DECEMBER 2019 # 83

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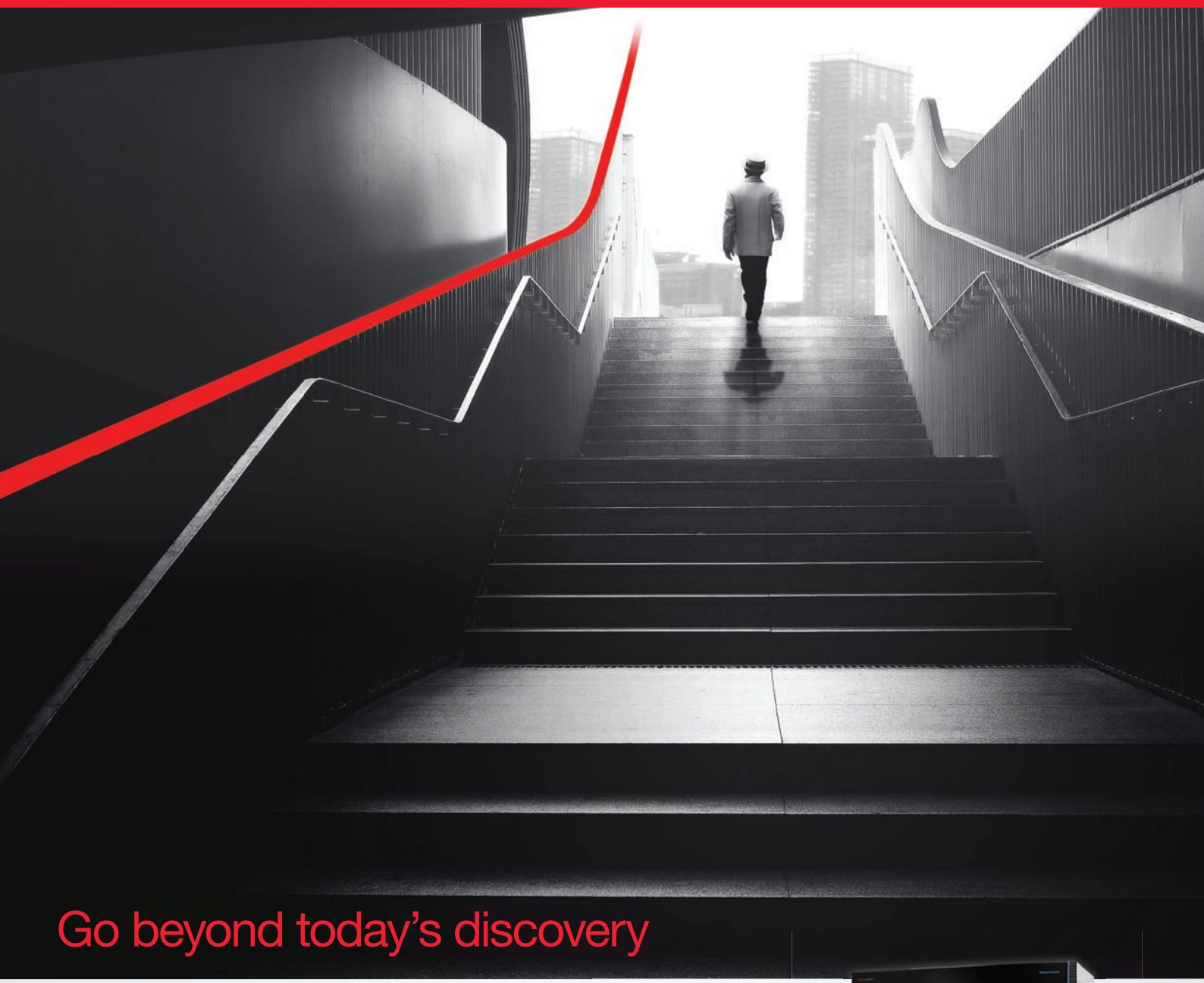

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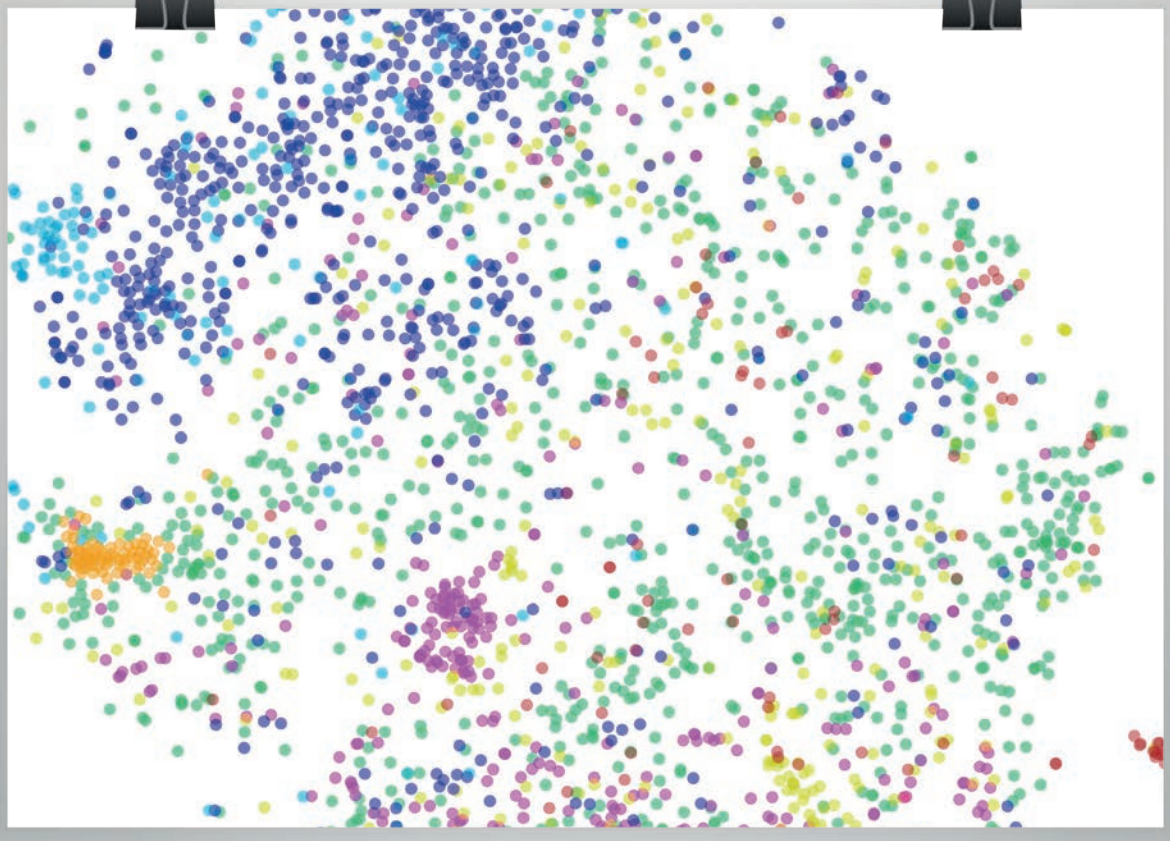

Sticking Together

Co-regulation map demonstrating associations between human proteins: nuclear (dark blue), nucleolar (pale blue), cytoplasmic (green), ribosomal (yellow), mitochondrial (pink) and secreted (red). Credit: Michael Schrader, University of Exeter, UK.

