research career in a joint project with a private company on food safety; it was the first step toward a fruitful and exciting interaction that still today inspires our research activity. In academia, we are free to decide what, why, when, and how. However, if we lose contact with real life and the needs of society, our findings are useless. Food production sustainability and benchmark quality are the real challenges for the future in this field. It is no coincidence that my research interests have changed direction from food safety to advanced food quality concepts, after experiencing the excitement of sensomics at the Technical University of Munich with Peter Schieberle, and more recently working in the food metabolomics domain.

Predictions: Within foodomics investigations, we readily adopt the best technology (LC×LC as well as GC×GC coupled with MS) and our community is quite open-minded when it comes to new approaches. However, thanks to the rapid evolution of mass spectrometry and the growth of multidimensional separation techniques, the risk is to undervalue their informative potential, limiting data mining to specialists and their complicated software. I foresee that more intuitive and user-friendly approaches will be the next step. It would be beneficial for all consumers and, of course, for science itself.

As a woman, mother and university teacher, most of my efforts in daily life are devoted to making complex concepts clear, simple and affordable; data mining and data elaboration approaches should follow this simple logic.

KELLY FLOOK

SENIOR MANAGER, PURIFICATION R&D, THERMO FISHER SCIENTIFIC, BEDFORD, MA, USA

Passion: The application of separation science towards higher quality biotherapeutics.

Pivotal moment: The realization of the broader applications of analytical chemistry beyond the traditional means of analysis.

Prediction: DNA-based therapies and virus based delivery systems.

CATHERINE FENSELAU

PROFESSOR, DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY, UNIVERSITY OF MARYLAND, USA

Passion: I have always been passionate about mass spectrometry and currently I am most passionate about top down analysis of intact ubiquitinated proteins.

Pivotal moment: One pivotal moment came early in my PhD research when my thesis advisor Carl Djerassi advised me never to ask the men in the lab to lift my heavy solvent bottles... Excellent advice!

Prediction: Technologies that provide good chromatographic fractionation of intact and modified proteins are badly needed for the development and production of protein therapeutics and in proteomic-based studies of immunology, cancer and other biomedical areas. Commercial production of a rugged and automated capillary electrophoresis-mass spectrometry system is a good start.

PAOLA DUGO

FULL PROFESSOR OF FOOD CHEMISTRY, DIPARTIMENTO DI SCIENZE CHIMICHE, BIOLOGICHE, FARMACEUTICHE ED AMBIENTALI, UNIVERSITÀ DI MESSINA, ITALY

Passion: My driving force is curiosity and willingness to acquire new knowledge. The evolution of techniques available for the isolation and characterization of natural molecules starting from the end of 19th century to now is fascinating; for many natural molecules, the exact structure was inferred many decades after their first isolation, meanwhile exotic names were assigned to remember their odor or the plant they came from – names that are still in use!

Pivotal moment: From 2002-2005 we took part in the RTN EU project COMCHROM (training young researchers in miniaturized comprehensive liquid chromatography), coordinated by Tyge Greibrokk (University of Oslo, Norway) and developed our first LC×LC system and applied it to the analysis of natural products in the "unusual" configuration NPLC×RPLC. It was a quite an unexplored field at that time and we were showing promising results. I was invited by Pat Sandra to present our work at HPLC meeting in Gent in 2003 and at ISCC in Riva del Garda in 2004 and 2006. The technique attracted a lot of interest, and has led to our group being involved in several new projects and collaborations over the last ten years.

Prediction: Many advances in the separation science field are changing our lives. In my opinion, the most significant will be those in the field of miniaturization. Other important trends are in the field of portable and integrated instruments, possibly also allowing for remote control and operation. In this way, women would be given a unique opportunity to carry on their research while having dinner ready for their family!

MONIKA DITTMANN

PRINCIPAL SCIENTIST R&D, AGILENT TECHNOLOGIES, GERMANY

Passion: I believe that a thorough understanding of the fundamental aspects is absolutely necessary to advance separation science. Even for mature fields, such as HPLC, there are still many topics that need to be addressed, in particular in the area of multidimensional LC.

Pivotal moment: The introduction of (U)HPLC in 2004 opened up a whole new field of fundamental and applied research. When I switched my focus from microfluidics back to HPLC, I had the chance to collaborate with many brilliant scientists, such as Gert Desmet and his group (especially Deirdre Cabooter and Ken Broeckhoven) and Dwight Stoll. Even after more than 10 years, there are still many interesting topics to work on.

Prediction: Multidimensional LC has the potential to multiply the number of components that can be separated compared to conventional LC. Coupling multidimensional LC to modern high-resolution mass-spectrometers will enable a much more detailed analysis of complex samples in fields such as proteomics or metabolomics.

KAREN FAULDS

PROFESSOR, DEPARTMENT OF PURE AND APPLIED CHEMISTRY, UNIVERSITY OF STRATHCLYDE, GLASGOW, UK

Passion: I am most passionate about multidisciplinary research and the role that analytical science can play at the interface between the different disciplines; in particular, the application of analytical techniques and methodologies to bioanalytical applications. I am most interested in the detection of disease related markers and in developing imaging techniques that have potential to be used to diagnose, predict or monitor disease progression in a sensitive and multiplexed manner. To solve the complex problems involved, we must build multidisciplinary teams of chemists, biologists, physicists, engineers and clinicians. I am also passionate about training the next generation of analytical scientists who are experts in multidisciplinary research.

Pivotal moment: After doing my PhD on the detection of drugs of abuse using SERS, I started a postdoctoral position with Duncan Graham on the detection of DNA sequences using SERRS. At this point, I realized how interested I was in bioanalytical applications of analytical chemistry and the potential for having a real impact on people's lives through improved disease diagnosis or monitoring disease progression. For me, research has always had to have a clear application and one that will benefit society, and it was during this time that I decided to pursue a career in academic research rather than move into industry.

Prediction: With the advent of the impressive array of miniaturized components – lasers, detectors, computing – I think over the next five years there will be some very impressive miniaturized spectrometers developed that will be game changing in terms of how and where they can be used. Equipment that is currently benchtop will become handheld, portable and battery-powered without losing capability – and costs will be reduced. These advances will enable the creation of complete solutions, consisting of simple devices and assays, that can be used at the point-of-use in clinical applications and in the developing world.

MELISSA HANNA-BROWN

TECHNOLOGY AND INNOVATION LEAD, PFIZER GLOBAL R&D, UK

EMILY HILDER

DIRECTOR, FUTURE INDUSTRIES INSTITUTE, AUSTRALIA

Turn to page 50 for Emily's Sitting Down With interview.

ISABELLE FRANÇOIS

UPC²/SFC & STRATEGIC SEPARATION TECHNOLOGIES BUSINESS DEVELOPMENT MANAGER FOR EUROPE AND INDIA, WATERS, GUYANCOURT, FRANCE

Passion: SFC and 2D are two technologies that are not mainstream in analytical labs today, but are close to my heart as they have been part of my life since the start of my analytical career. For both techniques, I see increased interest in academia as well as in the industry sparked by the significant improvements that instrument vendors have made in terms of performance and robustness.

Pivotal moment: Gaining my PhD degree has been most important in driving my career. It allowed me to build my skill set as an analytical scientist, and resulted in jobs at Exxon Mobil and then at Waters. A couple of years ago, my region was expanded from Benelux to Europe and India, so I can play a more significant role in the organization.

Prediction: I foresee that two different trends will continue to take place from a technology standpoint with performance and robustness as key features. On the one side, innovation is essential to drive research and technology further, both on the chromatography as well as on the MS side. Trends towards multidimensional separations and miniaturization will continue to develop, whereas innovations in MS, such as ion mobility and continuous improvements to the instruments, significantly aid in understanding the most complex samples.

SHARI FORBES

PROFESSOR AND ARC FUTURE FELLOW, CENTRE FOR FORENSIC SCIENCE, SCHOOL OF MATHEMATICAL AND PHYSICAL SCIENCES, UNIVERSITY OF TECHNOLOGY SYDNEY, AUSTRALIA

Passion: Developing and applying new analytical techniques to help police solve crimes. Much of my research focuses on understanding the volatile organic compounds produced by human remains and how cadaver-detection dogs can use these compounds to locate victims. Using advanced analytical instrumentation, we are gaining a better understanding of the complex decomposition odor profile and starting to identify the key VOCs that detector dogs use to search for human remains. Once we have identified these compounds, we can prepare better training aids and enhance their training protocols, ultimately increasing their chance of success when deployed to crime scenes.

