DECEMBER 2018 # 71

the Analytical Scientist™

Supelco®

Analytical Products

IMAGINE THE NEXT 350 YEARS

Supelco® analytical products from Merck. Accurate. Precise. Consistent.

We know only the most accurate analytical products will do. That's why Merck offers the Supelco® portfolio of analytical products. Whatever your needs, our portfolio is always fit for purpose, ensuring your results are accurate, precise and reproducible, and your systems fully certified. Our comprehensive portfolio, developed by analytical chemists for analytical chemists, covers a broad range of analytical solutions, and every product is meticulously quality-controlled to maintain the integrity of your testing protocols. And with Supelco® scientists dedicated to your analytical applications, the expertise you need is always on hand.

1668

Merck beginning with a pharmacy in Darmstadt, Germany

1827

Merck transformation into a research-based company

1850

Establishment of partnership E. Merck

1935

Sigma Chemical Company Founded

SIGMA

1951

Aldrich Chemical Company Founded

ALDRICH

1966

Supelco Founded

SUPELCO, INC.

1975

Merger to form Sigma-Aldrich Corporation

SIGMA-ALDRICH

1993

Supelco Acquired by Sigma-Aldrich

SUPELCO

1995

Establishment of Merck KGaA and public listing

SigmaAldrich.com / Supelco

The life science business of Merck operates as MilliporeSigma in the U.S. and Canada.

Lit. No. MK_AD2917EN 10/2018

Founders of Supelco

Dr. Walter Supina
Born in Hartford, Connecticut, Walt obtained his doctorate in chemical engineering in 1960

Mr. Nicholas Pelick
Born in Scranton, Pennsylvania, Nick obtained his master's degree in biochemistry in 1964

Footprint of Supelco

1966: Enters GC business with adsorbents and packed GC columns
1971: Enters carbon adsorbent business with Carbosieve®
1979: Enters HPLC with SUPELCOSIL™ line of stable 5 µm spherical particles with true monolayer bonding
1983: Enters the air sampling market by introducing a line of solvent desorption tubes for industrial hygienists to help protect workers from being exposed to toxic chemicals
1985: Enters sample preparation business with Supelclean™ SPE tubes
1993: Launches SPME fibers
1994: ISO 9001 – Quality Management System
2006: Sigma-Aldrich acquires Astec®: leader in chiral chromatography
2007: First to market globally Fused-Core® particles jointly with Advanced Materials Technology, introduced Ascentis® Express
2018: Supelco® expanded to include all analytical products from Merck KGaA for a comprehensive range of analytical techniques

TODAY

2015
Acquisition of Sigma-Aldrich®

2010
Acquisition of Millipore

MILLIPORE

Analysis with mobility and ease-of-use

Mobile Analysis

Reference materials for accurate results

- Cerilliant®, Certipur®, TraceCERT®

Chemical Standards and Certified Reference Materials

Comprehensive analytical portfolio

Chromatography, Titration, Spectroscopy, Photometry

«Our Ion Chromatographs are very robust and reliable»

Lledó Altava is a senior laboratory technician at IPROMA, a leading provider of laboratory testing, monitoring, and consulting services in Spain. Working at IPROMA's large environmental laboratory near Valencia, **Lledó relies on the robust performance of her fully automated Metrohm ion chromatography systems.** They are on duty 24/7 almost 364 days a year – helping IPROMA to keep its competitive edge in a highly competitive market.

www.metrohm.com

Metrohm

75 YEARS

PEOPLE YOU CAN TRUST

Image of the Month

Time Waits for No Man

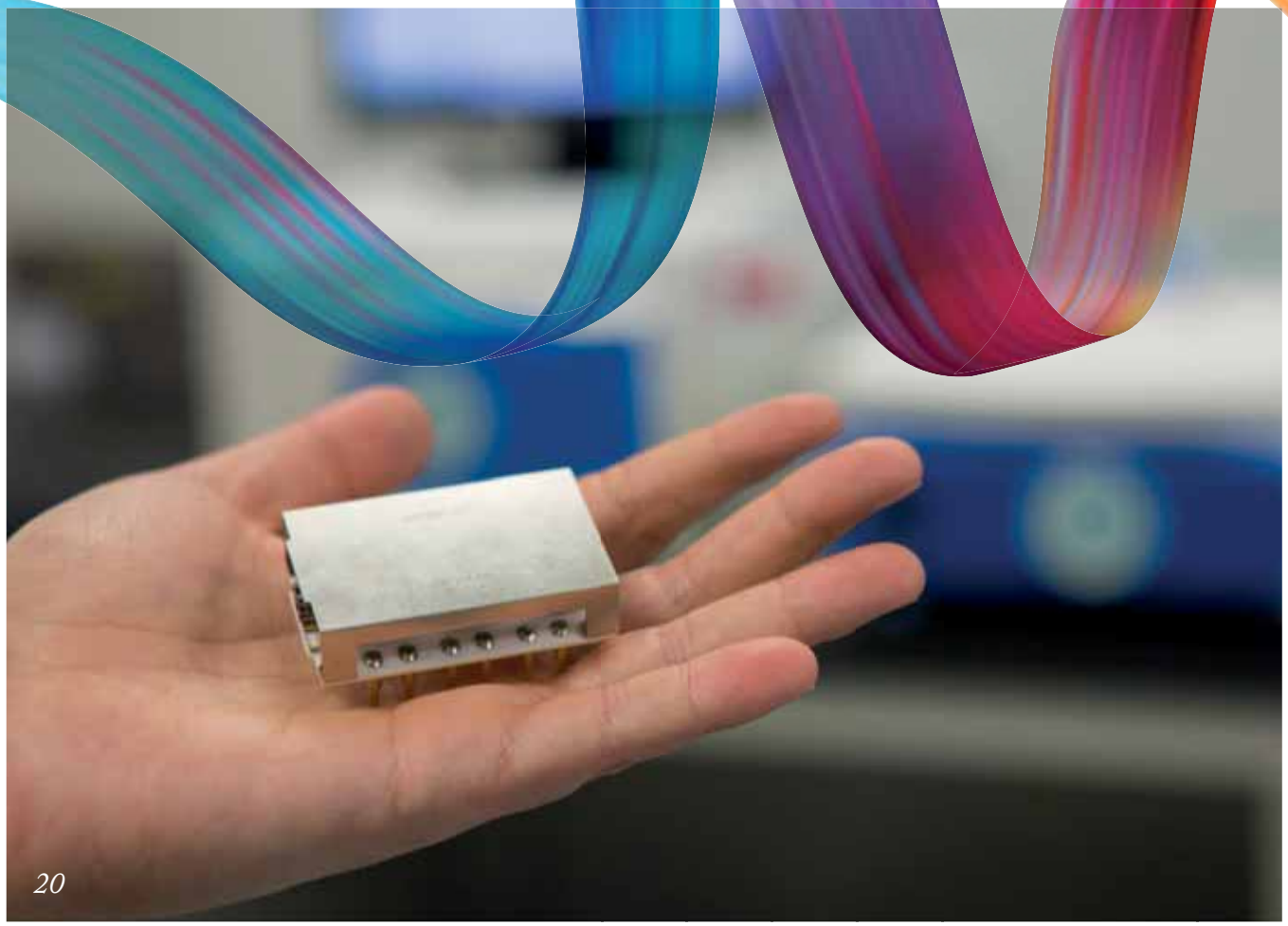
Hyperspectral imaging: analyzes the parts other techniques cannot reach. In-situ analysis of The Man with the Key, by sculptor Auguste Rodin, recently allowed researchers to assess various parts of the sculpture (either hidden or invisible to the naked eye), not only identifying two corrosion products – antlerite and brochantite – but also allowing the mapping of their spatial distribution.

Reference: E Catelli et al., J Spectral Imaging, 7, a10 (2018). DOI: 10.1255/jsi.2018.a10

Credit: Oslo kommunes kunstsamling (City of Oslo Art Collection).

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

Contents



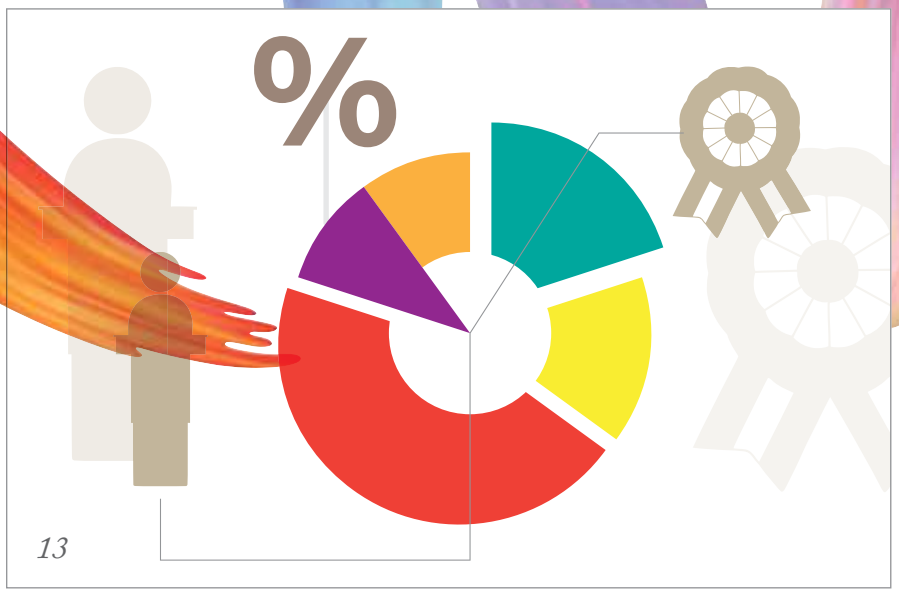
20

On The Cover

Brushing up on the best innovations of the year.

Upfront

In My View



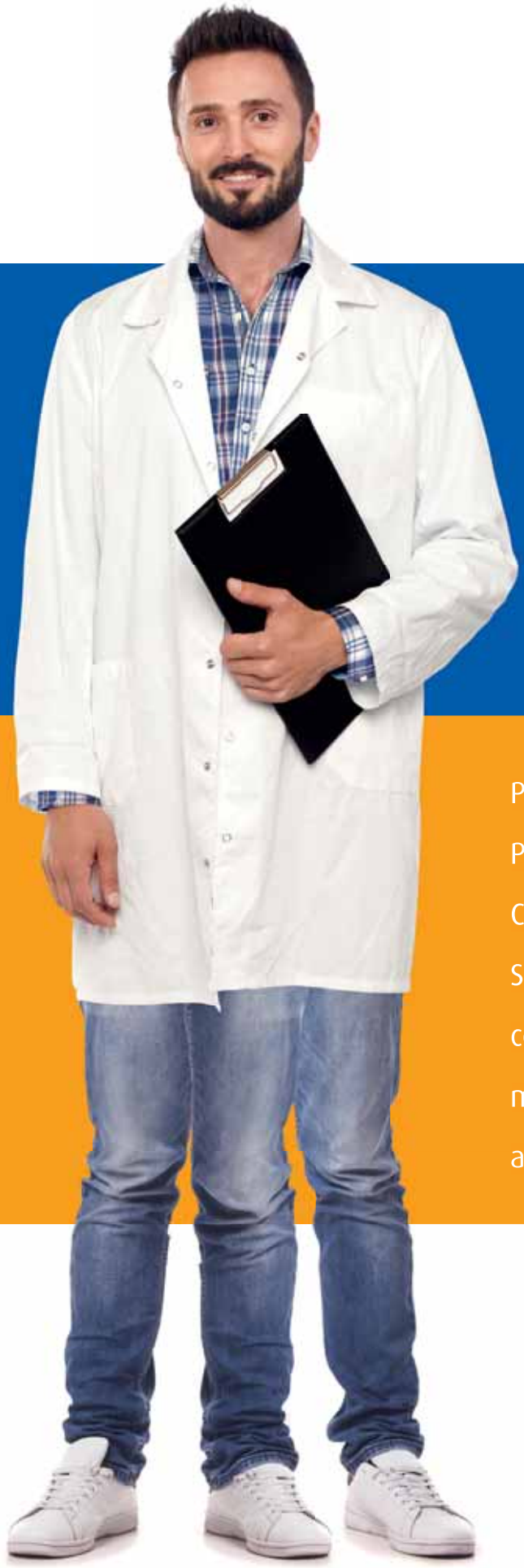
the **Analytical Scientist**

ISSUE 71 - DECEMBER 2018

Change of address
info@texerepublishing.com
Hayley Atiz, The Analytical Scientist,
Texere Publishing Limited, Booths Park 1,
Chelford Road, Knutsford, Cheshire, WA16 8GS, UK

General enquiries
www.texerepublishing.com | info@texerepublishing.com
+44 (0) 1565 745 200 | sales@texerepublishing.com

Distribution:
The Analytical Scientist (ISSN 2051-4077),
is published monthly by Texere Publishing Limited,
Booths Park 1, Chelford Road, Knutsford, Cheshire,
WA16 8GS, UK
Single copy sales £15 (plus postage, cost available on request info@texerepublishing.com)
Non-qualified annual subscription cost is
£110 plus postage



PSS

Perfect separation solutions for polymers, proteins and particles.

We go that extra yard!

PSS is your partner for **GPC/SEC**, Interaction Polymer Chromatography **IPC** or 2-Dimensional Chromatography **2D** – whether with our SECcurity² turnkey solutions, or with our expert contract analysis services. For the ultimate in macromolecular characterization, contact PSS and stay one step ahead of the game.

PERFECT
SEPARATION
SOLUTIONS

www.pss-polymer.com




Perhaps you have been a regular subscriber to The Analytical Scientist since the beginning (2013!). Perhaps you are a freshly-minted member of our ever-growing community. Or perhaps you browse our website, seeking out the content most relevant to you. Whichever type of reader you may be, we sincerely appreciate you and your support. And we ask each of you to join us in a moment of reflection. The festive season – with family get-togethers and (hopefully) an escape from typical daily demands – is always a good time to sit down, look back, and look ahead.

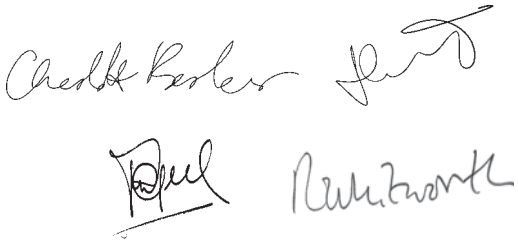
It's nearly six years since the first issue of The Analytical Scientist; how do we, the four editors, now see our role? Well, it hasn't changed: working with hundreds of contributors, we aim to share thought-provoking research, to highlight current developments from new angles, and to present you with diverse, substantiated viewpoints. Certainly, we do not wish to impose our vision on you, but rather to help you sharpen and hone your own ideas. And we do all this on a regular basis, through our monthly print magazines, our weekly e-newsletters and our online presence.

As we are a conduit for analytical science, it would be folly not to investigate ourselves as closely as we do the scientific content we publish. The observant among you will have noticed our newly designed website www.theanalyticalscientist.com, which will change the way we deliver content to you – but your opinion is essential for helping us choose the content that you want to read.

A good publication is made in constant dialogue with the reader. You keep us sharp. We invite you to tell us where we are succeeding – and how we can do better. Why not visit the new website and leave a comment on an article you do (or don't) like? Or alternatively email charlotte.barker@texerepublishing.com.

Wishing you happy holidays and a fruitful new year!