Reference: G Kustatscher et al., "Co-regulation map of the human proteome enables identification of protein functions", Nat Biotechnol, 11, 1361 (2019). DOI: 10.1038/s41587-019-0298-5

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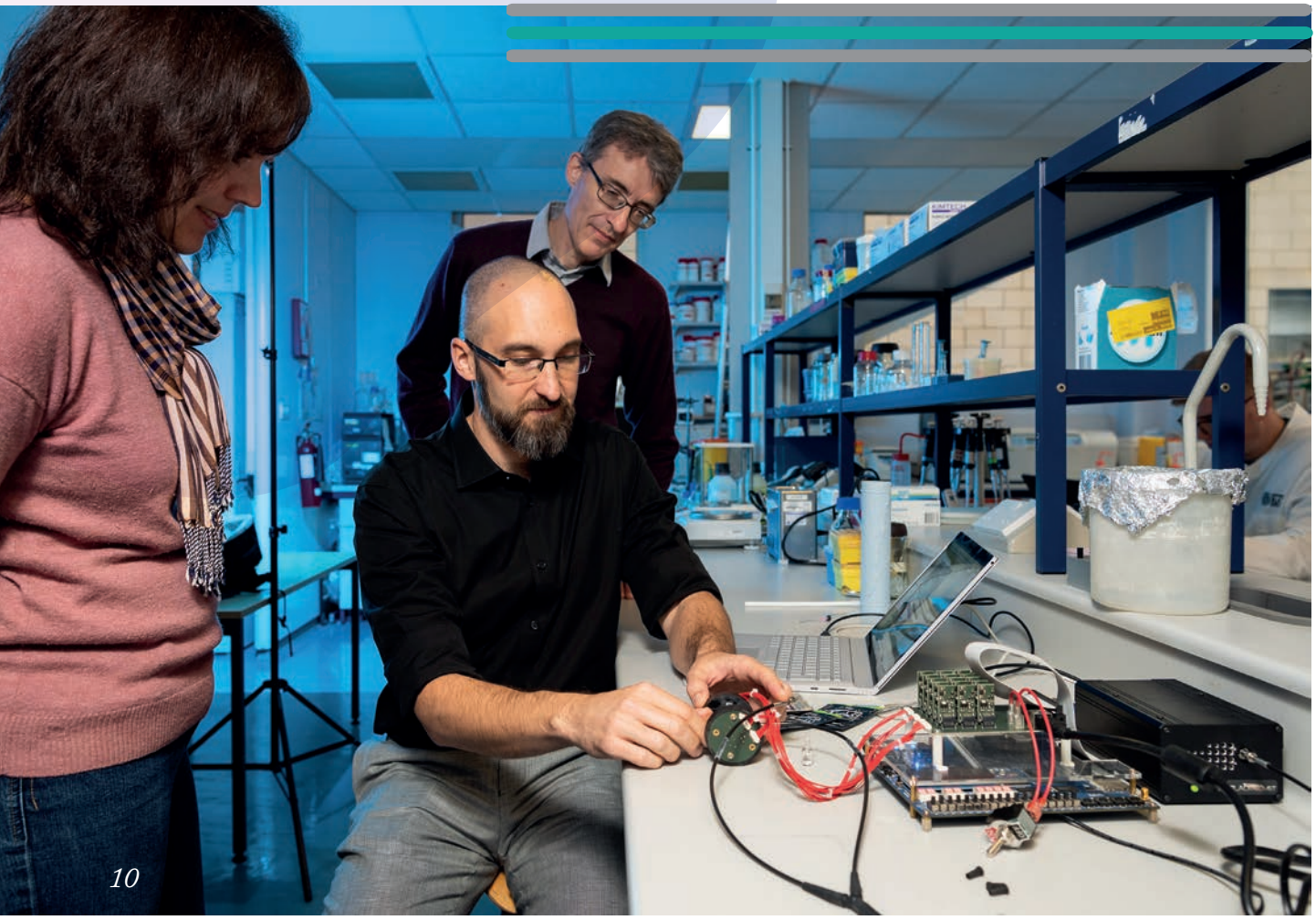

