JANUARY 2017 # 48

the Analytical Scientist

Landmark Literature

Six experts round up the most eye-catching papers of 2016.

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Image of the Month

7,000 Years in Tibet

Analyses of fossilized footprints on the central Tibetan plateau suggest that hardy humans resided there up to 4,000 years earlier than previously thought – long before agricultural crops were introduced. A collaborative team used three separate dating methods to analyze sedimentary quartz around imprints found on the site, and estimated that they were made between 7,400 and 12,700 years ago. This image shows a close up of the single-grain attachment with green laser used to measure the luminescence stored in individual sand-sized grains of quartz, one of the methods that allowed the research team to date the prints.

Credit: Laboratory for Luminescence Dating at the University of Innsbruck; photo by Robbie Shone.

Reference: 1. MC Meyer et al, "Permanent human occupation of the central Tibetan Plateau in the early Holocene", Science, 355, 64–67 (2017)

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

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On The Cover

The landmarks depicted represent the origins of our standout papers.

the Analytical Scientist

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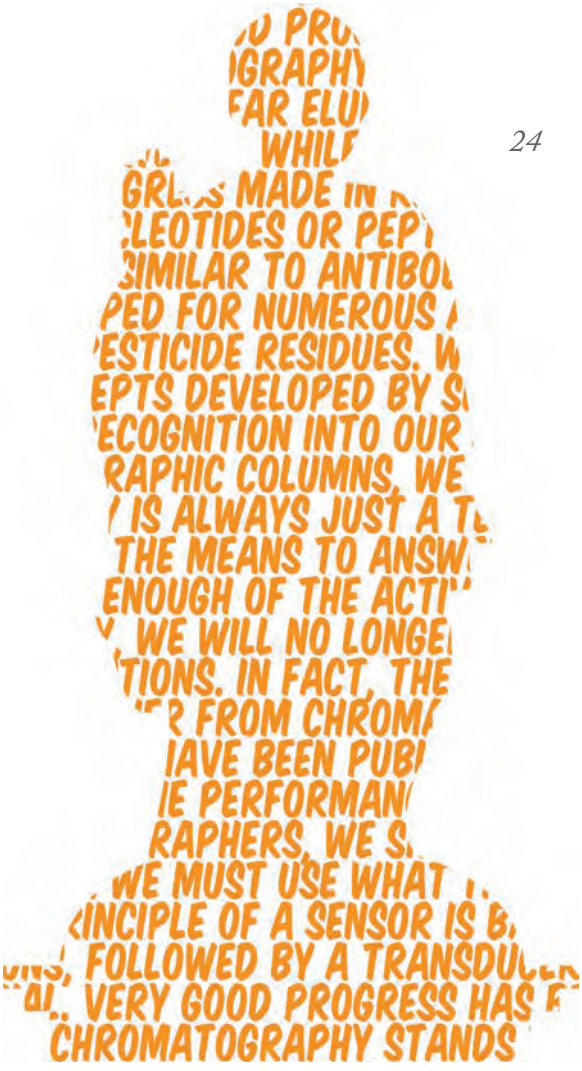

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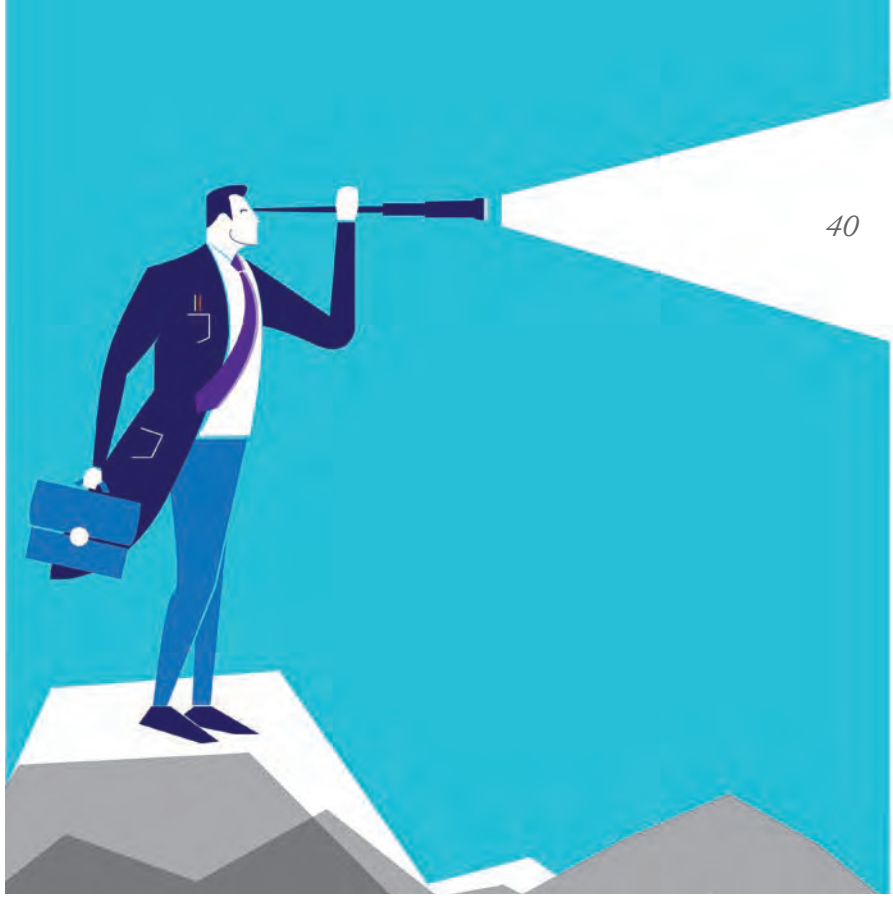

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In My View

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Sitting Down With

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New Year, New Faces, New Hopes, Age-old Challenges

What will the year 2017 mean for analytical science? At the very least, it should allow us to move forward.

It's fair to say that 2016 was an eventful year – particularly from a political point of view. How will those changes affect the analytical sciences? That's hard to say (I hope our political leaders will continue to pay at least some attention to what the science community has to say...) But I doubt it will mean a sudden and impressive influx of investment. Science funding will continue to be a battleground. To that end, I'm pleased to announce a new series of articles – "Adventures in Funding" – which we hope may shed some light on how analytical scientists in academia can secure the money needed to advance what I would argue is the most essential arm of science. Gert Desmet kicks us off on page 46, and I think his story represents hope for the field as a whole.

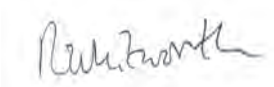
January is always a time for looking back – we cover the "Landmark Literature" of 2016 on page 24 – but it's also a time for looking forward. Analytical science is known for its incremental improvements (which ensures that we move in the right direction), but I'm always excited about the cutting-edge technologies and techniques that often surface over the course of a new year. In case you missed The Analytical Science Innovation Awards in the madness that is December (tas.txp.to/0117/TASIAs), our Top Five technologies are a showcase of advancements that move us forward more rapidly. A microfluidic CE-MS interface, real-time focus tracking for Raman, tandem ionization, a novel ion spray source, and a re-think of how GC systems should be built – they all have the potential to significantly change the way we approach measurement science. But application is everything, so we can also look forward to seeing how such groundbreaking technology will be applied in 2017, which innovations will become the new 'gold standard' and which will disappear into obscurity?

One thing's for sure: there is no shortage of analytical challenges, and therefore no shortage of opportunities to make a difference. I personally like Emily Hilder's vision for the future: highly-sensitive, real-time measurements in situ. Best get your 'thinking caps' on.

January is also The Analytical Scientist's birthday. We're four years old, have 48 issues under our belt – and yet we have more great content in the pipeline than ever before. And so in 2017, we will not be slowing down – quite the opposite, which is why I'm delighted to introduce our new editor: Charlotte Barker. Charlotte will be joining me, Frank van Geel and Joanna Cummings to ensure that The Analytical Scientist can move forward even faster.

All the best for the New Year!

Rich Whitworth
Content Director



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: charlotte.barker @texerepublishing.com

Purple's Reign

The sophisticated chemistry behind a simple – yet infectiously popular – purple dye

It all started with a vivid purple dye, discovered during the quest for anti-malaria treatments in the 1850s. William Henry Perkin was attempting to develop a synthetic form of quinine when he stumbled upon the formula for a purple dye, which he promptly patented as 'mauveine' in 1856.

During this period of the Victorian era, the demand for synthetic dyes was growing at a rapid rate, and the expensive method for producing mauveine gave it an extra air of exclusivity. The rapid growth in the dye's popularity led to it being dubbed 'mauveine measles', and even royalty got the bug – Queen Victoria and Empress Eugenie, wife of Napoleon III each wore mauveine-dyed dresses to state functions. As a result, competition to produce the dye was tough.

Now, researchers at Aberdeen University have discovered that in an attempt to fool his competitors and hide the true formulation, Perkin may have made several permutations of the dye – suggesting he had a more sophisticated approach than previously thought.

John Plater's team used LC-MS to analyze 15 six pence stamps produced with mauveine between 1865 and 1869, and compared this with Perkin's mauveine (obtained from the Manchester Museum of Science and Industry). They discovered striking chemical differences between the two (1). "The museum-stored mauveine, which is only available in four sites around the world, has two key ingredients, but the mauveine used on the majority of stamps analyzed has a very different composition to Perkin's mauveine and a different method of synthesis seems reasonable," Plater says. "This suggests that the samples given to the museums are true to the method used to manufacture the mauveine commercially, but are not the same as the mauveine made by his patented method."

Plater believes Perkin never fully revealed what he did to scale up production of his famous dye. "Mauveine is a very difficult thing to make because the yield is very low. The yields I have been able to reproduce in a lab give around five percent rather than the one percent from his patented method of 1856 [...] On this basis, it is clear to see why a more efficient method was needed for mass manufacturing," Plater says. "I propose that he used a very early form of traceless synthesis to modify the composition and improve the yield. And that indicates that far from being an 'accidental' chemist, he really was a true pioneer of his time." *JC*

Reference

1. *MJ Plater, A Rabb, "Mauveine and the mauve shade six pence stamp", J Chem Res, 40, 648–651 (2016).*

Moor Applications for Spectroscopy

Portable Raman allows in situ, non-invasive analysis of Alhambra polychrome decorations

Raman spectroscopy is highly prized in the field of cultural heritage because it allows non-destructive chemical analysis of artifacts. Portability further expands the application potential by allowing real-time, non-invasive field studies and by eliminating the need to take samples.

A collaborative group from the University of Jaen and the Conservation Department of the Alhambra and Generalife Council, both in Spain, recently launched a study of decorations in the Alhambra, a Moorish palace and UNESCO World Heritage Site (1). The team used a combination of analytical techniques that allowed most of the studies to be performed in situ. For example, portable Raman was used to detect the pigments and elucidate the techniques employed in the creation of the plasterwork – and to assess any potential conservation problems (2).

"Analytical techniques can provide the answers to many queries regarding the conservation state of assets under study or rehabilitation," says María José Ayora Cañada (Department of Physical and Analytical Chemistry, University of Jaen). "The characterization of decay compounds and the understanding of the degradation pathways – in many cases caused by chemical reactions between the original compounds and chemicals present in the environment – are crucial for the design of appropriate strategies of preventive conservation and intervention."

Ayora Cañada notes that, for the past few decades in the field of cultural heritage, interest has been focused on the development of non-invasive or non-destructive analytical techniques. "When dealing with artifacts, most of the challenges are around sample preparation, which is in many cases complex and labor intensive. In addition to preserving the artwork with a non-invasive study, the on-site investigation gives a more representative knowledge of the art objects, because the measurements are not limited to the samples that can be taken," she adds.

But in-situ measurements pose unique challenges – especially when working on top of scaffolding. "The vibrations made it difficult to maintain the laser beam in focus in prolonged measurements," says Ayora Cañada. "Daylight was a big problem; the Raman effect is very weak and background radiation from sunlight interfered with the spectra. The problem was partially solved by attaching a cover of dark foam to prevent the sunlight from reaching the objective aperture."

The team took to the lab to make other measurements that were simply not possible in the field, including analysis using a more sensitive Raman instrument. "Scanning electron microscopy equipped with energy dispersive spectroscopy (SEM-EDS) was also used to study the morphology and elemental composition of the samples – and to identify layers of different metals in gilded decorations," says Ayora Cañada. "And we used Fourier transform infrared (FTIR) microscopy to gain information about the organic materials employed as binders."

Ayora Cañada notes the need for a collaborative effort when it comes to protecting our heritage: "Conservators and restorers who wish to conserve cultural assets need to work in cooperation with analytical scientists – the professionals who can study the materials and the way those materials age in a given environment." *JC*

References

1. *P Arjonilla et al., Appl Phys A, 122,1014 (2016).*
2. *A Dominguez-Vidal et al., J Raman Spectrosc, 45, 1006–1012 (2014).*

MSB: Small Scale, Big Impact

Microscale Separations and Bioanalysis 2017 aims to highlight cutting-edge research at the frontiers of microscale separation science

The Microscale Separations and Bioanalysis (MSB) symposium has evolved over the last few years into a recognized forum for the discussion of new developments and ideas at the microscale – and their impact across various analytical fields. We talk to organizers Govert Somsen and Rawi Ramautar about the upcoming conference and why, when it comes to the future of analytical technologies, it may pay to think small...

Why are microscale separations important?

GS: Miniaturization of separation techniques is a dominating trend in modern analytical chemistry. Requirements related to quality, health, environment, safety, security, and costs are critical driving forces for this 'scaling down' of techniques. And it leads to exciting developments, not only in micro- and nano-LC, capillary electrophoresis, capillary GC and microfluidic separations, but also in lab-on-a-chip, sample pretreatment and detection methodologies.

RR: The importance of microscale separation techniques is also increasing in drug analysis, metabolomics, (glyco) proteomics, intact protein analysis and bioanalysis in general. Microscale analytical tools often provide better sensitivity and separation efficiency, and enhance the analytical performance of mass spectrometry-based methods, which is crucial for the reliable chemical profiling of complex samples.

What is the focus of the conference?

GS: MSB 2017 provides a forum for discussing fundamental and application aspects of microscale separations and related techniques. As indicated by the name, the symposium focuses not just on micro-separation science, but also on its applications in life science research.

RR: The MSB meeting especially encourages the exchange of ideas of unpublished scientific work on microscale separations in an intimate and confidential setting. To this end, MSB 2017 will be organized at an 'isolated' venue in Noordwijkerhout, providing closely grouped lecture and poster rooms.

Who do you hope will attend?

GS: Scientists exploring, designing and utilizing microscale separation technologies as an important component of their research and/or development program. MSB 2017 will be rewarding and inspiring both for fundamental micro-separation researchers and life science-oriented users seeking strategies to improve performance and impact by involving microscale techniques. We want to bring scientists together to debate challenges and explore new ideas,

with the aim of fully realizing the power of separations at microscale.