Pivotal moment: Being awarded a Canada Research Chair. The award provided a foundation for me to build a strong platform in forensic analytical chemistry in Canada through intensive research, infrastructure and human resources. Ultimately, this molded my future career as a research-intensive academic and resulted in the award of an ARC Future Fellow which allowed me to return home to Australia and continue to enhance my reputation in forensic analytical chemistry.

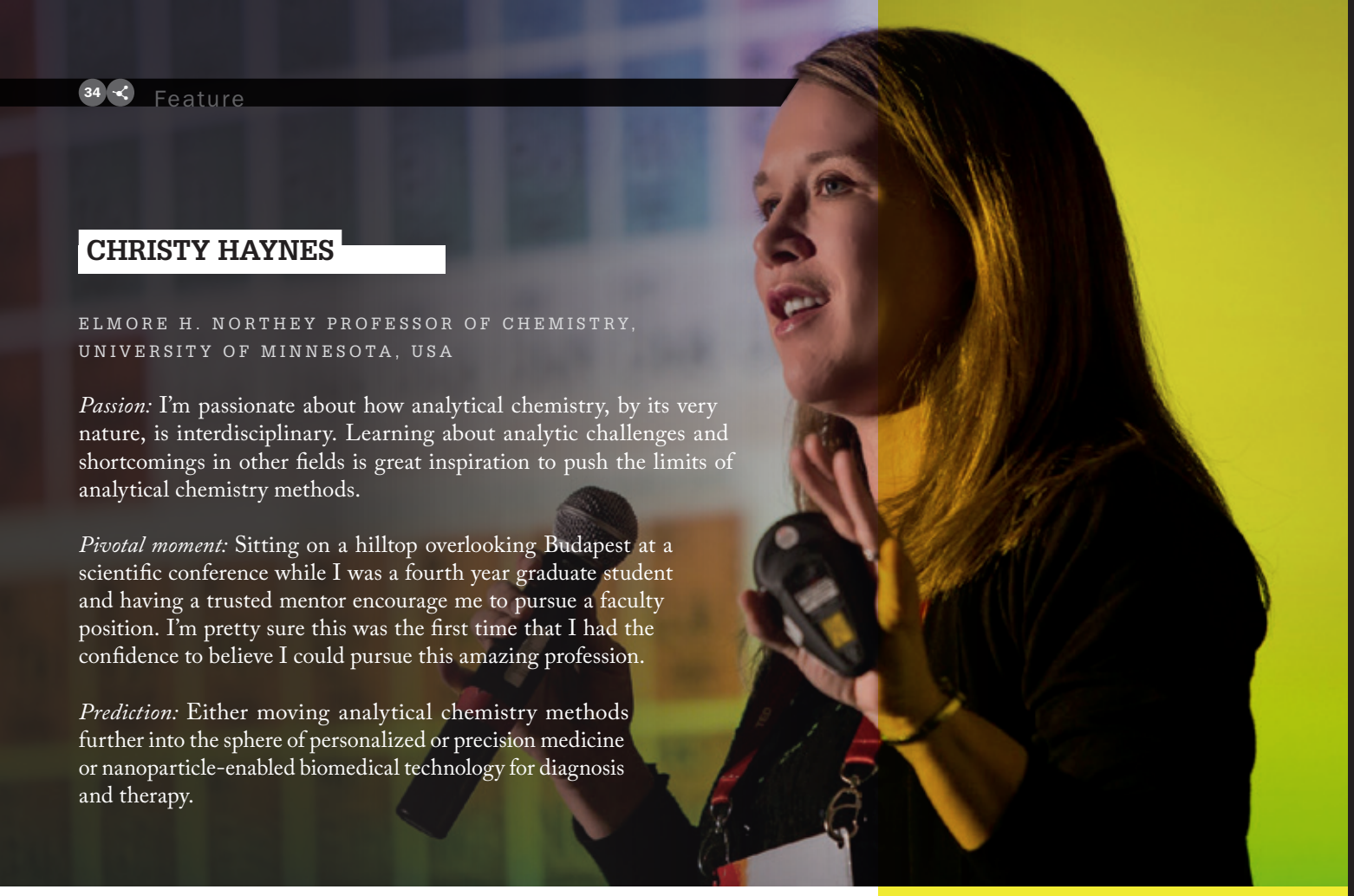
Prediction: Within the field of forensic chemistry, I hope to see more advanced techniques such as comprehensive two-dimensional gas chromatography and high-resolution mass spectrometry being employed in routine forensic analysis, which still relies on traditional chromatography and mass spectrometry. Within the field of analytical chemistry, I think the advances will come from the range of interdisciplinary research incorporating chemists, biologists, statisticians, engineers and other disciplines. The opportunities are truly endless.

ELENA IBANEZ

RESEARCH PROFESSOR, FOODOMICS LABORATORY BIOACTIVITY AND FOOD ANALYSIS DEPARTMENT, INSTITUTE OF FOOD SCIENCE RESEARCH (CIAL-CSIC), MADRID, SPAIN

Passion: I am most passionate about somehow contributing to the improvement of human life. Through the development and implementation of green analytical chemistry, I really think we can improve our world. I also believe that if we all contribute in a small way, we can absolutely make the difference – think big, act small!

Pivotal moment: The most important moment in my career was to create, together with Alejandro Cifuentes, our research group.



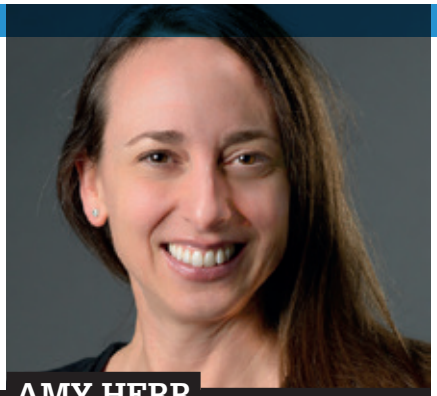
CHRISTY HAYNES

ELMORE H. NORTHEY PROFESSOR OF CHEMISTRY, UNIVERSITY OF MINNESOTA, USA

Passion: I'm passionate about how analytical chemistry, by its very nature, is interdisciplinary. Learning about analytic challenges and shortcomings in other fields is great inspiration to push the limits of analytical chemistry methods.

Pivotal moment: Sitting on a hilltop overlooking Budapest at a scientific conference while I was a fourth year graduate student and having a trusted mentor encourage me to pursue a faculty position. I'm pretty sure this was the first time that I had the confidence to believe I could pursue this amazing profession.

Prediction: Either moving analytical chemistry methods further into the sphere of personalized or precision medicine or nanoparticle-enabled biomedical technology for diagnosis and therapy.



AMY HERR

LLOYD DISTINGUISHED PROFESSOR, DEPARTMENT OF BIOENGINEERING, UNIVERSITY OF CALIFORNIA, BERKELEY, USA

Passion: Difficult measurement challenges exist at the interface of biology and quantitative science. Advanced measurement tools are already adding to our knowledge and capabilities in the areas of genomics and transcriptomics. As we push forward the frontier of quantitative, precise, and dynamic measurements, we'll see even more knowledge unlocked from nature and translated into improving the human condition. Dynamic protein measurements are a lynchpin to realizing these knowledge leaps.

Pivotal moment: Realizing that persistent, stubborn, "never-give-up" hard work wins out nearly every time. Also, realizing the power of connecting people and championing others – what a wonderful, scalable way to make a positive difference.

Prediction: We'll see protein measurement tools capable of stunning specificity and sensitivity, with measurement throughputs that firmly transport even single-cell resolution measurements into the realm of "big (quantitative) data."

GONGKE LI

PROFESSOR AND DIRECTOR OF THE INSTITUTE OF ANALYTICAL SCIENCES, SCHOOL OF CHEMISTRY, SUN YAT-SEN UNIVERSITY, GUANGZHOU, CHINA

Passion: The development of modern sample preparation technique and its application to trace analysis of complex systems.

Pivotal moment: The change of research field from atomic spectral analysis to chromatographic analysis.