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ISSUE 83 - DECEMBER 2019

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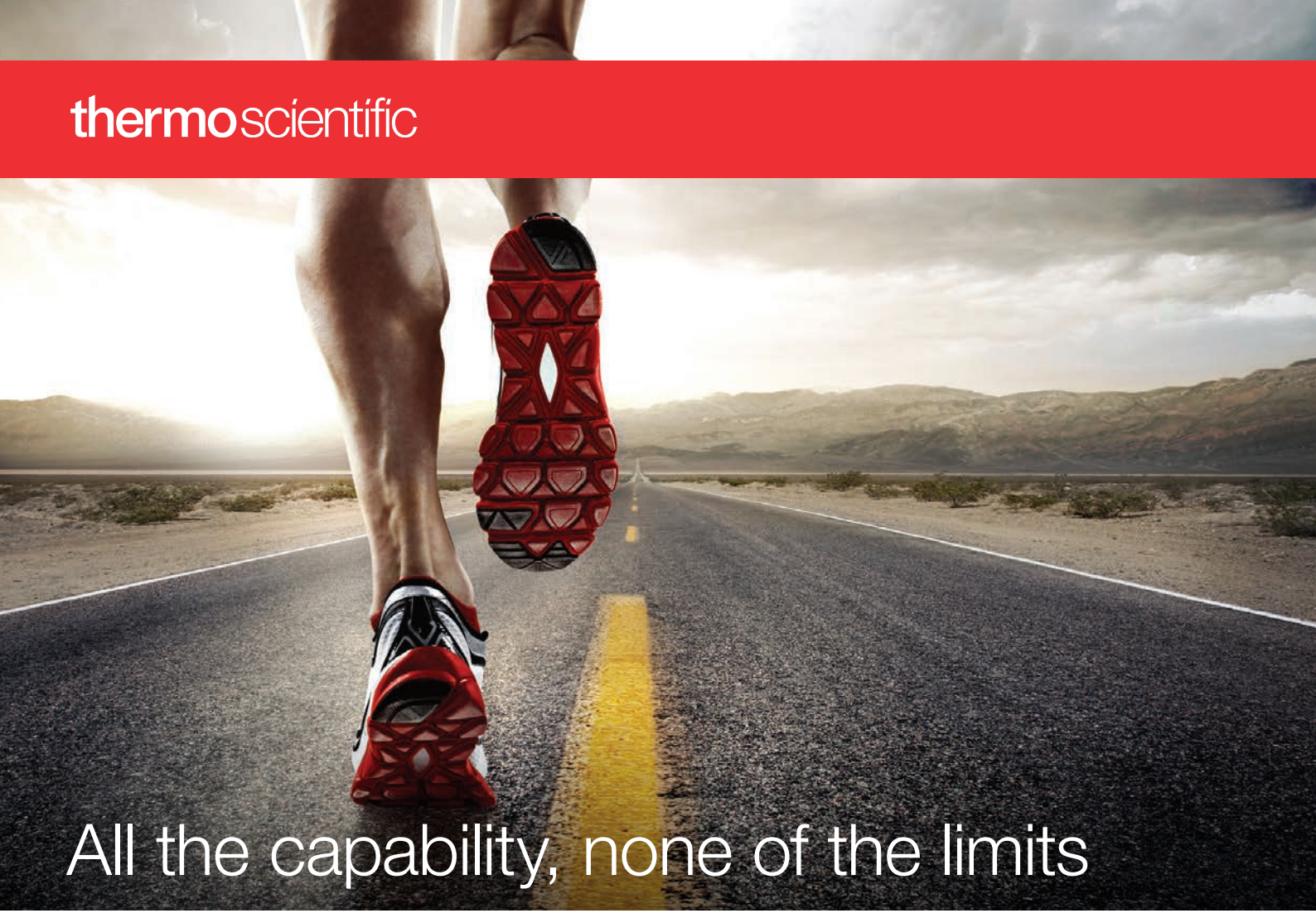

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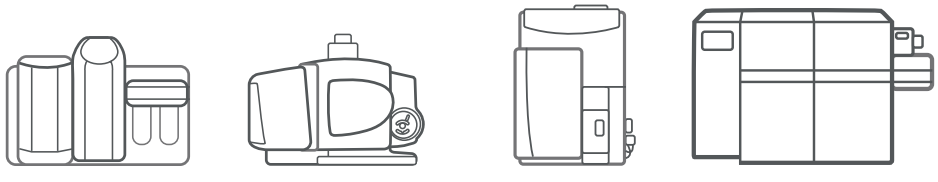

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A Call to Communicate

Public understanding of chemistry is lacking – but what does this mean for analytical scientists?

Chemists exist in bubbles, so to speak. We are educated among science enthusiasts, move into workplaces filled with graduates, and attend conferences that keep us connected with analytical minds around the world.

Outside the walls of our organizations, however, such discussion is scarce. Even the word "chemical" still incites fear among the public – a phenomenon branded "chemophobia" in a recent paper from Nature Chemistry. This phrase seems rather apt; 39 percent of 5,631 respondents surveyed in the same paper stated they "would like to live in a world where chemical substances don't exist" (1). I don't know about you, but the empty vacuum of space isn't the utopia I pine for.

A staggering 82 percent of the same sample was also unaware that synthetic sodium chloride and sea salt share the same chemical structure. Caught between the limited understanding of many citizens and the exponentially growing complexity of the field (see our feature on big data on page 32), it would be easy to give up entirely on communicating our research to the public. Why should we go the extra mile?

For one thing, public perception shapes political discourse and impacts the funding allocated to research. What's more, advances in research are bringing analytical power into public hands (as described by Michel Nielen in our October issue [2]) – as "citizen scientists" begin acquiring data from everyday settings, a rudimentary scientific knowledge could go a long way in preventing the spread of misinformation.

Communication and education are our greatest assets on this front. Many medical journals now request "lay summaries" alongside submitted manuscripts, which dispense key clinical data in an accessible fashion. Though such summaries might not be so suited to our field, I believe the movement could provide some much-needed inspiration. Efforts to communicate our research in a layman-friendly format would – at minimum – increase public awareness as to the existence and importance of analytical chemistry.

Education is a recurring theme in our December issue, with In My View articles from Victoria Samanidou and Michelle Misselwitz on the benefits of basic etymological and methodological insight, respectively. As usual, however, these articles detail efforts aimed at the practicing chemist.

Bringing analytical chemistry to the masses is a responsibility we should all bear. In time, these altered views could inspire the next pioneer in our field, or help drive political will to support scientific endeavors. So, what are we waiting for? The call to communicate is clear, and those heeding it could change the course of science (and history!) for the better.

Matthew Hallam
Deputy Editor

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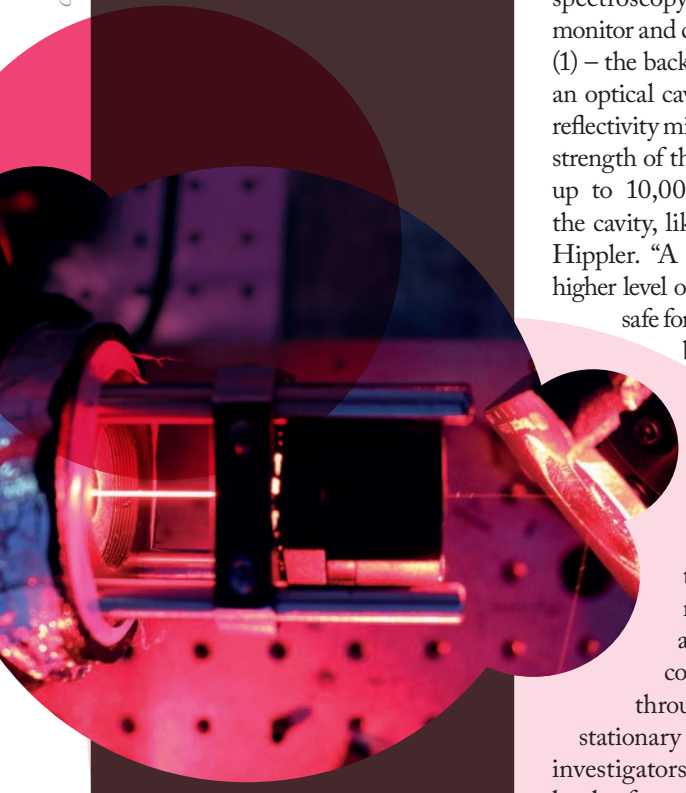
Upfront

