MARCH 2020 # 85

the Analytical Scientist™

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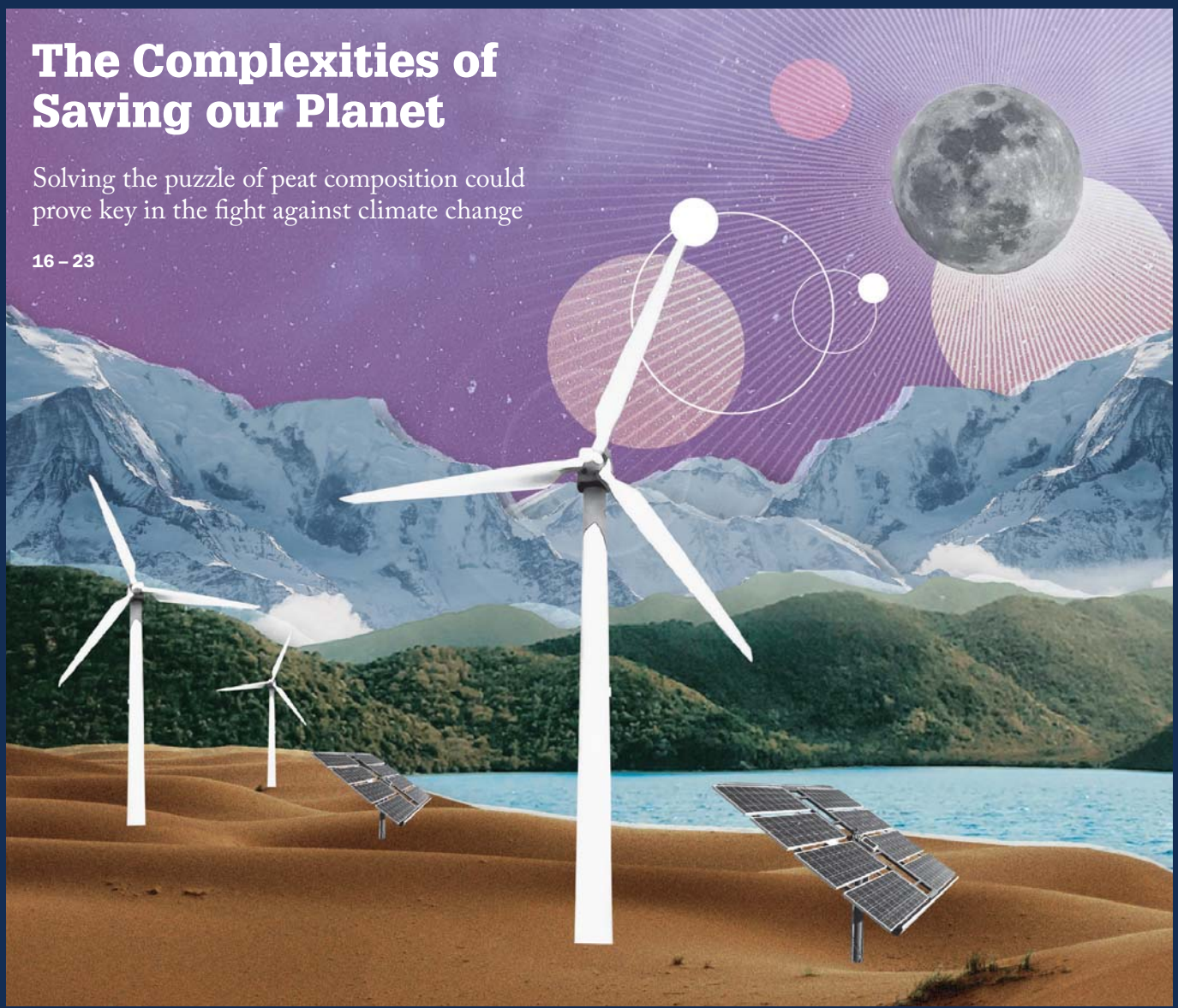

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Fighting Bad Guys in the Shadows

In times of darkness, analytical chemists offer a guiding light

Incredible applications for analytical technologies are published every day – sometimes (if not often) in response to rather troubling events. Peatland destruction, releasing millennia of trapped carbon? Nuclear magnetic resonance guides the way (page 16). Tainting of our water by so-called "forever chemicals"? Chromatography tandem MS techniques seek the truth (page 50). Brains turned to glass by pyroclastic flows of 520 °C? Proteomics investigates (page 9).

Analytical chemists act as unsung defenders on the frontline to tackle – and understand – our greatest threats; the recent development of a combined optics and magnetic particles technique for high-throughput COVID-19 coronavirus detection from saliva emphasizes this dedication (1). And, though the technology requires investment for expansion, the breakthrough exemplifies the resilient rise of analytics to combat insidious issues – a beloved vigilante, fighting bad guys in the shadows.

Collaboration is key to victory in our call to arms. In the case of clinical issues, instrument developers and clinicians must act in tandem to collect samples and validate methods; for environmental matters, analysts must side with governments to enact meaningful change and protect citizens; in forensics, the efforts of archeological experts ensure our analytical success.

The other secret weapon in our arsenal: information and data sharing. In the race to combat the COVID-19 coronavirus outbreak, ACS have released a free-to-read virtual issue of coronavirus research, facilitating open access to research-relevant articles. More widely, cloud-based platforms and databases of chemical information (such as METLIN – an MS identification database comprising over 500,000 molecular standards) allow us to easily capitalize on data acquired by our peers. Coupled with the rise of chemometric approaches for mass data management – and the rise of deep learning and artificial intelligence – it has never been easier to combine our forces (and expertise).

In short, you provide a light in the dark – guiding one another, and society, towards positive change. Though the darkness can be pressing (think pandemics and immediate nuclear threats), you persevere to navigate it – sometimes putting yourselves in harm's way to do so. And from this darkness sprouts progress, paving the way for the next generation of analysts to illuminate further recesses previously beyond our reach.

Matthew Hallam
Editor

Reference

1. *Bar-Ilan University, "New technology developed by Dr Amos Danielli may significantly reduce diagnostic time of coronavirus" (2020). Available at: https://bit.ly/2SUAYUv*

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Upfront

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On The Cover

No habitat is safe from climate change – our cover represents the shifting tides of habitability across the planet, and scientific efforts to combat them

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Study of peat composition represents a massive undertaking for analysts, but understanding nature's complex mixtures could prove key in protecting habitats and humans alike

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MS plays a crucial role in contemporary patient management; here, experts in the technique present their work across vital clinical application

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Upfront

Research
Innovation
Trends

Nuclear Magnetic Revelations

A new approach accurately determines the structure and stereochemistry of natural products that confound conventional methods

Natural products are a common source of drugs (many antibiotics, painkillers, and even cancer drugs are derived from natural products), but before they can be exploited, their structures and stereochemistry must be elucidated. And that's (unsurprisingly) easier said than done.

"Besides the X-ray diffraction, which can only be applied to crystallizable molecules, chemists usually use nuclear magnetic resonance (NMR) spectroscopy for structure determination. Most employed NMR parameters rely on the measurement of protons. But for molecules that only contain few protons, or flexible molecules that need more NMR data to define their conformational spaces, conventional proton-based NMR methods may not determine their structure and stereochemistry correctly," says Han Sun, a researcher at the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP) in Germany.

Another NMR-based parameter – residual chemical shift anisotropy (RCSA) – can accurately determine structure and stereochemistry, but requires specialized instrumentation. Now, Sun and colleagues have developed a method that simplifies the measurement of RCSA to make it more accessible.

"Our experiment involves bringing together natural products with a commercially available peptide – with a sequence of AAKLVFF," says Xiaolu Li, lead author of the work (1). "Dissolved in methanol, the peptides are transformed into liquid crystals, which gives the natural products a weak orientation in the magnetic field. This particular orientation enables us to measure the RCSA of the molecules as a parameter, which in turn provides accurate information about their structure and stereochemistry."

The team tested the technique by analyzing spiroepicoccin A – which was isolated from a marine organism that lives at a depth of more than 4500 m. The substance only has a few hydrogen atoms attached to its stereocenters, making it difficult to analyze with conventional NMR, but the new technique was able to successfully elucidate the compound's structure and stereochemistry.

Reference

1. *L Xiao-Lu et al., J Am Chem Soc, 142, 2301–2309 (2020). DOI: 10.1021/jacs.9b10961*

INFOGRAPHIC

Chemical Expansion

Analysis of 22 chemical inventories from 19 countries highlights booming chemical diversity

350,000

chemicals are registered for production and use in 2020

This number was **100,000** in 2000

66%

of chemical sales were contributed by the UK, Canada and Western Europe

BUSINESS IN BRIEF

Newborn hope

As part of a Parent Project Muscular Dystrophy (PPMD) New York State pilot program, PerkinElmer has announced that it will provide the assay for Duchenne muscular dystrophy screening in newborns. Approved by the FDA in December 2019, the GSP Neonatal CK–MM kit became the first commercially available newborn screening assay for the disease, and will be used to screen approximately 100,000 infants over two years. The program should help lay the framework for further Duchenne newborn screening across the US, and globally.

All roads lead to Delhi

In a new collaboration between academia and industry, Agilent has teamed up with Indian Institute of Technology Delhi as part of its corporate social responsibility initiative. Agilent's contribution will support ITT Delhi's incubator site for protein analysis, working to establish best global practices to ensure the quality of biotherapeutics on the Indian market.

Employer of the year

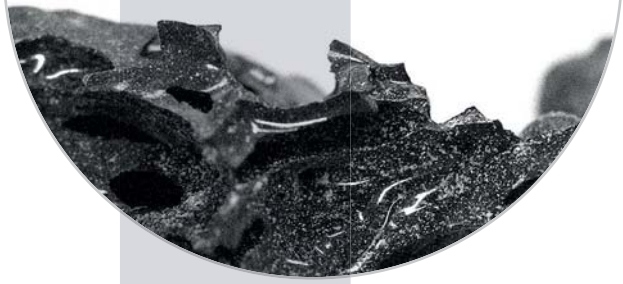
It's all smiles at KNAUER – a family-owned company that has been recognized as one of the top one percent of employers in Germany (and not for the first time). The evaluation, based on an independent meta-study of over 100,000 companies by the Düsseldorf Institute of Research & Data Aggregation, has earned the Berlin-based instrument manufacturer the title of "Leading Employer 2020" – an accolade supported by an average 8.8 years of service from employees.

Defying infectious disease

Thermo Fisher Scientific have announced a new collaboration with NanoPin Technologies (developer of the NanoPin diagnostic platform for blood samples) to streamline the development of sensitive analytical workflows for the diagnosis of infectious disease and subsequent patient management. The companies hope the partnership will provide a route to overcoming the limitations associated with current diagnostic solutions.

Setting an example of equality

BASF are taking aim at gender inequality. The company wants to increase the proportion of women in leadership positions to 30 percent by 2030 – a 7 percent rise on figures reported at the end of 2019, and almost double those figures reported for the three leadership levels below Board of Directors (15.8 percent females). The target will apply to BASF's operations in all countries.



Volcanic Vitrification of Brain Matter

What does glass from a skull at Herculaneum tell us about Vesuvius' volcanism?

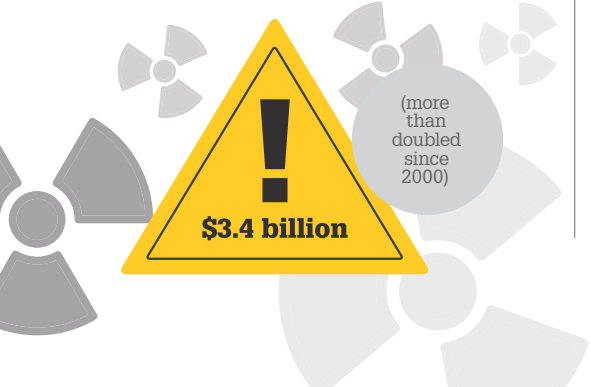
In 2019, Pier Paolo Petrone wrote of the instant vaporization of victims' bodily fluids when Vesuvius erupted in 79 AD. Now, further research in Herculaneum has revealed more harrowing consequences of the pyroclastic flow… Vitrified brains.