ELAINE HOLMES

PROFESSOR AND HEAD OF THE DIVISION OF COMPUTATIONAL AND SYSTEMS MEDICINE, IMPERIAL COLLEGE LONDON, UK

Passion: Recent decades have seen the recognition of the importance of the gut microbiome in human health. The microbiota are implicated in the aetiology or modulation of a wide range of diseases including inflammatory bowel disease, cardiovascular disease, type 2 diabetes, celiac disease, autism and certain cancers. There are multiple studies suggesting that modulation of the microbiome can be used to beneficially impact on disease risk or outcome, the most notable example being the treatment of antibiotic resistant Clostridium difficile using fecal microbial transplantation. Next generation sequencing techniques tend to focus on the composition of the microbiome rather than their functional activity. There is therefore a window of opportunity for metabolic profiling methods to generate functional readouts of the microbiome. Metabolites of either the gut bacteria themselves, or from co-metabolism of dietary substrates with the human host can be detected in biofluids such as urine, plasma and fecal extracts using 1H NMR spectroscopy and UPLC/GC-MS methods. Phenols, indoles, short chain fatty acids, methylamines (and other products of bacterial breakdown of choline), bile acids and biogenic amines can all be measured in either screening mode or by quantitative MS based methods. In this way, we can begin to learn more about the microbes underpinning specific disease states and move closer to developing new ways to target the microbiome in order to influence disease outcomes.

Pivotal moment: During my first postdoctoral appointment, I began to appreciate the value of combining computational pattern recognition and chemometric approaches to analyze and interpret NMR spectra and to develop bespoke multivariate statistical methods for interpreting spectral data. These approaches were able to efficiently detect the key metabolites that differentiated two or more biological states in an unbiased way. Application of this methodology to various toxic states promoted our understanding of mechanisms of toxicity.

Prediction: One of the most exciting technological advances is the development of rapid evaporative ionization mass spectrometry coupled to surgical devices. This technology allows almost real-time analysis of samples and has been used in conjunction with surgical knives in surgical removal of tumors, using a database of spectra acquired from histologically-typed tumor tissues to predict whether the tissue is malignant. This same technology has been used with some success to identify bacteria isolated from sepsis patients – looking forwards, perhaps this same technology could be directed towards rapid identification of antimicrobial resistant bacterial strains.

TUULIA HYÖTYLÄINEN

PROFESSOR OF CHEMISTRY, SCHOOL OF SCIENCE AND TECHNOLOGY, UNIVERSITY OF ÖREBRO, ÖREBRO, SWEDEN

Passion: I work in metabolomics, with the goal of identifying novel biomarkers for specific diseases and to gain understanding of the metabolic pathways leading to diseases. It is fascinating how much information we can produce with novel analytical tools, and it is like detective work to find the key information among the myriad data, and then to link the information with the metabolic pathways and disease mechanisms. Here, it is essential to work closely together with people from other disciplines. It is always inspiring to work together, learn new things together and, in the best cases, make some really novel discoveries that are not only scientifically interesting, but can also help find practical solutions to health issues.

Pivotal moment: There are several moments that have been important in my career, the most important one perhaps when I shifted the focus of my research from environmental studies to metabolomics. Actually, when I started my studies, I wanted to work both on analytical chemistry and biochemistry, but then the field was mainly limited to targeted analytical studies, which I found a bit narrow. With new developments in the instrumental side, metabolomics has moved to a fully different level and now I can combine my very first interests in research.

Prediction: There have been a lot of technological advances over the past decade, enabling better and more robust studies. Currently, the bottleneck is the efficient utilization of the data, and mining the relevant information from the huge amount of data produced. New developments in data preprocessing and data mining are needed and they are under continuous development. Also, in metabolomics, the development of more robust and rugged instruments in combination with the identification of novel biomarkers will allow personalized metabolic screening to enter into daily clinical practice.

BARBARA LARSEN

TECHNOLOGY FELLOW, CORPORATE CENTER FOR ANALYTICAL SCIENCE, DUPONT, WILMINGTON, DELAWARE, USA

Passion: My passion centers on "fitness for purpose": ensuring that the very best separation techniques matched with mass spectrometers with appropriate resolution, mass accuracy and sensitivity are applied to support research and plant problems providing critical solutions to the questions posed. It is critical to provide accurate and precise data, whether you are elucidating a structure or quantitating an active in a product. Most importantly, the data needs to stand the test of time. The analytical data produced will be used as a part of patent application, filing with a regulatory agency or determine the future of a corporate research platform. The field of mass spectrometry continues to change, making it possible to make measurements that were once unthinkable!

Pivotal moment: The pivotal moment was when I was interfacing electrospray ionization to a magnetic sector instrument I was using before these sources were commercially available. Using the resolution of this system, I identified the charge state of in-source fragment ions making it possible to sequence entire peptides. I knew then that electrospray was going to be a game changer in the field of protein identification.

Prediction: With the advances in instrumentation and novel ionization techniques, I predict mass spectrometers will be placed in users' hands to extract, mass measure, and sequence proteins directly from gels. Furthermore, with the research in biomarker identification, I foresee where physicians will be able to have instrumentation in their offices to provide real time analysis for patients to make accurate diagnosis, providing individualized care.

HILKKA KENTTÄMAA

FRANK BROWN DISTINGUISHED PROFESSOR, ANALYTICAL CHEMISTRY AND ORGANIC CHEMISTRY, PURDUE UNIVERSITY, USA

ELSA LUNDANES

PROFESSOR, SECTION FOR CHEMICAL LIFE SCIENCES, UNIVERSITY OF OSLO, NORWAY

SUSAN LUNTE

DIRECTOR, ADAMS INSTITUTE FOR BIOANALYTICAL CHEMISTRY, UNIVERSITY OF KANSAS, USA

LINGJUN LI

VILAS DISTINGUISHED ACHIEVEMENT PROFESSOR, JANIS APINIS PROFESSOR OF PHARMACEUTICAL SCIENCES AND CHEMISTRY, SCHOOL OF PHARMACY AND DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WISCONSIN, MADISON, USA

Passion: I am most passionate about developing novel analytical tools and strategies to solve challenging biological problems. We are excited about developing a suite of multifaceted mass spectrometric tools for functional discovery of neuropeptides and using these enabling technologies to improve our understanding about how the brain works. More recently, we have contributed to developing novel chemical tags for quantitative MS analysis and high throughput measurements in systems biology. I am also passionate about training and mentoring graduate students and postdocs during this process and helping them launch successful careers.

Pivotal moment: During my research career there have been many exciting moments, especially when we discovered neuropeptides that had not been reported before and deciphered their functions. Receiving the prestigious Biemann Medal from the American Society for Mass Spectrometry and delivering the award lecture to a few thousand colleagues and friends was another pivotal moment in my career. It was a tremendous honor and a humbling experience given that there are so many deserving individuals at a similar career stage. It was very encouraging and a strong endorsement for me and my research team.

Prediction: I would like to see single cell omics technology further advance and mature to enable real-time in situ measurements of biochemical changes in cells under healthy and diseased conditions. Such technology will greatly accelerate our pace towards individualized precision medicine.

LAURIE LOCASCIO

DIRECTOR, MATERIAL MEASUREMENT LABORATORY, NIST, GAITHERSBURG, MARYLAND, USA

Passion: I am most passionate about being able to lead an organization full of brilliant and talented individuals dedicated to making the world better through science. I love that all of the exciting big ideas in science today require multidisciplinary collaborative research.

Pivotal moment: A pivotal moment in my career happened when I assembled an extraordinary team of physicists, chemists, and bioengineers, and in a few short years, our ideas came to life in research that had a great impact on the field of microfluidics. It was a very productive time in my life in the laboratory before I moved into more senior leadership positions within my organization.

Prediction: There are so many potentially disruptive advances in the field of engineering biology right now – CRISPR genome editing, synthetic biology, CAR-T therapies. What a great time for research in the biotechnology/bioanalytical field!

LINDA MCGOWN

WILLIAM WEIGHTMAN WALKER PROFESSOR OF CHEMISTRY, RENSSELAER POLYTECHNIC INSTITUTE, TROY, NEW YORK, USA

Passion: I am most passionate about working with my students and collaborators to apply fundamental understanding of chemical measurements to challenging questions in analysis through establishment of thoughtful, innovative approaches. My recent entry into the field of astrobiology is particularly close to my heart; I have now come full circle, back to my childhood love of stargazing and my science fiction-inspired curiosity about the universe that led me to a career in science.