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

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



Credit: George Metcalfe

CERS: a New Tool for Biotech

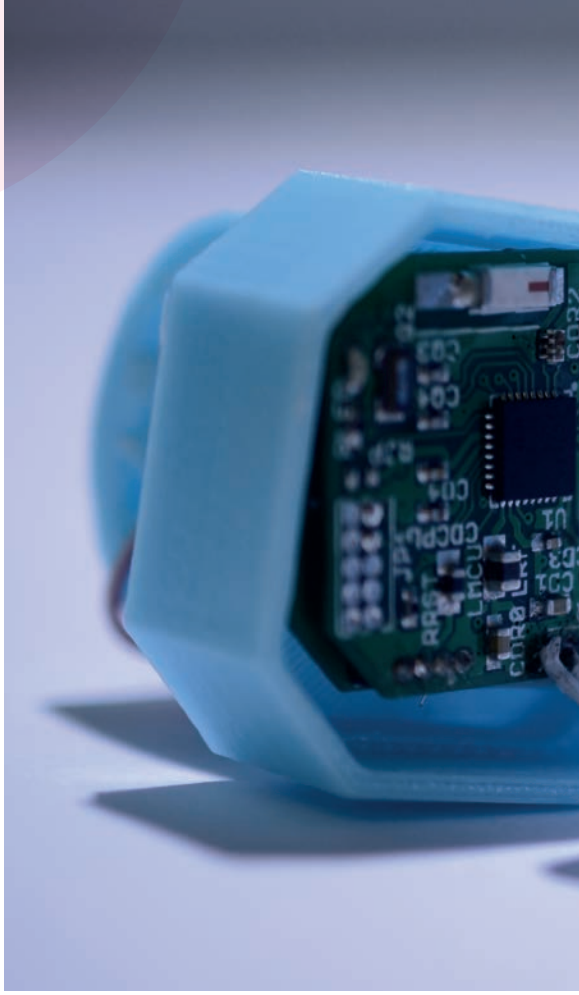
Is cavity-enhanced Raman spectroscopy the future of bioreactor monitoring?

Biotechnology. It's a broad term, representing a multi-billion-dollar industry that influences almost every aspect of our lives – from food and medicine production to biofuel manufacturing. Monitoring technologies play a central role in maintaining high standards and controlling processes, but current approaches are neither simple to use, nor cost-effective.

Now, Michael Hippler and colleagues (George Metcalfe, Saeed Alahmari and Thomas Smith) at The University of Sheffield, UK, have demonstrated for the first time that cavity-enhanced Raman spectroscopy (CERS) can be used to monitor and characterize bacterial growth (1) – the backbone of biotech. Employing an optical cavity composed of two high-reflectivity mirrors, the team amplified the strength of the Raman laser by a factor of up to 10,000. "Power accumulates in the cavity, like water in a reservoir," says Hippler. "A weak diode can generate a higher level of sensitivity, while remaining safe for routine use." CERS can thus be applied to monitor trace gases, including biologically relevant hydrogen, nitrogen and oxygen.

By using CERS in combination with carbon-13 sugar labeling to distinguish mixed sugar metabolism, the team was able to trace the growth of E. coli from the initial lag phase through exponential growth and stationary culture to cell death. To the investigators' delight, CERS delivered levels of precision comparable to existing approaches. "Here, we've demonstrated that CERS is amenable to in-situ multi-component analysis with excellent time resolution," says Hippler. "Historically, this kind of analysis would have necessitated the use of expensive GC- or MS-based instruments."

So, what's needed to make the jump from prototype to industry-ready technology? "To reach its full potential, CERS will need to be miniaturized, adapted for broader non-specialized use, and undergo further stabilization," says Hippler. No small feat, but the researchers remain confident that CERS prototypes will lay the groundwork for more sophisticated, spectroscopic-based approaches to large-scale bioreactor monitoring.



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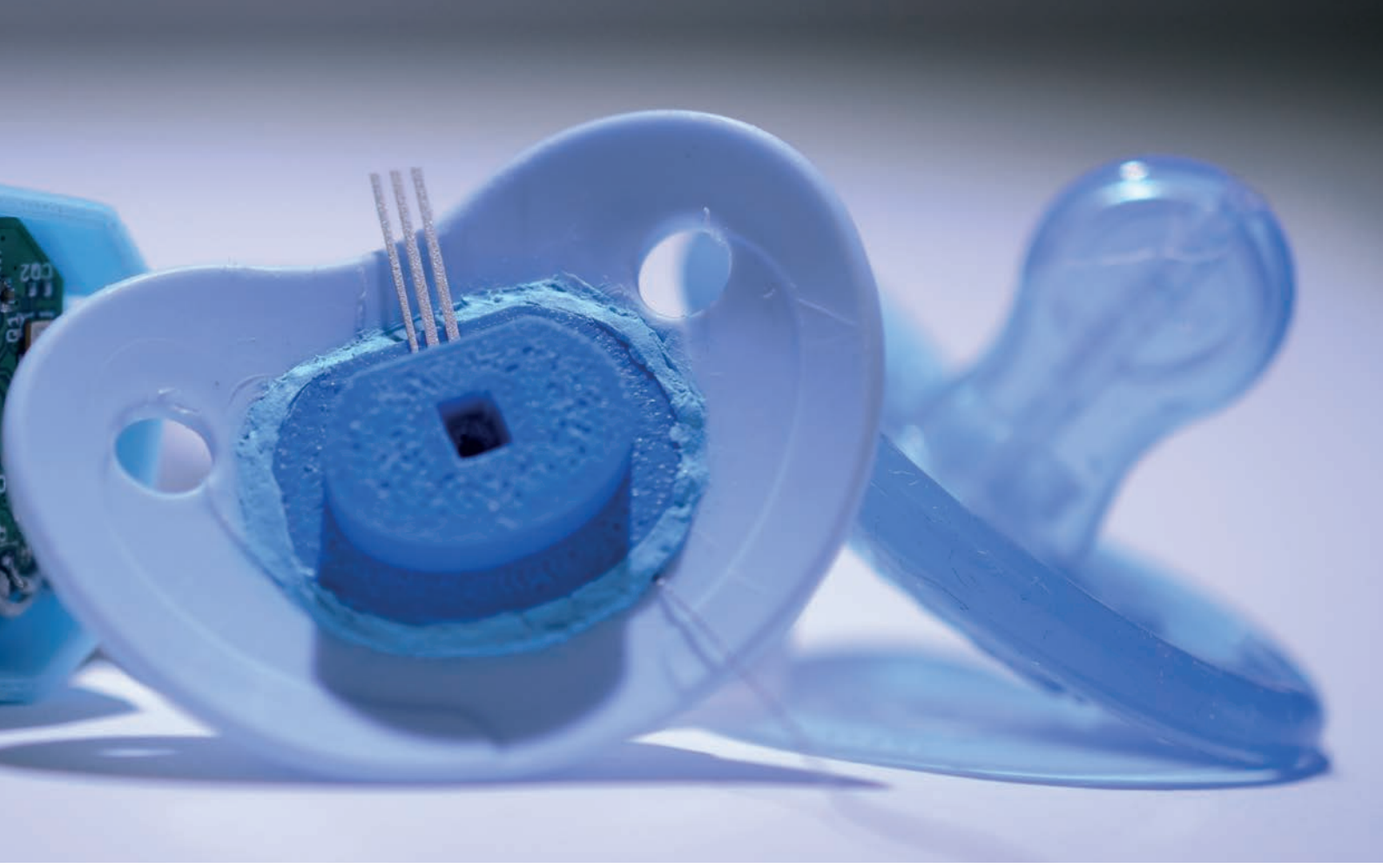