How has the conference changed in the past three years?

GS: The intention of the Strategic Planning Committee (SPC) in 2013 was to shape MSB into a forum of truly engaging dialogue and deep discussion. We know from experience that real discussion and interaction cannot be taken for granted, but needs to be actively stimulated and structured. Some key attributes for imposing the new format were: (i) a limited number of invited speakers, (ii) building at least 70 percent of the oral program from submitted abstracts, (iii) a double-blind peer review process ensuring that quality – and not who you are – gets you an oral presentation, (iv) at least a third of the duration of oral presentations reserved for discussion moderated by an active chair person, and (v) daily Science Café lunch seminars by vendors presenting and discussing advances in commercial separation technology.

Which techniques are emerging within the field?

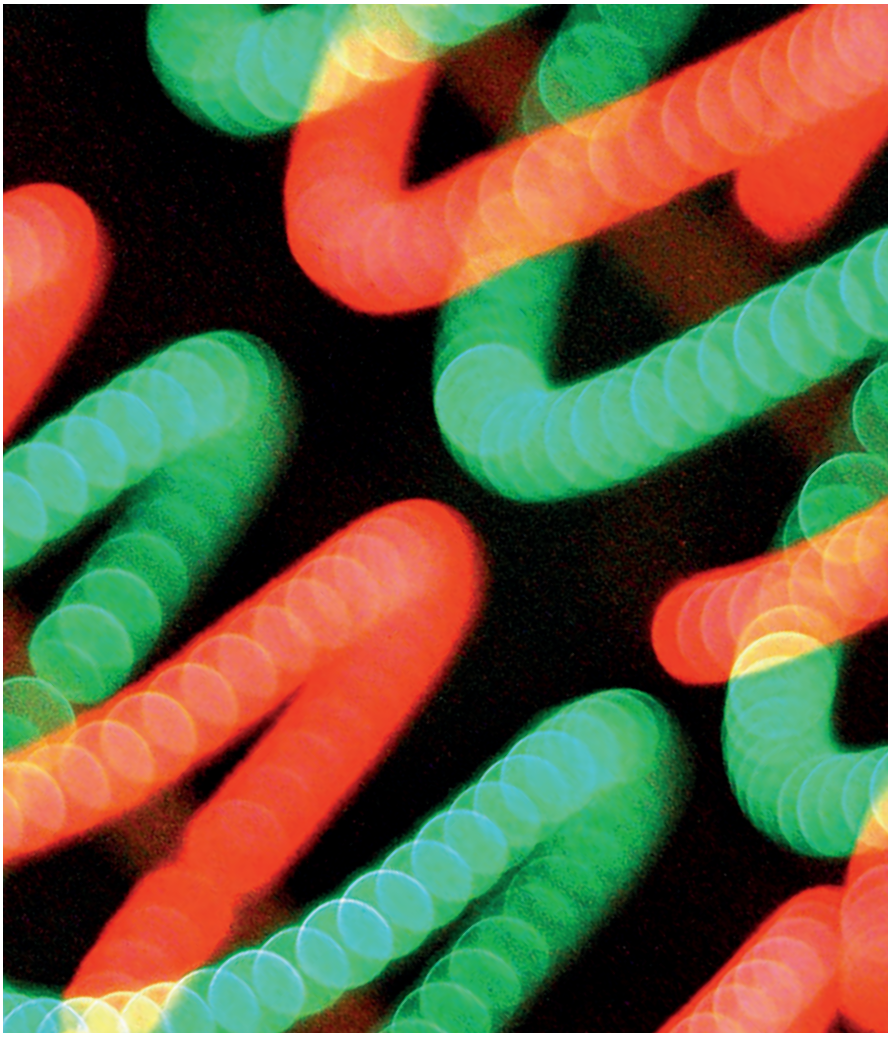
GS: Developments in microscale separation science continuously lead to improved analytical performances. For example, new multidimensional liquid chromatography systems involving micro- and nano-columns are yielding unprecedented peak capacities, advancing proteomics and biomarker discovery. Progress in CE-MS interfacing provides new possibilities for proteoform separations, aiding detailed characterization of biopharmaceuticals and endogenous proteins. Recent advances in ion mobility-mass spectrometry have opened new avenues for studying 3D structures of (macro) molecules from complex mixtures.

RR: Over the past few years, microscale separation techniques, including electrodriven and chromatographic methods, have been developed for analyzing small samples in a wide range of application fields. This will remain an active research domain in the future. I also expect major developments in the downscaling of sample preparation procedures, more effective hyphenation of microfluidic separation modules to nano-electrospray ionization (ESI)-MS, and microfluidic-based diagnostic assays with optical detection as the read-out.

MSB 2017 will be held March 26–29 at Conference Center Leeuwenhorst, Noordwijkerhout, the Netherlands. msb2017.org/

NoBody's Fool

Advanced mass spectrometry uncovers a tiny protein with important implications



Meet NoBody (non-annotated P-body dissociating polypeptide): a new, functional human microprotein, discovered and characterized by biochemists using cutting-edge gene sequencing and proteomics technologies at Yale University (1).

The team examined myeloid leukemia cells, first removing larger proteins, then using LC-MS-based proteomics to uncover the amino acid sequence of each of the more than 400 microproteins that remained. Having discovered a veritable treasure trove of previously unknown proteins, the researchers set out to find out their function (if any) in the body.

"Evolutionary sequence conservation is a great way to help you find function because if the protein sequence of a gene doesn't change, that probably means it is doing something important and changes to the sequence would be detrimental," explains co-senior author Alan Saghatelian. "Sarah Slavoff (co-senior author) decided to dig into the function of the gene for these microproteins, and through functional proteomics, linked NoBody to proteins that had been characterized in mRNA decay." In other words, NoBody helps to recycle genetic material in the cell.

Recent advances in gene sequencing have enabled detection of the small open reading frames (smORFs) that encode microproteins like NoBody, Saghatelian says. "Without RNA-Seq we could only have found about a third of smORFs. In addition, mass spectrometers have gotten so much more sensitive that it really allows us to dig a lot deeper into the proteome to find them. Ten years ago, the same experiment might have yielded 10–20 percent of what we are seeing today."

Saghatelian says that the discovery of NoBody has major implications: "First, it points to the fact that digging into the biology of microproteins is going to lead to new biological insights, and in some cases we will learn something about a disease, which we can use to develop new treatments." Second, he says, it has contributed to understanding the regulation of mRNA decay. "mRNA levels are used to do so much in biology, but most of this is considered from a production viewpoint (which is to say, transcription). However, degradation of particular mRNAs will be important too. The field has tons of room to grow – there is still a lot we don't understand."

The lab is now focused on finding and characterizing more microproteins, as well as building better technology to identify the most interesting ones to study. "In terms of biology and the relation to disease, my feeling is that we're only at the beginning," concludes Saghatelian. *JC*

Reference

1. *NG D'Lima, "A human microprotein that interacts with the mRNA decapping complex", Nat Chem Biol, 13, 174–180 (2016).*

Pittcon and All That Jazz

With a program of over 2,000 presentations, Pittcon covers all analytical bases. Here, we present our top picks for Chicago.

Pittcon is a highlight on many laboratory calendars, and Chicago 2017 looks set to be no exception. This year sees some exciting symposia on bioanalytics, the –omics and education, as well as sessions on the increasingly important role of analytical chemistry in the world of medical cannabis. And, of course, companies big and small will be displaying their wares on the endless exhibition floor. If you can't make it, we'll be live tweeting from @tAnaSci. If you are attending, here are our top picks from the vast program. *JC*

Awards and Symposia

1. Translational Microfluidic Platforms for Clinical Diagnostics (Sunday PM)
2. Frontiers in Sensors: From Ultrasensitive to Single Molecule Devices (Monday PM)
3. Novel Uses of Mass Spectrometry and Ion Mobility in Pharmaceuticals: From Small Molecules to Monoclonal Antibodies (Tuesday AM)
4. Measurement at the Speed of Thought – New Analytical Approaches for Monitoring the Brain (Wednesday PM)
5. Atomic Spectroscopy Instrumentation Development: A Disconnect Between the Research Laboratories and the Pittcon Floor (Thursday AM)

Oral Sessions

1. Metabolomics, Proteomics, and Lipidomics (Sunday PM)
2. Advances in Mass Spectrometry (Monday AM)
3. Advancements in Environmental Monitoring (Tuesday AM)
4. Developments in Forensics and Homeland Security Analyses (Wednesday PM)
5. Bioanalytical - LC, Sensors, and Microscopy (Thursday AM)

Organized Contributed Sessions

1. Advanced Concepts in Ion Chromatography and Recent Trends (Sunday PM)
2. Drug Detection in the Field (Monday AM)
3. From Discovery to Precision Medicine: Mass Spectrometry Through the Years and Beyond (Tuesday PM)
4. Frontiers in Atomic Spectrometry (Wednesday AM)
5. Supercritical Fluid Chromatography for Food Analysis (Thursday AM)

Networking

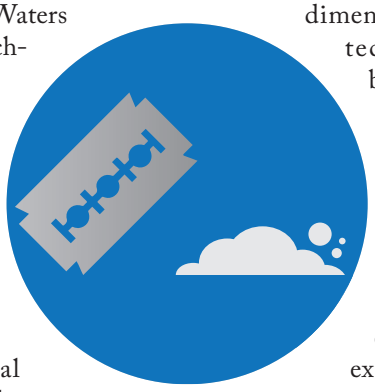
1. Analytical Chemistry in Developing Countries – Norman Fraley (Sunday PM)
2. Cannabis Testing Forum: New Opportunities for Enhancing Quality and Expanding Research – Joshua Crossney, (Monday AM)
3. Non-Invasive Biomedical Analysis – VOCs Are in the Air – From Cellular Metabolism to Crowd Monitoring – Wolfram Miekisch (Monday PM)
4. Defining, Refining, and Advancing Chemical Measurement and Imaging – Lin He/Michelle Bushey (Tuesday PM)
5. Steal My Strategy: Crowdsource Ideas to Improve Your Teaching! – Anna Donnell (Wednesday AM)

Pittcon 2017 will be held March 5-9 at McCormick Place, Chicago, USA: www.pittcon.org

Narco Polo

A new 20-minute method homes in on traces of illegal drugs

Chemists in toxicology labs are always looking for ways to improve detection of illegal drugs – especially as lengthy sample preparation procedures often cause delays that can compromise the analysis. In a recent paper (1) – and in collaboration with Waters Corporation – the Botch-Jones research group at Boston University School of Medicine slashed the time it takes to analyze illicit substances. "In forensic toxicology, we are challenged with providing comprehensive analytical testing as efficiently as possible," says group leader Sabra Botch-Jones. "For this research we wanted to reduce the amount of time required to prepare samples without sacrificing analytical sensitivity." And the time saved was indeed significant – illegal drugs were identified in urine samples in fewer than 20 minutes, compared to traditional techniques that can take hours for sample preparation prior to analysis.



The research team decreased sample preparation time by using a microextraction technique that eliminates the lengthy evaporation step typically following solid phase extraction. "Most traditional single dimension chromatography techniques would not be able to handle the high concentration of organic solvent used in this type of extraction," explains Botch-Jones. "With 2D-LC and a process called 'At-Column' dilution, a sample extract containing a high organic solvent content can be directly introduced in the LC system, which saves a significant amount of time."

The Botch-Jones lab have since completed several additional studies evaluating the use of the technique with complex matrices, such as bone, tissue and blood, and have demonstrated the ability to extract cocaine and metabolites from bone samples at trace concentrations. In addition, they have evaluated the use of the technique with new psychoactive substances, such as potent NBOMe compounds.

The team plans to share its methods with the analytical and forensic toxicology community, to help increase sample throughput in analytical toxicology laboratories – and ultimately hopes to see them used in forensics and law enforcement. "It was incredibly rewarding for our group to be a part of a research effort that will have such a positive impact on the analytical community," says Botch-Jones. "We feel that multidimensional liquid chromatography using this microextraction technique will grow in popularity." *JC*

Reference

1. *C Mallet, S Botch-Jones, "Illicit drug analysis using two-dimension liquid chromatography/ tandem mass spectrometry", J Anal Toxicol, 40, 617–627 (2016)*

Columns, Collaborations, and Chemical Detectors

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 the opening and acquisition of several food testing labs by SGS – and Agilent's latest Thought Leader Award goes to a pioneer in the field of infrared spectroscopic imaging.

Products

- Waters CE-marks IVD MassTrak Vitamin D Solution
- Premier Biosoft announces the release of SimLipid Software 5.50
- Waters expands Torus SFC Column Line with four new columns

Collaborations

- Bruker delivering 300 hand-held chemical detectors to German BBK
- Agilent Thought Leader Award for University of Illinois researcher
- Agilent and Transcriptic Inc. partner to automate discovery biology
- Singulex and Thermo Fisher Scientific partner for Sepsis ImmunoDx

Financings & Acquisitions

- Bruker acquires InVivo Biotech Services GmbH, MALDI imaging software firm SCiLS GmbH, and Active Spectrum, a pioneer of micro-ESR
- PerkinElmer to sell medical imaging business to Varian
- SGS acquires food-testing lab Laagrima in Morocco, a controlling stake in C-Labs SA, Chiasso, Switzerland, and a 70 percent stake in Biopremier, Portugal
- Agilent to acquire MDx firm Multiplicom NV for €68m in cash
- Eurofins acquires Exova's environment testing business in Eastern Canada for about CAD 13m
- Metabolon raises additional $15m from Essex Woodlands

People

- Stefan Traeger, Head of Life Sciences, to leave Tecan in 2017
- Waters appoints Sherry Buck as new CFO

Organizations

- SGS opens new food testing lab in South Korea, near Seoul

For links to original press releases and more business news, visit the online version of this article at: tas.txp.to/0117/BUSINESS

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

Why Science Depends on Diversity

The key to fostering diversity in technical and leadership positions? Invite, include and empower.

By Laurie Locascio, Director, Material Measurement Laboratory, NIST, USA.

I was proud to be named to The Analytical Scientist's 2016 Power List and among the top 50 most influential women in the analytical sciences. The list of luminaries represents how far STEM fields have come in welcoming people from under-represented groups into technical and leadership positions. But it's too soon to rest. Though the sciences are increasingly diverse, I still attend many meetings where I am the only woman in the room, and sometimes feel I must work to be heard. Some people are less persistent, and we consequently miss a great deal of valuable input.

As recently reported in The Washington Post (1), the women of the White House staff have a pact to amplify each other's ideas – by repeating and crediting them – to make sure they are heard. Let's all vow to follow their example, and help other voices be heard. Whether you are a leader of today or tomorrow, seek to amplify the voices of the people who differ from you – and not just physically. Of course, diversity is about demographic differences, but it is also about inviting people with different mindsets, world views, personalities, preferences, and working styles to participate.