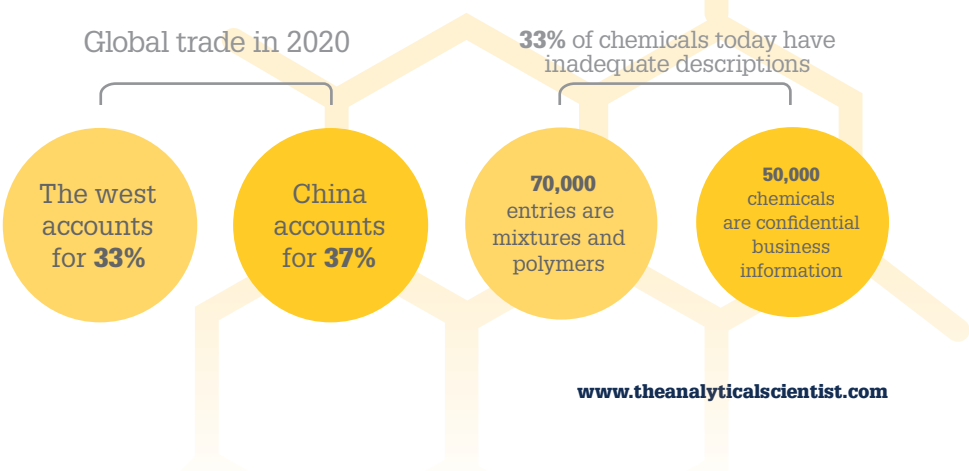
MS proteomics of atypical glassy material from "The Guardian" of the College of Augustales – an infamous Vesuvius victim with severe thermal damage – identified seven enzymes from the human brain and human hair fatty acids, alongside brain triglycerides. "The vitrification of human tissue indicates extreme temperature exposure followed by rapid cooling," says Petrone; reflectance analysis of charcoal samples indicate temperatures as high as 520 °C would be required.

"The preservation of ancient brain remains is extremely rare – this is the first discovery of ancient human brain vitrified by extreme heat," says Petrone.

Reference

1. *Petrone P. et al., NEJM,382, 383 (2020). DOI: 10.1056/NEJMc1909867*

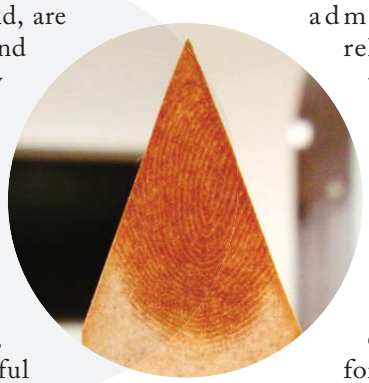




Coke Check

A simple fingerprint test could distinguish cocaine users from those who come in contact with the drug

Blood and urine are conventional matrices for drug testing, but both are biohazards – which has implications for storage and transport – and a potential invasion of privacy. "Fingerprint samples, on the other hand, are safe, easy to transport, and can be easily collected by non-medical staff," says Catia Costa, investigator of a novel method that uses fingerprints to detect illicit drug use. Donor identity can be imbedded on the ridge of the sample to stop cheats, making it particularly useful in drug rehabilitation centers, jails, and probation services.



"We started by exploring a range of MS techniques: desorption electrospray ionization, matrix-assisted laser desorption ionization, liquid-extraction surface analysis, paper spray, and LC-MS," says Costa. However, due to the "complex" nature of fingerprint samples (which compose sebaceous, eccrine and external contaminants), high-resolution MS (HRMS) was required to differentiate the sample components adequately. An extra layer of complication? The need to distinguish drug ingestion from environmental contamination.

Researchers set out to detect benzoylecgonine (a prominent cocaine metabolite) on fingerprint samples from non-drug users, patients admitted to a drug rehabilitation clinic testifying to use of cocaine in the last 24 hours, and volunteers who touched cocaine (seized by the Forensic Science Ireland) in controlled conditions for study purposes – before and after hand washing – using paper-spray HRMS. Oral fluid samples were also analyzed by LC-MS/MS to corroborate fingerprinting results.

The outcome? A method able to distinguish between cocaine ingestion and handling; benzoylecgonine could only be detected on the washed hands of individuals who had ingested cocaine. But the method is not without challenges. "The variable nature of fingerprints, and the differing secretion of this compound based on rates of secretion and pressure of contact between the finger and drug-testing matrix (triangular Whatman Grade 1 chromatography paper) complicates matters, especially in cases where quantitation is required," admits Costa.

Next? Testing therapeutic drugs to tackle treatment noncompliance – especially for leading killers, such as tuberculosis.

Reference

1. *Jang M et al., Sci Rep, 10, 1974 (2020). DOI: 10.1038/s41598-020-58856-0*

THC, or not THC?

Portable detection using Raman spectroscopy could streamline cannabis testing

Cannabis transport in the US is challenging: 11 states and Washington DC have legalized cannabis for recreational use, and medicinal use is legal in 33 states; 15 states have decriminalized it completely. In many states, the tetrahydrocannabinol (THC) content of hemp cannot exceed 0.3 percent by law – otherwise, it is considered cannabis. Clearly, there is a need for rapid determination of THC concentration.

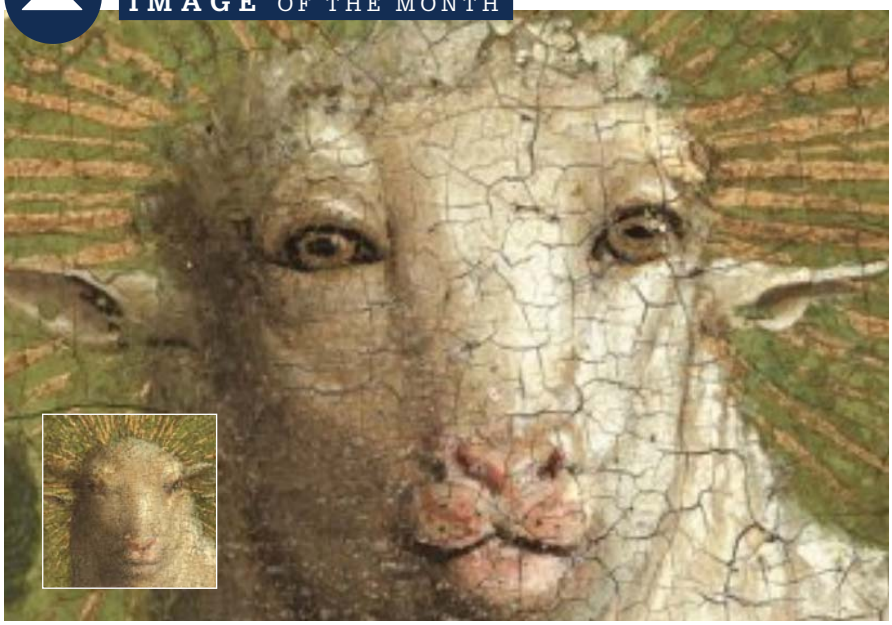
Enter Dmitry Kurouski – an investigator on the pulse of the issue. "We used Raman spectroscopy for non-invasive and non-destructive differentiation between hemp and cannabis with 100 percent accuracy," he says. The method overcomes the usual drawback of more conventional near-infrared cannabis detectors, which require dry, ground material – or high-performance LC methods, which are time consuming and laborious.

"Next, we plan to expand our method to identifying from which part of the US, Canada or Mexico cannabis and hemp plants originate," says Kurouski.

Reference

1. *L Sanchez et al., RSC Adv, 6 (2020). DOI: 10.1039/C9RA08225E*

IMAGE OF THE MONTH



Mutton Dressed as Lamb?

The "Adoration of the Mystic Lamb" (or the "Ghent Altarpiece") is supposedly the most stolen painting in history. Almost 600 years after its completion in 1432, researchers applied X-ray fluorescence scanning to reveal the original face of the central lamb, believed to have been painted over in the 16th century. Here we see the modified version (bottom left) and the original (uncovered) version of the painting. Some might say the elusive 16th century painter had the right idea – what do you think?

Image credit: @frajds (Twitter)

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QUOTE OF THE MONTH

"Looking forward, I'd suggest that correlation of blood chemistry acquired by MS with genetics and lifestyle choices will allow us to identify optimum nutrition for growth and help avoid fat storage, marking the beginning of a true age of personalized nutrition – and medicine."

By Donald Chace, Chief Scientific Officer at Medolac Laboratories

Critter Colony Chemistry

Ant brains aren't the easiest subject to probe, but capillary electrophoresis may lead the way in studies of bug behavior

Colony-specific behaviors of red forager ants (*Pogonomyrmex barbatus*) indicate potential neurological differences. Testing this hypothesis, Jill Venton and colleagues literally picked the brains of ants from nine wild colonies, extracting them and separating the contained amines by capillary electrophoresis (CE) coupled with fast-scan cyclic voltammetry.

Venton highlighted the strength of CE when it comes to detecting trace concentrations of analyte – "Perfect for ant brains," in her words. But the research was not without its difficulties. "The greatest technical challenge was aligning the electrode with the capillary and preparing samples from such small brains," says Venton.

Low detection limits were achieved for dopamine, octopamine, serotonin and tyramine – with dopamine present in the highest concentrations. The outcome: less amine variation was apparent within colonies than between them, suggesting environmental influences on neurotransmitter content in ants.

Reference

1. *M Shin et al, Anal Bioanal Chem (2020). DOI: 10.1007/s00216-019-02355-3*

In My View

Experts from across the world share a single strongly held opinion or key idea.

Surveying Diversity in STEM Disciplines

Inequity in science is a long-standing problem – but just how bad is it?

By Donna J. Nelson, Professor, Department of Chemistry and Biochemistry, University of Oklahoma, USA

The Nelson Diversity Surveys (NDS) are a collection of four datasets that quantify the representation of women and underrepresented minorities (URMs) among professors, by science and engineering discipline, at research universities collected during 2002, 2005, 2007, and 2012. The surveys were complete populations, rather than samples. Consequently, the Surveys quantified characteristics of STEM faculty that had never been revealed previously, drawing great attention nationally and gaining complete support from women and URM STEM faculty.

Women and URM science faculty had been concerned for years about perceived inequities in academia and were just becoming vocal. These groups believed that underrepresented students were increasing among PhD recipients without a corresponding increase among recently hired professors. Highly disaggregated federal data showed that female and URM PhD attainment were increasing, but no analogous faculty data existed to enable a comparison. Available faculty data were disaggregated by gender or by race, but not both, and neither was disaggregated by rank. A few concerned female scientists had compiled the disaggregated data for their own universities, but these data were too localized to support a national conclusion.

The NDS started as a student project – just two students and myself – with the intention of only examining chemistry faculty in the top 50 departments, as ranked by the National Science Foundation (NSF), according to research funding expenditures. They immediately drew so much press that female faculty from other STEM disciplines asked me to survey their disciplines, too. In a few weeks, the surveys grew from the top 50 departments in one discipline to the top 100 departments in each of 15 disciplines – chemistry, physics, mathematics, chemical engineering, civil engineering, electrical engineering, mechanical engineering, computer science, political science, sociology, economics, biological sciences, psychology, astronomy, and earth science.

Some amazing degrees of underrepresentation were revealed. For example, the 2002 survey showed that there were no Black, Hispanic, or Native American female faculty in the top 50 computer science departments. It also revealed that there were no Black or Native American assistant professors in the top 50 chemistry departments.

The hard part of the project – and the reason it had never been done before – was that whole populations were needed in these surveys. Some people may not know what that means; they may have heard a survey discussed in which 65 percent participation was obtained, so the researchers were happy. In some surveys, only 20 percent participation is considered adequate. The NDS required 100 percent participation. Why? Because it reports very small numbers of women and URM faculty. Reporting that there are zero Native

"Women and URM science faculty had been concerned for years about perceived inequities in academia and were just becoming vocal."

Americans in the top 50 departments of a discipline requires having data from all departments, otherwise, it could be argued that they might be in the missing departments. Therefore, we obtained data for all departments from department chairs. We also gave department chairs the opportunity to examine and correct their data before it was released. Finally, women and URM faculty had the documentation to support their concerns.

Our surveys unveiled the level (using data for one year) and rate (using data from 2002 to 2012) of faculty diversification, disaggregated by race, by rank, by gender, and by discipline. Researchers enthusiastically used the disaggregated faculty data in comparison with existing, analogous student data. I was cautioned by some researchers not to release my raw data (largely responses from department chairs) until I had fully reported their outcomes myself. However, my goal was not to get publications for myself, but rather to empower an army of concerned women and URMs to research the NDS data – a goal I believed to be of great importance (and I hope you agree).