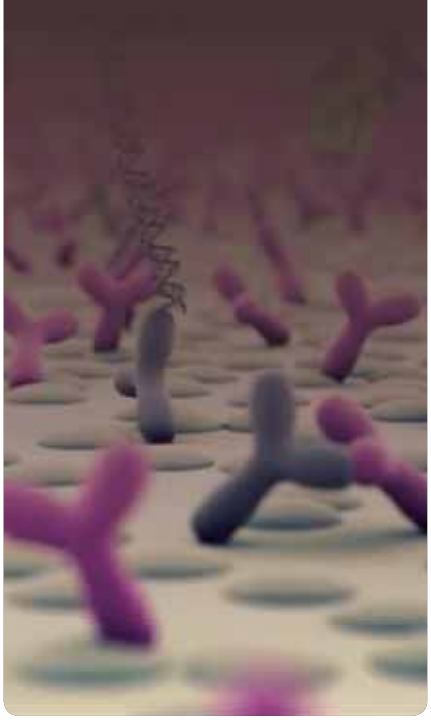
Charlotte Barker
Joanna Cummings
Frank van Geel
Rich Whitworth



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



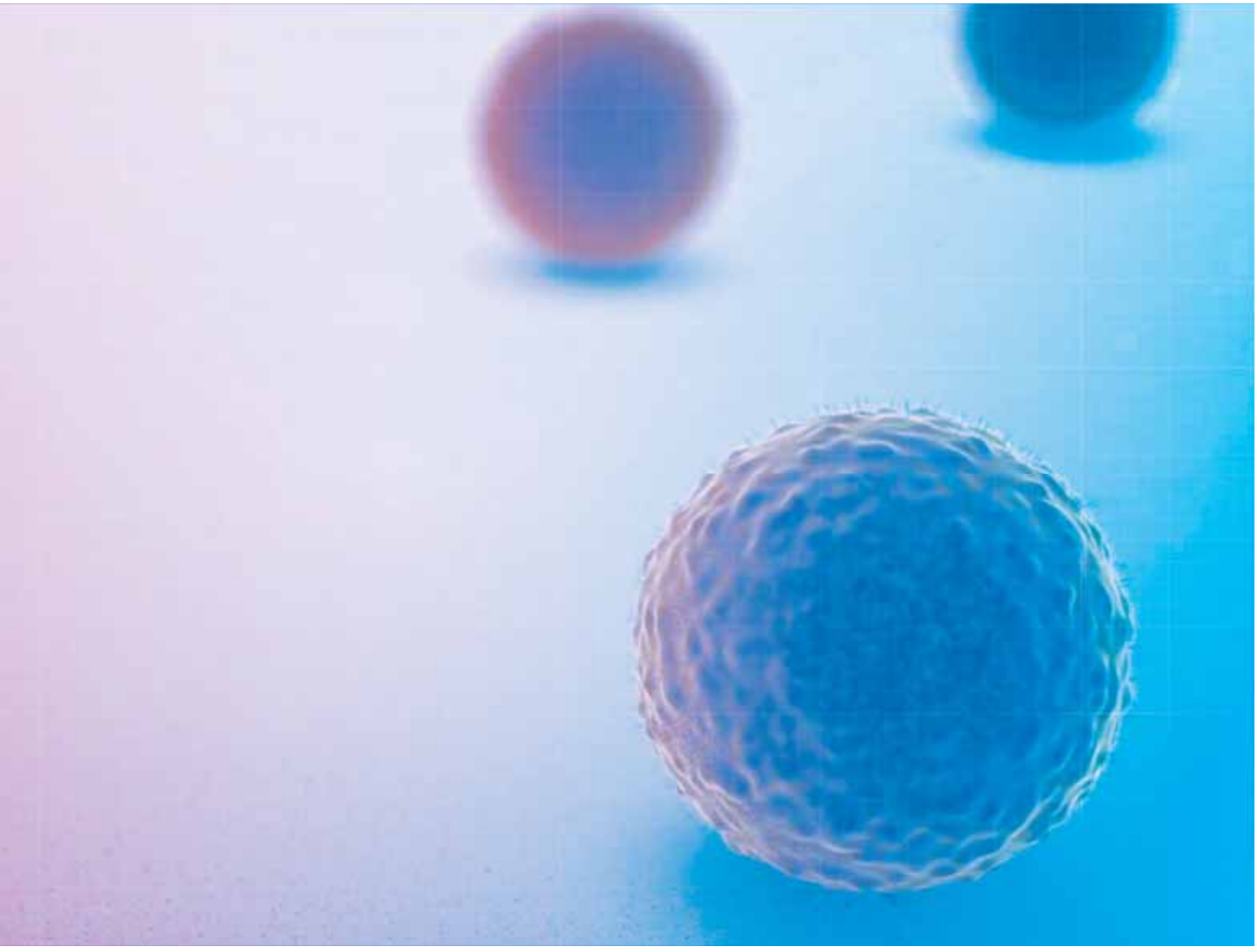
Sensing the Tiniest Change

A new biomarker sensing technology provides sensitive, specific monitoring for a wide range of patients

By Menno Prins, Professor, Department of Biomedical Engineering at Technische Universiteit Eindhoven, The Netherlands.

Molecules that are essential for the body, such as proteins and hormones, can often yield significant insight into a patient's health status. But most of these molecules are present in the blood in pico- or nanomolar concentrations – comparable to one grain of sugar dissolved in an Olympic swimming pool. The best-known assay to measure such low concentrations outside the body is ELISA, a test in which the sample passes through an elaborate process with multiple steps and biochemical reagents to yield a single concentration value. In contrast, continuous monitoring dynamically follows biomarker concentration in solution, leading to a stream of data rather than an isolated result. For continuous monitoring, molecular binding must be reversible and lead directly to a measurable signal without consumption or production of chemical reactants. The sensing principle should be self-contained, reversible, and stable over a long period of time. Still, the assay should be as sensitive and as specific as ELISA. That's the challenge we are addressing.

BPM refers to "Biomarker monitoring based on sensing of Particle Mobility." The technique exploits the fact that tiny particles in liquid are constantly in random motion because water molecules collide with them. What we did is couple the particles to a substrate via a flexible molecular tether, so that the particles wiggle back and forth. To detect a specific biomarker, the particles and the substrate are provided with affinity molecules; this enables specific, reversible interactions with the biomarker molecules in solution. When a biomarker molecule attaches to both particle and substrate, they form a molecular sandwich bond that greatly reduces the particle's mobility. When the biomarker is released, the particle regains its original mobility. So these mobility changes indicate the capture or release of a single biomarker molecule – and the number of changes



per minute reveals, with high sensitivity and specificity, the concentration of the biomarker in the liquid.

The beauty of the BPM sensor technology is that increases and decreases in biomarker concentration can be precisely monitored over time. We have demonstrated its use in monitoring protein and DNA, but the technology is widely applicable; affinity molecules such as antibodies and aptamers are available for almost all biomarkers.

We think that BPM sensing can become an early warning system that signals patient deterioration – useful for postoperative, immunocompromised, or chronically ill patients, as well as those in critical condition. Furthermore, patients who receive potent drugs with a narrow therapeutic range might benefit from a sensor that enables rapid and robust dosing regulation. Before that can become a reality, though, we need to develop assays for several medically relevant biomarkers and demonstrate the required analytical performance. This will be followed by clinical proof-of-concept studies, which should give solid grounds for subsequent development of a product. In total, we expect the process to take 5–10 years. We are now defining key applications and markets to determine our technical and clinical direction. Are we going to focus on measuring early warning markers, or on therapy monitoring? What patient group will we target? What value will we add? The answers to these questions will define our work in the coming years.

Continuous biomarker monitoring will go through several stages of maturity – and, in the future, may be as easy to perform as today's blood pressure or heart rate measurements. As technology development increasingly focuses on important medical needs, we have an interesting road ahead.

Reference

1. *EWA Visser et al., "Continuous biomarker monitoring by particle mobility sensing with single molecule resolution", Nat Commun, 9, 2541 (2018). DOI: 10.1038/s41467-018-04802-8*

Finding Narco

Forensic testing labs need to clean up their act

In forensics laboratories, unacknowledged background levels of previously analyzed drugs can affect the accuracy of ongoing analyses. A team from the National Institute of Standards and Technology (NIST) and the Maryland State Police recently set out to assess the levels of these "hidden" chemicals, by collecting samples from various work surfaces all around the lab (1). Edward Sisco, a research chemist in the Surface and Trace Chemical Analysis Group, NIST, tells us more about what they discovered – and why it's important.

What led you to initiate this study?

Our group's research has traditionally focused on trace detection of explosives and narcotics. Adoption of techniques like DART-MS is increasing the sensitivity of our analyses – to the point where the background levels of drugs in the laboratory need to be measured. We need to understand what's happening, minimize it, and account for it, so we can improve and define detection limits for sensitive analyses and improve cleaning protocols.

What techniques did you use?

We chose DART-MS for the screening component of the study – it is the leading analytical technique capable of trace detection and is being used or considered by many forensic laboratories. For quantitation, we wanted to use the most sensitive technique available in our laboratory – LC-MS/MS – and that turned out to be a good choice, because the levels we ultimately measured were significantly lower than levels that can be detected using current instrumentation (GC-MS).

What did you discover?

We found that background levels of drugs exist on most surfaces in forensic laboratories, with the highest concentrations discovered in the drug chemistry section – not entirely unexpected given that's where bulk materials are routinely handled. High levels were also found in balances, which reflects how difficult these are to clean. The data could be useful in doing risk assessments for analyst safety and in the implementation of laboratory engineering controls that help minimize background levels.

How does this compare with non-lab environments?

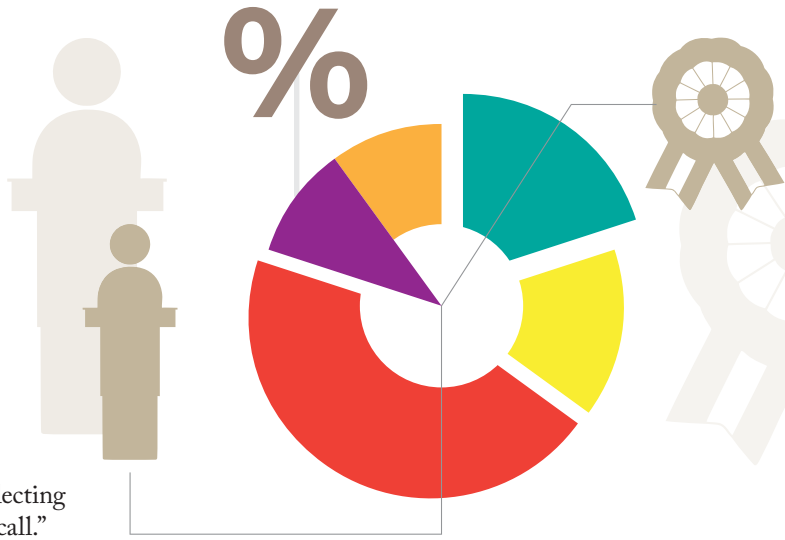
The levels in the laboratories were not that different from those reported in public spaces and police stations in other studies, but we hope this study highlights the importance of monitoring background levels on surfaces in forensic laboratories in particular. The study also provides labs with a protocol for self-monitoring and a dataset to help give context.

What happens next?

We are currently working on several follow-up publications that address: i) the capabilities of different cleaning agents at removing target analytes of interest from surfaces; and ii) a larger dataset that demonstrates background levels of 20 laboratory systems. We're hoping to draw conclusions from this larger dataset on how to help minimize background levels. We will also be running a workshop to discuss the results at the next American Academy of Forensic Sciences meeting (February 19, 2019).

Reference

1. *E Sisco et al., "A snapshot of drug background levels on surfaces in a forensic laboratory", Forensic Chemistry, 11, 47–57 (2018). DOI: 10.1016/j.forc.2018.09.001*



Variety Show

Need to diversify your list of conference speakers? There's a site for that

What?
An online directory of chemists, DiversifyChemistry aims to help – as the name suggests – "diversify" the pool of speakers, award nominations and so on, by providing a more diverse list of scientists. Entrants self-nominate, and can choose to identify themselves by gender, race, ethnicity and/or sexual orientation.

Why?
The directory aims to help with unconscious bias – and the limited human memory! From the website: "Studies have shown that a more diverse group is generated when candidates are identified from a list, rather than selecting based purely on recall."

Who?
The directory was created by Anne McNeil (University of Michigan), a chemistry professor frustrated by the poor representation of certain groups at conferences. "I wanted to bring visibility to those from underrepresented groups in the academic chemistry community," she said. At the time of writing, the directory lists 260 chemists.

What next?
The list continues to grow. If you are a chemist from an underrepresented group, why not sign up?

To add your name to the directory or browse the list, visit: https://diversifychemistry.com/ Twitter: @DiversifyChem

The MasSpec Pen. Credit: Vivian Abagyu.

From Imaging to Integration

Business in brief: What's going on in analytical science?

Products and launches

- Agilent launched the ICP-MS Water Analyzer, which aims to simplify ICP-MS analysis.
- Princeton Instruments launched the SpectraPro HRS-750 – a spectrograph and monochromator that has applications in a variety of spectroscopic techniques, including Raman, LIBS and microspectroscopy.

Collaborations

- Bruker has acquired Alicona Imaging. Alicona co-CEO Manfred Prantl said, "The Alicona InfiniteFocus, µCMM, and collaborative robot products […] combine nicely into Bruker's growing family of application-enabling technologies."
- A new collaboration between IntegraGen SA and Google Cloud will integrate IntegraGen's advanced genomic analysis tools, SIRIUS™ and MERCURY™ into the Google Cloud Platform.

Company and people updates

- Merck has agreed to establish an "innovation hub" in Guangzhou City, China. The hub will facilitate collaboration between companies and academic institutions, as well as showcase Merck's research and products.
- Livia Eberlin, co-developer of the MasSpec Pen, has been named one of the five Gordon and Betty Moore Foundation Moore Inventor Fellows. Each fellow receives USD$825,000 over three years to fund innovative research.
- The Society for Applied Spectroscopy Gold Medal Award (New York and New Jersey section) has been presented to Igor Lednev, professor at the University at Albany, for his spectroscopic work in the forensic field.
- Shire PLC's Facility Integration Project has been awarded "Facility of the Year" by the International Society for Pharmaceutical Engineering.

For links to original press releases, visit the online version of this article at: tas.txp.to/1218/BUSINESS.

Unity on Units

Measurement scientists from around the world have voted to re-define the International System of Units (SI)

Photograph courtesy of the BIPM

For 130 years the kilogram has been defined by the International Prototype of the Kilogram – a cylinder of platinum alloy housed at the International Bureau of Weights and Measures (BIPM) in Sèvres, France. Instead, the kilogram will be defined by the Planck constant – the fundamental constant of quantum physics. The ampere, kelvin, and mole will be defined by the elementary electric charge (e), the Boltzmann constant (k), and the Avogadro constant (NA), respectively.

When the changes come into effect on 20th May 2019, all SI units will be defined by reference to a fundamental constant, rather than a physical reference object (prototype).

Barry Inglis, Director of the International Committee for Weights and Measures said in a statement, "We will now no longer be bound by the limitations of objects in our measurement of the world, but have universality accessible units that can pave the way to even greater accuracy, and even accelerate scientific advancement."

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 charlotte.barker @texerepublishing.com

Playing the Polymer Game

We need to build a better suite of techniques for the analysis of macromolecules

By Harald Pasch, Professor, University of Stellenbosch, Department of Chemistry & Polymer Science, South Africa, and Taihyun Chang, Professor, Pohang University of Science and Technology (POSTECH), Pohang, Korea.

Over the last two decades, increasing attention has been paid to the analysis of complex polymers, particularly determining their chemical composition and microstructure using advanced fractionation and spectroscopic methods. Why do we need this information? So we can fully understand the behavior and properties of materials during processing and application. The precise analysis of such materials – which have multivariate distributions – is a difficult task, and a single separation/analytical method is often not able to provide comprehensive information.

The most commonly used techniques include size exclusion chromatography (SEC) and MALDI-MS.

However, it is important to be aware of the limitations of these techniques, and to keep an open mind to other separation techniques that can supplement them. For polymers with more specific applications, such as polymers with functional groups (for good adhesion and so on), block copolymers (for morphology control) and polymers with well-defined molar mass distribution with architecture, neither SEC or MALDI alone can provide sufficient information.