'Invite' is the operative word. We must do more than simply make room for people to express their opinions. It is human nature to want to form groups with people who seem like us; it's an instinctive effort to feel included and avoid conflict. However, our desire for inclusion does not always make us inclusive towards others. According to diversity expert Helen Turnbull, our neuropsychology makes it more difficult for us to empathize with people we don't consider part of our 'in group'. Don't worry; we are not doomed to homogeneity. We can challenge our brains to explore those biases and grow our capacity to welcome people who are different from us. We can work to help people feel that they belong, and that they will be heard.

To continue to prosper, civilization needs us to foster diversity. According to Stanford University researcher Margaret Neale, studies of working groups have shown that in more diverse groups each person brings a richer set of information to the table in anticipation of informing others and advocating for their ideas. Those discussions lead to more

"I still attend many meetings where I am the only woman in the room, and sometimes feel I must work to be heard."

innovative solutions. We will need that creativity to solve the existential issues facing humanity – safeguarding energy, food and water for all, fighting antibiotic resistance, and tackling emerging diseases will all require ingenuity. Our economic security is also at stake; today's business climate is marked by stiffer competition and constant pressure to adapt to new markets.

In the 1960s, the average lifespan of an S&P 500 company was 50 years but today, it's just 12 years (2). Businesses must change, or perish. In addition to the benefits of constructive conflict, teams of people with diverse views and experiences empathize with a wider range of customers, which leads to more readily adopted solutions. In other words, diverse teams respect what is unique about their clients. They are also successful change agents: research shows that diverse teams spread new practices faster within organizations because each team member influences a separate network (3).

How can we boost diversity? The US Department of Commerce cites a lack of female role models as one of the factors that contributes to low participation by women in STEM. Women hold less than 25 percent of jobs in science, technology, engineering, and math, but are nearly 50 percent of the total workforce. The situation is similar for other groups; Hispanic-Americans and African-Americans each hold about six percent of STEM jobs, although they constitute 11 percent and 14 percent of the American workforce, respectively. When members of under-represented groups see people like themselves in top positions in government, industry, and academia, they believe that they, too, can succeed as leaders. Our efforts to increase diversity today will pay off exponentially as each generation attains leadership roles and inspires still more diversity among upcoming waves of STEM workers.

As the leader of a large technical organization, my goal is to continue to build a culture of scientific excellence that will thrive into the future. To produce the best science, we need everyone to actively participate. And so I will continue to invite, include, and empower people who are different from me.

I invite you to do the same.

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It's Time to Push LC Limits Once Again

As the 45th International Symposium on High Performance Liquid Phase Separations and Related Techniques approaches, let's set a positive intention: to engage in meaningful discussions and debates that help our great field move forward.

By Michal Holčapek and František Foret, Chairmen of HPLC 2017 Prague

HPLC has come a long way over the years – and the HPLC symposium series has always been there to track its progress closely. It's also there to make sure we keep moving forwards! Well known as the world-leading forum for information exchange between researchers dealing with separations in liquid phases and supercritical fluids, the expectation is for each year's conference program to be bursting at the seams. HPLC 2017 Prague will not disappoint, covering aspects of fundamental and experimental approaches, as well as column technologies, cutting-edge applications and innovative instrumentation; as always, a large exhibition will play its essential role in the conference.

In more recent years, separations coupled with mass spectrometry have become increasingly important – and so a program track is now devoted solely to hyphenated techniques. Similarly, other new trends, such as microfluidics and nanotechnologies, have found their way into the program. Seeking out new trends – and deciding which ones are most likely to be embraced by a wider community – makes each HPLC meeting as exciting as the one before. And the chance to discuss these new trends – and forgotten fundamentals – with colleagues from around the world makes HPLC 2017 simply unmissable!

In particular, we look forward to

"We have decided that one of the main goals of the HPLC 2017 Prague symposium must be to attract the active participation of young researchers."

discussing some of the challenges and trends that will affect HPLC and its proponents. In recent years, there has been a shift from conventional HPLC to ultra-high-performance LC (UHPLC), and UHPLC is now a mainstream separation technology. We expect to see further reductions in particle size, but will technology limitations allow particles below 1 µm?

To push HPLC further, do we need to look to alternative column technologies or novel multidimensional methods – or both? On one hand, Gert Desmet is attempting to micromanufacture the perfect column (page 46) with the backing of a prestigious European Research Council (ERC) Advanced Grant. Meanwhile, Peter Schoenmakers is also pushing the limits of LC with his "Separation Technology for A Million Peaks" project – thanks to another ERC Advanced Grant. Both offer wonderful fuel for discussion...

Applied sciences are crucial. Theoretical achievements without possible applications are meaningless, so we also need to explore novel applications in medicine, biochemistry, clinical chemistry, pharmaceuticals, and so on – all topics covered in the program. The rising star of previous conferences has been supercritical fluid chromatography (SFC). Though the principle is not new, advanced commercial solutions bring reproducibility and robustness, which makes SFC (especially in UHPSFC configuration) more applicable to real-world analyses. For example, emerging applications of UHPSFC-MS in lipidomics and pharma illustrate the potential for real bioanalysis of low to medium polar compounds.

It's clear that success rarely happens overnight and few grand challenges are solved rapidly, so the future of our field also depends on its accessibility and appeal to the next generation. Therefore, we have decided that one of the main goals of the HPLC 2017 Prague symposium must be to attract the active participation of young researchers. We're very excited that, for the first time, one of the four parallel program tracks will be devoted solely to speakers under 35 years old, along with tutorial-style lectures from top experts to boost young researchers' know-how. The HPLC symposium has a history of supporting younger scientists in the form of awards, and we're pleased and proud to be able to present the following: the Csaba Horváth Young Scientist Award for the best young speaker at the symposium, the Best Poster Award, and the Georges Guiochon Faculty Fellowship for excellent young scientists in liquid phase separation sciences. Of course, all of this can only benefit those who attend the event, so we are pleased that a number of travel grants will be offered by various organizations for students and young post-docs. We've also reduced the student's registration fee down to only 240 euros – the lowest price for a decade.

The other three tracks in the main program include i) Fundamentals (FUN, covering research from mechanisms of mass transport phenomena to data analysis, validation and chemometrics), ii) Hyphenations (HYP, ranging from high-resolution separations-MS coupling to high-throughput data processing and bioinformatics), and iii) Applications & Instrumentation (APP, which includes a diverse portfolio of integrated –omics approaches and systems biology, clinical and environmental analysis, food analysis and/or (bio)pharmaceuticals and drug metabolism). As always, leading scientists from all over the world will present exciting and motivating plenary, keynotes, and tutorial lectures. Visit www.hplc2017-prague.org to see a continuously updated list of oral presentations.

This is just the first of several "In My View" articles that will explore the field of HPLC ahead of our meeting in Prague – we hope the opinions presented will act as 'food for thought'. Here, it would be remiss of us not to notify you of some important dates:

January 23 – Abstract deadline for oral presentations
March 6 – Abstract deadline for the Best Poster Award and for inclusion in the preliminary program
March 20 – Deadline for early registration payment
April 17 – Deadline for poster presentations
May 1 – Deadline for regular registration payment
May 1 – Final program
June 1 – Abstract deadline for late-breaking posters
June 18-22 – We welcome you to the HPLC 2017 Prague symposium!

Prague is easily accessible from all major European cities and many overseas destinations and offers a wide range of accommodation for all budgets. And we should note that the social programs will be just as exciting as the scientific one. For those who have not visited Prague before, our rich culture, historical treasures and great Czech hospitality awaits you. Those who have visited before know what to expect and we look forward to welcoming you back!

HPLC 2017 Prague takes place June 18–22 at Prague Conference Centre. www.hplc2017-prague.org

A Glowing Source of Inspiration

Solution-cathode glow discharge is a versatile new plasma source for atomic spectrometry. Could it topple traditional techniques?

By Steven Ray, Winkler Assistant Professor of Chemistry, State University of New York at Buffalo, USA

In the world of atomic spectrometry, the inductively coupled plasma (ICP) reigns supreme. New plasma sources for atomic emission and mass spectrometry are emerging, however, which promise to be vastly simpler, cheaper, and more versatile. One example that is under development in a number of laboratories worldwide is the solution-cathode glow discharge (SCGD), an atmospheric-pressure glow discharge operated out in the ambient atmosphere. The SCGD is particularly intriguing because this high-temperature, direct-current plasma is sustained directly on top of a liquid surface – a curious property that could make the SCGD a giant-killer.

To fully appreciate the simplicity of the SCGD, it helps to be familiar with its operating principles. The SCGD uses a continuous flow of a conductive analyte solution (for example, 0.1M HNO_3) cascading from the tip of a quartz capillary into a catch-basin. Once ignited, the SCGD is sustained between the liquid surface (cathode) and a positively-biased metallic counter-electrode (anode). Because the surface of the liquid represents the cathode of the glow discharge, the SCGD directly samples the liquid via a 'sputtering' action, ejecting material into the plasma for analysis by atomic emission spectroscopy (AES).

Amazingly, this humble 100-Watt discharge has demonstrated analytical capabilities on a par with

"This high-temperature, direct-current plasma is sustained directly on top of a liquid surface – a curious property that could make the SCGD a giant-killer."

"Plasmas are inherently versatile; often, physical traits, such as gas temperature, can be tuned to an intended application."

some conventional AES approaches. At analyte solution flow rates of 1 mL/min, limits of detection for many elements have been reported at levels near or below 1 ng/mL, with a linear response over three or four orders of magnitude; performance comparable to ICP-AES. More impressively, the SCGD has demonstrated limits of detection of 1–30 pg/mL for the alkali earth metals, significantly outstripping ICP-AES. Moreover, because the liquid surface sampled by the discharge is constantly renewed by the flowing analyte stream, the SCGD is a natural detector for chromatographic separations. Researchers have reported excellent performance with HPLC, ion chromatography, and capillary electrophoresis.

What I have described so far is relatively straightforward atomic spectrometry; however, the SCGD plasma is proving extremely versatile. For example, Shelley and coworkers have reported that biomolecules introduced into the flowing solvent stream are detected as intact molecular ions (and ion fragments) when the SCGD is analyzed by mass spectrometry (1). Researchers in the material sciences have used the SCGD to create nanoparticles directly from solution, environmental chemists have shown that the SCGD is an excellent means of disinfecting water supplies, and medical researchers are investigating the ability of plasmas to disinfect wound sites and enhance healing.

This seemingly disparate set of applications is possible because plasmas are inherently versatile; often, physical traits, such as gas temperature, can be tuned to an intended application. Open questions remain, however. For the SCGD to realize its potential, a more thorough fundamental understanding is required of the physical mechanisms that permit this highly energetic plasma to sit atop the surface of a liquid.

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Fishing for Insight

The power of metabolomics lies in casting a wide net.

By Coral Barbas, Professor of Analytical Chemistry, Pharmacy Faculty, Universidad CEU San Pablo, Madrid, Spain.

Analytical chemistry has always been the key to advances in scientific knowledge. It bridges the gap between a hypothesis and a theory by providing tools to test and validate our ideas. Nowadays, its power is greater than ever. Breathtaking advances in instrumental analysis and computational capabilities make it possible to separate and measure myriad compounds in very complex samples. In turn, these advances have opened the door to –omics technologies – including metabolomics.

Metabolomics is a powerful approach because metabolite concentrations, unlike genes or proteins, directly reflect the biochemical activity of a biological system. Metabolomics represents the phenotype, and gives real-time data on the end points that matter (for example, illness or response to a drug).

"Metabolomics is a powerful approach because metabolite concentrations, unlike genes or proteins, directly reflect the biochemical activity of a biological system."

"Metabolomics is like fishing with a huge net. You catch everything that is there, and while some of your haul will be plastic bags and seaweed, you are likely to find a variety of interesting fish."

Classical research is based on generating a hypothesis and developing the necessary assays to prove or disregard the hypothesis, which is time consuming and limited. New technologies have given us the opportunity to carry out a different type of research, looking at all the changes that occur in a system.

I often compare it with fishing. Traditional research is like fishing for salmon – you select the best place, time, rod and bait for the job, and you come home either with a salmon, or with nothing. Metabolomics is like fishing from a boat with a huge fishing net. You catch everything that is there, and while some of your haul will be plastic bags and seaweed, you are likely to find a variety of interesting fish. Every so often, you might even get lucky and catch a mermaid!

Detecting changes to the concentrations of metabolites in a perturbed system by differential analysis opens up an unlimited number of applications. We can identify biomarkers with potential as diagnostic markers, gather data to stratify patients or predict the trajectory of a disease over time. We can interpret metabolic changes to understand the mechanism of a disease, identify a target, and design new therapies. In cellular assays, metabolomics can give a broad picture of all the changes produced in response to a treatment. In summary, metabolomics can provide answers in basic research, personalized medicine, drug design, biotechnology and many other fields.

Luckily for analytical chemistry researchers, there is a lot of space for improvement in metabolomics workflow. To name just a few:

- The whole process should be validated to ensure reproducibility in results.
- Validation parameters and quality control procedures need to be established, with a joint effort of societies, journals and research groups to come to consensus.
- Metabolite identification is still one of the bottlenecks, together with data interpretation; in that regard, different groups and companies are working on cured databases and intelligent software systems.
- Reproducible ionization sources in LC are still a challenge for companies devoted to technical development.