I released the raw data immediately after each survey ended. The result? Many new programs increasing the representation of women and minorities among professors were launched. The NDS were used by the National Science Foundation, National Institutes of Health, Department of Energy, US Congress, Sloan Foundation, the National Organization for Women, universities, and many other organizations interested in diversity in academia. In only a couple of years, a new area of research was spawned – the Science of Broadening Participation.

As for the future of such surveys, I don't believe that NDS will be attempted again for multiple reasons – namely, obtaining data for such a large group is extremely difficult, and the surveys came along at a time when inequities in URM faculty representation were hidden but easily revealed. I still believe the Science of Broadening Participation is a much-needed research area, but we must go beyond headcounts in the future.

A full report of NDS, with all data, tables, and bar graphs, is in Chapter 2 of "Diversity in the Scientific Community Volume 1: Quantifying Diversity and Formulating Success" (https://bit.ly/2uzmrWi).

Great Minds Shaping IMS

Leading figures of ion mobility spectrometry–mass spectrometry explored the field and its future at the IMS Great Minds Summits. Here, we present their thoughts and conclusions.

Over the past century, we've seen the power that MS technologies bring to life-changing research. Now, as we transition into a new decade, it is important that we evaluate past successes, but also consider what can be achieved with future innovations. Ion mobility spectrometry–MS (IMS-MS) has played a role in breakthroughs across fields – from drug discovery and development to food and environmental analysis. And yet, despite successes and gaining traction, there is a shared feeling in the analytical science community that we have barely scratched the surface of IMS-MS' immense potential.

The IMS Great Minds Summits (GMS), hosted by Waters Corporation, brought together leading scientists from across the globe to discuss the latest IMS technologies and consider the path ahead. The events, which took place in Kerpen, Germany, and Indianapolis, USA, provided a unique opportunity for IMS-MS experts to help shape the instrumentation of the future.

Fundamentals of IMS

Matt Bush (University of Washington) and Erin Baker (North Carolina State University) explored the fundamentals of IMS-MS in Germany and the USA, respectively, each setting the stage for further discussion. Both Bush and Baker highlighted the key benefits of the method when interfaced with MS: a reduction in spectral complexity, maximized peak capacity, and enhanced selectivity. They also explored IMS-MS' ability to measure an additional molecular identifier in the form of the collisional cross section (CCS), which offers a number of advantages, including greater confidence in analyte identification and structural elucidation of compounds. Finally, Baker and Bush touched upon the latest technology and current challenges – namely the need for improved software integration.

Recent technological innovations

Kevin Giles, from the Waters MS Research Team, expanded on the theme of technological development at both GMS events, with a presentation that explored the development of traveling wave ion mobility and the exciting capabilities of the first commercial Cyclic IMS instrument. Unveiled at ASMS 2019 and having earned a place on the 2019 Innovation Awards from The Analytical Scientist, the SELECT SERIES™ Cyclic IMS offers greater resolving power and the ability to perform IMS^n experiments, enabling researchers to "zoom in" on a selected mobility range. Giles described that, as resolving power increases with the square root of the instrument's pathlength, the cyclic design permits greater mobility resolution with each pass, while maintaining a compact instrument footprint.

From male infertility to food safety – applications from GMS Europe

The afternoon session on IMS-MS applications at the European GMS was kickstarted by Sheba Jarvis, Clinical Research Fellow at Imperial College London, whose talk focused on the use of IMS-MS in a study that assessed the impact of obesity on male infertility in animal models. The greater peak capacity permitted by IMS was critical for the confident identification of deregulated proteins in the testes associated with a chronic high fat diet, and the novel candidates that her team identified in the animal model study were found to have human relevance. Next: future studies in obese men presenting with infertility.

The role of IMS-MS in sports doping analysis was explored by Mario Thevis from the German Sport University Cologne. He discussed the utility of CCS values as an additional confirmatory parameter in the screening of banned substances. Though not routinely applied in the field of doping control, his research suggests that CCS could provide crucial information to support investigations. A striking example highlighted during the lecture was the application of IMS-MS to doping control analysis of intact, rapid-acting insulin analogues; IMS-MS was able to distinguish human and synthetic insulins (which differ

by only one or two amino acids) in just 10 minutes – standard analyses take three times as long.

Applications for IMS-MS in tissue imaging and drug metabolism were also demonstrated. Laura Cole of Sheffield Hallam University, UK, presented her research studying metabolite distribution across whole-body tissue sections – which were clearer than those obtained through autoradiography. And Jan Boerma from York Bioanalytical Solutions started the second day by highlighting how IMS-MS speeds up metabolite identification through enhancement of low- and high-energy mass spectra quality. The former work highlights the potential role of IMS-MS in image acquisitions without the need for radiolabeling of compounds of interest, potentially reducing the cost of drug development, while the latter demonstrates the utility of IMS in reducing noise and resolving co-eluting metabolites.

Perdita Barran from the University of Manchester, UK, delivered an engaging account of her work detecting Parkinson's disease from sebum. Inspired by Joy Milne – a retired nurse with the ability to smell Parkinson's disease – Barran is using IMS-MS to identify compounds found at higher-than-usual concentrations on the skin of Parkinson's patients. IMS-MS is also being used to enhance food safety. Séverine Goscinny from Sciensano, Department of Food, Medicines and Consumer Safety in Belgium, outlined her progress in developing an extensive CCS library in collaboration with Michael McCullagh, Principal Scientist at Waters, to enable rapid detection of food additives. Both fortified and real substance samples have been identified using this method.

Bacterial "fight clubs," polymer analysis and structural biology from GMS US

John McLean, Department Chair and Stevenson Professor of Chemistry at Vanderbilt University, Tennessee, opened the US GMS event with an inspiring lecture that emphasized how IMS-MS with improved mass-resolving power helps solve the challenge of acquiring crucial biological data on short timescales. From aiding CRISPR gene editing experiments to creating bacterial "fight clubs" – that is, monitoring bacterial co-cultures with IMS-MS to discover new therapeutic compounds – the applications discussed were diverse and laid the foundations for another day of stimulating discussion.

Chrys Wesdemiotis from the University of Akron, Ohio, shared his IMS-MS analysis of polymers and other materials. In particular, he noted how some bioconjugates were proving to be impossible to characterize with any other method (including X-ray diffraction), and so IMS-MS represented a powerful technology in his toolbox.

Progress using IMS-MS in gas-phase structural biology was then explored by Brandon Ruotolo of the University of Michigan. His talk evaluated a new calibration method for CCS values to account for mass-to-charge ratio-dependent radial motion, and went on to discuss collision-induced unfolding – able to rapidly differentiate protein isoforms in gas phases based on differing unfolding patterns and stabilities. Potential applications, according to Ruotolo, include biosimilar studies and investigation of cell membrane-drug and cell membrane-protein interactions.

A fantastic finale

Both GMS events were concluded by David Clemmer from Indiana University, who delivered an energetic and informed review of the information that can be derived from studies of protein folding and dynamics. His presentation provided fascinating insight into the latest IMS-based methods for characterizing native and non-native proteins from solution. He also covered the use of IMS-MS for studying conformational changes in protein complexes and the extraordinary potential of charge detection MS, which can supply accurate information about the mass-to-charge ratio and charge of large bioparticles.

The future of IMS-MS – guided by great minds

The Waters IMS Great Minds Summits brought together leaders in the field and provided a forum at which to discuss a range of current topics surrounding IMS technology. From creating new research methods for Parkinson's disease to developing bacterial "fight clubs" for the discovery of new biological compounds, the applications of IMS technology were shown to be wide-ranging – proof of the great technological gains that have been made.

What challenges remain? Experimental design, data management and data interpretation will all demand increased scrutiny as the technique evolves. And the discussions held at the GMS events helped identify IMS-MS standards, data formats and the application of CCS as three immediate areas for attention.

By facilitating discussion – and the sharing of ideas and challenges, the IMS Great Minds Summits achieved a core objective: to shape the future of IMS-MS instrumentation.

THE COMPLEXITIES OF SAVING OUR PLANET

Part 1

Nature is complicated. Unfortunately, so too are the massive changes occurring in natural habitats across our planet – largely due to human interference in the form of pollutants, damage to land, and climate change. To resist (or even reverse) these changes, we must first understand them. Here, Nicholle Bell kickstarts a new series of environmentally-focused articles that shine a light on the researchers who are putting Earth first.

FOR PEAT'S SAKE

By Nicholle Bell, Research Fellow, School of Chemistry, University of Edinburgh, Scotland, UK

It's a little-known fact that peatlands are the largest store of carbon on the planet. In fact, they store approximately four times the amount of carbon found in all the world's standing forests, effectively equating to billions of tons. This may sound surprising, but peatland grows at a rate of approximately 1 mm per year, meaning that peat as deep as 11 m – as it is in parts of Scotland – has been accumulating carbon since the last ice age. Why is this important?

Peatlands can only store carbon when they are healthy and wet. And peat draining for agricultural or harvesting reasons opens up the land to oxidation. As you might expect, the result is the release of carbon – either into the atmosphere (in the form of carbon dioxide) or into water systems. For example, if all of the peatlands in Scotland were to become damaged, the release of carbon dioxide would be equivalent to the total carbon emissions of Scotland over the past 140 years. On a wider scale, we would have no hope of fighting the resulting climate-related effects.

Recognizing the importance of healthy peat is the main rationale for my research. I apply analytical techniques, such as high-resolution (HR) nuclear magnetic resonance (NMR), and solid and liquid-state high-resolution MS to study the chemical

The Peat Beneath our Feet

People tend to think that wetlands (often comprising a fair portion of peat) are effectively wasteland; you can't grow anything because it's too acidic. What's more, here in Scotland, they're very cold and there are no trees – so it looks like rolling barren land. There's very little education surrounding them, too, which has resulted in a historical non-appreciation of the incredible work this land conducts right beneath our feet. And when it comes to thinking about how we can meet our climate change targets, the sheer volume of peat in the UK (and elsewhere) makes this a viable target in terms of preventing massive carbon dioxide release.

The UK is number twelve in the list of countries with the most peatland, with approximately 3 million hectares of it. Unsurprisingly, the biggest peatlands in the Northern Hemisphere are in Canada, Scandinavia, and Russia. Then there are tropical peatlands, found in the rainforests of Southeast Asia and other such areas, which contain 30 million hectares of tropical peatland – approximately 10 times that found in the Northern hemisphere. However, this peat is completely different, owing to the differing source of organic matter (largely trees, rather than sphagnum mosses) and the hotter, more humid climate. Matter decomposes more quickly, and the peats are more swamp like as a result. One of the largest on a global stage is found in the Congo, but it's rather inaccessible and constitutes a whole other story...

composition of peat, which is widely considered the most complex organic mixture on our planet (containing anything between hundreds of thousands to a million of compound). In particular, my team aims to characterize and understand the differing chemical signatures of pristine and drainage-damaged peat – and whether this change is reversed upon restoration of the land, which is mainly achieved by rewetting the land by blocking drains with plastic dams.

Our process for progress

The good news: our main finding so far from our sites in Scotland is that the same compound classes do return to the peat upon its restoration. When we consider that around 80 percent of the UK's peatlands are currently damaged – a great cause of concern for our government – that really is good news. But it wasn't easy for us to arrive at this conclusion.

While we explored the use of HPLC and GC, these techniques failed to separate all the molecules in peat mixtures – as noted above, there were simply too many

A Toolbox for Success

Solid-state NMR

Can obtain information about the carbon compound classes within a peat sample without chemical extraction in tens of minutes.

Advantage: quick and easy.
Disadvantage: suffers from spectral overlap, and so cannot be used to determine individual molecules.

Liquid-state NMR

3D and 4D NMR (isotope-filtered) experiments are designed to obtain multiple chemical shifts from each tagged molecule, which allows their structures to be elucidated.

Advantage: allows unambiguous structural information to be obtained. There are also many NMR tricks one can play to reduce 3D and 4D experiments into their 2D versions.
Disadvantage: limited sensitivity. These NMR experiments can only determine the structures of major compounds present in the spectra of highly complex mixtures.

FT-ICR MS

Applied in solid-state (laser desorption ionization) and liquid-state (electrospray ionization) analyses to obtain accurate molecular masses (and hence formulae) for thousands of compounds in peat samples.