JULIE MACPHERSON

PROFESSOR OF CHEMISTRY, DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WARWICK, COVENTRY, UK

Passion: Developing sensor solutions based on conducting diamond electrode technologies that tackle real problems in the area of water quality. This also involves making the move from working with model solutions in the laboratory to real solutions out in the field, which itself brings about a whole host of challenges to tackle.

Pivotal moment: Winning my first fellowship funded through the University Royal Society Fellowship Scheme, which gave me the ability to be truly independent and develop my own research ideas and concepts.

Prediction: One area where I expect to see a huge rise in both the quality of the device, improvements in system integration and data reliability is in the area of wearable sensors. With easily accessible products on the market now for monitoring steps, heart rate, fitness levels, and so on, the public are becoming accepting and welcoming of personal healthcare technology. The move will be, I think, to drastically extend the range of responses that can be measured, especially when it comes to monitoring the chemistry of the individual, for example. Drastic improvements will also be seen in the placement of the sensor be it directly integrated into clothing or 'tattooed' or strapped onto the body. It will obviously need to go hand-in-hand with advances in thermal and power management (using heat from the body to power the device) and data storage and alert systems.

MARY ELLEN MCNALLY

TECHNICAL FELLOW, STINE HASKELL RESEARCH CENTER, E.I. DUPONT DE NEMOURS AND COMPANY, CROP PROTECTION, NEWARK, DELAWARE, USA

Passion: From a scientific viewpoint, it is the details. The theory of separations is not changing but our fundamental understanding of how influential the theory can be is consistently growing. The increase in understanding comes from digging deeper into the reason for chromatographic behavior, generally led by the need to solve a problem or to give a better answer. Molecules are 'talking' to each other whether in solution or in a chromatographic column; I want to know and understand exactly what they are saying. From the application of the science, I work in the agricultural industry, and our objective is to "Feed the World" by providing safe products to treat pests and weeds. The world's food supply is better because of what we do – so it is easy to get passionate about the work. A few years ago, DuPont introduced a product that was a game-changing insecticide. I remember seeing a picture of a farmer's crop after he used the product, the size of the cabbage he had grown had more than doubled, it changed his lifestyle, it changed the economy of the town he lived in. It was a product I had worked on since its inception and it was heartwarming to hear about the changes that had occurred because of the work we did.

Pivotal moment: There was a lot of competition when I first started my career. The concept of teamwork had not yet happened in the workplace – it was a brutal environment to try to do well and not become totally isolated from fellow scientists. Isolation did not fit my personality. One day, I realized that it was futile to keep this ever-increasing competition going, and I made the decision to compete only against myself. Since then, I have been able to accomplish remarkable things. Other scientists have contributed greatly to my success, and I am a better scientist for these positive interactions.

Prediction: As a separation scientist, it is almost a sacrilege to state, but the most game-changing technology will be one where separation will not be needed to identify, quantitate and understand the components of a mixture. This will likely not happen in 5 years, but it should be a goal for the next 10 or 15. We really are not that far away from the "Star Wars" image, where an item is placed behind a sliding door in the wall and what it is composed of is spit out in a manner of 30 seconds keeping the item intact.

SUSAN OLESIK

PROFESSOR AND CHAIR, DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY, OHIO STATE UNIVERSITY, USA

Passion: The world needs more sensitive methods for the analysis of trace components in complex matrices. For example, we need to improve our ability to detect trace pollutants in nature's water. We also need to improve our ability to detect trace levels of metabolites in body fluids. More and more evidence is appearing that shows, in both cases, that the combination of trace components in these complex matrices may have adverse effects on biota and on human health. We are developing nanoscale-based materials with plans to improve the efficiency of separation devices and to improve SALDI (surface assisted laser desorption ionization) techniques for mass spectrometry. We need faster and more efficient separation techniques that are compatible with mass spectrometry. SALDI-MS needs higher ionization efficiency to improve detection limits.

Pivotal moment: Early in my career, I received a call from a group in NASA who were working on the Cassini-Huygens probe. They had attended a talk of mine at a conference and they were wondering if I could contribute column technology for the Huygens probe. I was floored. We were so thrilled to make this contribution. When the Huygens probe visited Titan, I was even more thrilled!

On a different front, at a similar time in my career, I worked with my daughter's elementary school teacher to launch the Wonders of Our World (WOW) science outreach program (http://wow.osu.edu), which assists whole elementary schools once a month with science experiments using volunteer scientists. All schools who have stayed in the program for the entire three years of the program have seen substantial improvements in their science and math standardized test scores. Today, we have alumni of the early days of the program volunteering. Scientists must continue to show their enthusiasm for science to the rest of the world. It is a leadership responsibility that we must accept.

Prediction: Major advances are happening in 3D printing. If this technology can improve to the point of printing at the nanoscopic level, it will be huge.

KIM PRATHER

DISTINGUISHED CHAIR IN ATMOSPHERIC CHEMISTRY, DIRECTOR OF THE CENTER FOR AEROSOL IMPACTS ON CLIMATE AND THE ENVIRONMENT, DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY AND SCRIPPS INSTITUTION OF OCEANOGRAPHY, UNIVERSITY OF CALIFORNIA, SAN DIEGO, USA

Passion: Working to better understand how atmospheric particles and microbes influence clouds, climate, and weather. Our overall goal is to help better understand how clouds form so that we can make effective solutions to address climate change.

Pivotal moment: When we first used the instruments I developed early in my career to understand the major sources of pollution in the "brown cloud" over India. It was exciting to realize we had developed a method that could be used to determine sources of air pollution all over the world.

Prediction: In climate change and atmospheric chemistry, being able to identify a significant fraction of the chemical species present in the atmosphere has been an elusive goal for many decades. Thus, the game-changer technology will be on-line mass spectrometers with the necessary sensitivity and selectivity to identify more species. An even loftier advance would be to identify the chemical species on the surfaces of aerosol particles, which ultimately play a critical role in controlling clouds and the heterogeneous reactions that occur in the atmosphere.

JEANNE PEMBERTON

PROFESSOR, CHEMISTRY, UNIVERSITY OF ARIZONA, USA

CAROL ROBINSON

ROYAL SOCIETY RESEARCH PROFESSOR, CHEMISTRY, UNIVERSITY OF OXFORD, UK

VALERIE PICHON

FULL PROFESSOR AT UNIVERSITY PIERRE AND MARIE CURIE; DIRECTOR OF THE DEPARTMENT OF ANALYTICAL, BIOANALYTICAL SCIENCES AND MINIATURIZATION; AND ASSISTANT DIRECTOR OF THE CHEMISTRY, BIOLOGY, INNOVATION INSTITUTE OF ÉCOLE SUPÉRIEURE DE PHYSIQUE ET DE CHIMIE INDUSTRIELLES DE LA VILLE DE PARIS, FRANCE

Passion: In many cases, when developing analytical methods and/or new analytical devices, you are expected to provide tools that will help people in their work or in their life. I am particularly interested in developing methods for the trace analysis of compounds in complex samples in fields such as forensics, medicine, pharmacy, environment, and archaeology. My research field allows me to work with researchers with different backgrounds, which is a very enriching situation.

Pivotal moment: I am still waiting for it!

Prediction: I think that the future lies in the development of smaller, faster, greener and cheaper analytical devices. Therefore, I believe in their miniaturization and particularly in their impact on personalized medicine.

MARJA-LIISA RIEKKOLA

PROFESSOR OF ANALYTICAL CHEMISTRY, HEAD OF THE LABORATORY OF ANALYTICAL CHEMISTRY, DEPARTMENT OF CHEMISTRY, UNIVERSITY OF HELSINKI, FINLAND

Passion: Analytical chemistry taking advantage of major developments in electronics, information technology, materials and instrumentation.

Pivotal moment: When the Faculty Council of University of Helsinki selected me, the youngest and only woman among ten competitive applicants to the position of full professor of analytical chemistry. The final decision was based mainly on the independent scientific assessment reports written by four highly respected and well-known international professors.