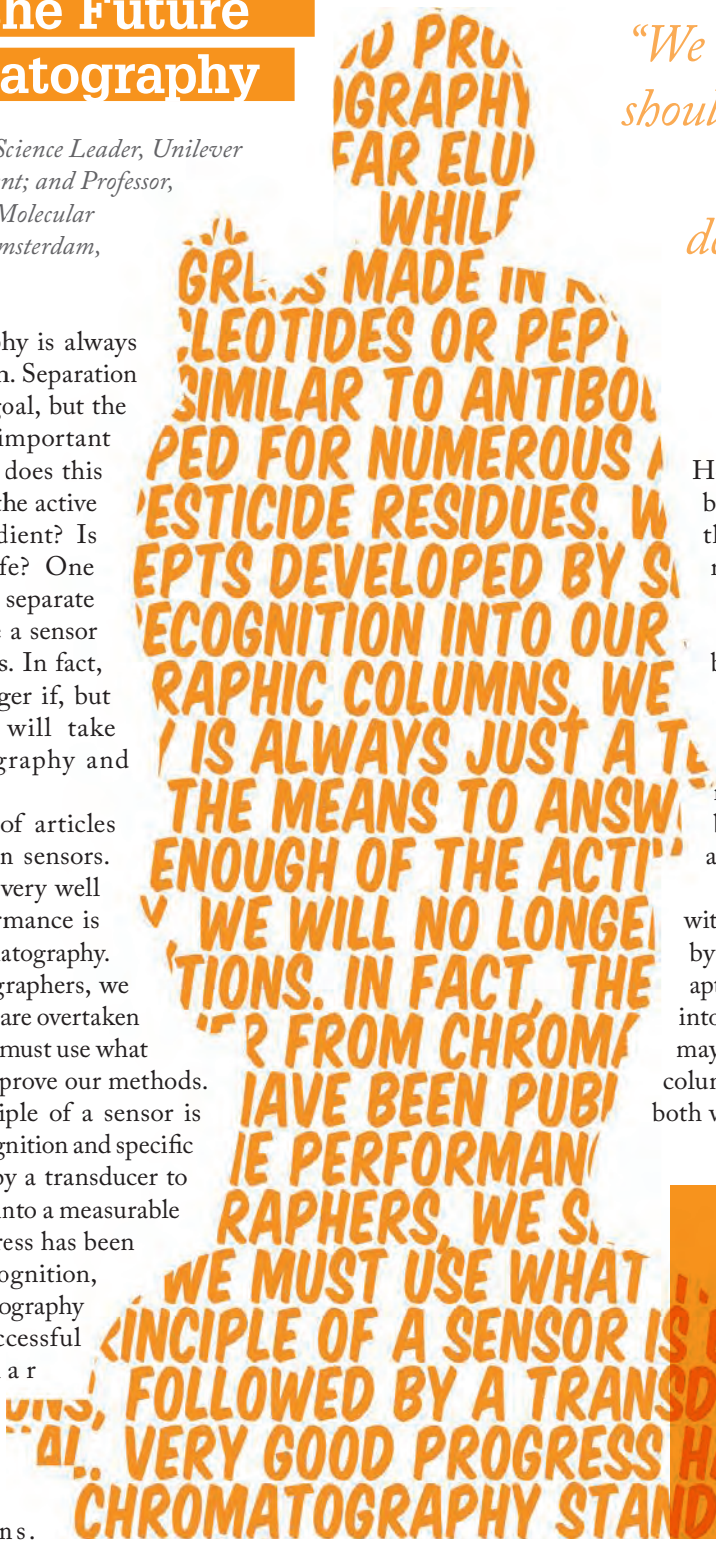
On a personal level, I have found metabolomics to be a very rewarding field of analytical chemistry. Firstly, it gives you the opportunity to work with state-of-the-art instrumental techniques and chemometric tools. Secondly, the nature of the field means that you have the opportunity to participate in multi-disciplinary groups, learn from different fields, and develop the ability to explain your knowledge to people from different backgrounds. It's a field in which you are always learning – from every project, every topic, every disease, and every research objective – which is both challenging and amazing.

LANDMARK LITERATURE

As we launch ourselves into 2017, our expert panel selects and reflects on six standout papers that truly advanced the field of analytical science in 2016.

Sensing the Future of Chromatography

By Hans-Gerd Janssen, Science Leader, Unilever Research and Development; and Professor, van 't Hoff Institute for Molecular Sciences, University of Amsterdam, The Netherlands.



For me, chromatography is always just a temporary solution. Separation of a sample is not the goal, but the means to answer an important question. For instance: does this pill contain enough of the active pharmaceutical ingredient? Is this food product safe? One day, we will no longer separate mixtures at all, but use a sensor to answer our questions. In fact, the question is no longer if, but rather when sensors will take over from chromatography and mass spectrometry.

A massive number of articles have been published on sensors. Some sensors perform very well but, overall, the performance is inferior to that of chromatography. However, as chromatographers, we should not wait until we are overtaken by sensor scientists. We must use what they already have to improve our methods.

The operating principle of a sensor is based on molecular recognition and specific interactions, followed by a transducer to convert the interaction into a measurable signal. Very good progress has been made in molecular recognition, and the field of chromatography stands to benefit. Successful use of molecular imprinted polymers has so far eluded me, and immunoaffinity isolation has only limited applications.

> *"We chromatographers should steal with pride from the concepts developed by sensor scientists."*

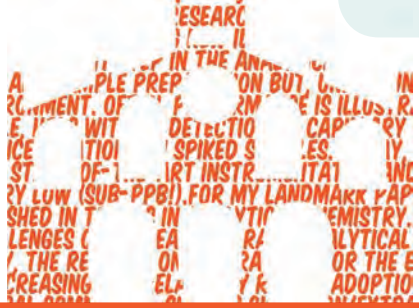
However, while reading an article by Dang et al., I was struck by the enormous progress made in recognition using aptamers.

Aptamers are single-stranded oligonucleotides or peptides that can bind with high specificity to target molecules, similar to antibody–antigen interactions. Selective aptamers have been developed for numerous applications, including bacterial toxins, veterinary drugs, and pesticide residues.

We chromatographers should steal with pride from the concepts developed by sensor scientists. If we can apply aptamer routes for selective recognition into our sample preparation systems or maybe even into our chromatographic columns, we can combine the best of both worlds.

Hans-Gerd's Landmark Paper

N Dang et al., "Advances in aptasensors for the detection of food contaminants", Analyst, 141, 3942–3961 (2016).



Espresso Extraction

By Pat Sandra, Emeritus Professor, Organic Chemistry, Ghent University; Founder and President, Research Institute for Chromatography, Kortrijk, Belgium

At RIC, research on sample preparation is one of our key activities. We are continuously evaluating new ideas (and re-evaluating old ones) to improve and automate this most important step in the analytical cycle. Many papers are published every year on sampling and sample preparation but, unfortunately, too many can never be applied in a routine environment. Often, performance is illustrated on outdated instrumental set-ups (for example, HPLC with UV detection or capillary GC with FID detection), at unrealistic high concentrations, in spiked samples. Today, sample preparation research should be performed on state-of-the-art instrumentation and at required sensitivities – which are often very low (sub-ppb!).

Despite the many disappointments in the recent literature related to sample preparation, some significant achievements were announced in 2016. My chosen landmark paper attracted attention in the first instance by a well-chosen title: "Hard cap espresso machines in analytical chemistry: what else?" We are all very familiar with espresso coffee machines in our laboratories, but Sergio Armenta, Miguel de la Guardia and Francesc A Esteve-Turrillas from the University of Valencia, Spain, demonstrated that they can very quickly, efficiently and cost-effectively perform extractions of solid matrices other than coffee!

A slightly modified hard cap espresso machine with a working pressure of 19 bar was used in combination with liquid chromatography and fluorescence detection for the determination of polycyclic aromatic hydrocarbons (PAHs) in soil and sediment samples. The PAHs were extracted from 5.0 g of sample, previously homogenized, freeze-dried and sieved to 250 µm. The sample was homogenized with dispersing agent and introduced in a refillable stainless steel capsule. 50 mL of 40 percent acetonitrile in water is percolated through the sample at 72 ± 3 °C with a total extraction time of 11 s.

The limit of detection for the PAHs is from 2 to 85 µg/kg and recoveries from spiked and aged samples ranged from 81 to 121 percent with relative standard deviations lower than 30 percent. Two PAH-containing certified reference materials – a clay soil and a sediment – were used for evaluation of the extraction efficiency and the trueness of the espresso method. Comparison of the results with the certified values indicated good agreement.

Five real soil samples were analyzed by the developed procedure and also by an ultrasound extraction (USE) method using 100 mL acetonitrile and an extraction-sonication time of 30 min. The ∑PAHs ranged from 34 to 827 µg/kg, which tallies with other studies performed at urban and industrial areas. The hard cap espresso data and the USE data were statistically comparable. USE is a relatively cheap method, but time-consuming and less green than the espresso method. Other methods that can be successfully applied for the same application, such as supercritical fluid extraction, microwave-assisted extraction and pressurised solvent extraction/accelerated solvent extraction, suffer from the same cons as USE; moreover, they require expensive equipment.

The paper does have some important weaknesses. LC-fluorescence detection was selected for the determination of the individual PAHs, which is fine, but two pairs of PAHs are co-eluting, namely benz[a]anthracene-chrysene and dibenz[a,h]anthracene-benzo[ghi]perylene. Dedicated PAH columns are available from different companies on which the two pairs are completely separated. On the other hand, the LC-fluorescence chromatograms shown in Figure 4 of the paper are far from state-of-the-art PAH analysis, and it is surprising that a journal like Analytical Chemistry has accepted these chromatograms for publication!

Despite this last remark, I would like to congratulate the authors for their ingenuity. The 'espresso approach' is unlikely to find its way into environmental laboratories dealing with hundreds of samples every week, but it could prove a valuable tool in R&D and for educational purposes.

"The 'espresso approach' is unlikely to find its way into environmental laboratories dealing with hundreds of samples every week, but it could prove a valuable tool in R&D and for educational purposes."

Pat's Landmark Paper

S Armenta et al., "Hard cap espresso machines in analytical chemistry: what else?", Anal Chem, 88, 6570–6576 (2016).

Nuclear Fusions

By Apryll M Stalcup, Professor of Chemical Sciences, Dublin City University, Ireland.

For my landmark paper, I have selected a review on nuclear forensics published in Trends in Analytical Chemistry. The article highlights some of the unique challenges of nuclear and radioanalytical chemistry: the importance of mass spectrometry, the reliance on separations for the elimination of isobaric interferences, and the increasing but relatively recent adoption of approaches developed in the broader analytical community, such as chelation/extraction chromatography. Alongside these special considerations, radioanalytical chemists face the same challenges as the broader analytical community, such as demands for fast analysis, measurement robustness, sample preparation, sensitivity versus selectivity, matrix effects, and availability of standard reference materials. This paper highlights some of the interesting approaches that have evolved to address these issues (e.g., borate fusion as an alternative to hydrofluoric acid digestion).

The paper caught my attention partly because I was involved in nuclear forensics projects shortly before moving to my current position in Ireland. The area is absolutely fascinating, for several reasons. First, many of the current analytical methodologies in nuclear and radioanalytical chemistry are based on technology that evolved during the Cold War. Second, researchers are problem-driven, and work in the broader analytical community is being adapted and adopted into the nuclear and radioanalytical chemistry areas. Third, my curiosity to explore completely new areas like this helps me refine my checklist of analytical questions that apply to other problems I might be working on.

For instance, in the less familiar spectroscopies (alpha, beta, gamma) mentioned in the article, what is the specific information obtained and how are the emitted particles/radiation detected? How is signal resolution accomplished? Are there parallels to spectroscopies (fluorescence, mass spectrometry, and so on) that I am more familiar with? How does the radioanalytical community perform background correction strategies to compensate for matrix effects and quenching? Does common terminology such as isobaric interferences, background correction or quenching describe fundamentally different or related phenomena and are there differences in peak shape analysis in the two communities? What constitutes a standard reference material when the substance being measured is continually changing through radioactive decay?

The analytical chemistry community is broad and sometimes divided by a common language. But like an aging relative at a family gathering, by having conversations across divides and communities, we can all learn a lot. In short, papers like the one I have selected are able to promote dialogue and cross-pollination.

> *"Many of the current analytical methodologies in nuclear and radioanalytical chemistry are based on technology that evolved during the Cold War."*

Apryll's Landmark Paper

IW Croudace et al., "Recent contributions to the rapid screening of radionuclides in emergency responses and nuclear forensics", Trends Anal Chem, 85, 120–129 (2016).

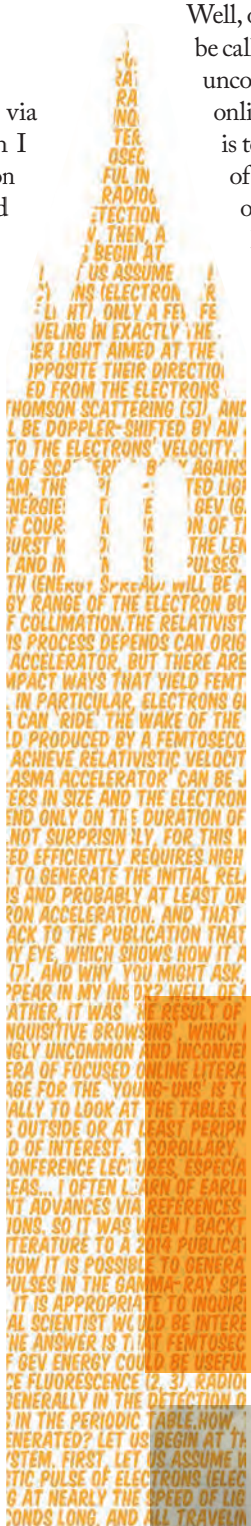
Finger on the Femtosecond Pulse

By Gary M Hieftje, Distinguished Professor and Robert & Marjorie Mann Chair, Analytical Chemistry, Indiana University, Bloomington, IN, USA.

I often learn of earlier, highly important advances via references from recent publications. So it was when I backtracked from recent literature to a 2014 publication that reveals how it is possible to generate femtosecond photon pulses in the gamma-ray spectral region (1). First, it is appropriate to inquire why an analytical scientist would be interested in such pulses. The answer is that femtosecond photon pulses of GeV energy could be useful in nuclear resonance fluorescence (2, 3), radiographic imaging (4), and generally in the detection of many elements in the periodic table.

How, then, are such pulses generated? Let us begin at the 'business' end of the system. First, let us assume we have a relativistic pulse of electrons (electrons traveling at nearly the speed of light), only a few femtoseconds long, and all traveling in exactly the same direction. A beam of laser light aimed at the electrons, perfectly opposite their direction of travel, will be scattered from the electrons (a process termed Thomson scattering [5]), and the scattered light will be Doppler-shifted by an amount related to the electrons' velocity. In a preferred direction of scattering, back against the incident laser beam, the Doppler-shifted light will possess photon energies in the MeV to GeV (gamma-ray) region. Of course, the duration of the high-energy photon burst will depend on the length of the electron and incident-laser pulses. Further, its bandwidth (energy spread) will be a function of the energy range of the electron bunch and its degree of collimation.

The relativistic electrons on which this process depends can originate from a suitable accelerator, but there are now better, more compact ways that yield femtosecond pulses directly. In particular, electrons generated within a plasma can 'ride' the wake of the electromagnetic field produced by a femtosecond laser pulse and will achieve relativistic velocities. Such a 'laser plasma accelerator' can be just a few centimeters in size and the electron-pulse length will depend only on the duration of the laser input (6).



Not surprisingly, for this whole sequence to proceed efficiently requires high laser power densities to generate the initial relativistic electrons and probably at least one extra stage of electron acceleration. And that brings me neatly back to the publication that initially caught my eye, which shows how it all appears possible (7).

And why, you might ask, did such a paper appear in my inbox? Well, of course, it didn't; rather, it was the result of what might be called 'inquisitive browsing', which is becoming increasingly uncommon and inconvenient in the modern era of focused online literature searching. My message for the "young 'uns" is to take time occasionally to look at the tables of contents of journals outside or at least peripheral to one's main field of interest. A corollary, of course, is to attend conference lectures, especially reviews, in other areas...

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Gary's Landmark Papers

S Steinke et al., "Multistage coupling of independent laser-plasma accelerators", Nature, 530, 190–193 (2016).
S Rykovanov et al., "Quasi-monoenergetic femtosecond photon sources from Thomson Scattering using laser plasma accelerators and plasma channels", J Phys B: At Mol Opt Phys, 47, 234013 (2014).