Diabetes Diagnosis ~~For~~ With Dummies

A microfluidic pacifier has been designed to measure biomarkers in saliva – starting with glucose

Diagnosing rare genetic disorders early can make all the difference to newborns – and neonatal diabetes is no exception. However, invasive tests for glucose monitoring in neonates have obvious drawbacks and, because of the very rare nature of the disease, genetic tests are used for definitive diagnosis rather than for screening. Now, Alberto Escarpa of the University of Alcalá, Spain, along with colleagues at the University of California San Diego, is pioneering a non-invasive approach: a pacifier – "dummy" in the UK – capable of monitoring glucose levels in saliva using a combination of microfluidics and electrochemical detection (1).

Saliva flows from the oral cavity into the exterior portion of the pacifier along a unidirectional flow channel before entering an electrochemical chamber. Here, glucose is converted into gluconic acid across a Prussian-Blue-GOx electrode, inducing a change in electrical potential, which is communicated to a computer or smartphone via wireless connection. "This is a truly non-invasive approach to measuring glucose levels in infant saliva," says Escarpa. "And because our device so closely resembles a typical pacifier in terms of esthetics, we don't anticipate rejection to be a major problem."

So far, the device has only been tested on diabetic adults; moving studies into neonates will present additional analytical and safety-related challenges. "Reflux of milk is very common in infants and has the potential to interfere with the signal. Saliva pH is also susceptible to this phenomenon, bringing into question the validity of any readings," says Escarpa, who must also further refine the design. "The device's saliva channel is composed of several pieces – each of which could present a choke or swallow hazard should it become disconnected. In an ideal world the apparatus would be assembled as a single piece – this is the goal," he says.

By integrating additional sensors, Escarpa believes he can increase the number of detectable biomarkers. "Conceivably, any saliva biomarker could be analyzed using this approach – including those indicative of infectious disease," he says. "The possibilities are practically endless."

Reference

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An Eye on Spice

Meeting the need for rapid detection of synthetic cannabinoid receptor agonists – introducing Chris Pudney (University of Bath, UK) and his portable analyzer

Chris Pudney (center) and colleagues test a prototype of their portable analyzer.
Credit: The University of Bath.

What is your research focus?

We focus on synthetic cannabinoid receptor agonists, which are so-called "novel psychoactive substances" and collectively referred to as "Spice." They mimic some of the active compounds in cannabis by interacting with endocannabinoid receptors, but do so with increased potency and exert enhanced effects. Interestingly, these compounds – which share some structural similarities with compounds from the plant – potentially also act on different receptors in the body, meaning their effects are difficult to predict.

The actual chemistry or strength of these products is often not known, which presents a serious problem – an accidental overdose of the wrong synthetic compound could lead to, for example, a stroke or send them to the emergency room. It is also difficult to discern exactly what drug a patient on suspected Spice may have taken, so there's an acute need for a point-of-care test from both health and harm reduction perspectives. And that's the overarching aim of our work.

How does it work?

The molecules in question fluoresce strongly, and we leverage UV excitation to capitalize on this by studying the detailed structure of the emission spectra obtained using fluorescence spectral fingerprinting – and piles of good old-fashioned math (1). What makes the method so effective for Spice analysis is this stepwise approach, whereby we identify synthetic materials and then apply numerical modelling to identify parent compounds and combusted materials. Such broad sensitivity allows us to cope with high levels of heterogeneity in the samples we process, but then we can also drill down into the details.

Techniques such as Raman and infrared spectroscopy are great for identifying specific molecules, but we are often faced with mixtures, which complicates the signal and complicates analysis. Coupled with the use of a biological medium, the challenge is intensified further. Despite the use of infrared as the de facto standard, it's clear that new approaches are necessary for analyzing Spice and further synthetic compounds.

Where did the idea for the technology come from?

The idea came to me when I was working on a technology to predict protein stability. My partner is a psychiatrist and she asked me if the approach could be applied to detecting drugs, and I was surprised to find that the drug molecules resembled the chemistry of proteins I used for spectral fingerprinting in a number of ways. I tried it, and the initial lab results were promising. It was by serendipity that the team had a great relationship with the Avon and Somerset Police (UK). Soon we were working with seized materials from the police, and our method showed excellent discrimination between molecules in as little as five minutes using a saliva sample.

What makes the need so great for these specific compounds?

We have studied these molecules for many years – after all, they were once available through legal means in headshops on the high street. Eventually, however, serious side effects (violence, psychotic episodes, strokes and epileptic seizures, to name a few) emerged, and legislation adapted to move these poorly understood compounds out of public hands. Today, they're still used largely in prisons and homeless communities because they're readily available and incredibly cheap.

Our focus is not for application in law enforcement or detecting criminal activity – very specific chemical information is needed for such purposes. We are conducting this work with the aim of reducing the harm caused by these compounds in vulnerable communities. That's the philosophy shared across our collaborators at the University of Bath.

What's next?

We have developed a robust and minute portable device prototype, which has acted as the much-needed proof of concept for making these measurements. The next stage is for us to make the analysis as user-friendly as possible, and to demonstrate use in real-world settings. Troubleshooting will also be important before we can move the instrumentation into the hands of users.

In terms of instrument development, the next phase will be to use real samples – something we have been limited with thus far due to ethical and moral considerations – and to build our spectral libraries of how these drugs manifest themselves in different user populations, such as drug addicts and the homeless. Eventually, we'd like to give the technology away to charities and groups working with homeless people, and perhaps also sell it to companies and institutions to which it would offer value.

Reference

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Turtle Recall

Collagen analysis is tracing the evolutionary tree of ancient marine turtles, providing powerful proof of concept for future taxonomic investigations

Several features of collagen make it an ideal candidate for the taxonomic investigation of archeological bone. It is abundant, resilient, and harbors species-specific chemical traits. Thus, "collagen fingerprinting" – a technique that extracts chemical signatures using MS – complements morphological examination and DNA sequencing in the acquisition of species identity in ancient bone.