Prediction: It is very difficult to predict, but perhaps advancements in biotechnology and nanotechnology? Portable technologies? Augmented reality and wearable devices?

VICTORIA SAMANIDOU

PROFESSOR, DEPARTMENT OF CHEMISTRY, ARISTOTLE UNIVERSITY OF THESSALONIKI, GREECE

Passion: Sample preparation and the ability to discover the unrevealed information in any sample matrix using novel pre-treatment approaches and materials.

Pivotal moment: Although I started my PhD working using atomic absorption spectrometry, in the late 1980s, I had the chance to work with HLPC. My perspective of analytical chemistry totally changed and this determined my whole career.

Predictions: Concerning HPLC columns, I believe that core-shell materials will prevail, providing the required high performance using conventional HPLC hardware. With regards to sample preparation, nano-materials will enable more selectivity, as well as multi-class extractions, driving towards application of more environment-friendly (green) techniques.

LOURDES RAMOS

RESEARCH SCIENTIST, DEPARTMENT OF INSTRUMENTAL ANALYSIS AND ENVIRONMENTAL CHEMISTRY, INSTITUTE OF ORGANIC CHEMISTRY, SCIENTIFIC RESEARCH COUNCIL (CSIC), MADRID, SPAIN

Passion: The idea of lifelong learning and the ability to provide practical solutions to new problems.

Pivotal moment: Probably one of the most pivotal moments was my decision to start working on the design and development of miniaturized and hyphenated approaches for the determination of trace organic compounds in (semi-) solid samples during my post-doc. At that moment (late 1990s), such analytical approaches were available for liquid samples but an equivalent analytical strategy had not been assayed for solid matrices. The current demand for faster, more cost-effective and green sample preparation procedures in this application area makes research on this topic still active and attractive.

Prediction: Progress in the analytical sciences over the last few decades has been huge. In the next five years, in my field, I expect to see an increasing use of novel engineered and nano-structured materials and solvents with improved and tailored properties for sample preparation; advances in comprehensive two-dimensional separation sciences; and more powerful mass spectrometers.

ANDREA SINZ

FULL PROFESSOR, DEPARTMENT OF PHARMACEUTICAL CHEMISTRY AND BIOANALYTICS, MARTIN LUTHER UNIVERSITY HALLE-WITTENBERG, GERMANY

Passion: Introducing people to the field of mass spectrometry – and the fact you can get answers to (almost) every chemical, biochemical or pharmacological question using this technique.

Pivotal moment: When I was introduced to protein mass spectrometry – something that happened just by chance.

Prediction: It is obvious that cryo-electron microscopy will change the field of protein structure analysis. But luckily, mass spectrometric techniques, such as native MS and cross-linking/MS, will continue to make valuable contributions.

PAULINE RUDD

PRINCIPAL INVESTIGATOR, NATIONAL INSTITUTE FOR BIOPROCESSING RESEARCH AND TRAINING, DUBLIN, IRELAND; VISITING INVESTIGATOR, BIOPROCESSING TECHNOLOGY INSTITUTE, ASTAR, SINGAPORE; INDEPENDENT CONSULTANT IN GLYCOSCIENCE: GCON

Passion: i) Visualizing the molecular structures and dynamics of glycoproteins to understand more about molecular interactions, where molecules come from and where they go to after I have observed them at some point in their life cycle. ii) Understanding how therapeutic drugs interact with the biochemical pathways in the patient. iii) Building teams in which I can help to develop the skills of younger scientists and see them succeed in their careers after they leave my group.

Pivotal moment: In 1958, when I was at school, a friend and I started a Biotech company called Wessex Biochemicals. We made rare sugars and sugar phosphates in our spare time with basic equipment like washing machines, liquidizers and some of the very first ion exchange resins. After I completed a chemistry degree I joined the company full time. Eventually we employed about 30 people, and in order to expand further, we made an agreement with Sigma whereby we kept control of the science and became Sigma London and they funded the purchase of the site in Poole where Sigma is still located. The excitement of extracting and purifying natural products and crystallizing molecules that had never been crystallized before remains with me still.

Fast forward to 1985 when I returned to full time work after a 15-year career break to raise my four children. I joined what became the Glycobiology Institute in Oxford, directed by Raymond Dwek. It was extremely difficult for women returning to work then – I began as a glass washer – but Raymond has always gone out of his way to support women in science. Without his commitment, I probably would not have had the career that I am enjoying now.

APRYLL STALCUP

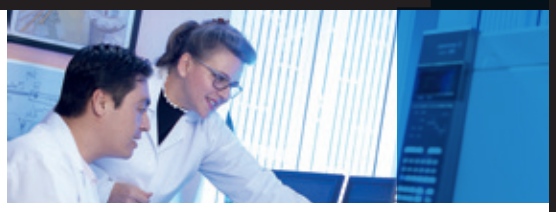
PROFESSOR AND DIRECTOR OF THE IRISH SEPARATION SCIENCE CLUSTER, DUBLIN CITY UNIVERSITY, DUBLIN, IRELAND

Passion: Early in my academic career, I did a lot of work in chiral separations and came to view both chromatographic and capillary electrophoresis columns as basically amplifiers of very subtle differences in intermolecular interactions. I want to understand how I can exploit that knowledge to obtain separations or use my separations to understand intermolecular interactions under other conditions (for example, in vivo, in vitro).

Pivotal moment: Finding myself in the middle of a hazardous waste dumpsite analyzing air samples all by myself at 3am, which inspired me to go back to graduate school! Meeting Dan Armstrong, who introduced me to chiral separations, and later attendance at a Chirality conference in Montreal proved seminal for my early independent research program.

Prediction: The most game-changing technologies or advances in the next five years will evolve from the liberation of people's imagining of separation science. There will be increased emphasis on new platforms, surface chemistries and separation modalities.

ELENA STASHENKO

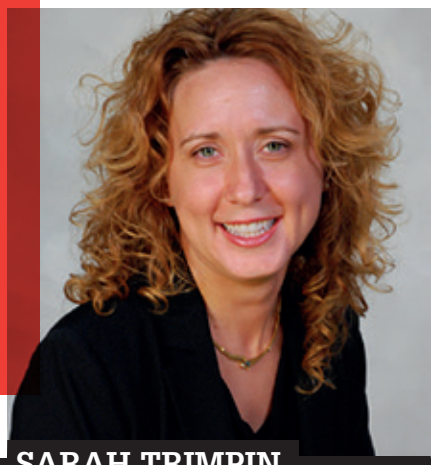


DIRECTOR, RESEARCH CENTER FOR BIOMOLECULES - CIBIMOL RESEARCH CENTER OF EXCELLENCE, CENIVAM UNIVERSIDAD INDUSTRIAL DE SANTANDER BUCARAMANGA, COLOMBIA

Passion: I'm passionate about the study of the biodiversity of tropical vegetal species through the prism of chemical substance analysis.

Pivotal moment: The approval of a project to create a Research Center of Excellence dedicated to the study of Colombia's biodiversity.

Prediction: A very important development in our research field is the complete on-line characterization of complex mixtures by the coupling of LC with GC and MS detection systems.



SARAH TRIMPIN

PROFESSOR, DEPARTMENT OF CHEMISTRY, WAYNE STATE UNIVERSITY, DETROIT, MI, USA

Passion: Developing ionization technologies for mass spectrometry. MS requires the conversion of molecules into gas-phase ions and even though the advent of electrospray ionization and matrix-assisted laser desorption/ionization were great leaps forward, there remain multiple problems that require advances in ionization technologies.

Pivotal moment: The first pivotal moment came when we observed highly charged ions in what was expected to be a MALDI ionization process that primarily produces singly charged ions. The second came from the study of the fundamentals of this matrix-assisted ionization process. We observed the formation of multiply charged ions (even from proteins) when the analyte was incorporated into a special matrix compound and exposed to the vacuum of the mass spectrometer without using heat, a laser, or any other energy source. The method has been found to be both simple to implement and highly sensitive.

Prediction: Within the field of mass spectrometry, development of ion mobility interfaced with mass spectrometry and developments in ionization technologies are currently transforming the field, but five years from now, simplification and miniaturization of mass spectrometry will likely be the most game-changing development in moving MS towards end-user applications, such as bedside diagnostics. We are positioning our ionization technologies to be a part of this development.