Entering the Fourth Dimension

By Davy Guillarme, Senior Lecturer, School of Pharmaceutical Sciences, University of Geneva/University of Lausanne, Geneva, Switzerland.

Ten years ago, the average analysis times in HPLC were in the range of 20–30 minutes, and the field was largely focused on developing faster chromatographic processes. Now, it is possible to routinely achieve HPLC separations within a few minutes or even less, while maintaining excellent quantitative performance: speed of HPLC is no longer the issue. The problem now facing the field is that our samples are increasingly complex, particularly in the –omics (lipidomics, proteomics or metabolomics). Therefore, there is a need to develop analytical strategies able to separate a huge number of compounds contained within a complex sample.

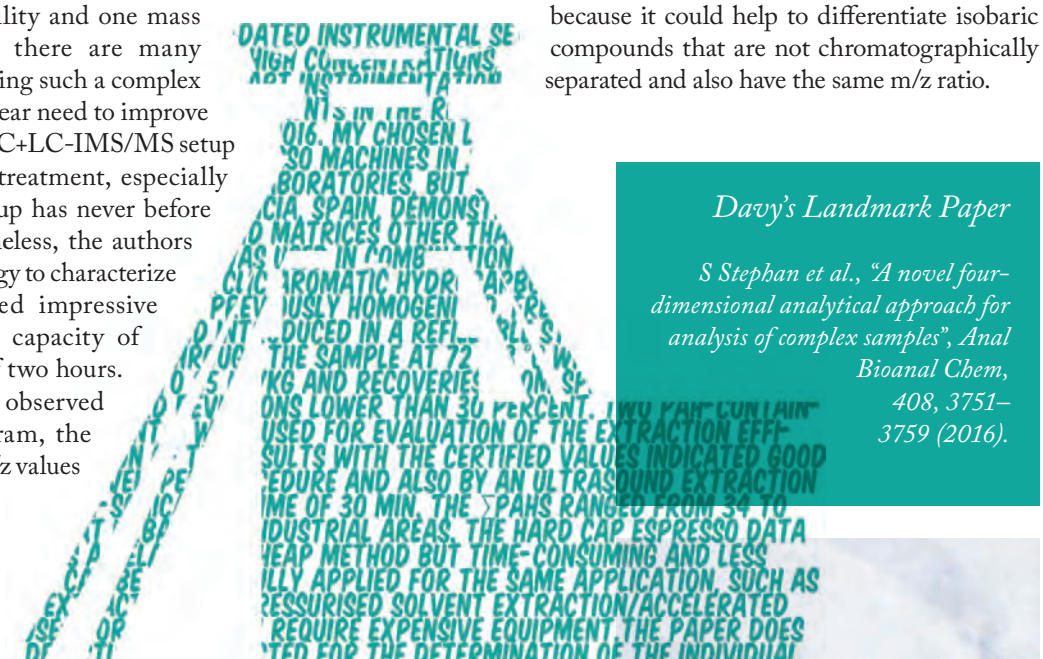
For this purpose, comprehensive 2D-LC has emerged over the last few years as a promising (but more complex) alternative to very high-resolution 1D separation. Beyond separation techniques, high-resolution mass spectrometry (HRMS) becomes ever more popular and powerful, particularly for untargeted analysis of complex samples. Also in the field of mass spectrometry, there is increasing interest in ion mobility spectrometry (IMS), which can be added ahead of MS to further increase its resolving power.

My selected paper describes the combination of 2D-chromatography and a powerful mass spectrometry approach (IMS-HRMS), which enables the separation of complex samples in four dimensions (two chromatographic, one mobility and one mass spectrometry). Obviously, there are many constraints when implementing such a complex analytical setup. There is a clear need to improve the software to manage the LC+LC-IMS/MS setup and – above all – the data treatment, especially because a 4D analytical setup has never before been implemented. Nevertheless, the authors successfully applied the strategy to characterize plant extracts and achieved impressive performance, with a peak capacity of 8,700 for an analysis time of two hours. In addition, for each peak observed on the 2D-LC chromatogram, the collision cross section and m/z values are available.

> *"The paper proves that chromatography and mass spectrometry should always be combined rather than opposed."*

The paper is remarkable in that it combines the latest progress in both chromatography and mass spectrometry. It is difficult to find research groups with expertise in these disparate and complex analytical strategies – and trying to combine so-called LC+LC and IMS-HRMS is impressive. The paper proves that chromatography and mass spectrometry should always be combined rather than opposed. The limited resolving power of IMS-MS means that combination approaches like LC-IMS/MS or LC+LC-IMS/MS are certainly the best and most powerful strategy.

In the future, I would like to see this approach evaluated for the characterization of –omics samples, as the number of detected features could certainly be strongly enhanced when using these multiple separation dimensions. Another application could be the analytical characterization of biopharmaceuticals, including monoclonal antibodies, antibody–drug conjugates, and bispecific antibodies. The addition of IMS to the more commonly used 2D-LC-MS setup would be of particular interest because it could help to differentiate isobaric compounds that are not chromatographically separated and also have the same m/z ratio.



Davy's Landmark Paper

S Stephan et al., "A novel four-dimensional analytical approach for analysis of complex samples", Anal Bioanal Chem, 408, 3751–3759 (2016).

Luminous Leap

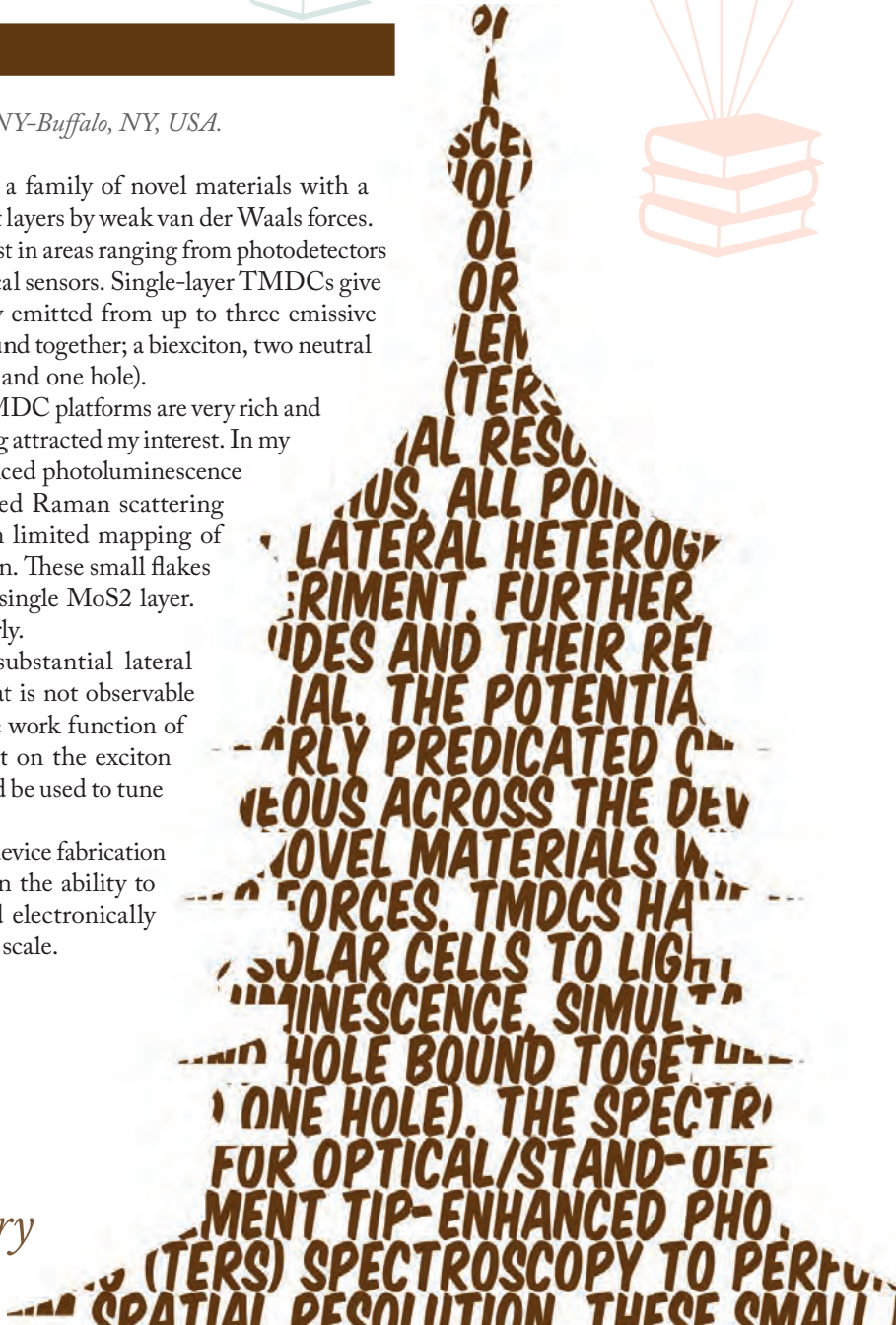
By Frank Bright, Henry M Woodburn Professor, SUNY-Buffalo, NY, USA.

Transition metal dichalcogenides (TMDCs) are a family of novel materials with a hexagonal-layered lattice that is bonded to adjacent layers by weak van der Waals forces. TMDCs have generated significant scientific interest in areas ranging from photodetectors and solar cells to light-emitting devices and chemical sensors. Single-layer TMDCs give rise to strong photoluminescence, simultaneously emitted from up to three emissive excitons (a neutral exciton, an electron and hole bound together; a biexciton, two neutral excitons bound weakly; and a trion, two electrons and one hole).

The spectroscopy and applications of these 2D TMDC platforms are very rich and their potential for optical/stand-off chemical sensing attracted my interest. In my landmark paper, the authors implement tip-enhanced photoluminescence (TEPL) microscopy in concert with tip-enhanced Raman scattering (TERS) spectroscopy to perform sub-diffraction limited mapping of single-layer MoS2 flakes at 20 nm spatial resolution. These small flakes are a few microns in size and are composed of a single MoS2 layer. Thus, all points on the flake should behave similarly.

What Su et al. discovered is that there is substantial lateral heterogeneity in this system on a 20 nm scale that is not observable by a traditional confocal experiment. Further, the work function of the metallic tip (Ag, Au) had a profound impact on the exciton amplitudes and their relative distribution, and could be used to tune local excitonic processes within the 2D material.

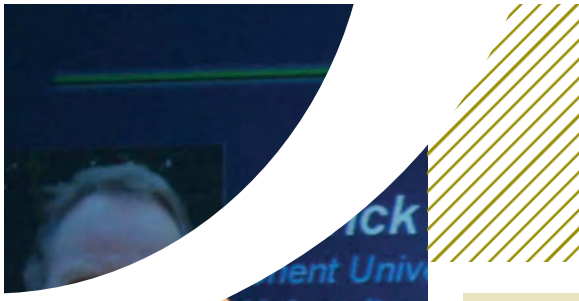
The potential of 2D TMDCs for optoelectronic device fabrication and heterostructure design is clearly predicated on the ability to make materials that are actually chemically and electronically homogeneous across the device's operating length scale.

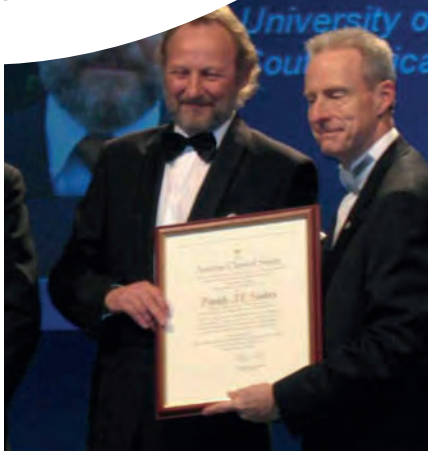


"The spectroscopy and applications of these 2D TMDC platforms are very rich and their potential for optical/stand-off chemical sensing attracted my interest."

Frank's Landmark Paper

W Su et al., "Nanoscale mapping of excitonic processes in single-layer MoS2 using tip-enhanced photoluminescence microscopy", Nanoscale, 8, 10564–10569 (2016).





Clockwise from top left: At Riva - the forum on microcolumn separations, 1983. Teaching a course in Mumbai, 2014. Accepting the American Chemical Society Chromatography Award 2005, San Diego, USA. Receiving the John Knox Award for Innovative, Influential Work in the Area of Separation Science, Royal Institute, London, UK, 2009. State-of-the-art instrumentation, RIC, 2016.

Thirty Years of Chromatography Research

Pat Sandra founded the Research Institute for Chromatography back in 1986, and it has acted as an outlet for his passion for separation science ever since. Here, Pat reflects on three decades of change, challenges and success – and offers a glimpse of our field's future.

An interview with Pat Sandra

I grew up in a region of Flanders, Belgium, known as the "Texas of Flanders" because of its entrepreneurship and bustling small family businesses. At the end of 1985, I had some tough discussions about the research program in separation sciences within our department at Ghent University. My proposals were not taken seriously. Based on my 'innate entrepreneurship' and the fact that industrial collaboration was not really accepted in an academic environment at that time, I decided to quit the university on February 1, 1986. And I had a plan.

In the beginning, the structure of the Research Institute for Chromatography (RIC) replicated Rudolf Kaiser's Institute for Chromatography in Bad Dürkheim, Germany. For the most part, we survived on teaching courses and on sponsorships from Carlo Erba, Italy, and later from Hewlett-Packard (now Agilent Technologies). In 1986, we began collaborating closely with a local industrial laboratory named Servaco – and moved our instrumentation from our garage to their facilities. At the same time, Frank David, my first PhD student, joined RIC.

When my mentor and PhD promotor retired from Ghent University, I was invited by the Dean of the Faculty of Science to restart my activities at the university and also to lead the separation sciences group. I only accepted a part-time position. One of the advantages of being back in the academic world was that we could recruit several coworkers from my group of PhD students, which guaranteed a very smooth integration in the RIC activities. I am delighted to say that all of them are still with us. Starting RIC France was another adventure, and credit should be given to our first collaborator, Pascal Hoogenbosch, for successfully integrating the company's philosophy in our French division.

I'm proud of our achievements. We've been able to establish an institute with high-quality, state-of-the-art instrumentation and a staff of 35 well-trained and productive co-workers active in Belgium and France. Above all, I am proud that our customers are highly satisfied with our work and what we offer. I suspect part of our success stems from the fact that we add value in terms of both quality and speed; we do what we do relatively fast (and in direct contact with the customers) – but we can also dig very deep into the details. Our customers come to us because of our strong history – and because they know we are close to the science.