In the case of samples from tropical climates, where hot, humid conditions degrade bones and their biomolecules, collagen fingerprinting is particularly valuable – a fact capitalized on by Virginia Harvey and colleagues. The team (including collaborators from the University of Manchester, University of Florida, Florida Museum of Natural History, University of Copenhagen and National Museums Scotland) applied the technique to examine the proteins preserved in 130 fragmented archeological remains of marine turtle bones up to 2,500 years old from the Caribbean and Florida's Gulf (1). The work represents the first instance of this technique's application to marine turtle identification.

"We found that 63 percent of the collagen-containing bones belonged to green turtles, with smaller numbers of hawksbill and ridley turtles," Harvey said of the results. The team also used this data to study the evolutionary relationships between identified species and found that the phylogenetic relationships generated by these protein sequences were identical to those routinely obtained from genomic studies. Unusual chemical signatures in four of the bone samples suggest that they may belong to a species of sea turtle no longer present in our oceans today; unfortunately, DNA from these samples was insufficient to provide confirmation.

Why is this research important? As co-investigator Michelle LeFebvre says, "Within the context of understanding human impacts on globally vulnerable or endangered sea turtle species, we are able to use collagen fingerprinting to construct species-specific historical baselines of human capture, use, and consumption of sea turtles through time." In a broader archeological context, the study supports further use of proteins to decipher relationships between species, offering an alternative for investigations otherwise hindered by physical sample damage or DNA degradation.

Of course, the approach has its limitations. "We sometimes need up to 5 million years of evolutionary divergence to induce detectable chemical changes between collagen species," says Harvey. And, as is often the case, she notes that the research is currently presenting more questions than answers.

Credit: Nicole Cannarozzi, Florida Museum.

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In My View

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

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

Contact the editors at charlotte.barker @texerepublishing.com

The Principle of the Thing

How do we ensure future generations understand the basics of GC-MS?

By Michelle Misselwitz, Environmental Chemist, Chemistry Matters, Bellefonte, Pennsylvania, USA

Here's a seemingly straightforward question for you. If pressed, could you explain how GC and MS technologies operate on a fundamental level? Struggling? You're not the only one. The analytical community is facing a crisis in that increasing numbers of analysts no longer understand the basic principles underpinning our work. The consequences will be dire: stifled progress and questions raised regarding data validity.

What should the community do to address this problem? In the 1940s and 1950s, GC and MS were only just beginning to emerge as commercially viable instruments and the language describing their operation was simplistic. A few years ago, I worked on a project to build a historical timeline for GC and MS measurement of polychlorinated biphenyls in the environment. What began as a dauting task soon became a passion, as I morphed from analytical chemist to history detective; I wanted to know not just how the technology evolved, but why.

Reading through the earliest papers was enlightening – I learned a lot, and gained an appreciation for how far GC-MS and environmental analysis has come. One of my favorites is a paper from 1943, which states the following: "In general, a mass spectrometer is a device for sorting molecules. Before the molecules are sorted, they are given an electric charge, so that they can be forced to move by the combined action of electric and magnetic fields" (1). While this description might not capture the nuances of the sophisticated technology, it does introduce meaningful terms that most can understand. The objective, after all, was to educate. When ideas and concepts are introduced in a way that isn't intimidating, they become easier to learn.

Unfortunately, the entry-level and repetitive nature of many analyst jobs leaves little time to devote to learning basic principles. What's more, on the job training primarily consists of how to do said job – not how and why an approach works. I've been the recipient of enough technical service calls to know that many analysts have merely

"In the past, scientific vendors were largely responsible for educating their customers – it was all part of the service."

been taught how to make an instrument run, but are woefully unprepared for any problems that may arise. Learning fundamentals is left largely to the individual to pursue independently; few employers have the time or resources to devote to day-long seminars and immersed training opportunities.

Creating innovative training experiences that take into account the limited availability and resources of the average analyst might offer one solution, but who should take responsibility? In the past, scientific vendors were largely responsible for educating their customers – it was all part of the service.

The first handbook on vapor fractometry (GC) was published in 1955 and freely distributed by the vendor (2). The book is easy to read, and clearly focused on education rather than number of sales. Today's approaches are radically different, with many vendors preferring flashy marketing and advertisement over educational value. Maybe it's time to once again prioritize education, and how we communicate to the broader scientific community. Raising the average user's knowledge has far-reaching benefits, and might just underpin the next technological leap forward.

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Industry Invisibility? A Response to the Power List

Celebrating achievements in our community is admirable, but we must work to ensure that key contributors are not forgotten

By Terry Berger, President, SFC Solutions, Sarasota, Florida, USA

I am a regular reader of The Analytical Scientist's Power List, but I feel there is a distinct gap in the 2019 edition that is deserving of comment. Of the 100 scientists listed, 92 are academics. What's more, the industry and national lab folks included are largely those in management positions, who do not spearhead invention efforts themselves.

Though I understand the List is based on a survey of readers – many of whom may not be fully aware of the inner workings of industry – I fear that this format risks overlooking the greatest source of innovation and invention in the field. That's not to say that those listed haven't made incredible contributions – they have, and I personally know and am proud of many of them. But it is important to recognize that their work often stems from the seeds sown in industrial settings.

Big instrument companies have almost stopped inventing since the 1980s, relying instead on new startups to develop technologies. These startups are then generally acquired on achieving viability. The ideas behind these startups may come from grad students or professors, but more often come from individuals with ideas that the big companies wouldn't listen to. This is my world – the world I find ignored in the Power List.

These big companies provide employment for some of the most talented grad students – those with research aimed at developing technologies would not flourish outside of instrument companies. These companies also tend to have enhanced resources, and quicker and simplified access to government funding, when compared with academic institutions. This is truly the environment for growing ideas into a reality, and there is incredible analytical talent in instrument companies that is generally not acknowledged.

"I fear that this format risks overlooking the greatest source of innovation and invention in the field."

Waters has initiated an award to honor industrial chemists: the Uwe D. Neue Award, named after a great contributor to separation science who

"I strongly encourage your readers to bear in mind their industrial peers when placing their nominations for the next year."

died far before his time. Nevertheless, there is no system akin to the Power List for honoring industrial chemists. I believe that these individuals are of equal importance to those frequenting the List, but are at a disadvantage as their managers do not encourage them to report on research until it is protected by patents or is part of a commercial product. Publication is not a usual job function in this setting, and these workers are seldom paid for time writing papers – and so, important insights from this space often go unreported. The result? Industry scientists often do not have a resume equal to those in academia regarding publications, but patent literature does act to fill the void somewhat.