SUSANNE WIEDMER

ADJUNCT PROFESSOR (DOCENT), UNIVERSITY LECTURER, DEPARTMENT OF CHEMISTRY, UNIVERSITY OF HELSINKI, FINLAND

Passion: Analytical chemistry has become highly multidisciplinary – it is inspiring to meet researchers from different scientific fields and communities.

Pivotal moment: When I gave a presentation as a young post-doc, a prestigious professor politely informed me that my argument was flawed. We had a long and incredibly helpful discussion, enabling me to refine and strengthen my argument before the manuscript was submitted. It impressed me that he acted out of a desire to mentor and assist – rather than criticize – a young researcher in his field.

Prediction: I believe that analytical scientists will pay even more attention to sustainable analytical chemistry solutions.

MARY WIRTH

W. BROOKS FORTUNE DISTINGUISHED PROFESSOR, ANALYTICAL CHEMISTRY, PURDUE UNIVERSITY, USA

Passion: Detecting extremely minute amounts of proteins in the bloodstream and characterizing their post-translational modification.

Pivotal moment: My wondering why chromatographic peak tailing never goes away no matter how pure the silica is. When I combined AFM and fluorescence microscopy to track individual adsorbed molecules on polished C18/silica surfaces, the pattern that emerged was that the molecules stopped at polishing marks. It seemed that this was either the most trivial result or else it was the answer. I decided to risk it being the answer.

Prediction: I would like to see an interface to a mass spectrometer that makes the sensitivity approach that of fluorescence spectroscopy.

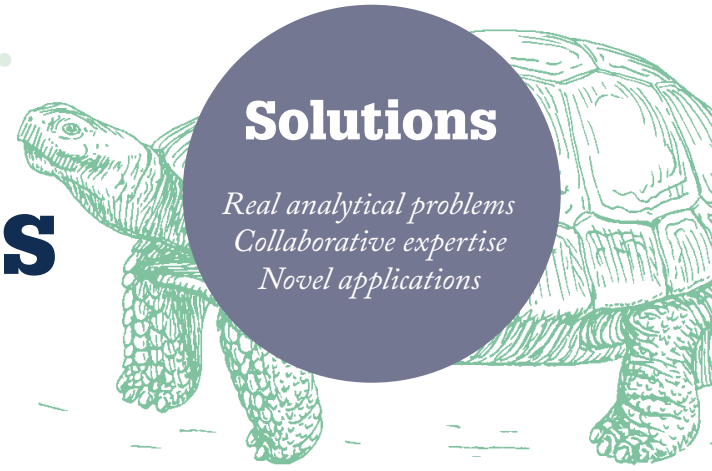
KELLY ZHANG

SENIOR SCIENTIST, GENENTECH, SOUTH SAN FRANCISCO, CALIFORNIA, USA

Passion: I am passionate about building/applying analytical technologies and strategies that have direct and crucial impact in drug research and development.

Pivotal moment: The approval of the cancer drug Cotellic is one of the pivotal moments in my career. It is really rewarding to see the science that my colleagues and I believed in and worked on for years to finally become a real medicine that saves people's lives.

Prediction: Technology that needs no or minimum method development but can still provide comprehensive information of a sample in a short time is highly desirable. Multi-dimensional HPLC coupled with hyphenated detection technologies together with platform strategies is a pragmatic way to fulfill this goal in the coming years.



What if Aesop's Tortoise Was Smarter?

Rethinking the chromatography component of routine LC-MS bioanalysis.

By Fred Regnier

The Problem

There is an increasing need for routine analysis of small numbers of analytes in complex biological samples – and the world is increasingly turning to LC-MS for answers despite the challenges of low throughput and high cost per sample.

Background

There is great interest today in measuring small sets of biomarkers in biological samples as a means to assess biological function, health, disease, and treatment efficacy (1, 2), which is in turn putting new demands on the separation sciences. How can we separate, identify, and quantify relevant markers in samples that contain 10,000 other components within minutes – millions of times annually? Many believe LC-MS will play a role in this endeavor.

A major problem in routine analysis via LC-MS is that the LC column captures most of the substances in a sample; all of which elute into the MS over the course of the separation. With samples containing 10,000 or more components (see Figure 1), analytes and non-analytes will co-elute (3), making analyte differentiation difficult. Additionally, co-eluting non-analytes cause ion suppression, add background noise in spectra, and produce fragment ions of mass similar to analytes. Although MS is capable of millisecond analyses, analytes elute from LC columns over long periods of time; throughput is low, and elution times vary with instrument type, temperature, column lot, and column aging. As a consequence, the MS must continuously collect and examine huge amounts of useless spectral data to assure that analyte data is captured. Clearly, the MS is being poorly utilized.

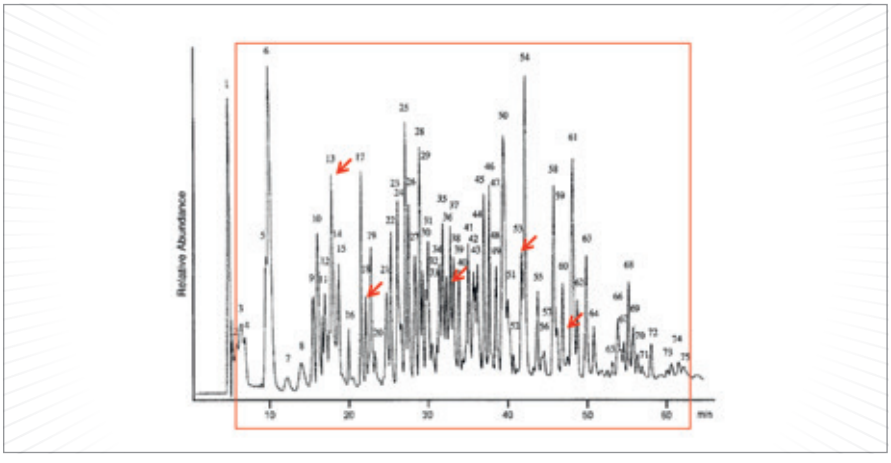


Figure 1. An illustration of problems encountered in LC-MS analysis of small numbers of analytes in complex biological samples. Red arrows show targeted analyte elution positions while the red box contains analytes that enter the mass spectrometer. Adapted from Reference 3 (highlighting added).

The scenario brings to mind Aesop's tortoise and the hare; in an LC-MS/MS version of the fable, chromatography would be mister LC Tortoise and the speedster would be mister MS Hare. One realizes that, although illogical, this fable is played out millions of times annually in routine analyses. MS is fast and underutilized while LC trudges along. In the real world, LC Tortoise would have to be cleverer to survive – insisting on rules that include i) allowing him to finish in a few steps, ii) greater exploitation of his unique skills, iii) a course that is difficult for MS, and iv) requiring MS to do more work to finish. LC could dupe MS into accepting this rule change by telling him: "These new rules will make the race a little stressful but it will be over quickly, proving how fast you are. It will be more like a sprint than a marathon, so falling asleep and waking up in time to win will no longer be a problem for you!" In actual fact, LC has skewed the rules far in his favor.

The Solution

There is clearly a problem with the way LC is

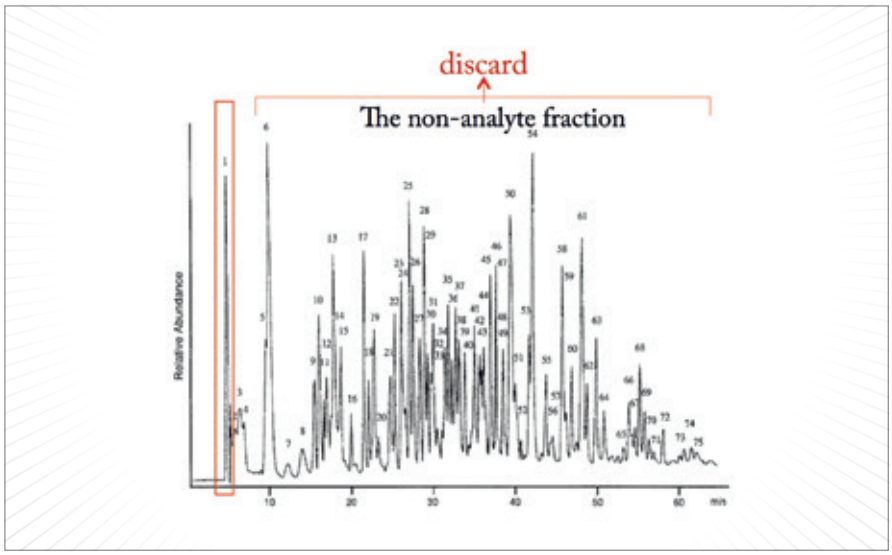


Figure 2. An MASC solution to the problem illustrated in Figure 1. The red box is where affinity selected analytes would coelute. All other substances would be discarded before entering the mass spectrometer. Adapted from Reference 3 (peaks highlighted in Figure 1 have not actually been removed from Figure 2).

being used in routine analytical applications. Although MS can resolve the highlighted analytes (see Figure 1) a thousand times faster than LC, it cannot rid the effluent of non-analytes. The primary function of the LC should be to provide the MS exclusively with analytes of interest (devoid of non-analytes), rather than dividing complex mixtures into hundreds of fractions.