In short, the characterization of polymer molecular heterogeneity demands the use of a wide range of analytical fractionation techniques, preferably those that are selective towards a specific type of heterogeneity. We call this "analytical LEGO" and, just like in LEGO – where kids put toy bricks together to build complex structures - we combine analytical components to build complex analytical instrumentation. For example, multidimensional and multidetector column- and channel-based fractionations provide exciting avenues in method and technology development (1-3). (And complex polyolefins represent a good example of when such complex methods are necessary, as only a combination of different analytical methods can address all the molecular parameters [4-6]).

Another interesting multidetector fractionation technology is field-flow fractionation (FFF), of which thermal FFF is a subtechnique. Thermal FFF can fractionate micelles, vesicles, nanogels and other polymer assemblies according to size, composition and molecular topology (7).

Research on these approaches – and more – will be presented at the International Symposium on Separation and Characterization of Natural and Synthetic Macromolecules (SCM). This biannual conference brings together scientists who share an interest in the separation and characterization of "large" molecules, and is one of the most important forums for discussing the basic principles of multidimensional fractionations (and their capabilities in chemical composition and microstructure analysis). For us and our students, SCM is essential – it's an opportunity for chromatographers and spectroscopists alike to present ideas and take part in lively discussions.

This year, we are presenting a workshop called "Polymer Separation – Learn from the Best." Targeted at analytical and polymer scientists, chemical engineers and laboratory managers, as well as postgraduate students and lab technicians,

it will provide a state-of-the-art overview of polymer fractionation and characterization, addressing both fundamentals and the latest developments in the field. Our message is: if we want more detailed characterization of molecules in polymer analysis, it's time to get out the analytical LEGO. "Playing" is rewarding… and fun!

References

1. *H Pasch, B Trathnigg, Multidimensional HPLC of Polymers. Springer-Verlag, Berlin-Heidelberg-New York, (2013).*
2. *H Pasch, MI Malik, Advanced Separation Techniques for Polyolefins, Springer-Verlag, Berlin-Heidelberg-New York, (2014).*
3. *MI Malik, H Pasch, "Field-flow fractionation: New and exciting perspectives in polymer analysis" Progr Polym Sci, 63, 42–85, (2016).*
4. *PS Eselem Bungu, H Pasch, "Branching and molar mass analysis of low density polyethylene using the multiple preparative fractionation concept",Polym Chem, 9, 1116–1131 (2018).*
5. *P S Eselem Bungu, H Pasch, "Comprehensive analysis of branched polyethylene: the multiple preparative fractionation concept", Polym Chem, 8, 4565–4575 (2017).*
6. *A Ndiripo, H Pasch, "Comprehensive analysis of oxidized waxes by solvent and thermalgradient interaction chromatography and two-dimensional liquid chromatography",Anal Chem, 90, 7626–7634 (2018).*
7. *UL Muza et al., "Characterization of complex polymer self-assemblies and large aggregates by multidetector thermal field-flow fractionation," Anal Chem, 89, 7216–7224 (2017).*

Efforts Outside the Echo Chamber

What can we as individuals – and members of professional societies – do to promote gender diversity at conferences?

By Rina Dukor, President, BioTools Inc., Jupiter, Florida, USA.

For a few years now, there has been some form of gender diversity symposium at the SciX and Pittcon conferences. These symposia sought to encourage young women students to stay in science as a career, by showcasing talks by established and successful women scientists in academia and industry. One of the other reasons, at least from my perspective, was to show our male colleagues (and everybody else, in fact) that women do really great science and that they deserve the same opportunities as their male counterparts.

The 2018 SciX session held no diversity session. Not because we believe we have achieved equality – and not because we have given up the fight. Perhaps these symposia became an echo chamber, with the same arguments year after year, amongst many of the same participants.

What is the way forward? I would like to see the theme of diversity incorporated throughout the sessions, rather than segregating a women-only event at the tail end of conferences. In these mini-events, we need to involve men too; male colleagues need to understand the challenges we face and be positive advocates for women in their team. It would also be great to have networking opportunities built into the sessions, so there is value beyond the presentations themselves.

Meetings such as FACSS and Pittcon also need to recruit a balance of plenary speakers – after all, there is no shortage of excellent female scientists in the field. FACSS has featured a lot of women as general chairs and program chairs of SciX – but that isn't the case at most analytical/spectroscopy conferences. (I was the first woman to co-chair at ICAVS in 2005. It took 13 years for another woman to do the same, at ICORS.)

Professors also have a part to play in encouraging female students to attend conferences, to volunteer, and to present. I have learned a lot of skills through my work with SAS (Society for Applied Spectroscopy). Volunteering at SAS provided me with experience of listening to different opinions, negotiating, writing, clearly presenting my points of view and thinking outside the box.

Young women, who are often socialized to be less assertive than young men, need to learn how not to be intimidated by the number of people present at a meeting. My strategy has always been to make sure I'm part of the conversation. I make a point before every meeting or conference to spend a few minutes scanning a newspaper: who scored that home run? Who won the Nobel prize? Those are the icebreakers.

So, what can each one of us do to help young women scientists? I think it's the responsibility of every female scientist to be open and willing to help make connections. Younger scientists are understandably intimidated to approach the big names in the field – and who, admittedly, are often surrounded by many people. So if you're an established scientist and see a younger counterpart on the edge of the group, pay it forward; step up and introduce yourself, and offer to introduce them to key researchers. One day, that young woman might be President of the conference, a society or a company. She might mentor other young minds or make an amazing discovery. I know from experience she will always remember you – the one who helped her break her first barrier, the one who took one minute from a conversation to say hello, the one who showed her how to support others.

Your Efficiency Challenge – Part III

Taking the next step on the road to efficiency

"Your Efficiency Challenge" is an exciting project from Agilent Technologies and The Analytical Scientist that helps you identify and address inefficiencies in your lab. Part I introduced the project – and kicked off a survey gathering views on efficiency in liquid chromatography from over 1,400 respondents. In Part II, we shared some of the results of the survey, and determined topics for a series of lively roundtable discussion webinars. Parts III–V bring together key points from the survey results and webinars, to help move the conversation forward.

In the first roundtable video, we sat down with pharma pioneer Kelly Zhang (Genentech) and LC expert Udo Huber (Agilent) to discuss efficiency at the analytical scale – and to discover how the right technology can help you push your results to the next level.

Read Part I: tas.txp.to/0918/efficiency-I
Read Part II: tas.txp.to/0918/efficiency-II
Watch the webinars: tas.txp.to/0918/YEC

What does analytical efficiency mean to you?

Kelly Zhang: In the pharmaceutical industry, our primary goal is to get first- and best-in-class medicines to patients as fast as we can. To do that, we need the data to be not only fast, but also informative. If we acquire data quickly but then have to spend a long time analyzing it to get the information we need, the overall process is not efficient.

Udo Huber: To me, analytical efficiency is everything that helps you to get better quality data, so you can be sure that you see all the peaks and all the impurities in your sample. In turn, higher quality data gives you more confidence – and I think that's very important, especially for the pharmaceutical industry.

In our survey, the most important considerations in liquid phase separations were robustness of the entire workflow – 87 percent of people thought that was very important or important. Does that number surprise you?

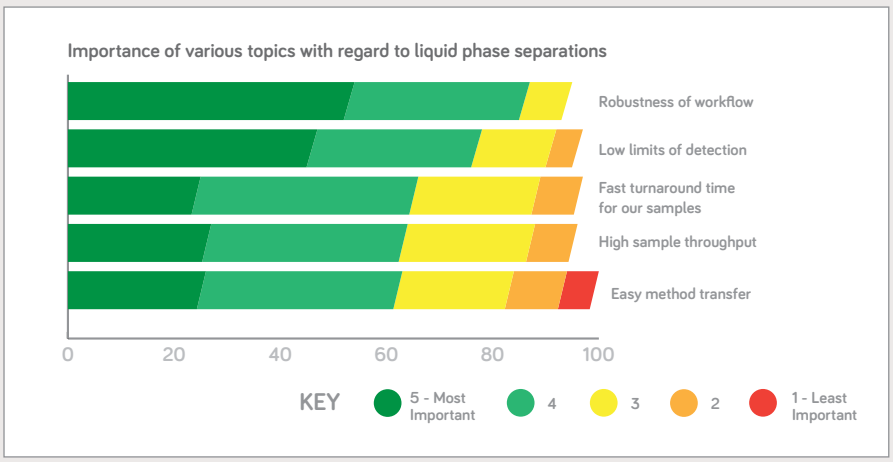
Udo: I'm not surprised. Remember that robustness is more than the instrument and the chromatographic run – if you think about the whole workflow, there are so many points where something can go wrong. Nobody wants mistakes – and that's true in all industries, not just pharma.

Kelly: I would also rate robustness number one. When it comes to patient safety, nothing can compromise the robustness; without a robust method, and technology generating quality data, we cannot make sure that our medicines are safe enough.

The second most important consideration was low limits of detection (78 percent) – but another part of the survey says that only 30 percent of users operate close to the limits of detection. Any comments?

Kelly: I think it depends on who you ask. My high throughput automation team, running hundreds of thousands of samples, are less concerned with sensitivity; they care more about how fast you can analyze one sample. But for the project team, sensitivity is a critical quality attribute – we don't want to miss any impurities, especially if they are toxic.

Udo: It doesn't surprise me that it



shows up high on the list. For industries such as food safety or environmental analysis, the regulatory agencies are setting lower and lower limits, and customers can't achieve that with the current instrumentation. I am surprised that separation performance or power wasn't higher, however. What we hear from the pharmaceutical industry – as well as from other industries – is that customers are afraid they are missing compounds in their chromatograms.

How do we drive the analytical workflow to improve robustness?

Kelly: Simple: all methods must be validated. We need to follow the validation protocol, making sure we can achieve the same result day to day, instrument to instrument, site to site and operator to operator.

Udo: People also need to ensure they include basic system care in their standard operating procedures; it's an occasionally forgotten element that helps keep your analysis or your system robust.

How can we improve robustness from a technology point of view?

Kelly: We always try to get the best instruments we can from the most reputable vendors; for example, we are now moving to UHPLC. We also try to reduce human error – so automation is another area where we can try to make the technology more robust.

Udo: I always recommend that you choose the system according to your application. For example, if you need to run a shallow gradient for your analysis, you should use a binary high-pressure mixing pump – because by design those pumps have a higher performance for shallow gradients. It may mean you have to invest in a binary or even a UHPLC pump. You could consider investing in a thermostat for your autosampler that keeps the temperature constant. Such simple investments really pay off after a relatively short period of time.

36 percent said they would run legacy methods even if newer established methods were better or faster, with 19 percent prevented from applying the latest methodology because of regulatory risks. How can scientists stay at the cutting edge?

Kelly: We think about this constantly. We always try to keep ourselves at the cutting-edge, but it depends on the stage and the purpose of the technology. For example, we can apply a new technology within the research lab, but when it goes into a regulatory environment, it is not that straightforward. You have to make sure you do a full method evaluation. And there are always regulatory concerns. If you have an established method that works, not many people will be motivated to change it.

Udo: We always get this request from our customers and so we invest a lot of R&D resources into ensuring that our customers can run their legacy methods even on the new instruments. We understand that customers may be reluctant to move away from their legacy methods; however, it's always possible to make small changes that improve and speed up the method.

Any final pearls of wisdom?

Udo: I think there is a way for everyone to improve analytical efficiency – but you really have to commit it! People sometimes don't want to change, but without change there will be no efficiency gains.

Kelly: When we talk about overall analytical efficiency, we certainly need incremental optimization to make current processes more robust and faster – but we must also be on the lookout for game-changing technologies. For example, when we analyze a sample, we must normally use multiple methods – but what if there was a single technology that could provide us with all quality attributes at the same time? It would be a huge improvement in efficiency!

The Road to Improved Efficiency

Are you a scientist, laboratory analyst or lab manager – or all of the above? Are you willing to challenge your perception of efficiency or do you already know you need to make efficiency gains?

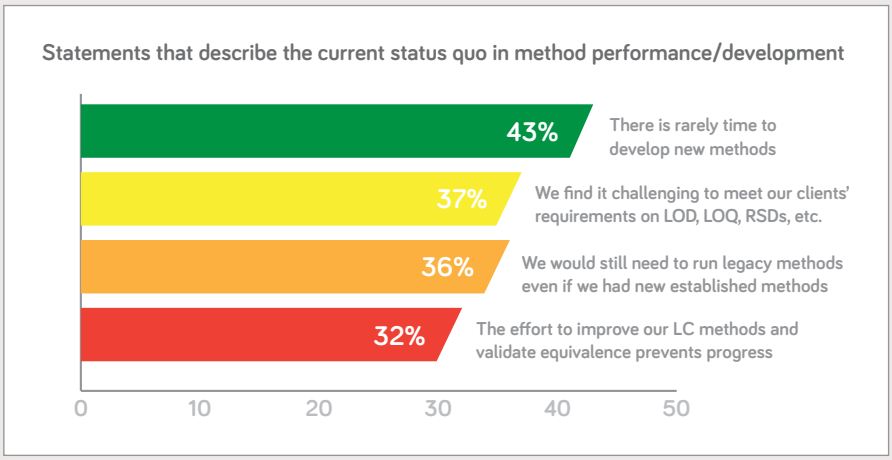
Join our experts – Kelly Zhang, Udo Huber, Stéphane Dubant, Wolfgang Kreiss and Oliver Rodewyk – for an exclusive series of video webinar masterclasses:

Webinar 1 – Analytical efficiency: How to push your results to the next level by selecting suitable technology

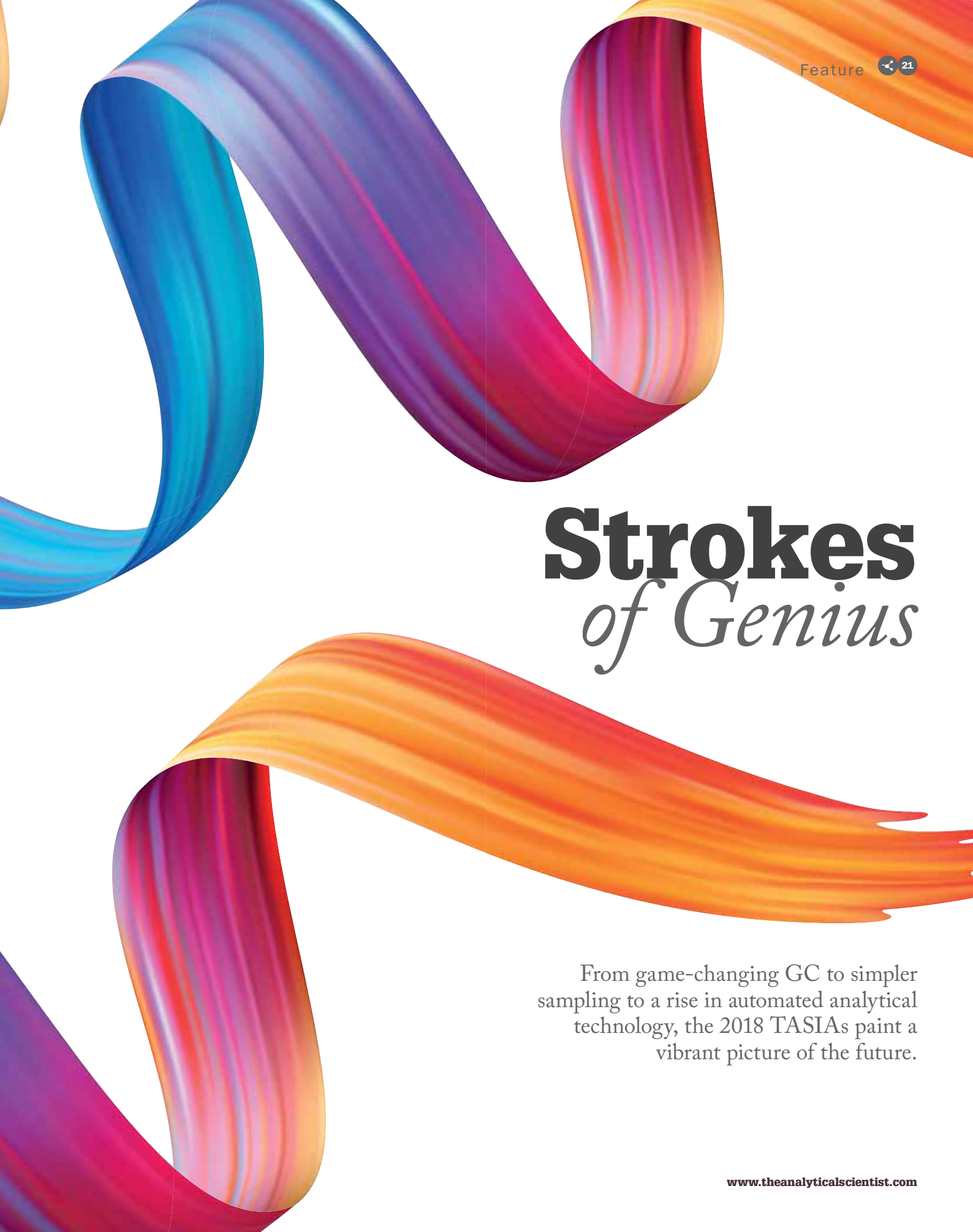
Webinar 2 – Instrument efficiency: How to survive the sample onslaught and even create a little breathing room

Webinar 3 – Laboratory efficiency: How to plan for success and secure your future

For more details, visit: http://tas.txp.to/0918/YEC




THE
INNOVATION
AWARDS
2018
the
Analytical Scientist



Strokes *of Genius*

From game-changing GC to simpler sampling to a rise in automated analytical technology, the 2018 TASIAs paint a vibrant picture of the future.