Advantage: sensitivity and resolution.
Disadvantage: can only see what is ionizable, and assigning a formula does not equate to a molecular structure.

different molecules. Instead we decided to focus initially on fingerprinting peat samples by compound class, rather than individual molecules. In this regard, NMR is the most effective method – in part because it allows for analysis performance in the solid state, meaning that harsh chemical extractions and the like are not required at the preparation stage. We were able to measure a carbon spectrum immediately from a ball-milled peat sample, and applied a statistical approach to decipher exactly what compound classes were in our samples of damaged, restored and pristine peat.

Once we had identified the relevant compound classes, we needed to transition to individual molecule analysis to gain more information – and that demanded alternative analytical routes to the norm. The answer: multidimensional NMR and enriched isotopes. We designed a novel method in which carbon-13 was inserted into molecules in specific locations to replace targeted functional groups; three- and four-dimensional NMR spectra were then allowed us to decipher the chemical structures surrounding the carbon-13 tags (1, 2). After extracting chemical shifts from our tagged samples, we were able to piece them together like a jigsaw puzzle to obtain the compound structures. So far, we have determined the structures of phenolic molecules from peat, but there are many more waiting to be solved.

> "It's a little-known fact that peatlands are the largest store of carbon on the planet. In fact, they store approximately four times the amount of carbon found in all the world's standing forests, effectively equating to billions of tons."

There were numerous sample prep and workflow considerations involved due to the significant number of confounding factors: peat doesn't dissolve in anything and

> "One of my main motivators in becoming an NMR analyst was the problem solving needed to interpret outcomes and attain structures."

molecules often interact with one another in these samples, aggregating and making the analyses increasingly complex. We overcame this by producing a standard protocol, starting with methylation within an organic solvent (a strong base), which results in a large fraction of peat – but, of course, not all of it – in solution.

Onwards and upwards

Now that we have an idea of the compound classes that constitute the difference between damaged and restored peatlands in Scotland, we are aiming to apply our method to peats from elsewhere in the UK, Canada and Sweden to assess the consistency of results across geographies – and to decipher if it is the same specific molecules that are important in each case using our molecular tagging and advanced NMR experiments.

Improving our methods is also a primary concern. At the moment, we take 50 cm cores from areas of peat for analysis; taking peat out of the landscape is not an ideal approach – and we have found an unlikely surrogate for analysis: teabags (3). Teabags represent another complex mixture, and they also contain similar compound classes to peat. Clearly, they are by no means the same compounds, but the classes present are similar enough that we can

assess their loss and restoration between pristine, damaged and restored teabags buried in soil across the UK, Canada and Sweden to further add to our understanding of the processes in peat. To this end, we have designed NMR experiments to help us decipher the molecular changes that take place within tea samples (4).

There are many teams working to monitor peatland restoration, but this is often conducted in terms of vegetation, hydrology and gas fluxes – but there have been instances where peatlands thought to been returned to a "healthy" state have yet deteriorated. Such failures really underscore the need for a molecular understanding of the process so that we can assess – with certainty – whether these systems are healthy or not.

In short, there's a fair way yet to go regarding our work, but advances in chromatography, such as two-dimensional separations and long columns, will make these analyses even more powerful in the future. One of my main motivators in becoming an NMR analyst was the problem solving needed to interpret outcomes and attain structures. Peat, as the most complex mixture on Earth, is therefore one of the biggest jigsaw puzzles on the planet – and one my group is determined to piece together.

References

1. *NG Bell et al., "Isotope-filtered 4D NMR spectroscopy for structure determination of humic substances", Angew Chem Int Edit 54, 8382 (2015). DOI: 10.1002/anie.201503321*
2. *NG Bell et al., "Isotope-filtered nD NMR spectroscopy of complex mixtures to unravel the molecular structures of phenolic compounds in tagged soil organic matter", Analyst, 131, 4614 (2016). DOI: 10.1039/c6an00999a*
3. *NG Bell et al., "Molecular level study of hot water extracted green tea buried in soils – a proxy for labile soil organic matter", Sci Rep, 10, 1484 (2020). DOI: 10.1038/s41598-020-58325-8*
4. *J Sakas & NG Bell, "Reduced dimensionality hyphenated NMR experiments for structure determination of compounds in mixtures", Faraday Discuss, 218 (2019). DOI: 10.1039/C9FD00008A*

Peak Protection: Safeguarding Your Lab Gas Supply

For many labs, it is important to have an up-and-running gas generation system 24/7. We talk with Jim Warren, Field Service Engineer for Peak Scientific, about his role – and why the service his team provides needs to be "the best in the business."

What does your job as a field service engineer (FSE) involve?

We're out there to provide the customer with a direct interface to Peak Scientific and our products. We have an extensive network of FSEs, so we can always get someone there to help our customers if they have any trouble with their equipment, resolving any problems quickly.

Most of our time is used performing annual preventative maintenance for our service contract customers. Regular servicing is essential to keep the machine in its finest upkeep, so that it will provide good, long-lasting service.

Despite this, our job still involves maintenance call-outs – sometimes a gas generator will need a repair and we will need to fix that problem. Whether it is something to do with the inevitable wear and tear of moving parts, or something out of the ordinary – we are problem solvers. That's what we're there to do.

How did you get into your role?

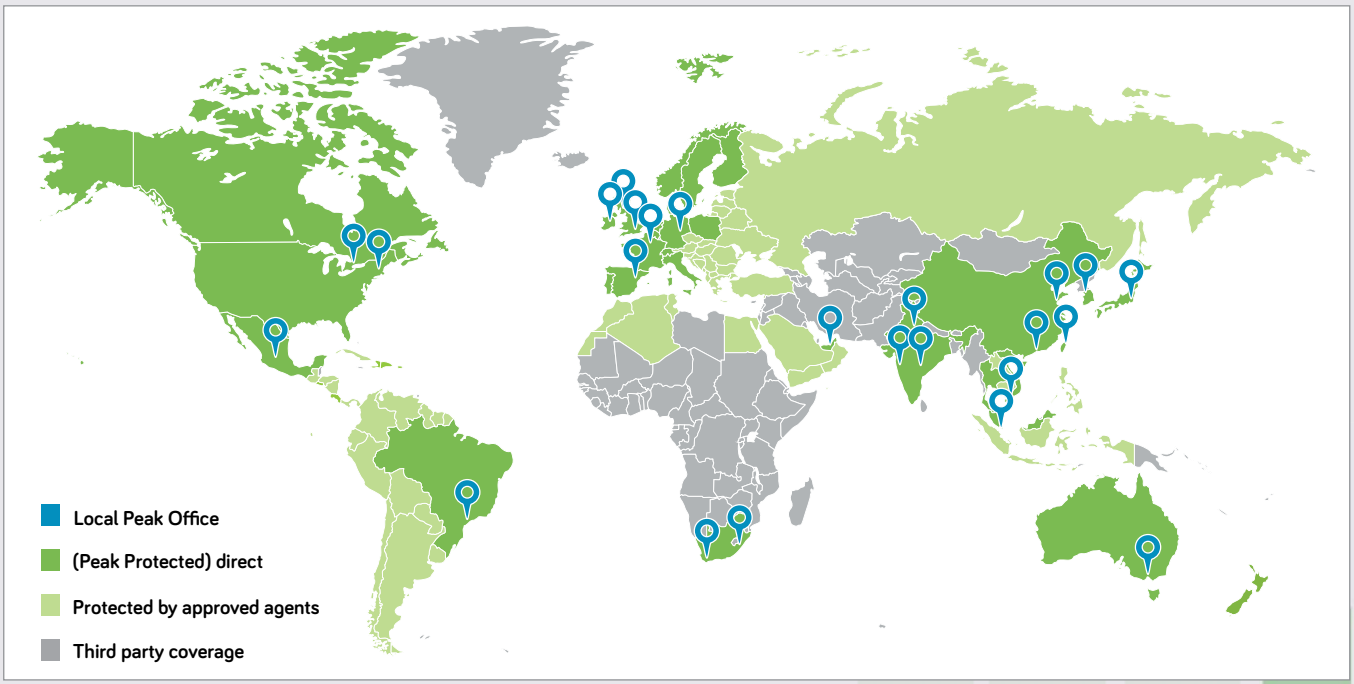
I was working for another company doing installation work for Peak Scientific. Peak looked like a great company to work for, so I joined them!

I enjoy working on equipment and I enjoy working with customers. The two together have brought me here to this point – it fits my personality.

What kind of training have you received at Peak?

Much of my career has been in rotating equipment and compressed gas. Here, we work on Peak equipment and only Peak equipment, so we are given extensive on-boarding training. You learn the principles of operation when you go through the corporate book training, and then you learn the physical properties of operation by shadowing senior FSEs. We do both annual and monthly testing to keep us current and fresh – and this makes us a really strong team.

There are also training and social events, which are great for team-building as well as being able to get together with your comrades and enjoy some time to catch up. Due to the nature of the job, none of us really interface with each other day-to-day – so it's nice to get together.



PEAK SCIENTIFIC

What do you enjoy most about your job?

I am a problem-solver, so I enjoy the challenges of maintenance calls. I really enjoy being able to go out and help the customers there and then – if the customer is down, they're losing money. I get to go out there and get them back online as quickly as possible, enabling them to perform at maximum potential again. That provides a lot of personal satisfaction for me.

I also enjoy industrial installations, because they're large, they're detailed, and they're a big solution for the customer. Where they once had maybe 10 small machines, we put in one large central system – it's a great challenge and very satisfying.

What is the reason behind most of your maintenance call-outs?

To be honest, most problems are caused by customers who either neglect their systems or attempt to service their equipment themselves – unfortunately, it never works out very well. It's not that the systems are incredibly complex, but if you don't understand the equipment fully, you can get into problems very quickly.

We'll get called out, analyze the problem and realize that someone's put the cup seals on the compressors upside down! The customer stands over your shoulder and you show them what you're doing, and they'll say, "Oh, that's actually a lot more complicated than I thought it was… We're just going to put you on contract next year!"

I know we're not flying rockets to the moon, but even a relatively simple system needs a deep understanding to get the best and most reliable performance.

Where are you and your colleagues based?

We have more than 94 FSEs in different cities globally in over 20 countries – across the US, South America, India, China, South Africa, Oceania and Europe.

I manage Houston and the Gulf Coast area, Louisiana, encompassing Baton Rouge, New Orleans and Lafayette, Louisiana. I also work in other areas in Texas, if we need extra coverage. We have around 20 FSEs across major cities in North America, including three here in Texas – so we can get to places quickly.

How quickly?!

We have a variety of contract levels depending on client requirements. The highest level is our Premium Protected contract, for customers who cannot afford downtime – it means we'll get an FSE to their doorstep within 24 hours (and, of course, it comes with annual preventative maintenance). The goal for us is to make sure we don't have to go back out there again, but for the customer, it's essentially an insurance policy. If they do have a situation, we will be there to resolve it, rapidly.

Here in the US, a large number of our customers are toxicology labs – they're high production, high throughput, and they need their equipment to operate. They need us to fix a problem within 24 hours and we make sure we get there – whatever it takes.

I personally see how tremendously valuable that is to customers. The less downtime they face, the more money they make.

How do your customers respond?

My customers tell me that we are unique in what we do – and that we do it very well. In this business, customer service is everything.

In my mind, we are the best in the business – we've set an industry precedent. We're noted for our ability to keep our promise of getting customers back online within 24 hours. For a business like ours to succeed, keeping promises is essential – our customers rely on us to maximize lab uptime and productivity, and we take that very seriously.

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THE FIGHT AGAINST DISEASE IS IN NO WAY AN EASY ONE – COULD THE POWER OF MASS SPEC PROVE TO BE MANKIND'S SECRET WEAPON?

The role of MS in screening, monitoring, and subsequently improving patient health has far-reaching implications – from giving premature babies a fighting chance to evaluating environmental factors that contribute to disease. These applications span the clinical research spectrum, from the operating room to the lab bench, and – thanks to instrumental advances and the increasing power of data processing methods – are becoming increasingly important. Here, four influential analytical scientists – Candice Ulmer, John Yates, Donald Chace, and Peter Nemes – detail how they are wielding the power of mass spectra to identify, support and treat patients now and in the future.