A family business

My wife, Martina, has a chemical–technical education, and was involved in RIC from the beginning, operating chromatographic instrumentation in our garage. She also took care of the admin – something I always hated. My son, Tom, has a chemical engineering degree, and joined the company in the late nineties. He worked with all instrumentation, with the main task of developing and validating methods – and drafting standard operation procedures. With the fast growth of RIC at the beginning of the century, he became increasingly involved in managing the Institute. Tom's input into the growth of RIC (including RIC France) has been of paramount importance – the rest of us were often 'too scientific' and academic!

At around the same time, my other son, Koen, obtained his PhD in biochemistry and started to work in a spin-off company from Ghent University (Pronota), where his role was to build a proteomics platform for discovery and verification of biomarkers in biological fluids. In 2008, when the platform was finished and in full operation, Koen joined RIC and introduced life science activities (the –omics) and biopharmaceutical analysis. Today, Koen is Scientific Director at RIC and R&D Director at a recently founded company called anaRIC biologics – a joint venture with Anacura, a company with 15 years' excellence in GMP.

To make the family story complete, the wives of Tom and Koen are also employed at RIC.

At the end of 2011, the management of RIC Belgium and RIC France was officially transferred to Tom and Koen. I'm still spending several hours a day at RIC, discussing current projects and difficult analytical problems with co-workers. And I'm also active in coordinating the scientific outcome of RIC (publications, application notes, and so on). At the new company, anaRIC biologics, I'm simply a scientific advisor – without any administrative tasks at all. Thank goodness.

The analytical chemist who saved Belgium

There have been several key moments throughout RIC's history, but the most important has probably got to be the dioxin crisis.

Everybody, including the government, was convinced dioxins were the problem. At that time, only two or three laboratories in Belgium could do dioxin analysis – but thousands and thousands of samples had to be analyzed. (We estimate that, before the crisis was over, more than 50,000 food samples had been analyzed.)

I immediately came to the conclusion that it was impossible for a small country like Belgium to analyze all food samples for dioxins and, based on intuition, I postulated that precursors of the dioxins, namely polychlorobiphenyls (PCBs), should be present in our food and at much higher concentrations. We took a very high risk (both from a scientific and a business point of view) by stating on the national TV news that the analytical focus should not be on the dioxins but on the analysis of PCBs. This is much simpler and much cheaper.

The Belgian authorities did not agree with us at first, but the European Community accepted our proposal, and the postulation was scientifically verified, first by us and then by other laboratories. In fact, addition of used transformer oil (PCBs!) to animal feed was the cause of the polluted food. At the same time, we described a method to analyze at least 100 samples per day, per technician, per instrument, including sample preparation. Ultimately, RIC received an accreditation in a couple of days and analyzed about 7,500 samples for the government.

The whole incident gained us international recognition. RIC was continuously in the newspapers and TV news. We were already well known – but that really established the 'brand'.

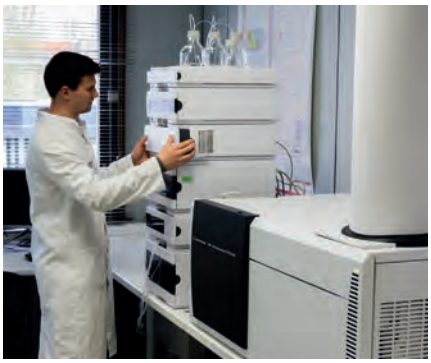
Career... so far

- Founder and director of RIC Belgium and RIC France
- Professor at Ghent University
- Director of the Pfizer Analytical Research Centre at UGhent
- Professor at the Stellenbosch University, South Africa
- Visiting Professor at the Technical University of Eindhoven, The Netherlands
- Chairman (1983-2012) of the International Symposium on Capillary Chromatography
- Organizer of 22 International Symposia
- Co-founder of anaRIC biologics

Clockwise from top left: Highly productive coworkers at RIC, 2016. Accepting Doctor honoris causa in Pharmacy from the University of Turin, Italy, 2004. Colleagues and coworkers of the Pfizer Analytical Research Centre, UGhent, 2008. Receiving the John Knox Award for Innovative, Influential Work in the Area of Separation Science, Royal Institute, London, UK, 2009.

The RIC timeline

- 1983
  Pre-RIC: from an academic environment to the garage – the “Chromalab” period.
- 1986
  Founding RIC: from the garage to an industrial park – the “Servaco” period.
- 1991
  Moved to Kennedypark 20, Kortrijk (500 m^2)
- 1992
  IOPMS foundation - ISCC
- 1995
  The “Schumacher” case
- 1999
  The Belgian dioxin crisis
  ‘Twister’ (stir bar sorptive extraction, SBSE) developed
- 2001
  RIC France established
  RIC becomes exclusive Belgian and French distributor of Gerstel GmbH and Value Added Reseller (VAR) of Agilent Technologies
- 2006
  Move to Kennedypark 26, Kortrijk (1,000 m^2)
- 2008
  Start-up of life science activities, focusing on –omics (Metablys) and biopharmaceuticals
- 2016
  Founding anaRIC biologics, offering non-GMP and GMP services for biopharmaceuticals
  Belgian and French distributor of Antec instrumentation



Clockwise from top: Golay Award winners Ray Dandeneau and Ernie Zerenner in Riva, 1989. A coworker at RIC, 2016. Receiving the Csaba Horvath Medal, Siofok, Hungary, 2013. RIC researcher, 2016.

Fundamental shifts

Things have certainly changed over the last 30 years. Something we observe frequently is how knowledge is decreasing, because the present generation are not being educated in the fundamentals as we were. And that is a great pity. It's a consequence of the current situation; not enough people are trained in analytical science at universities and high schools. More and more people apply chromatography and mass spectrometry as techniques, but the number of systems that are sold to people who've never had an education in chromatography and spectroscopy is unbelievable. In fact, they are not at all interested in being highly specialized in chromatography – it's purely application-oriented.

In the past, we ran a full course program in-house that included the fundamentals of gas chromatography (GC), GC combined with mass spectrometry, interpretation of mass spectra, liquid chromatography, sample preparation, and so on. The courses were mostly fully booked before 2000 but then the interest in fundamental courses decreased, while demand for on-site customized courses on specific applications, instrumentation or software increased.

Regardless, the present main focus on applications means that if you have a problem, you don't always know how to solve it. For us, chromatography has always been at the center; for many scientists today it is simply a tool – and that's a big difference. The solid fact remains that the better you know the fundamentals, the better you can apply the technique.

I think the only way to correct our trajectory is to re-introduce fundamental basic courses, covering the consequences and the theory – and how to apply techniques. We need to take great care in what we learn fundamentally; for example, interpretation of mass spectra, method development, and even the many different LC columns available. Take the latter example – there are hundreds of similar columns for reversed phase liquid chromatography. What do you select if you're a newcomer or just an application guy in your lab, if you don't know anything about the fundamentals of the technique? People rely on commercial leaflets – on what they're being told at the conferences or, later on, perhaps what's in The Analytical Scientist or other magazines. Most people using chromatography or mass spectrometry today don't look in detail at the literature, which is, admittedly, nearly impossible as there are so many (too many) publications. To cope, you have to select papers that are closely linked to your own field, but that doesn't give you the broad 'helicopter' view that we had in the past.

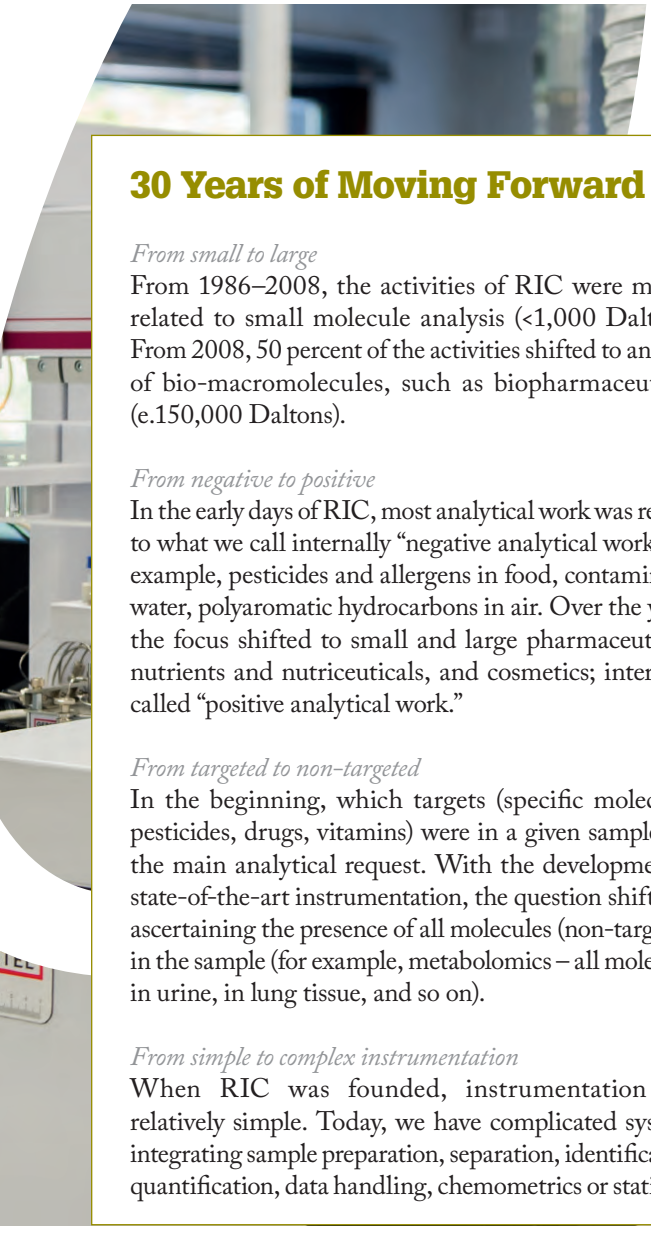
Our customers are very well aware of the possibilities and also of their limitations, and that's the reason why we can continue to be successful. To be honest, if our customers had the same level of knowledge and know-how as us, then we would have no reason to exist. And I guess, in a way, my call for more – and better – training in fundamentals could actually be bad for business, but I'm not overly concerned...

Old science, old technology, old sample preparation... Let's not get old

Quality of analytical data depends on the quality of the sampling procedure and the sample preparation – basically, the better your sample prep, the better your data. In recent years, we have made important progress in sample preparation and its automation, but introduction of these achievements in labs is rather slow.

It's just incredible what is still going on today. We still have official methods, not only in Europe but also in the US, that rely on huge quantities of sample and potentially toxic solvents – even in environmental methods, ironically. For example, one of the official methods in European countries (which I will not name) requires that you take one liter of wastewater, and extract with 100 ml dichloromethane – manually. Then you start to evaporate the dichloromethane and perform the analysis. Clearly, that's not at all state-of-the-art. You can easily miniaturize the whole procedure – and even do in-vial extraction in an autosampler. Unfortunately, such procedures are often not accepted by regulatory authorities, who apparently prefer the old technology. Another example is the still intensively applied Soxhlet extraction, invented in 1879, for solid matrices.

Going back to the dioxin crisis, the PCB method we developed for the industry long before the crisis was extremely advanced



30 Years of Moving Forward

From small to large

From 1986–2008, the activities of RIC were mainly related to small molecule analysis (<1,000 Daltons). From 2008, 50 percent of the activities shifted to analysis of bio-macromolecules, such as biopharmaceuticals (e.150,000 Daltons).

From negative to positive

In the early days of RIC, most analytical work was related to what we call internally "negative analytical work", for example, pesticides and allergens in food, contaminated water, polyaromatic hydrocarbons in air. Over the years, the focus shifted to small and large pharmaceuticals, nutrients and nutriceuticals, and cosmetics; internally called "positive analytical work."

From targeted to non-targeted

In the beginning, which targets (specific molecules: pesticides, drugs, vitamins) were in a given sample was the main analytical request. With the development of state-of-the-art instrumentation, the question shifted to ascertaining the presence of all molecules (non-targeted) in the sample (for example, metabolomics – all molecules in urine, in lung tissue, and so on).

From simple to complex instrumentation

When RIC was founded, instrumentation was relatively simple. Today, we have complicated systems integrating sample preparation, separation, identification, quantification, data handling, chemometrics or statistics.

back in 2000 – and it could be applied immediately. The method included ultrasonic extraction and matrix solid phase dispersion, a precursor of dispersive SPE in QuEChERS. Using 'official' methods, you can only analyze a couple of samples per day rather than hundreds. And yet, even though we proved that the method performed perfectly well, what happened at the end of the dioxin crisis? The government decided to go back to the old official method… I guess change really can be hard.

Sadly, people still do not consider that sample preparation is the most important step of any analytical procedure. Understanding the goal of the analytical method and the potential limitations of your sample preparation is essential. Let's take some examples:

i. *Tributyltin in water samples at the LOD of 60 (ppq) pg/L.*

State-of-the-art instrumentation allows us to measure extremely low concentrations (in standard solutions) but the following remarks are often not addressed: what is the blank value in your laboratory? Does your water sample contain suspended material or sediment? How do you cope with this? How do you take a subsample? What is the purity of your derivatization agent?

ii. *Analysis of phthalates.*
We always have doubts when phthalate concentrations are reported in the literature in environmental samples, biological fluids, etc. The bank values in analytical labs are very high and special precautions have to be taken. Even chromatographic instrumentation has to be decontaminated from phthalates for ppb determinations. Apparently, we are one of the few labs who report blank values! Miniaturization and automation is also the way to go here.

iii. *Pesticides in food using the QuEChERS method in combination with GC-MS.*
The following details are often NOT included in publications: What is the purity of your extract? 'Adapted' QuEChERS – how? Different results using GC and LC? How is the sample injected in GC? What inlet and inlet liner are used? What about contamination with non-volatiles of your system? Long-term performance?

iv. *Pharmacokinetic studies in blood and plasma samples.*
What about removal of proteins, lipids in high throughput analysis? What about ion suppression effects?

We all have to think carefully about – and then, crucially, invest in – good sample preparation. Sample loads are increasing, which means that automation surely must be the way forward.

All that said, I do also understand the difficulties. If you are an official organization, and you have a method that works – and if to implement a new method, you have to go through a complete new validation – very often, you're going to prefer the old method. There is no doubt that, for example, EPA methods work. But they are often based on old technology and old science – including the

RIC Belgium and RIC France teams, 2016.

sample preparation. We need to change our mentality and review long-lasting methods. Likewise, I often refuse articles submitted to me for review if the paper explores a new method of sample preparation, but uses old chromatography and detection methods in its evaluation. It makes no sense.

Academia versus business

I'm frequently asked if I prefer being a company chairman or a professor. I cannot say I prefer one over the other, but I can say that I love being able to do both. Being independent and working with industry is something I like, because I get to solve real problems – and that leads to great job satisfaction. If we can help in some way to introduce a novel biopharmaceutical onto the market, it's extremely rewarding – even more so than a great publication in the best journal. Industry is very often about reaching dynamic, practical conclusions. Conversely, being in academia means independence and research freedom – you can make more mistakes with fewer risks in the academic environment.