The problem could be circumvented if the small number of recurring analytes in the sample were structure-specifically selected and eluted concurrently in a cluster – unretained and relatively pure in a first chromatographic peak, and ahead of solvents and non-analytes – such that analytes could be rapidly transferred to an MS together (see Figure 2). The LC would be delivering a small group of highly purified, structure-specifically selected analytes to the MS for fractionation, identification, and quantification while discarding non-analytes. Being able to achieve this in two steps within minutes would have relatively large ramifications.

Structure-specific selection of analytes from complex mixtures is something that MS cannot do, whereas the LC could do so in minutes with high reproducibility. Moreover, nothing of analytical value would be eluted into the MS beyond the first chromatographic peak. The major work of the LC would be finished after delivering a single fraction to the MS. Non-analytes could be discarded by valve switching. Moreover, it would enable reduction of ion suppression, suppress background noise, and diminish fragment ion overlap in the MS. Structure-specific selection by the LC would be a critical component of the analysis, but the MS would be doing most of the work. The tortoise would be doing a critical thing MS cannot – quickly separating a small group of targeted analytes from the thousands of non-analytes in samples. Moreover, there would be no reason to fractionate all the non-analytes in a sample as shown in Figure 2, saving a huge amount of time. The tortoise would have crossed the finish line in two steps while the MS must do a large amount of work to finish. I think Aesop might have liked this "clever Tortoise" version of his fable...

We have achieved rapid, group-specific selection of a small number of analytes from complex mixtures as suggested above by developing a new type of chromatography. We call it mobile affinity sorbent chromatography (MASC) and first presented it at HPLC 2016 in San Francisco.

LC separations have long been based on differential partitioning of substances between two, immiscible phases; one being an analyte transporting mobile phase (Pm) and the other a stationary phase (Ps) through which Pm is flowing. MASC is different, because a third, structure-specific analyte sequestering transport phase (Pt) is added to

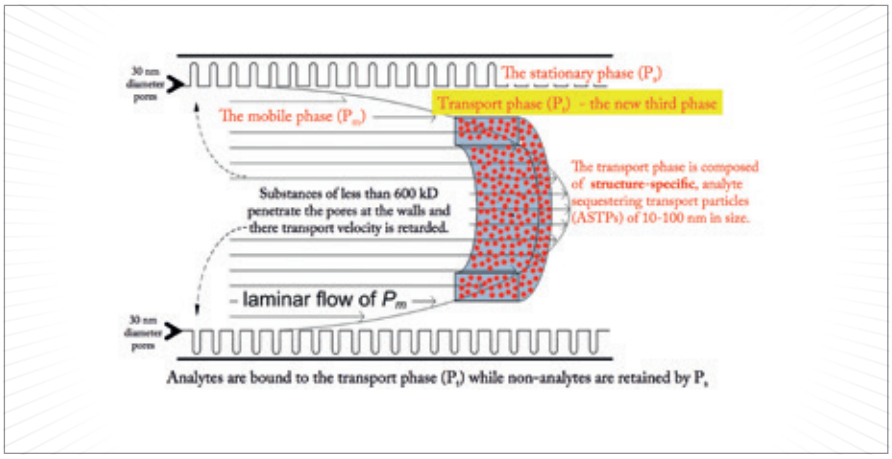


Figure 3. An illustration of the mobile affinity sorbent chromatography (MASC) model, demonstrating the three phases involved in separation processes. The function of the transport phase (Pt) is to sequester and accelerate the elution of analytes while that of the stationary phase (Ps) is to bind and retard elution of non-analytes. The mobile phase regulates partitioning between these two phases. This rapidly separates analytes from non-analytes.

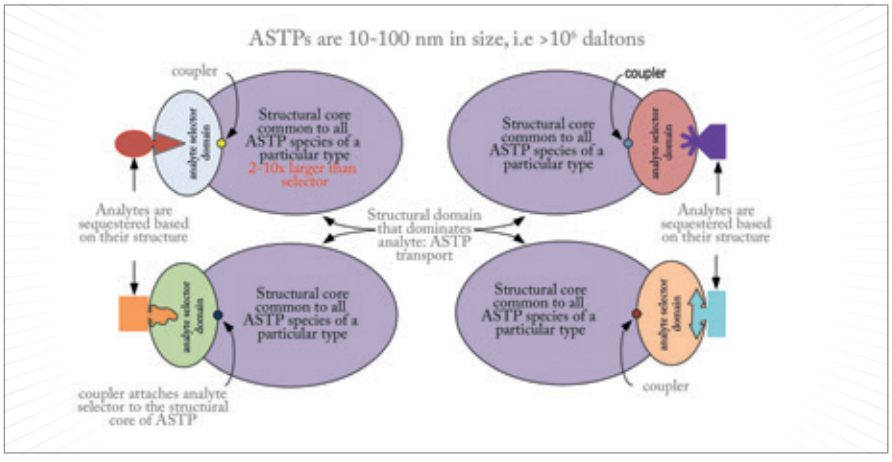


Figure 4. An illustration of the components in an analyte sequestering transport particle (ASTP).

the conventional two phase LC system (see Figure 3). The function of this new transport phase is to i) sequester analytes of interest with high selectivity and affinity, based on their structure, ii) preclude their interaction with Ps, and iii) transport them though the column unretained. Pm still plays the role of mediating partitioning and transport.

The Pt used in our early MASC experiments is composed of 20-80 nm hydrocolloids with coupled affinity selectors. These analyte-sequestering transport particles (ASTPs) are larger than most substances in plasma while being sufficiently small to pass readily between the particles in a size exclusion chromatography (SEC) column or restricted access media (RAM) system. Single-structure specific-affinity selectors (Sa) were a component of each ASTP (see Figure 4) and, in our early studies, were antibodies (Ab) with an analyte association constant typically exceeding 106. Subsequent to association with the Ab, analytes are transported through MASC columns without desorption from the ASTP (4).

ASTP particles of ~60 nm eluted in the void volume of a 30 nm pore diameter SEC column designed for the separation of water soluble substances (see Figure 5). Non-analytes of less than ~400 kilodaltons (kDa) enter the SEC pore matrix and elute after ASTPs; the retention time of ASTPs being in the range of a minute based on column dimensions and flow rate. Beyond enabling ASTP:analyte elution in the column void volume, a second advantage of MASC with an SEC column is that non-analytes have a short retention time, in contrast to the reversed phase chromatograms in Figure 1 and 2.

MASC was achieved in two ways; either by continuously adding ASTPs to Pm or by pre-equilibration of ASTPs with samples followed by injection of a small aliquot of the sample bearing analyte:ASTP complexes. The latter of these two separation modes is referred to as zonal MASC in view of the fact that the small zone of analyte:ASTP complex acts like a short column from which weakly adsorbed substances are being continuously stripped as the particles move through the SEC column. Zonal MASC has multiple advantages, with the most important being that analytes bind to the ASTP before introduction into column, circumventing the need for in-column association of analytes with the Pt, which minimizes band spreading. Zonal MASC also minimizes antibody consumption and results in non-specifically bound substances being actively removed from equilibrations with ASTPs. Finally, fresh sorbent can be used in each analysis; minimizing carryover – equivalent to using a new affinity chromatography column for each analysis.