OMICS AND PUBLIC HEALTH

By Candice Z. Ulmer, Research Chemist & Associate Service Fellow, Clinical Chemistry Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA

As a Clinical Research Chemist at the Centers for Disease Control and Prevention, my responsibilities include the planning and execution of programs for the harmonization and accurate reporting of chronic disease biomarkers – and other biomarkers deemed important by stakeholder organizations, including parathyroid hormone (PTH), anti-müllerian hormone, follicle stimulating hormone, luteinizing hormone, and steroid hormones.

We study these markers to enhance the diagnosis and treatment of select endocrine diseases and advance CDC Standardization Programs – aimed at improving the accuracy and precision of these same measurements, any many more, in patient care. In fact, I now ensure the accurate reporting of 17 such analytes, including the examples mentioned above, in addition to further roles generating population data, training laboratory professionals, and acting on the International Federation of Clinical Chemistry and Laboratory Medicine Committee on Bone Metabolism and the Clinical Chemistry Committee for the American Society for Mass Spectrometry.

A current focus of my research is the development of a reference measurement procedure for the accurate quantitation of PTH and its related fragments by ultra-high-performance LC-high-resolution MS (UHPLC-HRMS). This method currently serves as the only top-down proteomics method for PTH quantitation, with the lowest limits of quantitation for an MS-based method (10 pg/mL). We apply this approach to measuring PTH, which is a key biomarker in the diagnosis and treatment of chronic kidney disease-mineral and bone Disorder (CKD-MBD), hypo- and hyperparathyroidism, hypercalcemia, and vitamin D deficiency. Currently used tests suffer from issues with sensitivity, PTH instability and measurement variability, while MS allows for the accurate measurement of this analyte over four orders of magnitude in serum and plasma with a high specificity. PTH also has many fragments with potential clinical relevance, which may go unconsidered without MS-based measurement.

I've also conducted significant work in MS-based lipidomics. In this work, I developed multi-omic metabolomic and lipidomic methods, including their translation into biomedical and environmental applications to predict risks to human health. Notable projects include monitoring the effects of environmental exposures on human and marine life, predicting health risks for diseases, such as type 1 diabetes and melanoma, as well as the first interlaboratory lipidomics study, which assessed lipid measurement variance to develop a standard reference material (SRM).

As for the future, I expect to see MS incorporated into a number of broader clinical applications. A key element of this will be the transition from single analyte biomarker assays to quantitative panels able to measure multiple biomarkers and thus assess numerous disease states simultaneously.

EVERY SECOND COUNTS – NEWBORN MASS SPEC SCREENING

By Donald Chace, Chief Scientific Officer at Medolac Laboratories – one of the primary developers of newborn metabolic screening using tandem MS

My main focus has historically been metabolite identification – detecting rare, inherited metabolic disorders through "newborn screening." In fact, my team developed a tandem MS technique for the detection of phenylketonuria – an inherited metabolic disorder caused by the toxic buildup of phenylalanine in the blood that can lead to nervous system damage – from newborn dried blood samples. Our method works by analyzing the phenylalanine:tyrosine ratio within 24 hours of birth. We have since expanded these tests to study further inborn errors of metabolism.

Confounders complicate the task, however; many false results in newborn screening are due to abnormal metabolite elevation not caused by inherited disease – especially in premature, very-low-birth-weight infants. Why? In part because of immature systems, and in part due to the practice of nutrition, where the goal is to get an extraordinarily tiny

baby to grow – either of which can result in abnormal metabolism and toxicity that mimics metabolic disease. The goals of our research have been to define baseline values and understand what causes abnormal profiles that are not of genetic origin.

Because our MS method is used to measure multiple metabolites in newborn screening, it is the first true metabolomic application. And the data processing is as essential as the method itself. Each metabolite detected requires quantification and standardization (using stable isotopes), which converts an ion signal intensity to a relative ratio, and finally to a concentration. Once completed, it is referenced to population means and cutoff ranges. Because each disease exhibits a different pattern, these concentrations must be interpreted from metabolite concentrations relative to one another (a key example being the phenylalanine:tyrosine ratio mentioned earlier).

High-performance LC can also be used for such approaches, but the tandem MS screening approach I developed ditches the chromatography, which takes longer per analysis and makes high-throughput analysis challenging.

Dried blood samples offer a number of advantages, including simplified transport, lower risk of infection, and the low volumes needed (around 10 microliters, compared with around ten times that volume from a heel stick). Such a difference is, of course, highly significant in the case of newborns.

Looking forward, I'd suggest that correlation of blood chemistry acquired by MS with genetics and lifestyle choices will allow us to identify optimum nutrition for growth and help avoid fat storage, marking the beginning of a true age of personalized nutrition – and medicine.

THE THERAPEUTIC PROMISE OF PROTEOMICS

By John Yates, Professor, Department of Molecular Medicine, The Scripps Research Institute, CA, USA

The use of MS in clinical chemistry is growing rapidly. It is already the dominant clinical method in a limited number of applications, including newborn screening for metabolic disorders and bacteria identification, and many other applications, such as vitamin D and insulin-like growth factor-1 testing. These tests are being increasingly being performed with MS. A broader implementation of MS technology in a clinical setting may require a "killer" application that cannot be achieved with other methods – 3D proteomics may be just that application.

Most disease diagnostics are currently based on the presence/absence or increase/decrease of target molecule(s) – often a protein. Yet, the development of 3D diagnostics, where diagnosis is based on disease-induced conformational changes, may improve test specificity. 3D proteomics, an MS-based method that measures protein conformations on the proteome scale, seeks to determine whether disease status or associations can be predicted based on these conformations, and whether they can be reliably measured.

Protein misfolding drives many diseases, including Alzheimer's, Lewy body dementia, cystic fibrosis, and cancer, but our current understanding of this comes primarily from in vitro measurements of protein structure. We are pursuing an improved understanding of in vivo protein misfolding in these diseases with MS-based 3D proteomic methods, which quantify protein conformations using surface accessibility and cross-linking. My laboratory is currently studying in vivo folding of the cystic fibrosis ion transport regulator (CFTR) when affected by various non-trafficking mutations, and under different kinds of rescue conditions, including drug treatment. A number of analytical techniques have contributed to this research, but the implementation of 3D proteomics to examine CFTR confirmation in the context of the whole in vivo proteome promises to significantly advance our mission, opening doors to conformational 3D diagnostics.

Despite the utility of a 3D proteomics strategy, its scale remains limited today. Improvements in MS and related software for mapping quantitative MS data onto crystal structures have been helping to drive the technique's applications, but getting 3D proteomics to work across entire, complex proteomes is a work in progress. In addition to the diagnostic potential of these methods, they provide important insights into the basic biology associated with protein misfolding diseases – and new avenues for structural drug development.

Other conformational methods are being developed; certainly, we are not the only ones working on this approach. This is a growing area with great potential. To date, conformational diagnostics have been implemented principally through antibodies designed to bind to specific protein conformations or contrast agents used in imaging methods. Conformational antibodies are tricky to make and imaging methods provide confirmation of disease. Diagnostic methods based on protein conformations using methods like 3D proteomics in an easily obtained biofluid like plasma could potentially provide earlier diagnosis, if protein signatures can be found. Within the next ten years, we hope to provide a new parameter for the proteome by measuring its conformational alterations as a function of disease.

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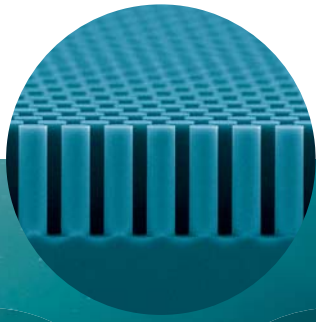

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UNDERSTANDING DEVELOPMENT, ONE CELL AT A TIME

By Peter Nemes, Department of Chemistry & Biochemistry, University of Maryland, College Park, MD, USA

My lab builds microanalytical MS instruments to study how cells orchestrate molecular programs as they give rise to complex tissues, organs, and organisms during normal and impaired development. Understanding these mechanisms is key to identifying biomarkers and developing specific and sensitive assays and therapeutics – all key to advancing personalized medicine. The molecular mechanisms uncovered could, for example, be used to grow tissues or organs for clinical applications on demand.

We have constructed ultrasensitive instruments to measure metabolic and proteomic reorganization in single differentiating cells and cell clones in the South African clawed frog (*Xenopus laevis*) and zebrafish, as well as single neurons and functionally important nuclei in the mouse brain. By conducting such experiments, we are unraveling the incredible complexity of development at the level of single metabolites' effects on embryonic cell fate and organogenesis. In fact, our MS approach allows the acquisition of single-cell omics data across the entire embryo; we were recently able to identify chemical differences underscoring embryonic patterning during *Xenopus* development.

How do we do it? We perform microdissection or use fine-fabricated capillaries to collect very small quantities of material from individually targeted single cells in live embryos. These custom-built, electrophoresis-based instruments are able to analyze samples as small as 1/10,000th the size typically required for contemporary spectrometers and related analytical sample processing workflows; our new-generation electrospray ionization interfaces effectively ionize these biomolecules with ~200 zeptomole sensitivity. Molecular compositions identified by MS then allow us to form hypotheses, which we test through functional biology experiments.

The details unveiled will hopefully open the door to inducing specific types of tissues for medical applications in the future. To help maximize the impact of our studies on translational research, we collaborate with numerous experts in cell biology, developmental biology, cancer biology, genetics, animal sciences, neuroscience, and so on – in both industry and academia. We have several projects on understanding the molecular aspects of cancer and impairment in embryonic patterning, hearing, vision, circadian cycle, and stress. Alternatively, the information we extract may allow us uncover molecules in the body (for example, natural metabolites) and in the environment (for example, toxins) that may impact embryonic development.

Our research brings many challenges – from maintaining a healthy colony of live frogs (!) to building and using complex MS instruments. But the potential knowledge to be gained – and its vast applications in medicine and elsewhere – mean that we relish facing those challenges head on.

Besides conducting our own original research using our technology, we also want to empower other investigators who can benefit from ultra-sensitive measurements. And so, it is highly rewarding to see that our tools and approaches have been adopted or adapted by several laboratories thus far.

Step Up For Cannabis Processing

From jelly babies to aromatic flowers – cannabis products can be a complex material to work with, in more ways than one. Kate Monks, Head of Applications & Academy and Quality at KNAUER, explains how the company jumped regulatory hurdles to develop a suite of systems that allow analysis and easy scale-up of cannabis purification.

How did KNAUER first get involved with cannabis?

Our involvement in the field was driven by feedback from our customer base. From the mid-2010s, customers and distributors started making noises about cannabis; by 2017, the demand was too loud to ignore!

At first, we were cautious – working with cannabis means a tremendous amount of paperwork and regulatory restrictions (1). But from a technology standpoint, it's a great fit for us and we knew we could serve this market well. We are known for the quality and reliability of our high-performance liquid chromatography (HPLC) instruments, and those are important attributes for customers in this emerging sector.

We decided to take the plunge and, three years on, we have a suite of three cannabis-specific HPLC systems at three different scales – quality control, purification, and production.

You have been busy! Where did you start?

We started small and scaled up over time, accumulating licenses (and enhanced security!) along the way. First, we developed the Cannabis Profiler, which allows quick and easy determination of six important cannabinoids (in line with the German Pharmacopoeia). Then we went on to develop more sophisticated analytical methods for up to 16 cannabinoids. We then extended our license to include larger samples, allowing us to move up to preparative-scale HPLC. The resulting Cannabis Purifier makes it straightforward to produce high-purity starting materials for applications in the pharmaceutical industry, for example. Finally, we moved into larger-scale continuous liquid chromatography, with the simulated moving bed (SMB) chromatography-based Cannabis Producer, designed for high-throughput purification.

Of course, we were not starting from scratch: all three products have our well-established AZURA® HPLC systems at their core.

What are the challenges faced by your customers in this area?

From the practical side, the matrix is typically the biggest challenge. There are some technical challenges in working with any plant material – in particular, sample preparation is often difficult, requiring multiple extraction steps. That means that the process has to be absolutely reproducible; otherwise, any differences will be amplified at each stage – a problem that is compounded once you move up to preparative and continuous scales.

However, the greatest hurdle by far is regulation. Just last week we had to cancel a planned project because – although both sides have a license to work with cannabis – we were unable to obtain a special license to transport the material from their lab to ours. While it is exciting when shipments arrive with an armed police guard, regulations are not always conducive to easy collaboration in this area. As license extensions, amendments and renewals are relatively longwinded, it is important to plan enough time (and patience) into these projects.