A Power List for industrial innovators (not managers) might be one idea – but I can't say how exactly one would go about doing that... In any case, the Power List – as it stands – fails to tell the whole story.

I strongly encourage readers to bear in mind their industrial peers when placing their nominations for the next year, so that we may celebrate the achievements of scientists across all sectors of our community.

Nominate scientists in industry now – before the official nomination process begins – by emailing: matthew.hallam@texerepublishing.com

It's All Greek to Me

Chemistry etymology: how the language of a small country can make a big difference

By Victoria Samanidou, Associate Professor, Department of Chemistry, Arisotle University of Thessaloniki, Thessaloniki, Greece

When I attended a Master's thesis defense in Austria some years ago, I was astonished to hear one student asked (among other things) about the etymology of the term "chromatography." I thought, "OK, that's a good way to break the ice in what is an admittedly awkward situation – being questioned in front of a live audience." But it would appear I was wrong. The question posed was a serious one, which made the student uncomfortable and didn't prove so easy to answer.

I love to narrate this true story to my sixth semester students of instrumental analytical chemistry. I feel it's important to familiarize the students with scientific terms when I teach the introductory chapters of chromatographic techniques, but I always receive the same reaction. They don't believe it is pragmatic. For them, the meaning of the word is more than obvious. Chromatography is derived from Greek words: chroma (color) and graphein (to write).

Of course, this is far from the only Greek word in the wider scientific terminology. Medical students, for example, will encounter numerous words

"I feel it's important to familiarize the students with scientific terms when I teach the introductory chapters of chromatographic techniques."

of Greek origin, but they aren't they only ones. Many chemistry terms also find their roots in the Greek language (ancient and modern variants alike); analytical (and analysis), organic, inorganic, physical, and

"In most cases, the etymology is clear, as is the case in terms like atom, ion, dialysis, osmosis, chiral, enantiomeric, stereomeric, and isomeric."

biological are just a few examples. Even the word chemistry has Greek origins (though there is debate as to whether it is actually derived from the Arabic word "alchemy"). In the former case, the word has been altered to give a spelling that means "to pour" – giving the science of liquids.

In most cases, the etymology is clear, as is the case in terms like atom, ion, dialysis, osmosis, chiral, enantiomeric, stereomeric, and isomeric (and if it's not clear: they are all Greek!). But why is such knowledge important? Some chemical elements are named using Greek words that describe their physical or chemical properties – useful information, I'm sure you'd agree. For example, the suffix "-gen" – as in hydrogen, nitrogen, oxygen – means "giving birth," and the first part of the word indicates what is produced from a reaction with these elements (such as the production of water through hydrogen combustion).

These elements are not alone. Chlorine and iodine are named after the colors green and violet, respectively, chromium is derived from the word for color, barium comes from heavy, and so on. Elements like helium (sun), selenium (moon), lithium (stone), argon (slow, inactive), neon (new), krypton (hidden) and praseodymium (from leek-green color and twin) also have names indicative of their properties. What's more, Greek words can also be found in prefixes and suffixes of numerous other terms. Number-based prefixes like mono, poly, di, tri and tetra are all Greek, as are prefixes, such as iso- (equal), anti- (opposite), meta- (1,3 substitution), ortho- (adjacent substitution), para- (directly opposite substitution), glyco- (sweet), amphi- (both), micro- (small), mega- (big), and meso- (intermediate). Aromatic (derived from aroma), aliphatic (derived from fat), pentane, hexane, octane, energy, enthalpy, entropy… The list goes on and on, even extending to the names of techniques andinstrument components.

I would argue that Greek scientists have an advantage in their studies. Even if they are unaware of the meaning of a word, they can come to some (accurate) conclusions with relative ease. When it comes to me and my students, I guess this is one of the few instances where the expression "it's all Greek to me" means the opposite of what was intended… For the rest of you, when it comes to understanding fundamental chemistry and the techniques employed in analytical labs, I'd say a little Greek knowledge can go a long way!

THE INNOVATION AWARDS 2019

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Nexera is a new ultra-high-pressure LC (UHPLC) system combining excellent hardware performance and analytical intelligence. Analytical intelligence (AI) is a new concept for analytical instrumentation, which Shimadzu defines as a system that can monitor and diagnose itself, handle any issues during data acquisition without user input, and behave as if it were operated by an expert. AI features within the Nexera system include: automated system start-up with FlowPilot functions to protect the column; a unique device and mobile or computer application to minimize the risk of mobile phase shortage (known to lead to system failure and column damage); detection of solvent flow anomalies by the system followed by automatic correction to enable stable data acquisition; and unique post-run processing technology, offering accurate peak integration and the determination of overlapping peaks.

Potential impact

Automated data acquisition from thousands of samples through high-speed UHPLC sampling and a high-capacity plate changer dramatically improves operating efficiency. However, overall analytical efficiency depends not only on hardware and software, but is also affected by the skill and experience of the user. And, while efficient training is a time-consuming process, the number of experts available in the analytical workplace is dwindling. AI functionality can help improve data reliability regardless of the analysts' skill and experience. It supports the acquisition of high-quality, reproducible data for both routine and demanding applications by foreseeing and correcting common issues.

REBEL

=14

An at-line bioprocess analyzer for fresh and spent cell media

Produced by 908 Devices Inc.

The Rebel is a first-of-its-kind, integrated analyzer for fresh and spent media analysis. The instrument aims to simplify media analysis, and its compact, self-contained footprint fits alongside bioreactors in process development and cell culture labs. Samples can be run at-line in less than 7 minutes, eliminating the core lab wait time, and calibration and data analysis are completed automatically for a panel of more than 30 analytes (including critical amino acids, biogenic amines, water-soluble vitamins and dipeptides). Built for GMP environments, Rebel integrates reporting, automated performance qualification and 21 CFR Part 11-compliant software. By accelerating process development cycles and maximizing bioreactor utilization, Rebel will enhance research across biopharma.

Potential impact

Media composition is critical for maximizing cell line productivity and biotherapeutic quality; thus, optimization of media represents a coordinated effort between numerous teams. Due to limited access to analytics among cell culture scientists, media preparation teams and bioengineers, third-party labs are usually involved in the analysis of amino acids, dipeptides and vitamins, but results from these sites may take several days to return. The Rebel operates at-line alongside bioreactors to eliminate this delay. What's more, the instrument does not require special sample preparation beyond filtering and dilution, and uses minimal sample volumes, which facilitates rapid analysis earlier in process development.