The additional financial responsibility is a major difference. When you're responsible for the well-being of around 20 families, the decisions you make must be more balanced. In the early days, my primary concern in industry was how to survive; if you work as a professor, you don't worry about that – in one or another way, everything is paid for. Indeed, colleagues working in the academic world often have no real idea of the cost of their activities; for example, I know of university labs who charge less than 500 euros per day for using a Q-TOF-MS while easily paying over 1,500 euros per day for a service engineer to maintain that system... In academia, when you make a decision to buy instrumentation, you simply ask, "what will we buy this year?" In industry, if you decide to buy something, it has to bring in money – it's a completely different selection process.

I've been happy with my career. I've been able to combine both the academic and business worlds, and I am not sure one would have happened without the other – I guess I am one of those people who can survive in both environments.

Top six analytical milestones

- Miniaturization and automation of sample preparation
- Multidimensional chromatography
- (2D-GC and 2D-LC)
- Smaller particles (porous and core shell) in LC
- Ultra-high pressure and high temperature LC
- High resolution mass spectrometers and MS/MS
- Data handling software and advanced chemometrics

From the past to the future

When I look back, I see some key trends (see sidebar: 30 Years of Moving Forward):

- A growth from small to large
- From negative to positive
- From targeted to non-targeted analysis
- From simple to complex instrumentation
- From straightforward to complex software (data analysis time)

Over the next years, a substantial part of our energy is likely to go into biopharmaceuticals. At the beginning of this year, we started a new company together with Anacura, anaRIC biologics, because customers asked us to assist them beyond research. We are well known for our method development and for the characterization of biopharmaceuticals, and now we're moving into good manufacturing practice (GMP) territory. It's completely new for us and also very challenging – and significantly different to research and development, but it is also a natural progression and an important move.

Analytical chemistry is a wonderful field to work in. I believe analytical chemists are special. You solve problems, develop methods – and you need a special mentality. Whenever you visit international meetings in analytical chemistry, whatever the technique, it's obvious that many of the attendees don't simply 'work' in the field – it's a hobby and something they genuinely hold dear. Personally, I find myself amazed every day. We published a paper on skin lipidomics in which we identified over 1,000 lipids from a very small surface layer, which is just unbelievable.

I'd like all analytical chemists to recognize the power of what we do and motivate themselves to become more enthusiastic about the fundamentals. Many people only use analytical chemistry as a tool, when they should be appreciating its real beauty.

QUO VADIS, CAPILLARY GAS CHROMATOGRAPHY?

How mature is capillary gas chromatography (CGC)? Are we close to the maximum achievable for daily routine analyses? Can we reduce or even stop research into CGC technology? Here, we offer personal opinions based on 30 years of service to the industry.

By Frank David, Koen Sandra and Pat Sandra

Looking at all the different chromatographic techniques, capillary gas chromatography (CGC) is by far the most mature. Here, we define 'mature technique' as a technique that has reached a state of 'satisfaction', with a stable but low growth rate. Indeed, over the past decade, few groundbreaking developments have been realized in CGC. Since the invention of the technique by Golay in 1957 (1), most theoretical fundamentals of CGC were described in the 1960s and 1970s. Indeed, few studies have added valuable extensions to that fundamental work; exceptions include the papers by Blumberg and Klee (2, 3), who introduced novel and practical concepts, such as speed flow rates and optimal heating rates in CGC. Notably, this work has hardly been applied in practice for optimizing GC separations! Does this reflect that knowledge (and know-how) has been decreasing over recent years?

One of the most important milestones in achieving the 'mature' state of CGC was the invention of fused silica capillary columns (4), which opened the way to produce columns in a very reproducible way, with efficiencies reaching the theoretical maxima. High quality, inert, temperature stable columns in various dimensions and coated with a range of stationary phases are presently available from different vendors. However, only a limited number of CGC column technology innovations have been applied in practice in recent years – partly because CGC is increasingly combined with mass spectrometry (MS), which provides an additional level of specificity that reduces the need for other stationary phase selectivities. The introduction of ionic liquids as stationary phases for CGC is an illustration of a notable exception.

In the field of sample introduction, often considered the Achilles' heel of CGC, most fundamental work was performed in the 1980s

"WE ARE MORE AND MORE CONVINCED THAT APPLICATION OF GC×GC IS OFTEN UNREALISTIC AND UNPRODUCTIVE FOR A LARGE NUMBER OF APPLICATIONS."

and 1990s. Theoretical and practical aspects of split, splitless and cool on-column injection have been studied and described by Grob (5, 6) and many others, while programmed temperature vaporization (PTV) injection was pioneered by Vogt, Poy and Schomburg (7). With the exception of some developments in gas or pressurized liquid injection and hyphenation of different sample preparation techniques (thermal desorption, dynamic headspace, derivatization, and many others) to CGC, hardly any research is presently devoted to further development and performance evaluation of inlet systems.

Even at the level of detection, only marginal improvements and evolutions seems to take place, with the exception of the giant leap in performance between mass spectrometers (low and high resolution, MS and MS/MS, hard and soft ionization, and so on). Spectroscopic detectors receiving new attention in recent years, such as VUV and FTIR, have some applicability for specific problems, but will they ever be as universally applied as the well-known 'old' detectors?

In contrast to the above, one might get the impression that multidimensional CGC and, in particular, comprehensive gas chromatography (GC×GC), is the only field of current CGC development performed by academia and research groups. Working at RIC, an analytical laboratory providing analytical solutions to the industry, to institutions, and to other laboratories using CGC-MS in various application areas, we are more and more convinced that application of GC×GC is often unrealistic and unproductive for a large number of applications; for example, the routine analysis of pesticides in food and beverages. All too often, GC×GC is used for hype rather than for need!

At the same time, we are also concerned about the lack of optimization, validation, and critical evaluation of CGC methods under development or being published. We have the impression that the quality of recent scientific publications in the field of CGC is quite variable. Such observations put pressure on CGC as a mature technique of great value...

THE STATE-OF-THE-ART: CONTROVERSIAL PUBLICATION

A typical example of the pressure on CGC was exemplified by the controversial paper entitled "Thermal degradation of small molecules: a global metabolomic investigation" (8). The paper questions the correctness of data produced by GC-MS in life sciences. The authors claimed "[...] a significant amount of spectra data generated in GC-MS experiments may correspond to thermal degradation products."

Consequently, the paper formed the basis for 'heated' disputes (9) and comments (10). One could easily argue that the applied experimental design using off-line heating of standards and biological samples, followed by LC-ESI-MS analysis, can in no way simulate what happens in a CGC column and system. Moreover, using LC-MS under aqueous conditions to analyze silylated samples, dedicated to CGC analysis, is not common practice – or done at all, which led to a striking statement of the paper: "[...] the productive effect of derivatization was not found to be significant."

The above claim – and others in the paper – can be simply counteracted by looking into the performance of CGC over the past few decades. A good example is the routine quantitative analysis of steroids in medical laboratories –

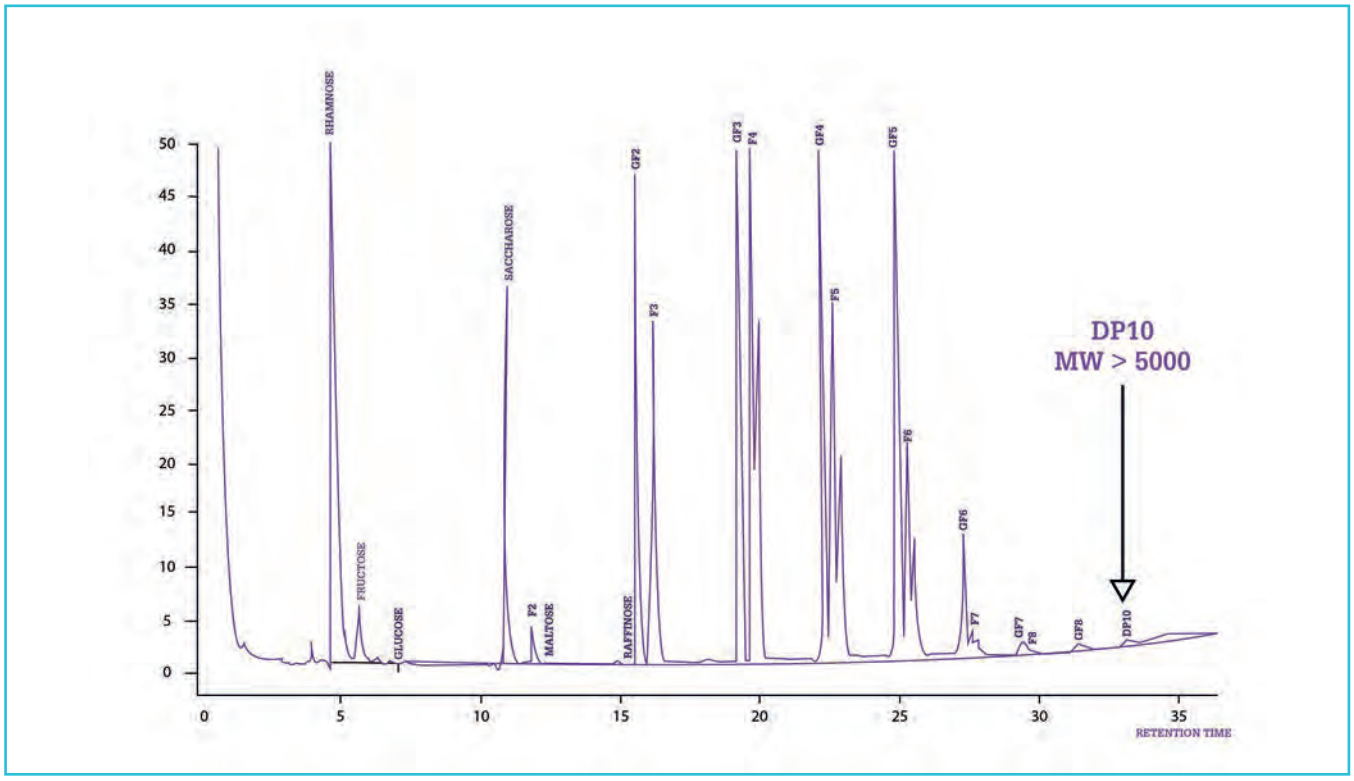


Figure 1. Analysis of Oligofructose by HT-CGC. Data from D Joye, Tiense Suiker. Analytical conditions: column MXT-500 SimDist (6 m x 0.53 mm ID x 0.15 µm); cool on-column injection, carrier: 8.5 mL/min He constant flow, oven temp: 85°C - 10°C/min - 430°C

a foolproof method, based on derivatization by oximation and silylation followed by GC analysis and direct injection, was published in 1975 (11). A more recent example is an oligosaccharide analysis that is routinely performed by CGC in quality control in food laboratories. As illustrated in Figure 1, using oximation and silylation, an appropriate sample introduction method (cool on-column) and high-temperature CGC analysis, fructose oligomers can be determined quantitatively up to decamers, representing molecular weights close to 5000 dalton. These successful routine applications are not considered as 'innovative' or 'novel' and don't make it into scientific papers. They do, however, prove the power and maturity of CGC.

In our opinion, the major – in fact, only – value of the paper is that it represents a wake-up call for the GC community (and for the chromatographic community in general). Indeed, since most centers of GC expertise from the 20th century have re-oriented or been absorbed into other faculties or institutions, there is a slow but important loss of knowledge on the fundamentals of GC – and also an attrition of know-how. Young scientists entering the field can no longer rely on in-house expertise and, in their quest for rapid publication, they often focus exclusively on recent (review) papers, missing out on groundbreaking fundamental work. Consequently, attention is often focused on applying 'hyped' developments without a critical appraisal of important aspects, such as what injector liner to use and what mode of operation will obtain decomposition-less profiles. With this in mind, we would like to cite Koni Grob from a presentation given in 2000 (12): "Splitless injection [...] is one of the major sources of error in trace analysis by GC and not sufficiently well controlled. Losses through the septum purge outlet, for instance, often exceed 30 percent (overloading of the vaporizing chamber), and frequently less than 60 percent of the sample is transferred into the column. Some of the injectors on the market are simply inadequate. Should it be performed by a short or a long syringe needle, with an empty or a packed liner of 2 or 4 mm i.d., with a fast or a slow autosampler? Methods just state '2 µl splitless injection', not even specifying whether or not this includes the volume eluted from the syringe needle, probably because no clear working rules have been elaborated."

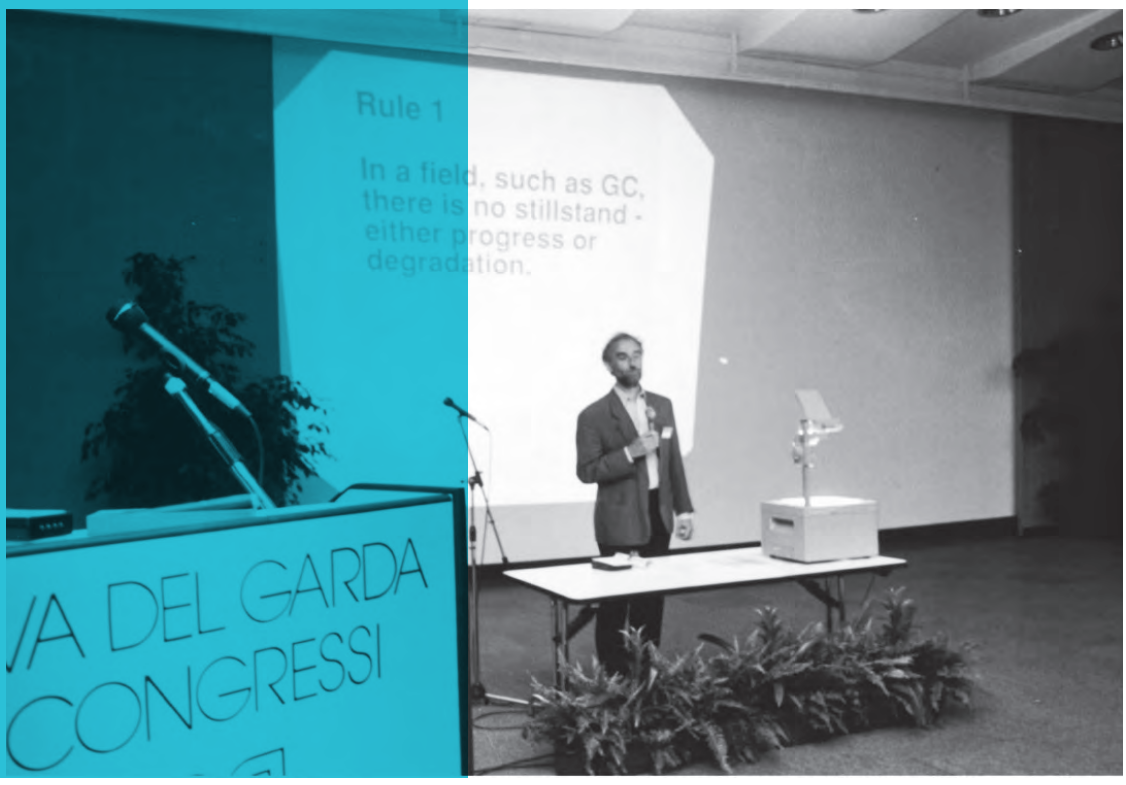


Figure 2. Koni Grob at ISCC 2000.