How do you tailor your products to this market?

We've been involved in projects with customers from industry, local pharmacies, and law enforcement. Many do not have chromatography expertise within their organization. So we aim to make our systems user-friendly – as close to "plug and play" as we can. We are also ready and willing to provide technical support and advice – particularly at a preparative scale, where our scientists often help set up the application and make sure all is running smoothly.

What sets KNAUER's solutions apart?

Crucially, we offer the ability to go up to a continuous production level using SMB technology. Systems are modular, so a semi-preparative scouting system can be upgraded to a preparative scale relatively easily.

What is the worst thing about working with cannabis?

The bad jokes! People assume that we are getting high in the lab or ask if they can have a sample. On the other hand, saying you work with cannabis is a real conversation starter at a dinner party....

What keeps you going when faced with a mountain of red tape or another bad pot pun?

Cannabis is a fascinating area because attitudes have shifted so dramatically in the last decade. I think it's great that we're opening up and moving away from fear, and towards respect and a better understanding of the plant. It's a new frontier, and that's why I do analytical science – to discover more about the world and to help keep it safe. I believe analytical science is a tool for humanity to achieve continuous improvement.

Reference

1. K Monks, "Regulation Rigmarole", The Cannabis Scientist (2019). Available at: https://bit.ly/2Ta3Zf0.

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INSIDE

36–38
Inductively Coupled Plasma Chef
Lu Yang discusses her career in chemical characterization by ICP-MS, and we take a brief look at the technique's development through time

Inductively Coupled Plasma Chef

Lu Yang is a chemist-come-cooking icon who is bridging gaps in our fundamental knowledge of the elements, one ICP-MS experiment at a time…

What are your main scientific responsibilities?

Currently as a Senior Research Officer at the National Research Council Canada (NRC), I've conducted leading research in inductively coupled plasma mass spectrometry (ICP-MS) and multicollector (MC)-ICP-MS for over 20 years. My main responsibilities in this role? Development of MC-ICP-MS for the accurate and precise isotopic characterization of materials for Certified Reference Materials (CRMs) purposes (including study of mass bias and mass bias corrections), representing the NRC in participating Consultative Committee for Amount of Substance (CCQM) intercomparisons to demonstrate the measurement capabilities of Canada, and – of course – communication of our findings via the usual channels – publications and conference presentations! Beyond the NRC, I also act as an editorial board member for the Journal of Analytical Atomic Spectrometry.

Which projects are you most proud of?

One is determining the atomic weight of ^{28}Si-enriched silicon to give a revised estimate for the Avogadro constant (1) – an international endeavour involving a few national metrology institutes, with the aim of determining the Planck constant and supporting redefinition of the kilogram.

Another was the use of MC-ICP-MS with the regression mass bias correction model to determine osmium isotope measurements (2); osmium isotope ratio measurements are somewhat complicated by severe memory effects, and our method provided the first calibrated measurements since 1937! Our results have also been adopted by IUPAC as the best available isotopic composition measurements – as is also the case for our results using a regression model and full gravimetric isotope mixture model for isotopic measurements of lead (3).

I also played a key role in determining the calibrated isotope ratio measurements of iridium (4) and hafnium (5), recently. I'm very proud and happy to be able to say that I made such vital contributions to determining these standard atomic weights. As we chemists are aware, such measurements are necessary for the conversion of mass fractions to moles, underpinning a great deal of our chemical knowledge.

What attracted you to research using MC-ICP-MS?

Both thermal ionization MS (TIMS) and MC-ICP-MS can be used to conduct high-precision isotope measurements. In the past decade, however, applications of MC-ICP-MS have increased significantly, owing to simple sample introduction, high ionization efficiency, and high sensitivity. Thus, in spite of the greater (approximately ten times greater) mass bias exhibited by MC-ICP-MS versus TIMS and subsequent need for correction, we at the NRC chose to apply MC-ICP-MS for our isotope ratios measurements. At the moment, we're applying the technique alongside a regression model to verify early isotopic CRM measurements – which may be subject to questions regarding their quality and validity – and are planning to further develop high-precision and high-accuracy measurement methods for other elements that lack calibrated isotope measurements or standards.

Where do you see the technique in 10 years' time – and what advances are needed to get there?

We have witnessed the rise of MC-ICP-MS for isotope ratio acquisition in a wide range of fields, from archaeology to provenance studies, medical science, nuclear and forensic sciences, geoscience, and studies of the environment. Over the next 10 years, I anticipate an explosion of these applications, particularly in medical and environmental fields. Regarding the advances needed? A full understanding of mass bias in MC-ICP-MS would be a strong start. Though mass-dependent fractionation is widely acknowledged, the reporting of mass-independent fractionation for some elements – which has a huge impact on mass bias correction models – indicates a need for improved understanding. The development of Si-traceable isotopic standards and state-of-the-art correction models is needed to push this area of metrology forward – alongside suitable instrumental advances!

Beyond the lab you have a successful cooking channel online – tell us more…

I always enjoyed cooking, but only got seriously invested in it after my son Maomao (a popular Chinese nickname, meaning "sweetie" in English) was born over 20 years ago. He was a very fussy eater and I had to create a lot of different recipes to please him. Given his name, my nickname soon became "MaomaoMom"… And this later became the name of my cooking blog, which I started to share my recipes after a friend suggested I should. Though the blog began in Wenxuecity, it quickly became popular among overseas Chinese, and I started my own website (Maomaomom.

A BRIEF HISTORY OF ICP

1940S
GI Babat

First experiments in induction-coupled plasma generation, describing electrical and magnetic properties, as well as circuit requirements and general appearance of capacitive and induction-coupled plasma (1)

1961
TB Reed

Flowing atmospheric pressure ICP developed for wound-healing applications, using a high-power induction torch source to grow refractory crystals and protecting the torch wall with a stream of argon (2)

1964
S Greenfield, Jones & Berry

Development of annular ICP suitable for use as a spectroscopic source (3) and filing for US patents

1965
RH Wendt & VA Fassel

ICP torch with laminar flow described, providing reduced turbulence and greater stability with low detection limits (4)

1969
GW Dickinson & VA Fassel

Detection limits established for annular ICP

1974

First commercial ICP-atomic emission spectroscopy instrument developed

1975-85

Mushrooming utilization of ICP approaches, driven by the advent of end-on observation (J Robin and C Trassy) in 1975, significant instrumental advances and the characterization of spectral and matrix interferences

1990S – TODAY

ICP experiments shift into routine use, with massively expanded applications. Instrumentation experiences cost reduction in the 2000s, and alternative plasmas (nitrogen, for example) hit the market in the 2010s.

References

1. *GI Babat, Inst Elec Eng (London) J 94, 27 (1947).*
2. *TB Reed, J Appl Phys, 32, 821 (1961).*
3. *S Greenfield et al., Analyst, 89, 713 (1964).*
4. *RH Wendt & VA Fassel, Anal Chem, 37, 920 (1965).*
5. *RS Houk et al., Anal Chem, 52, 2283 (1980).*

"There are a number of similarities in my approach to cooking and chemistry... At the end of the day, I guess I'm essentially conducting experiments in either setting!"

com) with the help of another friend in 2011. I've received many compliments on my dishes over the years, and today the website has over 43 million views! I've also published a number of books (electronic and hardback) and was interviewed by the Canadian Broadcasting Corporation Radio's All in a Day host, Alan Neal, and producer, Christine Maki, about the channel in November 2019.

If you could apply an analytical technology in your kitchen, which would it be and why?

Definitely a balance – to provide accurate and easily followed recipes for my fans.

In fact, there are a number of similarities in my approach to cooking and chemistry; for example, I might repeat cooking of a dish a small number of times with altered ingredient weights until I reach (as I'd say in the lab) optimal conditions. At the end of the day, I guess I'm essentially conducting experiments in either setting!

References

1. *L Yang et al., "Determination of the atomic weight of ^{28}Si-enriched silicon for a revised estimate of the Avogadro constant", Anal Chem, 84, 2321 (2012). DOI: 10.1021/ac203006jZ. Zhu, J. Meija, S. Tong, A. Zheng, L. Zhou and L. Yang, Anal. Chem., 2018, 90, 9281-9288.*
2. *Z Zhu et al., "Determination of the isotopic composition of osmium using MC-ICPMS", Anal Chem, 90, 9281 (2018). DOI: 10.1021/acs.analchem.8b01859Z. Zhu, J. Meija, A. Zheng, Z. Mester and L. Yang, Anal. Chem., 2017, 89, 9357-9382.*
3. *S Tong et al., "High-precision measurements of the isotopic composition of common lead using MC-ICPMS: comparison of calibration strategies based on full gravimetric isotope mixture and regression models", Anal Chem, 91, 4164 (2019). DOI: 10.1021/acs.analchem.9b00020*
4. *Z Zhu et al., "Determination of the isotopic composition of iridium using multicollector-ICPMS", Anal Chem, 89, 9375 (2017). DOI: 10.1021/acs.analchem.7b02206*
5. *S Tong et al., "Determination of the isotopic composition of hafnium using MC-ICPMS", Metrologia, 56, 044008 (2019).*

Invigorating Industry

The Royal Society of Chemistry (RSC) is extending a hand to industry chemists in 2020 – how can they support your research and development?

The RSC is a professional body that aims to advance excellence in the chemical sciences. As a not-for-profit organization, they invest any surplus income to achieve charitable objectives in support of the chemical science community. We spoke with Andrew Waterworth (Industry Engagement Manager for the RSC) to find out more.

What's the main focus of your role with the RSC?

The RSC's commitment to academic research is widely apparent, but we must also ensure that every great innovation has the potential to become a commercial reality. As Industry Engagement Manager, I work primarily with small-to-medium sized enterprises (SMEs) in the chemical industry – helping them access RSC support. Our support takes many forms, and – having obtained experience across many industry sectors myself – I'd say I'm well placed to understand a business' needs and guide them towards their full potential. I deal with stakeholders ranging from multinationals to regional catapults and trade associations to universities so that I can stay abreast of the whole field, meaning I can connect people to the right networks to enable growth.

Why is it important to support industry scientists?

Chemistry is "the industry of industries"; industrial chemistry not only provides a foundation for everyday well-being, but also provides stability in our economy. In the UK alone, the chemical industry contributes an annual turnover of about £50 billion. And, given that the majority of chemical companies in the UK are SMEs (around 97 percent), the need to support these companies by providing a voice that can influence policy, funding and government priorities is clear. Without this support, a great idea, concept, or innovation could fall through the cracks.

How could industry scientists benefit from RSC membership?

We have a dedicated in-house careers team comprised of specific chemistry specialists who can aid continuous professional development in a huge number of ways – including careers consultations, help with CV writing, and overseeing our professional mentoring scheme. We also offer professional development support for those in their early career, through RSciTech and RSci (which are highly sought-after by employers), and skill development grants. For those working on research and development in a chemical sciences SME, we have our EnterprisePlus scheme. The scheme supports companies in networking, profile building, recruitment support, access to funding options, and much more. There are vouchers available to employees of registered companies for training and skills development, and grants to support intern or apprenticeship schemes.

Our Synergy program brings experts together to solve complex chemistry challenges in industry, although this idea may sound simple, finding common ground between businesses that operate in completely different markets isn't always straightforward. And that's where we come in by facilitating collaboration across industry. Some of the big challenges in industry – like corrosion and sustainable material consumption – can only be solved through long-term collaboration between industry, academia, government, and with society. We provide a platform that unites different perspectives to facilitate mutually beneficial collaboration.

How do you plan to reach out to industry scientists in 2020?

We'll be sending numerous support teams to exhibitions and conferences across the world in the coming year, including Analytica and Arablab – the full list is available on our website.

Our Policy team is gathering evidence from industry, academia and trade associations to inform the UK Chemicals Strategy, and presented our recommendations in January at the Westminster Briefing.

We also run our Chemistry Means Business event annually, which hosts over 200 attendees and more than 60 SMEs, providing a great platform for European emerging technology companies. Attending these events ensures industry researchers are aware of the unique advantages made available through the RSC – and how these benefit their organization in the long term.

What is your unique selling point?