Analyte detection by MS in MASC is best achieved by dissociation of the analyte:ASTP complex after elution from the LC column. When the affinity selector is an antibody this entails antibody denaturation by heating or addition of an acidified organic solvent. With electrospray ionization-mass spectrometry (ESI-MS) high-temperature gas in the nebulizer spray was used to denature antibodies and desolvate the products before transport into the MS as seen in the detection of carbamazepine (see Figure 5).

Beyond the Solution

The intent of the discussion above was to direct attention to three key facts:

1. the best solution to a problem may not be the most widely used,
2. the LC component of LC-MS for

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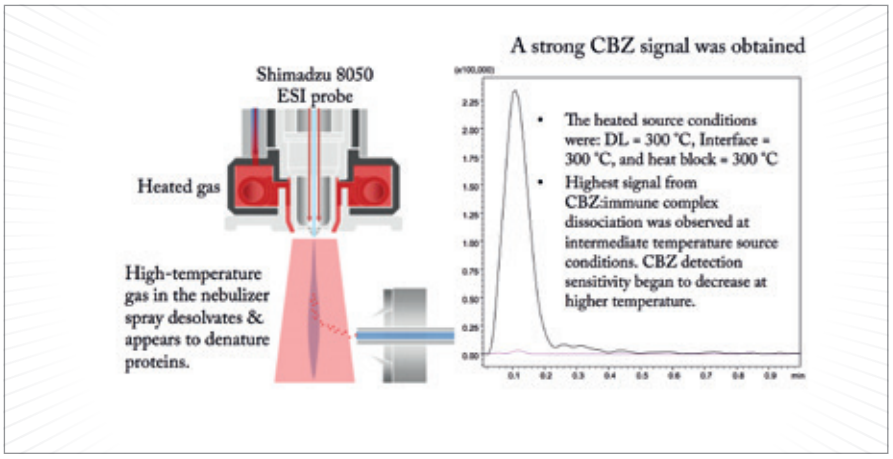

Figure 5. The inlet system used in ESI-MS analysis of carbamazepine.

routine analysis is low-throughput and unoptimized,

3. column parameters, such as particle size, theoretical plates, and peak capacity, are not always the dominant issues in an LC separation.

Although enormous gains have been made in structure-specific selection technology coupled to MS, adaptation in routine LC-MS has been disappointing. Structure-specific selection of analytes for MS analysis is actually an old technique – immunoaffinity assays using MS detection were first described in 1991 (6), followed by a host of MS-assisted assay methods ranging from mass spectrometric immunoassays (MSIA)7, affinity-MS8, and probe affinity mass spectrometry (PAMS, 9) to immunoMALDI (iMALDI, 10), surface-enhanced laser desorption ionization-TOF (SELDI-TOF, 11), and surface-enhanced affinity capture (SEAC, 12). These strategies all exploited either affinity chromatography with ESI-MS or affinity selection on MALDI plates as a means to simplify the purification of specific analytes – and they worked beautifully.

And yet, even with all of these powerful hyphenated-tools, reverse phase chromatography (RPC) still dominates sample preparation in routine LC-MS analysis of complex biological samples. As the LC-MS version of Aesop's fable suggests, the dominance of this old method is illogical. MASC with analyte-sequestering transport particles is simply another in a long list of structure-specific selection epiphanies (albeit one of the more powerful).

The Future?

Scientists often seek – or expect scientific explanations for – puzzling phenomena such as the LC-MS conundrum noted above in routine analysis. But perhaps the dilemma is not of scientific origin. Clearly, the issues noted above obstruct the delivery of high-throughput, inexpensive diagnostics to millions of human subjects; removing these obstacles would be of massive value. So why hasn't the LC-MS/MS enigma in routine analysis been addressed?

It is often overlooked by the scientific community that economics towers above the other 'omics'. Finding the 'right time' and mode of delivering a new technology often requires large investments. One skill of the investment community lies in guessing (or betting on) those elements and solutions that would provide the greatest return on investments, along with providing the requisite capital to back their bet. The manner and timeline in which a routine analysis revolution is triggered will more likely be a function of economic drivers than scientific issues.

As an afterthought, the 'clever tortoise version' of Aesop's fable should probably have included a venture capital (VC) investor who would finance the contest and declare a winner based on investment returns. Looking at this as a sporting event with betting and a P&L bottom line is perhaps much more exciting than increasing LC-MS throughput, decreasing ion suppression, and eliminating background noise in spectra.

Fred Regnier is J.H. Law Professor of Chemistry Emeritus at the Department of Chemistry, Purdue University, Lafayette Indiana, USA.

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Directing the Future

Sitting Down With... Emily Hilder, Director, Future Industries Institute (FII), University of South Australia, Adelaide, Australia.

Congratulations on your fourth appearance on The Power List...

I was surprised by my presence on the first Power List – as were a few other colleagues... The list may not be objective (influence is hard to measure), but it's done a lot to get people thinking about what's going on in the field and who's active. The controversy is all part of it! It's great to see a list profiling only women, which makes us all consider diversity more carefully. I believe that diversity is critical to high performance and something to be celebrated.

How did you get into analytical science?

It's always been about natural curiosity for me. My family loves telling the story of my fifth birthday party; I spent a good deal of it training my guests how to take the wheel off a bike – in a party dress. I like to learn how things work. When it was time for university, I believed that science would allow me to move into a whole bunch of different careers and I knew that I liked chemistry. I remember telling one lecturer that I would never do analytical chemistry again – it seemed boring and irrelevant. Later, in a mainstream chemistry class, a professor came in and started talking about chromatography with an enthusiasm I'd never seen before. It was Paul Haddad. I realized that it wasn't just about the science, it was about the people – and all the connections that come together to bring it alive.

How have you risen through the ranks so quickly?

I think it's important to be aware of the bigger picture; I guess one of my strengths is seeing connections between seemingly unrelated concepts. I also think it is important to actively listen out for problems that you can help solve with creativity. These days 'disruptive' is a buzzword, but not all solutions need to be disruptive – sometimes, articulating the real value in what you are doing is good enough to help you progress.

What's your underlying motivation?

Someone once described me as ruthlessly pragmatic. I guess that's because I really care about doing something meaningful. I'm not particularly driven by personal recognition (although it can be nice), but I'm deeply motivated by being able to create an environment where other people can succeed outside of their own expectations. In my family, academic achievement is no more important than any other; my father would simply say, "whatever you do, be passionate about it, be good at it, and make sure it's something useful."

What sparked your move to the FII?

Aside from the personal challenge (and I do love a challenge), I could see great potential in bringing truly interdisciplinary teams together to tackle some of the modern world's grand challenges – many of which cannot be solved by a single discipline. And I was also really motivated by the focus on being led by industry. It's a beautiful mix of collaboration and pragmatism. The real world doesn't respect discipline boundaries.

Your role is a testament to the change that's going on in analytical science...

The younger me certainly didn't appreciate the versatility that would come with being trained as an analytical chemist – or the impact that analytical science would have in general. My institute works across an incredible breadth – from mining through to basic biology – so at first glance, it doesn't seem to be the kind of place where you would have an analytical chemist at the helm. And yet, my groups have always crossed almost every aspect of what's possible in the institute. It's ironic really – the field is more relevant than ever, but also suffering in terms of unique identity more than ever... We need to ensure that training of the fundamental principles does not disappear in an avalanche of applications. If you get the fundamentals right, they can be applied to any field or problem.

"The younger me certainly didn't appreciate the versatility that would come with being trained as an analytical chemist."

Where is analytical science heading?

The really big and exciting challenge at the moment lies in developing tools for real-time measurements in situ – it's a game changer for understanding complex systems, particularly in the biological arena. It's also extremely challenging, because we often need to measure very small quantities of analytes in places that are not amenable to sampling. What we've been able to achieve over the last 10 or 20 years has already been phenomenal, but right now, we tend to measure what we can measure rather than what we need to. Translating some of that knowledge into highly-sensitive, real-time measurements is going to have a huge impact across a whole range of fields. And it won't be easy...

So the role of analytical scientists is still very much secure...

I think we're going to be very relevant for a very long time! Don't forget that until we develop new measurement tools, we don't even realize what we couldn't see before. And when we suddenly gain new information, it allows us to start asking questions we'd not previously thought to ask – that's where breakthrough science exists.

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