GC×GC HYPE

A typical example of what we perceive as 'hype' in analytical chemistry is the stampede towards GC×GC. The following statements made by some protagonists of GC×GC are worth mentioning: "Nearly 90 percent of the published studies utilized GC×GC, while only 10 percent used heart-cutting 2D-GC. It is hard to tell if this large discrepancy is because the maturity of heart-cutting 2D-GC makes such studies less 'publishable' or because users find GC×GC to be a more effective method for analyzing complex samples (13)," and "although GC×GC is a great multidimensional approach and has gained a lot of popularity, it is also true that in much published research, classical MDGC would have probably provided a better analytical result (14)."

Our experiences are fully in line with these statements. GC×GC can indeed perform an excellent job in 'sample imaging' for profiling and comparing complex samples, or in petrochemical group type separation, for instance. However, most GC×GC applications published over the last few decades are not really optimized (column selection, flow conditions, modulation, temperature programming, and so on), which results in overall performance much lower than what can be achieved. Moreover, the GC×GC literature is overwhelmed with applications that concentrate on the beauty of the contour plot rather than on producing useful data! Perhaps more worryingly, substantial information on sample preparation and sample injection – both of utmost importance when it comes to correctness and reproducibility of data – is not provided. Looking at hundreds of papers and presentations given at international meetings in recent years, it seems strange that these problems are non-existent when GC×GC is used. And though while all GC work should ultimately lead to quantitative data, this too appears to be a minor issue when applying GC×GC. Are colorful plots really more important than meaningful quantitative data? Apparently so. It is high time that the proponents of the technique proved its real performance by publishing validated studies, analysis data of certified reference samples, results of round robin tests, and so on.

Our criticism does not at all mean that we do not appreciate the power of GC×GC for a number of important of applications, such as characterization of petroleum products or non-targeted analysis in metabolomics studies. A recent publication clearly demonstrates that optimized GC×GC can indeed deliver its theoretical potential, namely increasing the peak capacity in a single run by an order of magnitude (15). However, to make the

"IN THE NEXT DECADE, WE EXPECT THAT SEVERAL EVOLUTIONS WILL TAKE PLACE IN CGC TECHNOLOGY, MAKING THE TECHNIQUE MORE USER FRIENDLY AND RUGGED."

shift from R&D to QA/QC, for example, for targeted analyses, performance should still be proved by developing standard operating procedures that can be validated by analysis of certified samples. It is our belief that for targeted analysis, it will be difficult to beat the performance of state-of-the-art 1D and 2D in the heart-cutting mode in combination with MS/MS detection!

SO, WHAT'S NEXT?

Many years ago at one of the Riva meetings, Koni Grob stated, "in a field such as CGC, there is no standstill, there is either progress or degradation (12)" – see Figure 2. Is it not time that we take that statement seriously once again? There is definitely a need for more fundamental training, including hands-on, in CGC. CGC is far from a black box technique and will, hopefully, never be so! New GC methodology and applications should be optimized according to the fundamentals described in key papers and results should be critically evaluated and correctly compared with existing technology before publication. Solutions should be fully validated in terms of accuracy, reproducibility and robustness. On that aspect, the controversial paper on thermal degradation of solutes in metabolomics studies can be considered an interesting contribution, given that it questions many aspects of routine CGC. It is therefore the task of researchers applying CGC to evaluate their data in a critical manner before submitting it for publication. In addition, journals should also adapt their requirements for 'novelty' and give quality and scientific correctness the highest priority.

From our experience in GC – and looking into some recent papers that do contain innovative ideas – we believe that CGC, including 2D-GC (heart-cutting and GC×GC), can indeed further grow at a steady pace, guaranteeing high quality, accuracy and robustness, and making the technique even more valuable in many application fields.

New CGC equipment, incorporating chip technology, new column formats, new column connections and flow chips, and so on, will help new GC practitioners set up optimized and robust GC methods. The recent introduction of the Agilent Intuvo 9000 GC already incorporates some of that technology. In the next decade, we expect that several evolutions will take place in CGC technology, making the technique more user friendly and rugged. In combination with new developments in sample preparation placed on-line with the CGC instrumentation, we will undoubtedly see a further expansion of GC as a powerful analytical tool for quality control in many application areas, including the life sciences, where it can prove its complementarity to LC-MS.

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Profession

Leadership
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Adventures in Funding

For all scientists, the quest for funding can feel relentless – but analytical science, in particular, struggles more than most, often finding itself at the back of the pack. Despite measurement science being the foundation of all (successful) scientific endeavors, it is all too often overlooked by grant reviewers, who tend to favor more attention-grabbing projects over the essential 'supporting' role played by analytical research.

An interview with Gert Desmet

In this new article series, "Adventures in Funding", we get the inside story from analytical scientists who have secured major grants. In each article, the 'winners' will talk us through the highs and lows of the process, share the factors that led to the reviewers' decision, and describe the impact on their work. By publishing their personal stories, we hope to build up a more detailed picture of the funding landscape in analytical science – and also offer some of the secrets to grant success.

To kick off the series, Gert Desmet shares the story of his recent 2.5 million euro European Research Council (ERC) Advanced Grant.

Tell us about the grant…

I recently received an individual European Research Council (ERC) Advanced Grant, worth 2.5 million euros. A number of Advanced Grants are awarded every year, and specifically target researchers who have already established themselves as top independent research leaders. ERC Advanced Grants are designed to allow outstanding research leaders of any nationality and any age to pursue high-risk, high-reward projects in Europe – and give them full freedom to develop their idea over a period of five years. It is a very attractive and highly sought-after grant.

"As the deadline approached and the perfect proposal eluded me, the stress levels rose!"

What is the funding for?

I applied for a grant to build the perfect chromatographic column, by arranging chemically perfected micro-particles in a minutely ordered 3D pattern. Calculations have proven that perfect arrangements of particles exist that produce up to 10 times more theoretical plates in the same time. This could unlock a breakthrough in the ability to detect low abundant molecules in very complex samples, which in turn could lead to fundamental new insights in the life sciences. In addition, we will be able to perform time-resolved analysis of very rapid processes involving short-living intermediates. It seemed to me that such an ambitious goal was ideally suited to an Advanced Grant so, with some trepidation, I decided to apply.

How was the process?

At first, the procedure to apply for the grant seemed simple enough. The ERC only requests a 15-page project description. Those 15 pages then needed to be reduced into a five-page summary, which in turn was summarized in a 2,000-word abstract. The abstract is then used to select reviewers and get a first impression.

Once the proposal is submitted, the waiting begins...

The applications are reviewed over several phases. During the first round,


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PROPOSAL

"I believe I convinced the committee members with my passion for the project and the importance of my goal; it is my life-long dream to make the perfect chromatographic column."

about 70–80 percent of the proposals are eliminated solely based on the abstract and the five-page summary. The full description is only read during the second round, where typically another half of the first round survivors are rejected. All in all, the entire selection takes around nine months.

What tactics did you use to perfect the proposal?

As anyone who has written a grant proposal will know, it's easier in theory than in practice. The summary and abstract proved particularly difficult, because the reviewing panels are composed of scientists from a broad range of disciplines. In my case, the best I could hope for was that the reviewers had a vague notion of what chromatography is. Finding the balance between an in-depth detailed chromatographic description and a project proposal that would be accessible and draw the attention of non-experts took up many hours. In the attempt to achieve this elusive balance, I must have rewritten the 15-page project description at least four times, not to mention the number of versions the abstract went through.

Needless to say, as the deadline approached and the perfect proposal eluded me, the stress levels rose! The last three weeks before the deadline, I decided to go 'under the radar' to ensure 100 percent focus while working full-time on the project application. I found the most effective technique was to surround myself with a small team for

brainstorming sessions and to evaluate different versions of the proposal. Furthermore, I also made sure I had good technical support, who could provide me with excellent graphics to enliven and illustrate the text, and – very importantly – a dedicated proofreader to review the text. Often, people hire professional agencies to do this work for them, but I am proud to say that I was able to rely on my own team.

How did it feel to win the grant?

When you get the news that the grant is yours, all the hard work and the stressful waiting are immediately forgotten. Writing the application was a tremendous effort, but the opportunities my research group now has are wonderful. The week after the news of my grant got out, our university rector saw me crossing the campus, and came running across the lawn to give me three kisses and congratulate me in front of a stunned audience of students and colleagues!

What do you think tipped the balance in your favor?

In hindsight, I believe I convinced the committee members with my passion for the project and the importance of my goal; it is my life-long dream to make the perfect chromatographic column, and I believe that showed in the proposal. By defining the need to realize this dream in layman's terms, I could also persuade the non-chromatography experts to take a chance and offer me the opportunity to start this scientific adventure.

As with all applications for funding, there is always a significant portion of luck involved. It is always possible that your project proposal ends up in the hands of an ill-disposed reviewer. Fortunately, that risk is limited for this type of grant, as each application gets at least eight review reports, such that these 'accidents' can be filtered out.

What's next for the project?

My goal will require a great deal of innovative science to achieve. First, we will need to develop radical layer-by-layer micro-particle deposition methods, working with nanometric precision over very large areas to address the typical length and width of a chromatographic column in one stroke. In other words, we aim to develop a nano-precision bricklaying technique, working at high speeds and over large areas. The benefit of these layer-by-layer deposition methods is that they should work with many different materials. It will also allow us to develop applications in totally new areas, such as the production of photonic crystals with new bandgap sizes. The latter prospect is really thrilling, as it will allow us to considerably broaden our research activities, acquire new know-how, and set up many new collaborations, including outside the field of chromatography.

"We aim to develop a nano-precision bricklaying technique, working at high speeds and over large areas."

What do you hope to achieve by the end of the funding period?

The grant will enable me to hire four PhD students and two postdoctoral researchers over the coming five years. Furthermore, I will be able to expand our lab infrastructure with a whole range of new nano-positioning and micro-optics set-ups. In five years, I not only hope to have achieved my dream to build the ideal chromatographic column, but also hope our lab has become a highly attractive hub for top-level scientists – junior and senior – from many different disciplines.

Gert Desmet is Professor, Chemical Engineering at the Vrije Universiteit Brussel, Belgium.

If you have a story to tell – positive or negative – about your Adventures in Funding, or would like to nominate a colleague to be featured, contact the editor at: charlotte.barker@texerepublishing.com.

Mass Spec Mentor

Sitting Down With... Barbara Larsen,
Technology Fellow at DuPont,
Wilmington, Delaware, USA.

How did you get into science and the analytical field?

My interest in science started in high school. The first teacher who took me under his wing was Mr Bailey; we went on field trips, digging in streams for fossils and shark teeth, which introduced me to scientific curiosity. I also took two years of chemistry in high school – unusual at the time – and the subject so fascinated me that I went on to do a degree in physical chemistry.

Why mass spectrometry?

For my senior research project at Ames Research Facility in California, I studied the origins of life – and that's where I started my first mass spectrometry (MS) experiments. I was immediately hooked. Putting my sample into the MS system created a puzzle; I had to figure out how to break something down into its component parts and how to put it back together. I love a challenge, and if I'm told I can't do something, I'm all the more determined. I still find the puzzle aspect fascinating today, but now I'm focused on protein sequences and modifications.

What prompted your move to industry?

After my PhD, I spent a year at Johns Hopkins in the School of Pharmacy at the NSF-funded Middle Atlantic Mass Spectrometry facility, which was at the interface of pharmacy, medicine, biology, and life sciences. I recognized it as the next frontier for the field of mass spectrometry. Ultimately, my own interests were more applied, so I moved to DuPont, where I'm still able to dabble in MS research and development, but in a more product-centric way. It's a great mix of fundamental and applied research. However, my year at Johns Hopkins also provided me with a very strong lifelong mentor – Catherine Fenselau (another Power List awardee and a huge supporter of women in science).

What makes a good mentor?

You have to be approachable and open – and you need to listen. My own mentors made the effort to know me, to understand what drives me, and to present opportunities for me to move forward. Now, I try to do the same for others by listening, making suggestions and asking probing questions. I've had three very strong mentors, and I still go back and ask them questions. You need people you can rely on when you're questioning yourself.

What is your current focus?

I work in DuPont's Science and Innovation Center, which is looking at new applications for cutting-edge technology. I'm currently involved in a long-term project to stabilize probiotics, and so enhance their shelf life. We're using a systems biology approach, combining genomics, transcriptomics, metabolomics, and proteomics to study changes over time. Notably, the approaches we are using will be applicable to a wide variety of commercial applications across multiple DuPont businesses. Outside of work, I believe strongly that we should all remember to give back to our communities by volunteering our time – whether it be to schools for career days, helping with illiteracy or, my personal passion, the local food bank (where I currently serve as president of the board of directors).

What are your top three career highlights?

One particular highlight came in the 1990s when my group and I pioneered the use of electrospray ionization together with magnetic sector instruments – before such sources were commercially available. I realized that it was a game changer and that the subsequent jump in resolution and mass accuracy would revolutionize everything we'd been doing up to that point. A second highlight was the development of a highly specific method for extraction of small molecules out of a polymer that is referred to by the US Environmental Protection Agency as "the Larsen method." It's based on very careful work with several papers published in the The Analyst; I'm particularly proud of the body of work. A more recent highlight has come from seeing the proteomics work that I've been engaged in for years finally being applied to products.

What have been the greatest milestones for mass spectrometry?

Matrix-assisted laser desorption and electrospray ionization have been the biggest leaps in instrumentation. The mass accuracy with these techniques is phenomenal. Another amazing advance is ion mobility, which gives us the ability to pull two molecules apart from each other based on tiny differences in the 3D structure. I truly believe that we are not far from seeing mass spectrometers in physicians' offices, where they will be used to help speed up diagnosis and select the right drug for the right patient – unthinkable 20 years ago. My next challenge to the instrument manufacturers: enable me to extract a spot out of 1D gels, without the laborious cutting and digestion. Why can't we use a laser or electrical beam to extract those molecules, and do the chemistry in the gas phase?

Women in science – do we need to do more?

I've been fortunate to work for the DuPont company which is very supportive of women; typically, 50 percent of new hires each year are women. There are a lot of female role models within DuPont, whether you want to stay in science or take a management track. I think universities should take a closer look at what DuPont does right. One of the things that I find astounding is that more than 50 percent of college graduates in the US are women, and yet women make up just 25 percent of tenured professors. The US needs to ensure a better representation of women in high-level positions through all sectors of academia, business and government.

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