15

"IONI" API-TOF

An atmospheric pressure interface for the modular ioniTOF platform

Produced by IONICON

All IONICON's PTR-TOFMS series products are based on the ioniTOF – a modular and flexible, entry-level to high-resolution time-of-flight mass spectrometer platform, featuring custom interfaces and high-performance IONICON hexapole ION-GUIDEs. IONICON has now taken the concept one step further and developed an atmospheric pressure interface for the ioniTOF.

The APi-TOF consists of a critical orifice for contact free sample introduction, two hexapole ION-GUIDEs for high ion transmission efficiency over a broad m/z range, and a high performance pump for high sample throughput. The interface is coupled to an orthogonal TOF analyzer equipped with an ion mirror for increased mass resolution.

One advantage of the IONICON hexapole ION-GUIDE over conventional quadrupole interfaces is that the energy in the multipole is lower, which decreases unwanted ion-chemistry artifacts. Another advantage is that the mass range transmitted through the multipole is much broader.

Potential impact

The APi-TOF enables its users to measure high-mass cluster ions and, simultaneously, the composition of precursor compounds and gas-phase impurities, which is important in the context of atmospheric ion clusters.

The APi-TOF therefore overcomes shortcomings of other commercial products that rely on TOFs with quadrupole ion-guides, which can only be tuned to either lower or higher m/z but not to cover the whole mass range of interest. Thus, particularly in atmospheric chemistry and environmental research, important data are inevitably lost, when the ions do not match these parameters.

A first APi-TOF prototype was tested at the CLOUD 12 campaign in fall 2017 at CERN, Switzerland, studying the influence of galactic cosmic rays in new particle formation. Currently, a new high-performance version of the APi-TOF is being tested at CERN.

14

ARC-I CATALYTIC COMBUSTION REACTORS

Developed for the measurement of carbon isotope ratios of steroids and alkanes

Produced by Dell Medical School

ARC-i (ARC-isotope) reactors were developed and characterized for carbon isotope ratio (CIR) analysis of steroids and alkanes, using gas chromatography combustion isotope ratio mass spectrometry (GCC-IRMS) for detection of synthetic steroid use in doping control and measurement of alkanes of interest in geology and the petroleum industry. Specifically, the reactors were custom designed to operate with combustion volumes consisting of a transition-metal catalyst to enable – for the first time – complete combustion of organics to CO_2 molecules at dramatically lower temperatures (620°C) than fragile metal oxide-filled reactors, which operate at ~950°C, constructed with ceramic tubes widely used for GCC-IRMS. With ARC-I, the 13C/12C isotope ratio can be measured with high precision.

Potential impact

Carbon isotope ratio (CIR) analysis is used for the detection of testosterone and other endogenous steroids in "doping" applications, as well as in geochemical and petrochemical laboratories. Quantitative combustion of organic analytes to CO_2 is required prior to admission to the IRMS. Since their introduction in the late 1980s, the high temperature furnaces used in all commercial systems have been a huge barrier to further innovation because of the limited range of materials available at 950°C. Availability of lower temperature combustion overcomes the major technical hurdle to implementation of high performance methods to deliver faster and better sensitivity for CIR doping laboratory analysis. The ARC-i reactor employs an oxidation catalyst that delivers complete combustion of steroids and other organic compounds at temperatures 300°C lower than previously achieved. The commercially engineered system is easily integrated into existing analysis systems and initial tests show the reactors to be as robust as commercially available equipment. In addition to providing a new modular solution for laboratories, it represents a proof-of-principle that encourages future refinements to further lower combustion reactor temperatures.

THERMO SCIENTIFIC FAIMS PRO INTERFACE

A differential ion mobility interface that boosts proteomics workflow performance

Produced by Thermo Fisher Scientific

The Thermo Scientific FAIMS Pro interface is a next-generation differential ion mobility device that provides the selectivity and ease-of-use needed for the most demanding analytical challenges in proteomics. Identifying and characterizing proteins and post-translational modifications through bottom-up mass spectrometry relies on the acquisition of high-quality MS and MS/MS data. The FAIMS Pro interface increases analytical performance through gas phase fractionation and selective enhancement of peptidic compounds, reducing the complexity of the MS spectra and improving analyte signal/noise ratio. When integrated with an Orbitrap Tribrid MS system, it further increases the breadth and depth of protein and peptide identification. Menu-driven software enables method design using pre-configured parameters, increasing productivity and simplifying use, while reduced sample fractionation saves time and costs. Designed to improve nano, capillary and microflow applications, the interface achieves high data quality on even sample-limited studies, delivering selectivity and productivity in high-resolution MS across proteomics applications.

Potential impact

Today, there is increasing demand for improved protein coverage during proteomics experiments, greater dynamic range to comprehensively characterize and validate proteins and their post-translational modifications, and more accurate quantitation of many thousands of proteins in a single run with shorter analysis times. The FAIMS Pro interface is expected to reduce sample and spectral complexity, improve selectivity and increase coverage of the proteome, delivering greater productivity across a range of proteomics workflows. One early user reported, "FAIMS Pro enables considerably more sample depth per unit time and could eliminate the need for pre-fractionation of peptides for most applications."

AQS³PRO

12

Protein characterization through five measurements: aggregation, quantification, stability, structure and similarity

Produced by RedShiftBio

Microfluidic modulation spectroscopy (MMS) is a proprietary technology that directly addresses the limitations of current technologies and provides an efficient tool for direct, label-free protein analysis.

The AQS³pro is built on MMS technology. With its greater sensitivity, it makes it possible to characterize proteins from 0.1 mg/mL to over 200 mg/mL, the concentration range found across the full spectrum of drug development. No other similarly capable technique, including FTIR, circular dichroism and differential scanning calorimetry, is capable of this range of analysis, and so the AQS³pro enables scientist to see changes that they might currently miss. As a flow technology with built-in real time referencing, MMS instruments can also be automated. The AQS³pro is a true walk-away instrument, capable of running through well plates automatically to provide characterization of aggregation, quantitation, similarity, stability and biophysical structure.

Potential impact

As protein structure directly impacts drug efficacy and safety, protein chemists and formulators rely heavily on structural characterization techniques to develop stable, commercially viable products. When multiple instruments have to be used at different stages of the drug development pipeline, it is both inefficient (raising development costs) and far more challenging to make comparative measurements. The ability to conduct five measurements using a single instrument – with a high degree of automation, high sensitivity and wide concentration range – could help solve these problems for the protein scientist and result in a more efficient and accurate drug development process.

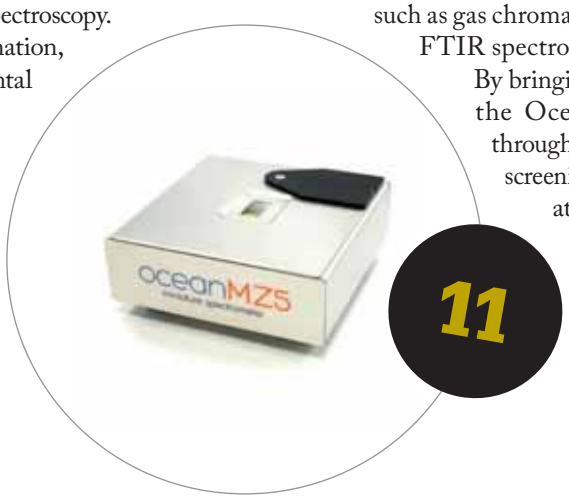
OCEAN MZ5 ATR-MIR SPECTROMETER

A self-contained, economical alternative to traditional FTIR spectroscopy

Produced by Ocean Optics

The Ocean MZ5 is a miniature ATR spectrometer with measurement capabilities from 1818-909 cm-1 (5.5-11 µm). This fully self-contained instrument – including sample interface, light sources and detector – provides a compact, fast and scalable alternative to traditional FTIR spectroscopy. Applications include chemical discrimination, food and flavorings analysis, environmental testing and scientific research.

Ocean MZ5 works straight out of the box and does not require any external equipment, such as a light sources or fibers. Ocean Mirror, the software that comes with the system, is designed for measuring absorbance and transmittance of liquids placed on the instrument's crystal surface.



11

Potential impact

With the counterfeiting of goods from foods to fuels now a global problem, the task of authenticating materials, such as biodiesel, essential oils and dairy products, demands robust, simple-to-use tools based on sound science.

Mid-infrared spectroscopy is especially useful for identifying adulterants, which often have well defined absorption characteristics within the IR fingerprint region. The Ocean MZ5 ATR-MIR spectrometer, which measures liquids, is more compact, more portable and simpler to use for screening than alternative technologies, such as gas chromatography, mass spectrometry and FTIR spectroscopy.

By bringing the instrument to the sample, the Ocean MZ5 can offer screening throughout the supply chain. For example, screening milk for quality and adulterants at remote collection centers could save thousands of dollars by discovering adulterated milk early in the food chain instead of during the dairy production stage.

CENTRI

An automated multi-mode sampling and concentration system for GC-MS

Produced by Markes International

10

Centri offers versatility and performance in the sampling and preconcentration of volatile and semi-volatile organic compounds from solid, liquid and gaseous samples, prior to GC-MS analysis. Centri combines several popular sample introduction modes – with full automation and trap-based preconcentration in a single platform: i) headspace or immersive high-capacity sorptive extraction using HiSorb™ probes; ii) headspace sampling; iii) solid-phase microextraction (SPME); iv) analysis of sorbent-packed thermal desorption (TD) tubes.

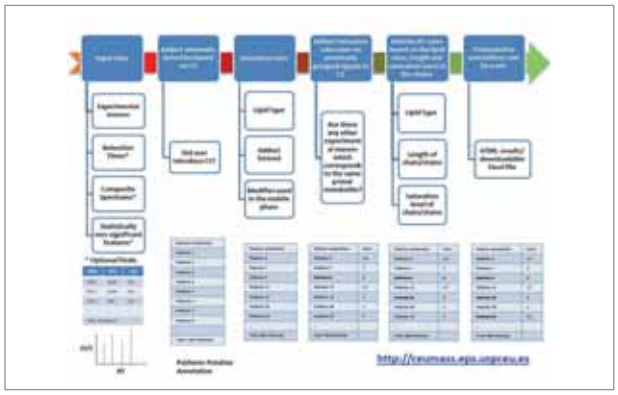
The system can accommodate standard 20 mL or 10 mL vials, has capacity for up to 50 TD tubes, and is automated by leading robotics technology, with the full automation of high-capacity sorptive extraction being a significant instrumental advance.

Potential impact

Centri could benefit environmental, food, fragrance and clinical GC-MS laboratories that struggle with time-consuming manual sample preparation, and want to improve productivity through the introduction of automated solvent-free methods. Further benefits are provided by the availability of economical cryogen-free trapping – a standard technique for TD and sorptive extraction protocols, but one that is used less often for SPME and headspace sampling. Trapping improves sensitivity to the ppt level, allows selective purging of interferents, such as water and solvents, and offers the ability to split and re-collect a single sample onto a clean sorbent-packed tube; the re-collection capability of Centri is particularly important, because it eliminates repetition of lengthy sample extraction steps, brings greater peace of mind by allowing storage of valuable samples, enables analysis of a wider concentration range by changing split flow ratios, and permits easy validation of complete analyte transfer.

What the judges say:

"It is often not immediately clear upfront which of the different sample preparation techniques for the analysis of volatiles will give the best results – this instrument simply combines them all."



CEU MASS MEDIATOR

09

Software for metabolite annotation in untargeted metabolomics

Produced by CEMBIO

CEU Mass Mediator (CMM) is an online software tool developed at the Centre for Metabolomics and Bioanalysis (CEMBIO) that allows researchers to filter and score the putative annotations for MS-based metabolomics studies, with the aim of saving time and reducing misidentifications. It uses a knowledge-based system with rules related to: i) the propensity to form certain types of adducts depending on the metabolite type; ii) the relation between different signals coming from the same experiment and iii) the retention time of the metabolites in the separation column. CEMBIO believes that CMM is the first tool to use a knowledge-driven approach to support metabolite annotation.

Built on J2EE technologies, CMM performs searches using HMDB, KEGG, LipidMaps, Metlin, and MINE databases, as well as an in-house library. Furthermore, the compounds from these databases have been unified whenever possible, avoiding repeated compounds among the results.

Potential impact

Metabolite identification is the main bottleneck in untargeted metabolomics studies; annotation is the first step of the identification. The task is cumbersome, time-consuming and prone to errors. The number of putative identifications for one single mass is very high, and increases along with the number of compounds present in databases. Many researchers use Excel files to handle metabolite annotation, integrating the results from several databases, and then applying their own biochemistry knowledge to manually discard or retain them.

Using a single interface, CMM offers automation of these tasks – even the steps guided by biochemistry knowledge – and it is freely available on-line. Furthermore, it supports identification of oxidized lipids from MS/MS information and provides a system for calculating the quality of MS/MS spectra for identification purposes. Such services enable the user to speed up and improve the identification of metabolites.