RSC Select is a great example of the flexibility apparent in our support. This service offers on-demand access to groundbreaking research in chemistry across disciplines. In this way, the RSC can continue its commitment to advancing excellence in chemistry.

Personally, I think the standout benefit of the RSC is the fact that it provides something for everybody. As well as tailored membership offerings for all stages of a chemist's career, we provide a variety of products and services to non-members. The RSC is for all.

To find out more about the RSC and their plans for industry, visit www.rsc.org. If you're interested in joining the RSC as an individual member, email membership@rsc.org. To enquire about EnterprisePlus, email enterpriseplus@rsc.org.

Business

Economic drivers
Emerging trends
Business strategies

One Vision, One Culture, One Team

Agilent CEO Mike McMullen tells us how he's investing in innovation and why culture is the key to reaching business goals

How do you describe what you do – and analytical science in general – to those unfamiliar with the field?

Highlighting analytical applications tends to start interesting conversations that most people can easily relate to. After all, analytical science touches all of our lives in many ways. I point out that the air we breathe, the water we drink, the food we eat, the drugs we take are all assumed to be safe – and link it back to the science. Once I've introduced them to the hidden world of analytical chemistry, I can switch gears and introduce the role of Agilent, which I describe as a mission driven company. For example, I'll talk about how we help researchers find new ways to treat disease by providing the underlying tools and technology.

In recent years, we've had a big push into the diagnostics arena – heralded by our acquisition of Dako in 2012. Now, we can also highlight the link between a drug that people may have seen on a television commercial and the companion diagnostic that supports its use. Being involved in the fight against cancer connects us to a very real world.

These messages also resonate within the company. We're all really motivated by the fact that we do make a difference – something that's said more often than it's true.

What other motivating stories stand out for you?

One that immediately comes to mind is a compelling story I heard during my first management meeting as CEO back in 2015. As part of the proceedings, we invited a student from the University of California, Berkeley, to speak. She began by telling us how her presence on that day was only made possible by the technologies brought to market by Agilent. An athlete and non-smoker, the woman had been diagnosed with lung cancer. Genetic testing – enabled by our genomics products – revealed a mutation that could be treated by a specific drug. The whole room was completely silent.

Another example: we've just built a second facility that produces GMP-grade oligonucleotides for RNA-based therapeutics – a new class of drugs that target rare diseases, with often truly life-changing results. A company called Alnylam produces one such drug, patisiran (Onpattro) – the first small interfering RNA-based therapeutic approved by the FDA – which treats polyneuropathy in a severe and fatal disease called hereditary transthyretin-mediated amyloidosis. We supply Alnylam's oligonucleotides for patisiran, so we're now part of another compelling story – but the list goes on and on.

I really want my employees to be proud of the company they work for – and it turns out that's not such a tough job!

As a leader of a company that must innovate to succeed, how do you maintain momentum?

Innovation is in our DNA at Agilent – and that philosophy must extend beyond the R&D community. Yes, we must develop products at the cutting edge for our customers, but we must also be innovative when it comes to how we work with our customers – and how we run internal operations. It's easy to talk about these things – but do you actually run the business this way?

When I first took on this role in 2015, I discussed profitability goals with the investment community, as you might expect. "Well, Mike," they said. "Why not just cut your R&D budget in half, and you'll reach your goals much faster…

"That would destroy who we are," I replied. "We are an innovation-driven company." And that's why we are willing to invest such a high percentage of our revenue into R&D – over $1 billion in the next three years. We're also the only company in our space with a long-term basic research effort – Agilent Labs, staffed with world-class scientists developing the technologies of the future.

Innovation really means thinking carefully about the challenges that our customers face – both scientifically and economically. I call it "innovation with purpose."

So how do I keep the vision alive? First, we talk about it. Second, we fund it. And third, we recognize it. For example, we have an annual President's Award for innovation, with two top prizes – one for the most innovative technology development and the other for a process innovation. A couple of rounds of reviews produces ten teams who present their work at a special fair in Santa Clara. The two winning teams are announced at our version of the Oscars; both teams receive a financial reward, but I think most participants are more interested in the recognition.

What trends are driving innovation within Agilent?

Consider your smartphone – you're probably less interested in the underlying technology than the experience it enables. When it comes to analytical technology, while yesteryear's users may have built their own instrumentation, today's users simply want to ensure that it meets their workflow needs. Our technology is trending towards smaller, faster, easier to use, and better integrated – back to my analogy: everyone now has a far more powerful computer in their pocket than the one I had on my desk when I started at Hewlett-Packard...

Analytical instruments are tools that provide data, which can be turned into information that the user must be able to trust. And the more seamlessly the tool can perform that role, the better, which is why the latest generation of Agilent instruments feature smart capabilities that alert lab managers to the need for preventive maintenance. Today's users want more actionable information with fewer headaches – and that leads us directly back to my point about innovation with purpose.

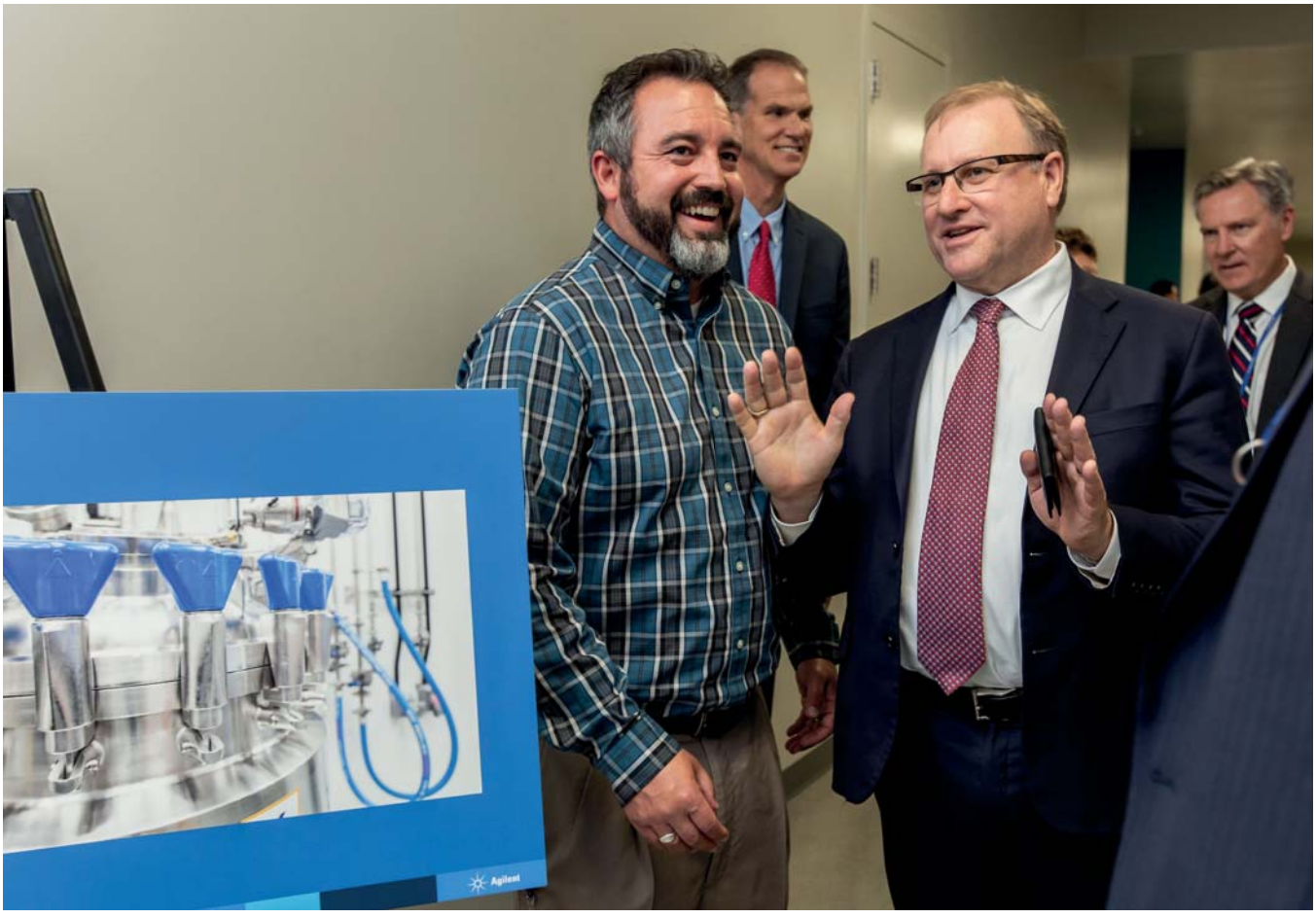
The scientists we serve have certain expectations that are set by their interactions in everyday life. How they shop online, search for information, receive customer support, connect with their technology – we must strive to mirror all of these aspects. And this is why we need that broader vision of innovation.

How does Agilent differentiate itself?

Funnily enough, a question oft-asked by investors is, "What's your sustainable competitive differentiation?" For me, it's all about the human element. We place a great deal of emphasis on our "One Agilent Culture," which is all about people truly working together as one team – and trusting each other.

All companies have great presentations about their amazing core values… But, at Agilent, we live them. When I became CEO, my number one priority was to improve certain aspects of our culture – the aforementioned drive towards collaboration and trust. If we trust


Agilent Technologies


Agilent

"What really makes it stand out for me is the technical capability and the passion of the people that call this place home."

one another in the company, it allows us to build trust with our customers. I honestly believe a major reason why Agilent has witnessed a rebirth in terms of growth and performance is because we are working together as one team on behalf of our customers.

The investors may be thinking: "Why is he talking about people and culture?" But clearly, companies are all about people. You joked earlier that "analytical scientists are people, too" – but that fact can get lost. We're having this conversation at the opening of this wonderful spectroscopy R&D facility on the Harwell Science and Innovation Campus in Oxfordshire, UK – and that's exciting. But, genuinely, what really makes it stand out for me is the technical capability and the passion of the people that call this place home. The people make the difference.

At the beginning of your career, did you ever envisage becoming the CEO of an analytical giant?

I can't remember ever looking that far ahead! And, in fact, when I dispense career advice, my first pearl is: "Don't over manage your career – because you never really know where it will take you." My second piece of advice: "Always follow the experience and accept opportunities to learn." I believe it's good to be naturally curious. When I finished my MBA at The Wharton School at the University of Pennsylvania in the 1980s, the next step should have been Wall Street. And though I had job offers on the table from investment banks, I recognized that I really didn't want to enter that world.

I wanted to work for a company with a mission – a company that developed and created a tangible product. At Hewlett-Packard, I knew that my ability to progress was only linked to my willingness to develop myself and take a few personal risks. I entered the company as a financial analyst, so perhaps dreamed of becoming the Chief Financial Officer one day… But as I moved through my career, grasping opportunities to gain experience, I ended up working in Japan as country sales manager for two years – an unforgettable experience… "What's a finance guy doing in Japan leading a sales team?!"

I learned that I had inherent leadership qualities – for one, I'm a big believer in the power of authentic communication. Next, opportunities opened up first in China and then the USA, where I had the chance to run a product line. "OK - so what's a finance guy – with sales management experience – doing running a technology business?!" When pushed, I used to say, "Well, I have a secret weapon: a chemist, who also happens to be my wife, so I go home and ask her!" More seriously, I really love technology but, rather than getting lost in the details, I'm passionate about what it can do for our customers.

Over time, I built up a track record of growing businesses and turning businesses around. When we created the new Agilent in 2015, I was asked to become the third CEO. Notably, my

"Everyone has the chance to grow and develop – and even become CEO one day. So why would they want to work anywhere else?!"

predecessors were both R&D engineers. And that links to another piece of advice: "Don't allow people to put you in a box or tell you what you can't do."

When new people join the company, I explain to them that I have been here for 35 years – unusual in itself – but my non-linear path also proves that everyone has the chance to grow and develop – and even become CEO one day. So why would they want to work anywhere else?!

In short, there are four constants throughout my journey: i) always going for experience over promotion (promotion will follow), ii) never compromising my personal values, iii) always being true to myself, iv) never allowing people to trap me with false walls.

What's your best moment as CEO (so far)?