08

THERMO SCIENTIFIC COMPOUND DISCOVERER 3.0 SOFTWARE

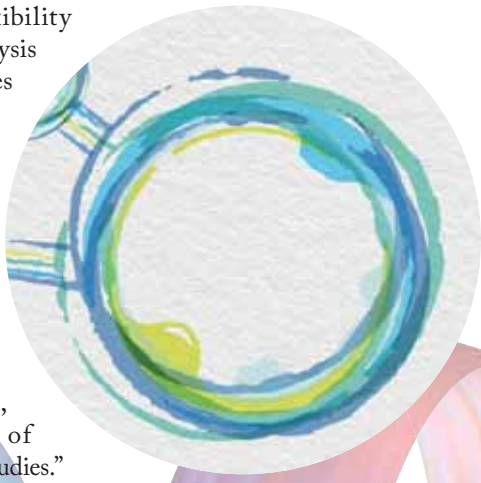
Easy-to-use software that advances small molecule analysis

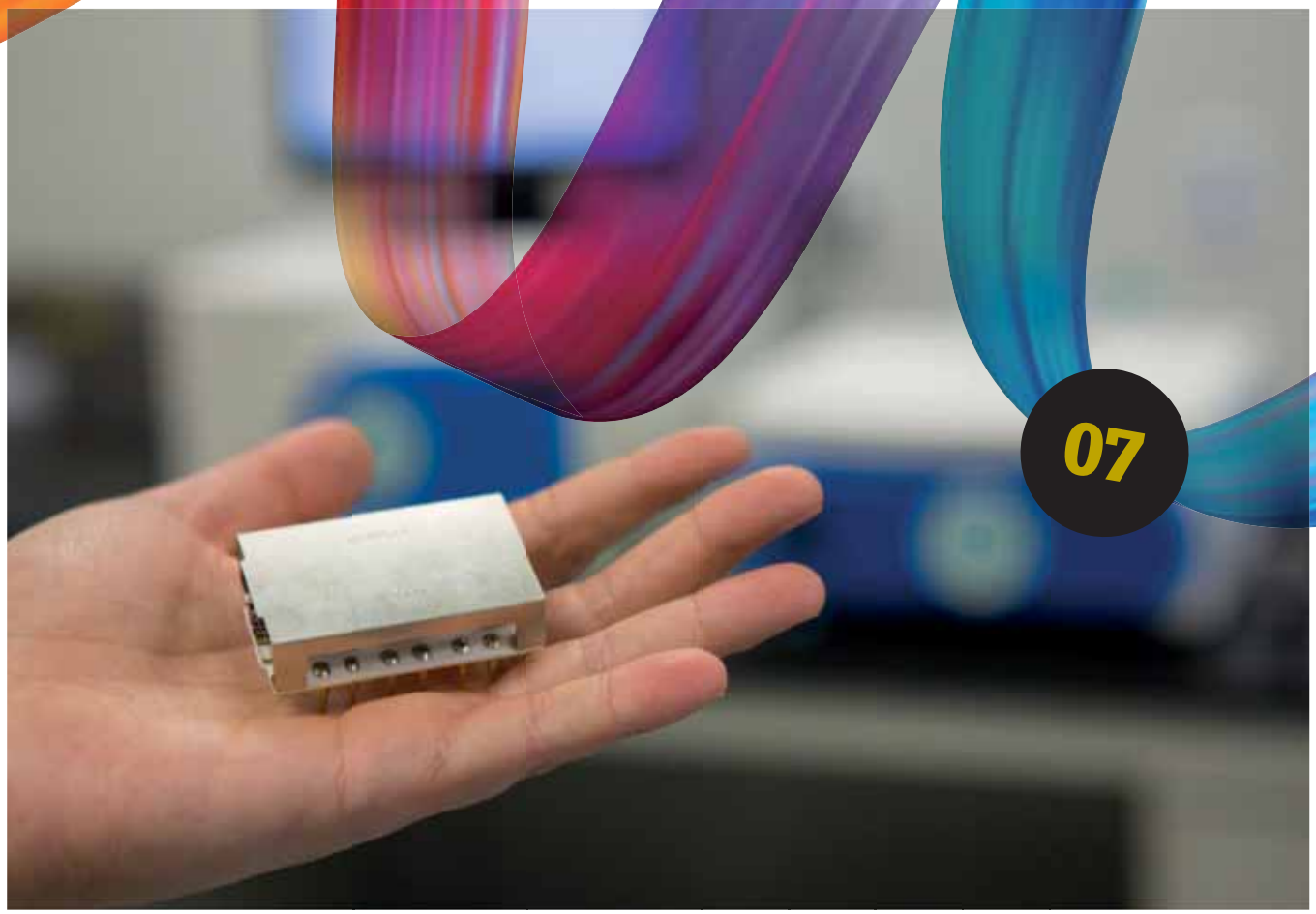
Produced by Thermo Fisher Scientific

The Thermo Scientific Compound Discoverer is an integrated set of databases, statistical analysis tools and online libraries (mzCloud) that streamlines and customizes high-resolution accurate-mass (HRAM) data analysis. Full-scan mass spectrometry generates large amounts of information in small molecule applications, often making efficient data processing and the confident extraction of real insight challenging. Compound Discoverer software processes the information-rich data from high-resolution accurate mass (HRAM) Orbitrap mass spectrometers and transforms it into meaningful results. The software simplifies and reduces processing clicks, enabling faster, more confident transition from analysis to insight. Customizable node-based workflows, integrated compound identification capabilities and statistical analysis all reduce the time involved in using multiple software tools to analyze results.

Potential impact

Compound Discoverer offers scientists working in metabolomics, pharmaceuticals, food safety, environmental and forensic applications the opportunity to more easily transform complex, unknown mass spectra generated from small molecule analysis into actionable data. This integrated toolkit is designed to require minimal training and expertise – however, highly customizable workflows offer the flexibility to match individual analysis requirements. Juan Moises Sanchez, associate scientist, bioanalytical chemistry at Intrexon, said, "Implementation of this software has reduced our bioinformatics lead time and improved the impact of our research in the areas of high-throughput untargeted metabolomics, structural elucidation of unknowns and carbon fate studies."





07

MICROSAIC PROTEINID

Point-of-need mass spectrometry to accurately identify proteins

Produced by Microsaic Systems

The Microsaic ProteinID is a mass identification technique that allows users to characterize proteins and small molecules at the point of need, throughout the whole bioprocessing value chain – from cell train and bioreactor, to capture and fill. The Microsaic ProteinID offers fast results over a mass range of 50-3,200 m/z, the broadest mass coverage for a small footprint mass spectrometer. And unlike other contemporary "compact" mass spectrometers, the Microsaic ProteinID offers laboratory-level performance on an industrial scale, but without large, noisy floor pumps or exhausts.

Potential impact

Bringing the power of the centralized laboratory to in-situ bioprocessing line measurements, the Microsaic ProteinID simultaneously analyzes the product and matrix parameters used to control upstream and downstream bioprocessing, either on-line or at-line, with the aim of reducing key bioprocessing analyses from days to minutes. With the Microsaic Protein ID, operators can monitor feedstocks, metabolites and target proteins in one measurement, potentially accelerating time-to-market for new biologics development, while also enhancing QbD capabilities and improving compliance with regulatory demands for CQA in biologics during pilot and full-scale manufacture. Mass spectrometry can now offer superlative performance to high-value manufacturing industries at the point-of-need, providing greater insights over ubiquitous optical sensors, such as UV, Raman, and NIR.

What the judges say:

"The most powerful tool available for protein analysis in the laboratory – mass spectrometry – is now also available for use in the factory and in production. Operation has been greatly simplified so that operators – not scientists – are sufficient."

AGILENT 8700 LASER DIRECT INFRARED (LDIR) CHEMICAL IMAGING SYSTEM

An innovative, easy-to-use infrared system that allows fast, high-quality chemical imaging

Produced by Agilent Technologies

The Agilent 8700 Laser Direct Infrared (LDIR) chemical imaging system is the newest instrument in Agilent's infrared spectroscopy portfolio and represents a new approach to chemical imaging and spectral analysis.

Using a Quantum Cascade Laser, the 8700 LDIR directs light over the sample to create a complete molecular map of the sample by analyzing the specific wavelengths of infrared light absorbed and then comparing the structure-specific signature to a reference database.

Designed to be used by experts and non-experts alike, the Agilent 8700 LDIR provides a simple, low-maintenance and highly automated approach for obtaining reliable, high-definition chemical images of constituents on a surface.

06

Potential impact

The Agilent 8700 LDIR offers rapid processing, building chemical images over large areas in less than 30 seconds, which could save labs both time and money. Imaging itself, which is fully controlled by the Agilent Clarity software, is an entirely automated process, taking the usual spectroscopy chores out of the hands of the operator, with a subsequent increase in the accuracy of results. Indeed, novice operators are able to run experiments from day one.

The Agilent 8700 LDIR does not use liquid nitrogen cooling but instead employs a single-element electrically cooled detector, which not only eliminates laser coherence artifacts that can reduce the quality and reliability of images, but also minimizes the need for maintenance.

Finally, the Agilent 8700 LDIR fits all of the above qualities into a reduced footprint, freeing up valuable lab space.

TOUCH EXPRESS OPEN PORT SAMPLING INTERFACE (OPSI)

A one touch sampling technique for solids, liquids, sample preparation tips, and fibers

Produced by Advion

The novel Touch Express Open Port Sampling Interface (OPSI) ambient sampling technique was developed by Gary Van Berkel and Vilmos Kertesz, of Oak Ridge National Laboratory. It incorporates a low-volume, open port of continuously swept solvent, which flows directly into the electrospray ion source of the Advion expression Compact Mass Spectrometer.

Potential impact

The OPSI source is a unique, prep-free sample technique that offers i) compound identification and impurity detection from almost any surface, ii) direct assays from sample preparation tips and SPME fibers, iii) easy screening applications for drug research, food safety, environmental, and forensics, and iv) large molecule applications, including proteins, peptides, oligonucleotides and polymers.

05

What the judges say:

"Allows rapid screening of a wide diversity of samples with little to no sample preparation. Offers more or less immediate results for rapid decision making."

04

THERMO SCIENTIFIC Q EXACTIVE UHMR HYBRID QUADRUPOLE-ORBITRAP MASS SPECTROMETER

A unique mass spectrometry platform that aims to expand our understanding of proteins

Produced by Thermo Fisher Scientific

The Thermo Scientific Q Exactive UHMR Hybrid Quadrupole-Orbitrap Mass Spectrometer is the first ultra-high mass range (UHMR) mass spectrometer (MS) to combine high m/z (mass to charge), MS2, and pseudo-MS3 capabilities in a single platform. Delivering high sensitivity that minimizes sample volume, and ultra-high mass resolution at up to 80,000 m/z, the system is designed to resolve the small differences in masses required to characterize intact biomolecular assemblies and other large molecule complexes. Ultra-high mass quadrupole selection and higher fragmentation efficiency allow improved native top-down analysis, providing structural detail that cannot be seen with other methods. By varying the in-source trapping energy, the instrument can release protein subunits for top-down sequencing or, with gentle activation, retain membrane proteins bound to multiple ligands, allowing whole complex analysis.

The Q Exactive UHMR Hybrid Quadrupole-Orbitrap Mass Spectrometer is designed to unlock a greater understanding of proteins and their interactions.

Potential impact

Native mass spectrometry is a powerful technique for studying the structure of large protein complexes, protein–protein, and protein–ligand interactions. It relies on maintaining a biomolecule's natural folded state and associated non-covalent interactions for MS analysis. Until now, technology limitations have prevented native MS from achieving its full potential. The Q Exactive UHMR Hybrid Quadrupole-Orbitrap Mass Spectrometer provides a unique combination of unprecedented resolution, highest sensitivity, MS2 and pseudo-MS3 capabilities needed to advance native MS investigations, overcoming previous technology limitations and providing a workflow for protein structural analysis. Albert Heck, Biomolecular Mass Spectrometry and Proteomics, University of Utrecht, used it to achieve "high-fidelity, hypothesis-free mass analysis of intact ribosome particles, revealing the substoichiometric association of even elusive small particles." The new system should give researchers the opportunity to gain a deeper understanding of protein function, disease mechanisms, potential drug targets and biotherapeutic compounds and advance the study of structural biology.

03 THERMO SCIENTIFIC ORBITRAP ID-X TRIBRID MASS SPECTROMETER SYSTEM

A mass spectrometry system with the potential to transform small molecule characterization

Produced by Thermo Fisher Scientific

The Orbitrap ID-X Tribrid Mass Spectrometer system combines quadrupole, Orbitrap and linear ion trap mass analyzer technology with novel automated data acquisition strategies and powerful structural analysis software processing tools. The combination provides a complete solution – from data acquisition to data analysis – and aims to significantly improve and accelerate the identification and characterization of small molecule compounds. The AcquireX data acquisition tool, method editor templates and ready-to-use experimental parameters ensure efficient acquisition of high-quality data, even for non-expert users. Coupled with the mzLogic data analysis algorithm, an online spectral library (mzCloud) and data processing software solutions (Compound Discoverer and Mass Frontier), the Orbitrap ID-X Tribrid mass spectrometer provides a solution for small molecule structural analysis, significantly increasing accuracy, efficiency, and overall productivity in drug impurity and metabolite identification, extractable and leachable analysis, and other related applications.

Potential impact

Interpreting the mass spectra of unknown compounds remains challenging and is a frequent bottleneck in many fields, including food safety, environmental monitoring and pharma/biopharma. The Thermo Scientific Orbitrap ID-X Tribrid Mass Spectrometer offers a complete, intelligent solution that accelerates small molecule identification and characterization by automatically capturing the maximum possible information about small molecules and translating it into confident identification of chemical compounds. By enabling the collection of a greater amount of structure-informative data, the system increases the depth of small molecule compound analysis for better structural characterization. The system brings greater confidence to the analysis and identification of degradants, extractables, leachables, metabolites and other classes of compounds, and aids in metabolomics, lipidomics and the study of natural products.

02 THERMO SCIENTIFIC PHENOM PHAROS DESKTOP SCANNING ELECTRON MICROSCOPE (SEM)

The first desktop SEM with a field emission gun (FEG)

Produced by Thermo Fisher Scientific

The Thermo Scientific Phenom Pharos desktop scanning electron microscope (SEM) is the first desktop SEM solution from the company to include a field emission gun (FEG). The Phenom Pharos microscope is easy to operate and incorporates an advanced hardware design for fast time-to-image and simple handling. A wide range of academic and industrial researchers now have access to the benefits of FEG in a desktop model, which can increase their throughput and result in high-quality images and resolution. In addition to providing advanced detectors that can acquire high-quality images with magnifications of up to one million times, the Phenom Pharos microscope also offers researchers:

- access to sharp, high-contrast images with resolutions below three nanometers;
- an intuitive user interface that enables researchers to get a live image in less than 25 seconds after inserting the sample;
- high-resolution imaging that can be obtained simultaneously with analytical techniques.

Potential impact

In the past, only highly experienced scientists have been able to operate and benefit from FEG- equipped scanning electron microscopes (SEM), but Phenom Pharos brings the benefits of FEG to users with different experience levels; it is easy to use, and installation can be done without the need for special room requirements. Installation is fully automated and once initialized, the user interface enables researchers, students and operators alike to analyze images and corresponding details at the nanoscale, from visualizing multiwall carbon nanotubes to capturing high-resolution imaging of Ag nanoparticles.

01

HYPERCHROM FLOW-FIELD THERMAL GRADIENT GC

Hyper-fast GC with cycle times of less than 60 seconds

Produced by Hyperchrom

The HyperChrom FF-TG-GC is a hyper-fast GC based on a new principle: flow-field thermal gradient gas chromatography. For the first time, an additional spatial thermal gradient is applied along the column in a commercial GC. In combination with temperature programming, a new mode of chromatographic transport and separation takes place. The benefits of this gradient elution are lower elution temperatures and an enhanced resolution.

The newly launched system is a fully featured GC and comprises many advanced technologies: standard separation columns can be utilized and changed easily; purged connectors avoid dead volume effects and enable back-flushing of the injector and the column. Real-time electronic control synchronizes high precision temperature and pressure ramps and the event control for valves on a millisecond scale. The employment of all these technologies leads to remarkable chromatographic resolution and stability.

Potential impact

The FF-TG-GC is a high-throughput GC measurement system, with fast heating rates and cool down times; the system cools down from 400°C to 30°C within 10 seconds, allowing laboratories to achieve much higher sample throughput rates. In certain applications, a single FF-TG-GC could replace at least 10 conventional GC systems, including peripheral instrumentation (for example, samplers), saving investment, labor, energy and consumables.

The high measurement speed provides fast analytical results; in industrial processes, it means results being collected in near real time with the analytical accuracy of classic GC-MS systems. Such speed is also an advantage in security applications where fast results (for example, the detection of explosives or drugs) or many measurements in a short time are required.

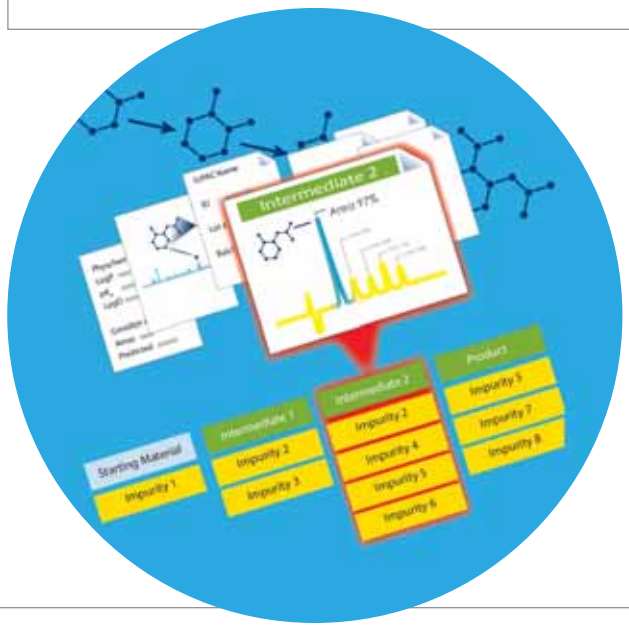
Despite the level of performance already achieved, the development of the technology is still in its infancy. Simulation-based improvements are in progress, as is the refinement of many embedded technologies. With the two-dimensional extension of the HyperChrom GC an even higher resolution with short cycle times will be available.

What the judges say:

"This is the largest innovation in gas chromatography since the introduction of comprehensive GC×GC some 25 years ago. This instrument allows us to do something that has been speculated about for decades; in short, GC can become much faster, more sensitive and more selective."

THE INNOVATORS 2018

Whether testing for impurities, ensuring national security, or speeding up sample prep – meet the companies advancing analytical science.



CUT YOUR TIME INVESTMENT IN IMPURITY DATA MANAGEMENT

Conveniently manage analytical data related to impurities and track their formation, fate, and purge in a single software

LUMINATA™ is an informatics system that enables organizations to establish effective impurity control strategies based on assembled analytical and chemical information, in a single environment.

Built on the multi-technique, vendor-agnostic ACD/Spectrus Platform, Luminata offers comprehensive data standardization – accomplished by aggregating chemical reaction information and the associated formation and fate of impurities with chromatographic and spectral data. Luminata facilitates efficient organization of the overwhelming quantity of analytical knowledge for processes and associated impurities – at every stage.

Luminata's unique assembly of searchable knowledge provides unprecedented visualization, decision-support and reporting capabilities, and facilitates collaboration between process chemistry and analytical research and development groups.

The software now also includes the capability to conveniently calculate carryover and purge factors directly from LC/MS data.

Learn more at www.acdlabs.com/luminata

CENTRI

Fully automated multi-mode sampling and preconcentration system for GC–MS

April 2018 saw Markes International launch Centri® – a breakthrough in versatility and performance for the sampling and preconcentration of VOCs and SVOCs from solid, liquid and gaseous samples, prior to GC–MS analysis. For the first time, it combines capability for several popular sample introduction modes with full automation and trap-based preconcentration, all on a single platform.

The techniques available on Centri are:

- Headspace or immersive high-capacity sorptive extraction using HiSorb™ probes
- Headspace sampling
- Solid-phase microextraction (SPME)
- Analysis of sorbent-packed thermal desorption (TD) tubes.

On Centri, all modes can benefit from economical cryogen-free trapping, which improves sensitivity to the ppt level, allows selective purging of interferents such as water and solvents, and brings the ability to split and re-collect a single sample onto a clean sorbent-packed tube.

Markes' Business Unit Director, Massimo Santoro, says "Centri is ideal for environmental, food, fragrance and clinical GC–MS laboratories who struggle with time-consuming manual sample preparation, and want to improve their productivity by replacing these with a variety of automated solvent-free methods."

Learn more at http://chem.markes.com/centri

ONE VALVE DRIVE FOR ALL APPLICATIONS OF LIQUID CHROMATOGRAPHY

Easy operation of KNAUER valves with an innovative solution

For more than 25 years, KNAUER has offered a wide range of valves for liquid chromatography applications. Now there is a new member in the portfolio – a single valve drive for all KNAUER valves, which allows the operation of two-position as well as multi-position valves. The Valve Unifier AZURA® VU 4.1 recognizes each valve automatically via RFID (radio-frequency identification) technology. Manual configuration is not needed, thereby preventing potential user errors. The smart valve drive adjusts torque and switching speed according to the mounted valve, which results in optimized switching and minimized backpressure. A further feature of the VU 4.1 is the precise position control; each port is approached with a precision of less than 0.5°. Consequently, carryover during fractionation and sample loss during loading are both minimized. In addition, the RFID technology allows storage of important GLP data for each valve – for example, the switching cycles are recorded, and the maintenance intervals monitored.

In addition to the control via keypad, the VU 4.1 valve drive also features various interfaces like LAN, USB, or analog control, enabling multiple operation modes. Several software packages (e.g. ClarityChrom®, OpenLab®, Thermo Scientific™ Chromeleon™ CDS 7, Mobile Control, etc.) are also supported.

KNAUER not only offers the valve drive as a stand-alone device for end users, but also provides diverse modular kit options for OEM customers. With various materials and bore sizes, the KNAUER valve portfolio is suited to a wide range of analytical and preparative applications.

Due to its variability, in combination with its small footprint, the new valve drive is ideal to easily update or complement already existing systems. A valve at the right position will optimize any liquid chromatography system. Beyond the usual sample injection, additional functionalities like fractionation, column selection, as well as special applications like heart- or end-cut become possible. With the innovative Valve Unifier VU 4.1, KNAUER offers a small but powerful product that suits customer needs.

For more information on the KNAUER portfolio refer to www.knauer.net/valves

BAYSPEC'S PORTABLE MASS SPECTROMETERS

Don't wait for answers…bring the lab to the sample with field portable mass spectrometers from BaySpec

BaySpec's miniature mass spectrometers were featured in the Canadian national news earlier this year, with the battery-powered device being deployed at supervised injection sites in Ottawa to screen recreational drugs for highly toxic substances such as fentanyl and carfentanyl. This compact, lightweight instrument based on linear ion trap (LIT) technology packs a surprising amount of performance with a mass range of 50–1100 amu, a mass resolution of < 0.5 amu, and a detection limit below 100 parts per trillion. BaySpec has designed the system with LIT to make it compatible with any ambient ionization method for in situ analysis. Most systems employ an atmospheric pressure inlet system with thermal desorption and electrospray ion sources. The device can distinguish isobaric compounds with tandem mass spectrometry capabilities. Intended for use by nurses, soldiers and police officers, the device is easy to use, low maintenance, and provides results within seconds. Suitable for bulk and trace analysis, this miniature mass spectrometer is solving problems within military, food and agriculture, public health & safety, and space exploration. What's your application?

Learn more at www.bayspec.com/

GERSTEL PYROVIAL

Pyrolysis for HPLC and more

The GERSTEL PyroVial performs pyrolysis procedures at temperatures up to 800 °C in a dedicated sample vial. Less volatile and thermally labile pyrolysis products can be taken up in a suitable solvent for subsequent GC/MS or LC/MS determination – or for analysis using other techniques. Volatile pyrolysis products can be sampled directly from the headspace for GC/MS determination.

Placing a sample into the reaction chamber is simple and the pyrolysis process is fully automated based on the GERSTEL MultiPurpose Sampler (MPS). PyroVial can be used as a micro-scale reaction chamber, the gas phase can be replaced with an inert gas or a reactant as needed. Food preparation processes, such as the Maillard reaction, can be simulated in micro-scale and the formed flavor compounds determined. Pyrolysis of polymers, for example those based on polar acrylic resins, can be followed by HPLC determination of the reaction products. Reagents or catalysts can be added before the pyrolysis step, enabling the simulation of complex industrial processes.

For more information about PyroVial and other GERSTEL solutions, please contact gerstel@gerstel.com or visit www.gerstel.com

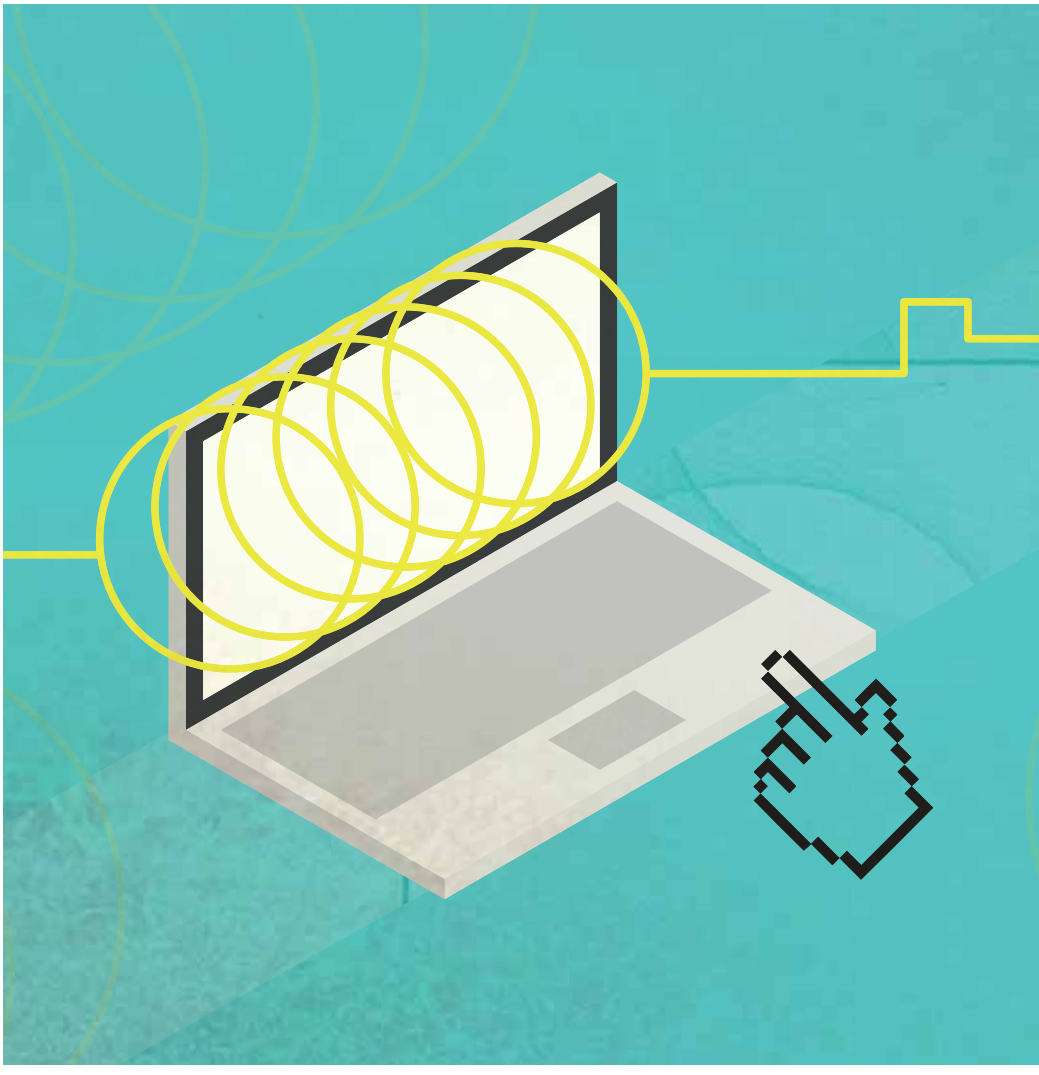
Solutions

Real analytical problems
Collaborative expertise
Novel applications

A GC in Your Laptop

Very few students get hands-on experience with a working gas chromatography system. I believe robust software tools are the next best thing.

By Jaap de Zeeuw



The problem

How can we give inexperienced trainees or potential users the chance to "play" with gas chromatography optimization – when there is no access to a GC system?

Background

When chemistry students cover physical separation methods, they typically learn about filtration, gravimetry, distillation and chromatography. However, the chromatography they are exposed to is very generic – at best a few injections are done by the instructor and the result are explained. When it comes to optimization methods, there is very little flexibility, as students are not usually allowed to work with a real GC.

Traditionally, you need plenty of "hands-on" GC experience to truly understand the impact of parameters such as oven temperature, flow, phase chemistry and column dimensions, on separation and analysis time. Back in my university labs, there were usually only a few gas chromatographs and columns available, so students could not spend the hours it would take to run experiments with various parameters – there is no time to "play." And this represents a major roadblock to learning.

"By simulating separations, it allows the user to change any GC parameter online and see how separations are affected."

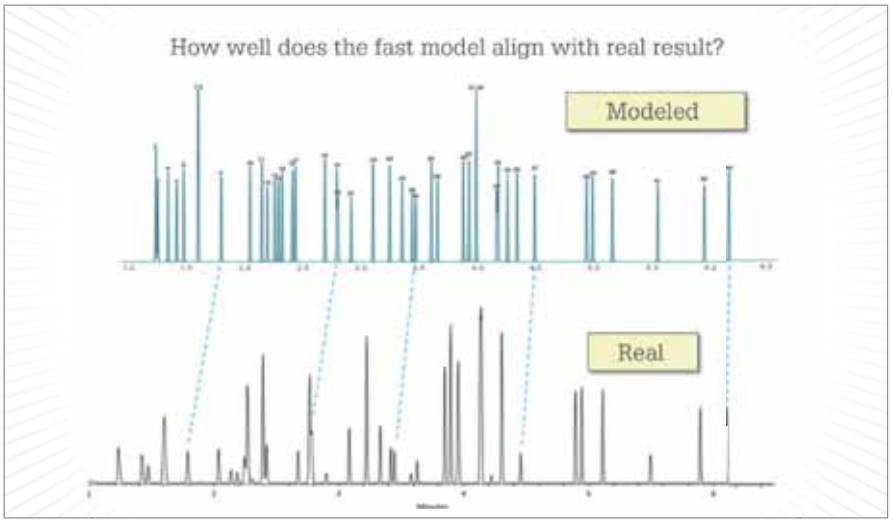


Figure 1. A modeled chromatogram of VOC versus the real result.

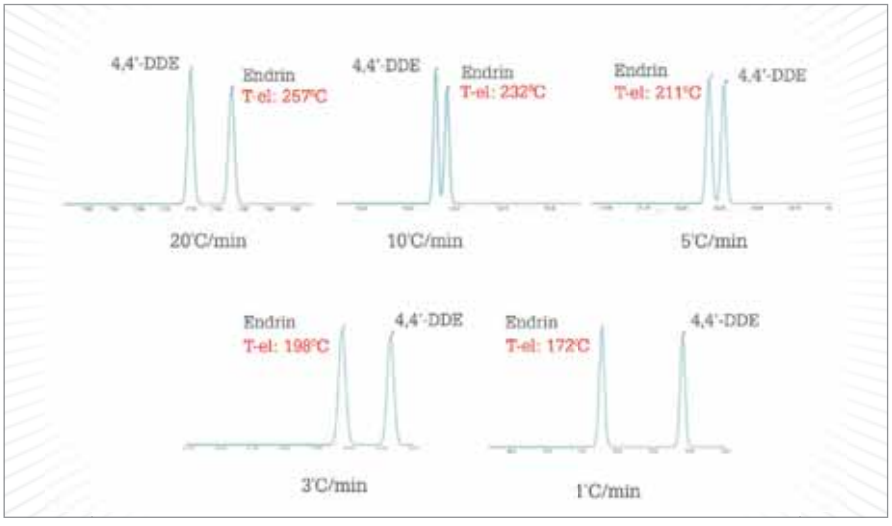


Figure 2. Principle of the proposed high-resolution semi-preparative LC system based on three operational sub-units: 1) pump-injector unit, 2) recycling and separation unit, and 3) fraction collection unit.