Easy: when we received the results of one of our leadership surveys – about three years into our journey. Every six months, we ask all 16,000 Agilent employees how we're doing. We recruit an external consultancy team to analyze the results and compare us with the best out there. Our scores for employee engagement had grown significantly over that relatively short period; apparently, we were "best in class." It's great to make investors happy with rising stock prices, and to see customers reacting more positively to their experience with us. But I am most proud and satisfied by how our employees feel about working at Agilent – because that's really how we've achieved our other goals. There's plenty of information out there pointing to the fact that companies with highly engaged workforces do well. And it was great to have proof that I wasn't just being a delusional CEO...

I always tell my team, "The best is yet to come" And the fact that we're all "in it together" and pointing in the same direction? Well, that gives the words real meaning for everyone – me included.

In July 2014, I was asked by the Agilent board of directors to be the next CEO. And I remember flying home from California to New Jersey, thinking to myself, "Great – I've got the job. Now, what am I gonna do?!" It was then that I decided that the transformation of the company needed to begin with the people – with "One Agilent Culture." And the results of that survey made me realize that it was not only the right move – but respected by the whole team

A great deal of attention is on biopharmaceuticals and advanced medicines, but small molecule drugs are still highly important. What trends do you see – and how is Agilent innovating in this area?

First of all, the pharmaceutical market is the largest market for Agilent, at over 30 percent of our revenue. We have been working hard to become a broader supplier to customers in that market. You've somewhat stolen my thunder with your question. I was with the investment community a couple of days ago in London and everyone wants to talk about biopharma, which is very exciting and has high growth rates – and, of course, Agilent has solutions in that space. But I'm always very quick to remind people that small molecule pharma is not going away – and it is being driven by the need to lower costs across the world. And that means they need new tools that allow them to do more with less, or to be more efficient in QA/QC, for example. And here, at the spectroscopy R&D facility, we have innovative technology on display that tackles certain bottlenecks in pharmaceutical manufacturing. But, as I mentioned earlier, supplying the right tools is only one part of the solution. My fundamental business strategy for Agilent was not only to help our customers do great science, but also to help them with the operations and economics of the lab. And so, in addition to easier to use, digitally-integrated solutions with smaller footprints, such as the Ultivo triple quadrupole LC/MS system, we've got a whole series of new capabilities for laboratory managers; for example, the potential to monitor instrument utilization and peak run times, to provide troubled asset reports, and so on. Rather than supplying a pinpoint product to an analytical lab, we look at the whole ecosystem – and consider how we can not only integrate into it but also add real value.

Where is Agilent heading?

Whatever our customer's application needs, we want to provide the leading solutions. Agilent is well known for chromatography, MS and spectroscopy in the lab environment, but we are also investing in new businesses. Back in 2015, we recognized the fast-growing area of cell analysis, and so we've built up great new business in this space through a series of strategic acquisitions – most recently, BioTek – a leader in plate-readers and cell imaging systems.

As well as supporting our existing customer base, we will always push to be at the leading edge and follow where the science is headed. The Agilent story is far from over.

The 44th ISCC and the 17th GC×GC Symposia is a "hyphenated" meeting which will be held again in wonderful Riva del Garda (Italy), from 24 - 29 May, 2020.

Apart from the most recent advances in the fields of pressure and electrodriven microcolumn separations, and comprehensive 2D GC. This year particular emphasis will be directed to all Comprehensive Separation Technologies in combinations of capillary chromatography and 2D GC with various forms of MS… from unit mass to high resolution, and from single to hybrid analyzers. Consequently, both the importance and complementary nature of chromatographic and MS processes will be given to the sample preparation process, in both oral and poster sessions. The ISCC/GC×GC scientific program will be a rich one, it being characterized by:

- invited contributions from leading scientists reporting the latest most exciting developments
- keynote lectures from promising young researchers
- very active poster sessions
- discussion sessions
- workshop seminars presenting the most recent novelties in scientific instrumentation
- a world-class GC×GC course
- a world-class LC×LC course

Researchers in all areas relevant to the subjects of the symposia are invited to submit abstracts. As is traditional for the Riva meetings, the majority of presentations will be in a poster format and the Scientific Committee will select contributions for oral presentations. As always, many awards will be assigned in both the ISCC and GC×GC events, recognizing excellence in both established and young scientists, in oral and poster presentations. Exhibitors and sponsors are a fundamental part of the meeting (without them…Riva wouldn't be Riva!) and are encouraged to participate by reserving booth space, becoming a sponsor and to promote the ISCC and GC×GC events.

Last, but not least, the traditional "Riva" social program.

Please keep visiting our web site (www.chromaleont.it/iscc) for new information as it becomes available.

Looking forward to meeting you in astonishing Riva del Garda!

44TH INTERNATIONAL SYMPOSIUM ON CAPILLARY CHROMATOGRAPHY

AND

THE 17TH GC×GC SYMPOSIUM

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UHPLC Analysis of Commercial Monoclonal Antibodies at Elevated Temperatures Using YMC-Triart Bio C4

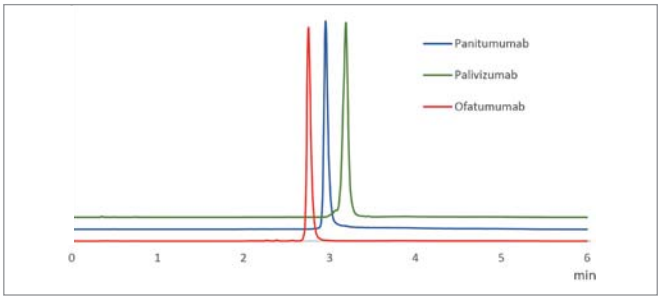

Figure 1: UHPLC analysis of different monoclonal antibodies using YMC-Triart Bio C4.

MAbs are becoming increasingly important in the treatment of different types of cancer and autoimmune diseases.

Intact antibodies are usually analyzed by IEX, SEC or HIC because of their high molecular weight. However, use of a wide-pore, temperature-stable stationary phase – such as YMC-Triart Bio C4 – can provide a successful analysis of MAbs in RP mode. Due to the extended temperature stability of YMC-Triart Bio C4, it is possible to use temperatures up to 90°C.

This application note, developed by the Department of Analytical Pharmaceutical Chemistry, University of Geneva, demonstrates the robust chromatographic method using the commercially available MAbs: ofatumumab (Arzerra®), panitumumab (Vectibix®) and palivizumab (Synagis®).

A YMC-Triart Bio C4 UHPLC column with a linear gradient (25–50% B) in 4 minutes is used. The application demonstrates that elevated temperatures such as 90°C result in higher recovery and sharper peaks for all three MAbs.

Learn more about YMC-Triart Bio C4 at www.ymc.de

Spotlight on... Technology

Compact Preparative System

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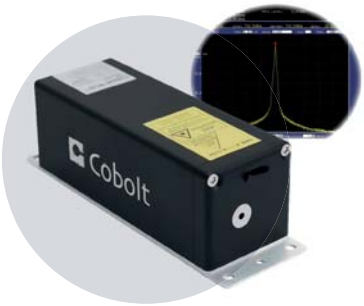
https://www.ecomsro.com/systems/compact-preparative



Robust 785 nm Lasers for Raman by Cobolt

HÜBNER Photonics – a leading supplier of all laser wavelengths to Raman – introduces the Cobolt 08-NLDM 785 nm, with enhanced spectral purity. HÜBNER Photonics now offers the widest selection of Cobolt lasers for Raman spectroscopy, and all with the same footprint. Run your system or experiment knowing the laser is dependable.

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CDS 7550S Thermal Desorption Autosampler

The CDS 7550S is a stand-alone, 72-position thermal desorption autosampler. Equipped with the second-generation autosampler platform, the CDS 7550S offers worry-free 24/7 automation. With the high-temperature 350°C oven, and the optional Peltier electric cooling module, the system is capable of handling C2-C44 level VVOC.

https://www.cdsanalytical.com/thermal-desorption-7550s

Highly Flexible Thermal Desorption Instrument: UNITY-xr™

UNITY-xr is a world-leading analytical thermal desorption instrument for the simultaneous analysis of VOCs, SVOCs and thermally labile compounds. UNITY-xr is perfect for any laboratory starting out in TD with low throughput requirements, or those needing a versatile thermal desorber for all their TD applications (accommodating tubes, canisters, or online).

http://chem.markes.com/TAS/UNITY

WITec alpha300 Confocal Raman Imaging Microscope Series

The WITec alpha300 series is a versatile, modular line of confocal Raman imaging and correlative microscopes that offer industry-leading speed, sensitivity and resolution – simultaneously. Raman, AFM, SEM and SNOM systems can be configured to fulfill individual requirements, and reconfigured over time as experiments evolve.

www.witec.de/assets/WITec-alpha300-Brochure.pdf

CONTAMINANT CHARACTERIZER

Sitting Down With…
Stefan van Leeuwen,
President, Senior Scientist, Wageningen Food Safety Research, University of Wageningen, The Netherlands

What is the overarching theme of your work?

Environmental contaminant analysis is really the core of my work – particularly substances that persist in the environment for long periods. These so-called persistent organic pollutants (POPs) eventually enter our food chain, so they are of special concern for human health. I started my career studying polychlorinated biphenyls (PCBs) and brominated flame retardants with Jacob de Boer's group at Wageningen Marine Research, but, by the early 2000s, our international coworkers had pointed us towards a new pollutant of interest – perfluorooctane sulfonate. Soon many more per- and polyfluoralkyl substances (PFASs) were detected, and their study became a field in its own right. After 5 years at the VU University in Amsterdam, where I obtained my PhD developing analytical methods for detecting the occurrence of POPs in fish for human consumption, I started in my current position at Wageningen Food Safety Research, where research on POPs in food has continued.

Have there been any landmark moments during your time in the field?

In 2006, we published the results of the first international proficiency test for PFASs in environmental and human samples. The data was very scattered and not comparable between labs; it was obvious that these analytes required different analytical approaches than the field was used to. In the following years, enormous effort was made to improve method development – commercial standard providers have devoted considerable time and energy to developing high-quality standards and mass-labelled analogues. This has resulted in a huge increase in the quality of reported results, which will in turn improve our understanding of the effects associated with PFASs in the years to come. Regarding chlorinated paraffins, a new high-resolution MS (HRMS) and statistical approach from the Bogdal lab has recently provided researchers with a more powerful tool to probe these industrial contaminants in food.

What are the "tools of the trade"?

We use several techniques including LC-MS/MS and GC-HRMS to conduct targeted analysis of a number of environmental contaminants, such as dioxins, PCBs, and PFASs. Chlorinated paraffins in food present a particularly challenging phenomenon, requiring HRMS (Orbitrap) coupled with LC to ensure the resolution necessary for complete analysis.

What technological developments does the field need?

The OECD has published a list of over 5,000 PFASs; of these, we routinely analyze about 20 using a targeted LC-MS/MS approach. Although not all 5,000 PFASs may be relevant for food or environmental contamination, it's clear that a more holistic approach is needed. The solution lies in complementary approaches: in vitro effect assays, oxidizable PFAS detection, total organic fluorine detection, and untargeted identification. Several groups in our institute are joining forces to develop and combine these approaches, and so far, the results have been promising.

Elsewhere, the accumulation of contaminants in the "circular economy" is gaining considerable attention. When materials are recycled, undesirable substances like brominated flame retardants can be unintentionally introduced into products. We need to better understand how recycling processes lead to contamination and where these substances accumulate, which will – of course – require new analytical approaches.

What are the biggest misconceptions facing the field?

Some people say that environmental contaminants are no longer a problem. I disagree –evidence is mounting that even very low levels of contaminants such as dioxins, PCBs, and PFASs lead to subtle yet undesirable effects for organisms. Moreover, we've seen that chemical industries will cease production of a specific contaminant due to social, political, or environmental pressure, only to switch to another, similar compound down the line – potentially introducing yet another new contaminant to our food or drinking water. This surely provides more than enough evidence to support the importance of environmental analysis… And this importance will only increase over time.

What's next for your group?

I would like to further increase separation power when studying chlorinated paraffins by combining complementary analytical approaches. We hope to be able to separate individual isomers from mixtures of thousands of very similar compounds within a sample. This level of precision is crucial for food analysis, and to support toxicology studies into individual congeners.

Another important goal is to design strategies that will allow the identification of unknown PFASs. Untargeted identification of PFASs in food and environmental samples is currently very time- and resource-consuming; HRMS data evaluation is a particularly limiting step. Speeding up data analysis by using software and combinations of complementary techniques would not only be beneficial for studying PFASs, but also for identifying many other food contaminants.