The solution

The solution is simple: a web program called "ProEZGC." By simulating separations, it allows the user to change any GC parameter online and see how separations are affected. The program is free for anyone to use and calculates retention times based on real measurements.

Now, being a "hardcore" chromatographer, the word "simulation" immediately puts me on my guard, but once I learned how the program could benefit users, I realized that it is a very cool tool. Actually, it is designed for anyone to use, but I think it has a special value for students.

When a parameter is changed in ProEZGC, the result is displayed immediately. You can change the oven temperature, the column flows, the column dimensions and even the type of carrier gas and immediately see the predicted impact on the separation. In short, ProEZGC offers great educational

In the Classroom

Simona Tereza Popovici, a chemistry lecturer at the University of Applied Sciences, Vlissingen, explains how the chemistry department is using the software to teach gas chromatography principles.

ProEZGC is a very useful tool for teaching chromatography to students. It can be applied to experience the basics of GC on a large list of analytes (the effect of columns stationary phase and dimensions, oven program) but it can also be used for teaching about method translation in more advanced level chromatography lessons.

A well-known drawback in teaching is the limited time to practically coach students on the lab. Therefore simulation programs are a very important tool to help students visualize and understand the consequence of choosing one or other parameter. This tool pushes students to understand chromatography and stimulates their interest.

Third year students had a practical assignment that involved developing their own (non-validated) method to analyze BTEX by GC-MS in just six hours. The students approached the practical by exploring peer-reviewed literature, before using ProEZGC to translate the methods they identified to the column type and system that exists in the lab – with great success.

The disadvantage of using any simulation is the risk that users fail to understand the reasons behind their work, but ultimately this is the responsibility of educators. The advantage is obvious – motivating students by helping them to visualize the effects of parameter changes on predicted chromatograms. I'll add that it can also prevent frustration and wasted resources in the lab when time is limited.

value, it is fast and interactive, and – as the name suggests – it is easy (EZ) to use.

Equally importantly, it is also true to life; Figure 1 compares predictions from ProEZGC with the real separation, showing how accurate the model is. So how does it work?

In GC, we are lucky to have only a limited number of parameters that can influence separations. There is "selectivity," which depends on interactions of analytes with stationary phase. As pi–pi and van de Waals (London) interactions are dependent on temperature, changes (in temperature) will also have an impact.

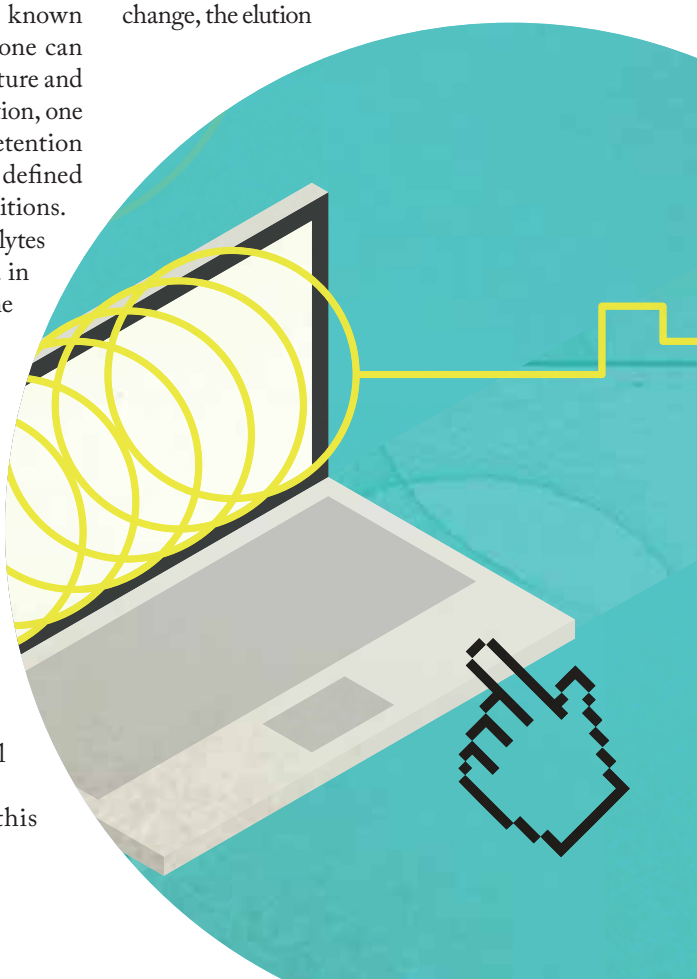
Then we have "retention," which depends on film thickness, column dimension, temperature and carrier gas velocity (and this velocity depends again on column dimension, type of carrier gas, pressure and temperature).

Once the relation of retention versus temperature for a component is known on a specific stationary phase, one can predict the elution time/temperature and create a model. To make a prediction, one must accurately measure the retention of the component under exact, defined temperature-programmed conditions.

A chromatogram of a list of analytes can be generated and optimized in the program, and when the same conditions are copied in real life, the same result can be expected. The power behind the ProEZGC is a huge database of nearly 8,000 components and how they behave on different stationary phases. As the main factors behind retention are temperature and interaction, the retention of components is measured on stationary phases using several defined temperature programs. This way, it is possible to model elution times very accurately.

I first got excited about this program a few years ago, when there was a helium shortage. I started to look at using nitrogen as the carrier gas in my GC. To compensate for loss of speed, I chose to use a shorter narrow bore (20m x 0.15mm ID) column instead of the standard 30m x 0.25mm, and ran this at a slightly higher flow, so I would get the exact same analysis times as obtained with helium. Using the program, I was able to predict the separation and the results matched very well with the eventual outcome. We tested the concept for four different GC phases and four different component classes (fragrances, PAH, pesticides and dioxins) – and all were a perfect match.

But for students, it's a valuable tool to see how separations are impacted by different parameters, not just in terms of time of analysis, but also peak sequence and separation. When temperature programs or column flows change, the elution



"We believe it will be a useful teaching tool for chromatographers worldwide."

temperatures of the eluting components change. As a result, the separations (elution times/orders) can change. Some separations improve, some separations get worse or can even disappear – a fact that is under-appreciated even by experienced scientists. For example, Figure 2 shows how separation between the pesticides endrin and 4,4'-DDE changes when different temperature programming is used. Elution temperatures for endrin change from 257°C to 174°C and make this peak elute in a completely different position.

A useful exercise is to ask students to optimize a separation, while providing a number of practical limitations. For example:

"I have a MS system and I need to optimize throughput to reduce cost per analysis."

The limitation of the MS system is often the vacuum pump capacity, being approximately 2 mL/min. So it would be a very interesting exercise to optimize the analysis using a higher flow rate. Alternatively, you could explore using a smaller diameter or a shorter column to reduce runtime. One can even compare separations on different stationary phases and select the most suitable phase before doing the optimization of the GC parameters – everything can be modeled and visualized. Plus, all models are interactive – and they can be saved and revisited.

Beyond the solution

Of course, there are limitations to any modeling system. In ProEZGC, you can only model the components that are in the database, so you must always consider that there may be more selective phases available. Also, the program displays the components as Gaussian peaks, whereas in real life peaks may have tailing caused by the injector, transfer lines, ionization source or column. Similarly, the program assumes ideal injection, whereas real-life peaks may show overload due to sample composition or poor loadability of the column.

We have been presenting the capabilities of ProEZGC as a half-day workshop at several universities, and believe it will be a useful teaching tool for chromatographers worldwide.

Jaap de Zeeuw is International GC Specialist, Restek Corporation, Middelburg, The Netherlands.

You can register for ProEZGC at: http://www.restek.com/proezgc.

PITTCON® 2019
CONFERENCE & EXPO

The Visible Difference
In Laboratory Science Expositions

Join thousands of chemists and scientists from around the world at Pittcon, the leading annual conference and exposition for laboratory science. This all-in-one event offers a high-caliber technical program, skill-building short courses and a dynamic marketplace of the latest scientific instrumentation and services. Start collaborating with individuals in a variety of scientific disciplines and find solutions to your greatest laboratory challenges at Pittcon 2019.

Pennsylvania Convention Center | Philadelphia, PA | March 18 - 21 | www.pittcon.org

the Spectroscopist

INSIDE

MRR on the Up

Molecular rotational resonance (MRR) is based on the established technique of microwave rotational spectroscopy. Could chiral tagging be the springboard for its rise to fame? We spoke to Justin Neill, Chief Technology Officer at BrightSpec – the company hoping to bring MRR into the spotlight.

What does MRR bring to the table?

What's long been recognized about microwave spectroscopy is its capability to resolve different compounds – particularly isomers in a mixture – without having to separate components. MRR is unique among spectroscopy techniques; different isomers have different moments of inertia, but with MRR we can resolve them and actually do computational work to determine the pattern of each isomer in the spectra – allowing us to identify it unambiguously. In terms of specificity, there are also amazing advantages to the technique over other methods, especially in the spectroscopy realm – and sample preparation centers on volatilizing the sample.

What advantages does MRR have over chromatography?

MRR identifies and quantifies molecules on the basis of their unique 3D structures, through microwave and millimeter wave spectroscopy. Because of the high selectivity and resolution, pure reference standards of each component of interest are not needed – components can be identified directly in mixtures. This eases a major burden in chromatographic method development. MRR is extremely sensitive to small changes in structure, including diastereomers, regioisomers, and enantiomers, which are often difficult separations. Because of the fast measurement times and method development, MRR is particularly advantageous in reaction monitoring; for example to monitor the yield and specificity of small-molecule continuous flow syntheses.

MRR has never really met with commercial success – what has changed?

HP (Hewlett-Packard) tried in the early

In MRR, coherent microwave or millimeter wave pulses are broadcast through a vacuum chamber, where they excite gas-phase molecular samples. After the pulse is switched off, resonant molecular emissions are recorded - which are Fourier transformed to give the information-rich rotational spectrum.

1970s. The major developments in the past few years that enabled BrightSpec to commercialize the technology arise from the availability of high speed electronics, new micro- and millimeter-wave components, and dramatic advances in computational chemistry. The most recent breakthrough is the ability to resolve between enantiomers – which in the pharmaceutical industry is crucial.

Along the way, researchers around the world have made a steady stream of improvements that enable fast, high-resolution spectroscopy results in an <15-minute cycle time for a new sample.

How are enantiomers resolved?

Similar to chiral solvating reagents used in NMR, enantiomers can be converted into diastereomeric complexes by introducing a small chiral molecule with known stereochemistry. Because of the sensitivity of MRR to small changes in molecular structure, these diastereomer complexes have distinct MRR spectra that can be used to accurately determine the enantiomeric excess of each individual component directly in a mixture, without the need for separation. It's all in the gas phase, there's no sample preparation and you can do it all in one measurement.

We've developed an instrument for chiral analysis that comes in two configurations; the first is for use in a large central lab where the nature of the problem will change from one month to the next. The follow on targeted instrument is intended for a production setting.

What impact could this have on the pharmaceutical industry?

The current application we see is in pharmaceutical development and process control. Analyzing chiral purity in a short timescale is an unmet need. For pharma, one of the biggest challenges is characterizing all the possible impurities that can come out of a sample. In an R&D context, MRR eliminates the need for the synthesis of all these impurities for calibration standards. The ability of MRR to identify and quantify based on structure opens up fast new analyses that are not otherwise possible.

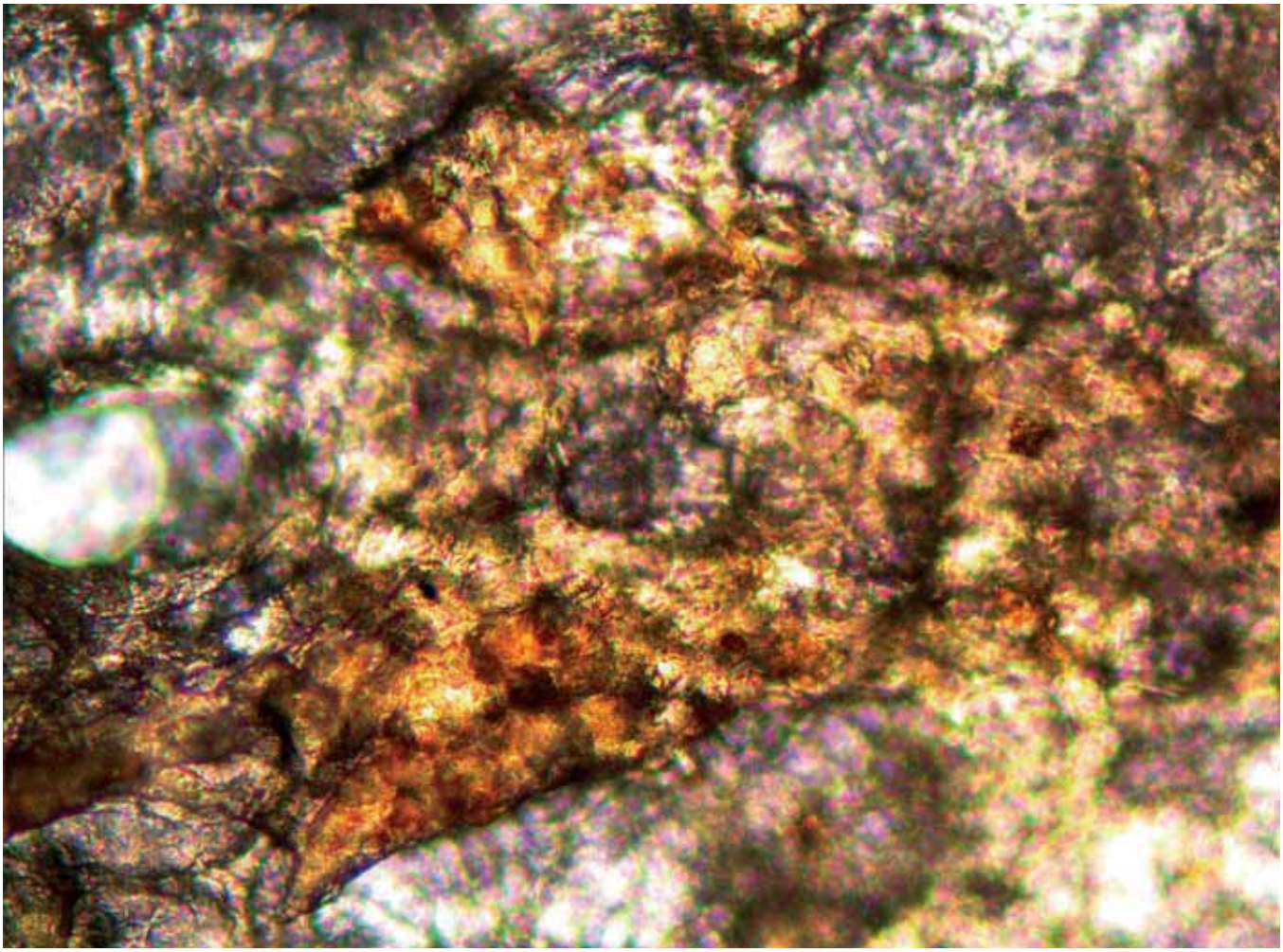
Is it already being used?

Yes – we have instruments in the US and Europe at present. In one example, an academic pharmaceutical research lab is using it to re-engineer the process chemistry for flow synthesis of a set of existing drugs that are of global health importance. In this instance, MRR was used for critical analysis of an anti-malarial compound, artemisinin (or DHAA), and for an anti-HIV drug antiretroviral. This has been at core of our recent work. A number of applications for other pharma/chemical compounds arose out of these two drugs, which were good analogs for a whole series of other analytical challenges with other molecules in development. Of course, it's important to remember that the foundations for this work have been established by over 110 different research groups around the world, who have long been using this technique in fundamental research. We just happen to be the first to commercialize it.

Justin Neill is Chief Technology Officer at BrightSpec, Charlottesville, Virginia, USA.

The browning of the otherwise translucent sample eggshell matrix represents the formation of N-heterocyclic polymers.

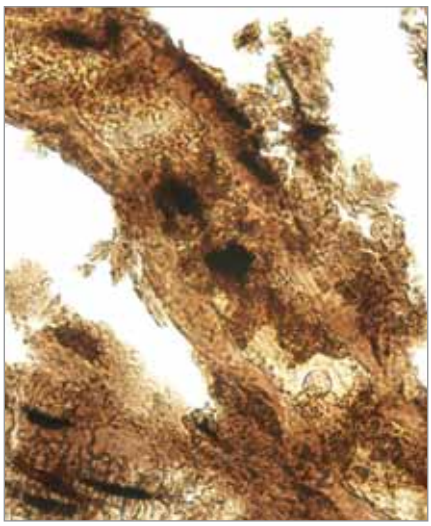
Credit: Jasmina Wiemann/Yale University



Hard Luck

Raman microspectroscopy unearths the secret to dinosaur bone preservation

The longevity of proteinacous matter in vertebrate hard tissue is estimated at around 3.8 million years. So why are soft tissue remnants still found in 100 million-year-old dinosaur bones? A team that included researchers from Yale University and the American Museum of Natural History analyzed 35 samples of decalcified fossil bones, eggshells and teeth using Raman microspectroscopy, discovering that in more oxidative environments, soft tissue had converted into advanced glycoxidation endproducts (AGEs) and advanced lipoxidation endproducts (ALEs). These N-heterocyclic polymers – structurally comparable to burnt toast – are resistant to decay.



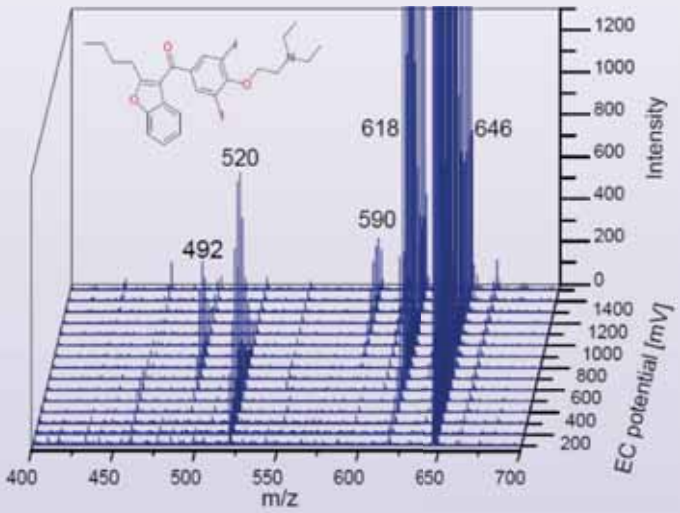
Reference

1. *J Wiemann et al., "Fossilization transforms vertebrate hard tissue proteins into N-heterocyclic polymers", Nat Commun, 9, 4741 (2018). DOI: 10.1038/s41467-018-07013-3*

ROXY™ EC System

Comprehensive Drug Metabolism using Electrochemistry-MS (EC-MS)

- **Mimicking/predicting oxidative metabolism (CYP450)**
- ***In-electro* as alternative to *in-vivo* and *in-vitro* techniques**
- **Fast: Phase I and II reactions in minutes**
- **Clean: no interferences with biological matrices**
- **Generating intermediates and reactive metabolites**



Oxidative "fingerprint" (MS Voltammogram) of Amiodarone (*antiarrhythmic agent*) m/z 646 and its major oxidative metabolites m/z 618, 590, 520 and 492 generated by on-line Electrochemistry-MS using the ROXY EC system equipped with µ-PrepCell2.0 and connected to an MS. Total experimental time 15 min.

ROXY™ Potentiostat

µ-PrepCell™2.0

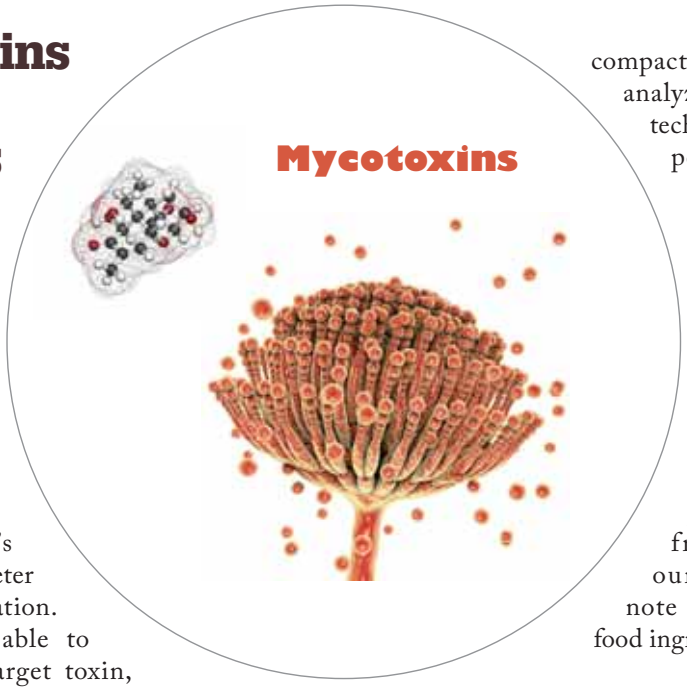
Antec® Scientific

www.AntecScientific.com

Detecting Toxins in Food with Portable Mass Spectrometer

A case study for residual mycotoxin screening in wheat flour

Samples provided by a Canadian Agriculture firm were analyzed by TD-ESI coupled to BaySpec's Portability™ mass spectrometer without any sample preparation. The portable device was able to detect ppm levels of the target toxin, deoxynivalenol. Featuring light weight and compact size, BaySpec's novel mass analyzers based on linear ion trap technology are the most sensitive portable devices available on the market with parts-per-trillion detection sensitivity. These extremely compact instruments are simple to operate and maintain, and they are ideal for a variety of bulk or trace on-site detection in real time.



Learn how you can bring the lab to the sample with portable analytical tools from BaySpec by reading our educational application note for toxin detection within food ingredients.

Find out more at www.bayspec.com/

Superior Characterization of Protein Therapeutics by Electrochemical Reduction of Disulfide Bonds

On-line electrochemical reduction of S-S bonds in top-down and bottom-up proteomics for enhanced peptide sequencing and S-S bond assignment

J-P. Chervet[1], N. Reinhoud[1], Pablo Sanz de la Torre[1] and M. Eysberg[2]

[1]Antec Scientific, Zoeterwoude, Netherlands

[2]Antec Scientific (USA), Boston, MA, USA

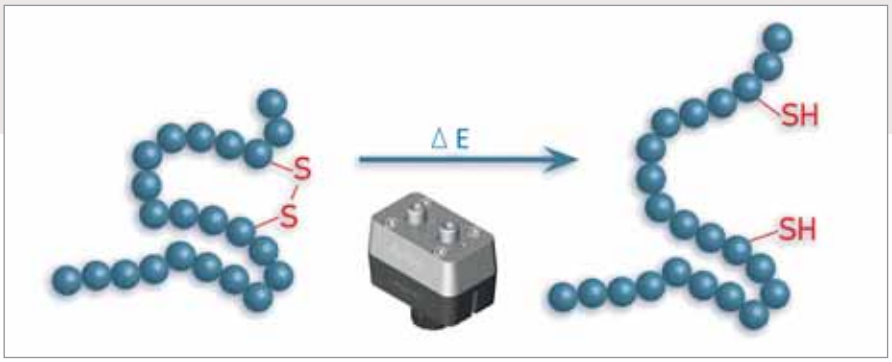


Figure 1. Schematics of a disulfide bond reduction in a peptide chain. During the flow through the electrochemical cell the S-S bond of the intact peptide gets cleaved instantaneously thereby forming the reduced peptide with 2 thiol (S-H) groups. Typical reduction potential applied 1 V (pulse mode).

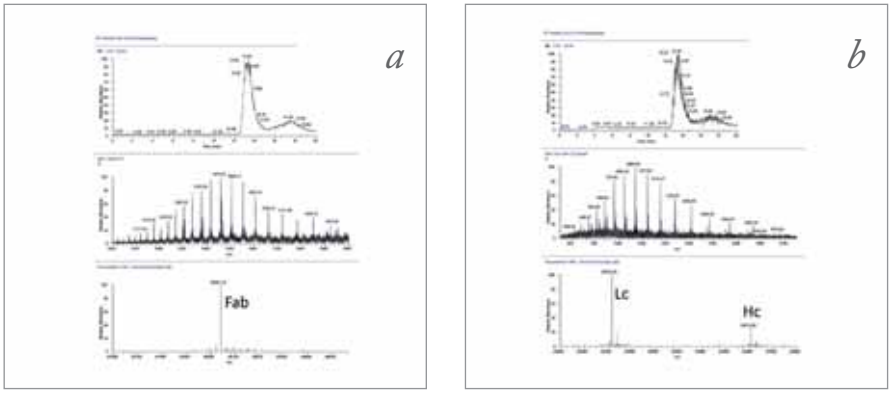


Figure 2. On-line LC-EC-MS of intact Fab fragment (A) and Fab fragment with electrochemically reduced S-S bonds (B). From top to bottom for (A) and (B): TIC, MS spectrum and deconvoluted MS spectrum with monoisotopic mass, measured on Orbitrap Fusion Lumos (Thermo). Courtesy: Dr. Theo M. Luider, Yesim Ikiz and Dr. Martijn van Duijn, Erasmus Medical Centre, Rotterdam, The Netherlands.

Disulfide bonds are one of the most important post-translational modifications of proteins. They stabilize the protein's 3D structure and are crucial for their biological function. The reduction of inter- and intramolecular disulfide bonds is necessary for successful characterization and assignment of the bonding sites by MS. Off-line reduction is performed using highly concentrated chemical agents, e.g. dithiothreitol (DTT) that needs to be removed prior LC/MS analysis. Alternatively, thiol - free reducing agents such as TCEP (tris (2-carboxyethyl) phosphine) can be used. However, sample preparation remains laborious and difficult to combine with on-line LC/MS. Moreover, the possibility of on-line electrochemical (EC) disulfide bond reduction can be beneficial for the determination of disulfide bond arrangements in top down proteomics strategy, which relays on fragmentation of intact proteins without enzymatic digestion.

The use of (LC)-EC-MS has shown great potential for the fast assignment of S-S bonds in biopharmaceuticals. With the introduction of a new electrochemical cell, highly efficient and robust online reduction of disulfide bonds in proteins/peptides is now possible. The new µ-PrepCell-SS (see Figure 1) consists of a two-electrode configuration with a new counter electrode design and allows for continuous operation of several days without contamination or loss of reduction efficiency. The flow cell can be used in pre- and post-column HPLC configurations prior to MS detection and is ideally suited for reduction of high disulfide-stabilized proteins. Online reduction occurs within several seconds as compared to conventional offline chemical methods which can take hours or longer to achieve a similar result. A high-pressure version for HDX-MS and a low-dispersion variant to preserve chromatographic separation are also available. Overall much higher sequence coverage has been found in HDX-MS when compared to chemical reduction (TCEP, DTT) and new cysteine peptides could be identified in-post column settings.

In Figure 2 the spectra of the intact and reduced Avastin (bevacizumab, Roche) Fab fragment after HPLC separation on a C4 column are shown. In Figure 2A the intact Fab fragment is shown with the post-column electrochemical cell off and in Figure 2B the reduced Fab fragment is depicted with the cell on (1 V, pulse mode)

From the deconvoluted MS spectrum in Figure 2B and the two fragments with mass 23435.25 Da for the light chain and mass 24612.86 Da for the heavy chain, the reduction of both the inter- and intramolecular disulfide bonds is unambiguously confirmed.

Conclusion: With Antec Scientific's new dual electrode µ-PrepCell-SS efficient and robust reduction of S-S bonds in top-down and bottom-up proteomics becomes possible in routine.

Extracting the Best – from Students and Samples

Sitting Down With…Valérie Pichon, Director, Laboratory of Analytical Sciences, Bioanalytics and Miniaturization, National Center for Scientific Research (CNRS), Paris, France.

Did you enjoy your recent role as co-chair at the 31st International Symposium on Chromatography (ISC 2018)?

I really enjoyed it! Everything went well and we didn't have any unpleasant surprises! My co-chairs – Didier Thiébaut and Jean-Luc Veuthey – and I received a very positive response from all the speakers we invited, so we were able to put together an exciting program.

Any sessions you were particularly proud of?

The session dedicated to teaching and analytical chemistry was a highlight for me. It allowed a cross-section of the scientific community – PhDs, postdocs and researchers from industry and academia – to express their needs and expectations in terms of education. Our aim was to get a better idea of the needs of industry, and to be sure that we, as academics, are giving our students the tools they will need to meet those needs.

What's your view on diversity in conference programs?

Well, it's noticeable that very few women are recognized for academic prizes at analytical chemistry conferences. Many male scientists still don't seem to see a problem – but I hope that we are becoming more aware of the issue as a society.

Walk us through a typical day in your role…

My time is divided between teaching and supervising students, assessing research activities conducted in the laboratories, evaluating applications, and management responsibilities both for my own laboratory and for the wider unit, which houses some 120 people. I also search for new partnerships and write proposals to finance our research activity.

What does your group focus on?

The aim of the analytical chemistry department is to develop separation methods – gas, liquid and supercritical fluid chromatography, and electrokinetic methods – particularly for the analysis of new or challenging classes of compounds, including glycoprotein drugs, metabolites, petroleum additives, ions, and so on. We have to face the demands of different sectors – the police, defence, government and industry. My own group is devoted to selective extraction. We develop stationary phases based on antibodies, aptamers and molecularly imprinted polymers to allow us to selectively extract targets present in trace quantities in samples. Our work is applicable to a range of fields; for example, we work with the nuclear industry to develop methods for extracting ions, and with the cosmetic industry to extract pollutants from the oils used in their products.

What aspect of your job do you find most interesting?

I love the excitement of starting a new collaboration and discovering a whole new field of activity or area of research. It's interesting in itself, as well as a good way for me to broaden my skills. I also like supervising students during their masters or doctoral internships; it's rewarding to help them develop their research skills.

How has your role changed over time?

In the last few years, I have spent more and more time on my administrative role, trying to find funding for research. It's not necessarily a lack of funding per se, but we are investing a great deal of time and energy into identifying and applying for funding from many different organizations, each of which has a very high rejection rate. This situation is particularly difficult for young people starting in academic positions; if you're well known and have been selected for projects before, it is easier to secure funding. Such a reality is a shame, because academia relies on young scientists with fresh ideas to keep a field evolving and improving.

"I love the excitement of starting a new collaboration and discovering a whole new field of activity or area of research."

Is it easier to find funding from industry?

Definitely. With industry, if they have confidence in your research activity and think it can help them, we just discuss the project, perhaps write a one-page summary, and then get started. To apply for an national grant can take months and several lengthy proposal documents – and, after all that, only about 6 to 10 percent of projects will be funded.

Tough odds! What keeps you motivated?

The collaborative projects that we still manage to get! This allows me to pursue the research that interests me in various fields. But my favourite part of the job is sharing my experience with my students. I love to see them find success, either in terms of results, publications or in finding a job quickly.

- Extraction, derivatization, addition of standards
- Solid Phase Extraction (SPE), Filtration
- Evaporative concentration (^{m}VAP)
- Agitation, ^{quick}MIX
- Centrifuge
- MAESTRO PrepAhead Productivity – even through the holidays

Something you can rely on

The GERSTEL MPS handles Your Sample Preparation and Introduction efficiently, accurately and reliably, automated to your specifications.
Setup and start by mouse-click: Your MPS works day and night, using less solvent and without anyone watching over it.

Intelligently automated GERSTEL Solutions for GC/MS and LC/MS: Dependable Productivity and Less Stress for Laboratory Staff, the Workplace and the Environment.

What can we do for you?

Agilent Technologies
Premier Solution Partner

GERSTEL

www.gerstel.com