13

TOSOH LENS$_3$ MALS DETECTOR

Directly measures molecular weight and size of macromolecules in solution with less than 2 ng of sample loading

Produced by Tosoh Bioscience

The LenS3 utilizes Rayleigh light scattering to obtain the molecular weight and size of macromolecules in solution. How does it differ from current multi-angle light scattering (MALS) detectors? A novel optical design that allows for light scattering measurements at angles as extreme as 10, 90 and 170 degrees. How? By "dumping" the incident beam and minimizing the "stray light" effect. The detector makes use of an optical "flow path" of largely non-refractive bio-inert PEEK, which splits the sample into two streams, elongating the flow path, maximizing the interaction of the incident beam with molecules of interest and significantly increasing light scattering intensity. The MALS detector can measure the angular dissymmetry of scattered light for molecules as small as 2 nm in size – well below current detection limits.

Potential impact

MALS is routinely used in conjunction with HPLC-size-exclusion chromatography to identify and quantify levels of aggregawtion in monoclonal antibodies and other therapeutic proteins and peptides. LenSTM3 can reproducibly detect and quantify levels of aggregation at much lower levels of sample loading, allowing scientists to extend the level of species detection and leading to more informative analyses using less sample. Plus, by extending the size detection limit down to below 2 nm, scientists can reliably use the radius of gyration to better understand the conformation of macromolecules in solution. Polymer scientists can use LenS3 to characterize chain branching and obtain data across the entire distribution of molecular weight, and the combination of gyration radius with hydration radius can provide shape factors of proteins and antibodies.

12

SCIEX TRIPLETOF 6600+ LC-MS/MS SYSTEM

Enhancing low-flow LC-MS with ultra-fast scanning acquisition and high-resolution data

Produced by SCIEX

The TripleTOF 6600+ LC-MS/MS System incorporates low-flow source technology to deliver accessible, sensitive and precise quantification at ultra-fast scanning speeds of up to 100 Hz MS/MS across a broad dynamic range. The instrument utilizes Scanning SWATH Acquisition to make four-dimensional records of all detectable analytes, and is equipped with an OptiFlow Turbo V Source – a single source for all micro- and nano-flow applications. The high-resolution data can be shared through integration into the SCIEX Cloud, supporting meta-analyses, omics and big data applications. Markus Ralser (Senior Group Leader, The Francis Crick Institute, London and Director of Biochemistry, The Charité, Berlin) says, "The TripleTOF 6600+ System with Scanning SWATH retains the sensitivity and data quality we have come to expect but adds the fast scanning capability that is critical for the next generation of proteomic applications that we have increasingly become dependent on."

Potential impact

To make the most of limited samples with many trace analytes, scientists are turning to highly selective and sensitive micro- and nano-flow LC-MS/MS. Small injection volumes mean greener and cheaper analyses, while scanning SWATH acquires vast, precise and correlated datasets, empowering researchers and facilitating data-driven decisions. Data-sharing in a cloud-based environment maximizes the utility of this richly defined data, enabling powerful meta-analyses that extract and translate findings into meaningful macro-level conclusions.

Judge's verdict

"Tiny amounts suffice to collect the highest quality spectra – no longer will we need to be nervous about whether the tiny volume of sample collected is enough for doing all the MS experiments required, or whether the sample will be gone before all data are collected."

PRECISION HYDROGEN SL

A small, easy-to-use hydrogen generator for GC-flame ionization detection

Produced by PEAK Scientific

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Peak Scientific's Precision Hydrogen SL line provides an efficient hydrogen gas solution for GC flame detectors at a purity of 99.9995 percent. The smallest laboratory-grade hydrogen generator in its class, Precision Hydrogen SL produces hydrogen at the push of a button whilst taking up minimal bench space. Available in both 100 cc and 200 cc, Precision Hydrogen SL is simple to use and easy to maintain, requiring only the simple replacement of a sealed-capsule desiccant system and de-ioniser cartridge, both of which can be changed in one minute by the user. Featuring advanced fail-safe technology with minimal gas storage, SL provides laboratories with a safer alternative for supplying hydrogen gas to GC detector flames."

Potential impact

Precision Hydrogen SL is less than 20 percent the size of its predecessor, eliminating the need for additional space preparations in and around the lab. Extremely compact in design, Precision SL reduces footprint requirements to the bare minimum while improving safety by removing the dangers of manhandling heavy pressurized gas containers – very little hydrogen gas is stored. The automatic failsafe technology also shuts down the generator in the unlikely event of leak detection. Delivering reliability in its simplicity, Precision Hydrogen SL comes with only one button for startup and shutdown, and the user-friendly maintenance is just as simple - no engineer is required on-site, minimizing instrument downtime. Eliminating repeated deliveries means that labs can have gas available 24/7 – and reduce their carbon footprint.

TASSO ONDEMAND PATIENT-CENTRIC BLOOD SAMPLING KITS

Painless, at-home collection of blood samples

Produced by Tasso

The Tasso OnDemand platform consists of five components: (1) a kit containing a novel and painless blood collection device that patients use to collect blood samples; (2) patient-facing prompts to ensure adherence to blood sampling protocols and collection of additional contextual data points; (3) logistics management tools for the distribution and receipt of kits; (4) a certified laboratory partner to handle sample analysis; and (5) a secure data access protocol to deliver results to the necessary parties. Tasso OnDemand is currently used for remote pharmacokinetic and therapeutic drug monitoring applications, and has now started expanding to include additional test panels.

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Potential impact

Tasso OnDemand enables comprehensive at-home care by adding blood tests to the virtual care experience. This means that a typical clinic visit can now be completed at home, expanding the amount of data that can be collected to support care delivery and analytics. Patients appreciate increased convenience, clinicians value more insight, and scientists benefit from faster discovery. Of course, high-quality data relies on high-quality samples; the OnDemand product is an enabling technology that will enhance clinical trials and general healthcare monitoring, while also translating findings into meaningful macro-level conclusions.

Judge's verdict

"The collection of a blood sample will no longer require a trip to see a healthcare professional. The patient is in full control, moving part of the laboratory analysis to the confident and secure home environment."

9

INFINITY LAB LC/MSD iQ

Bringing mass detection to a wider market

Produced by Agilent Technologies

The InfinityLab LC/MSD iQ is designed to support chemists and chromatographers seeking improved clarity in their LC results. Agilent's OpenLab CDS Software provides an efficient and reliable method for data collection, analysis, and reporting, developed with a focus on ease of use and data integrity. MS data acquisition is simplified by features such as the "Auto Acquire" mode, which makes method setup as intuitive as that of LC – no need to understand the underlying physics. A touchscreen-enabled interface and pre-configured analyses further streamline sample submission for open-access labs, minimizing the associated training requirement when coupled with the MassHunter WalkUp Software. The InfinityLab LC/MSD iQ also resides beneath the Agilent's InfinityLab HPLC stack, saving valuable lab space.

Potential impact

The instrument is aimed at labs performing small molecule analysis in pharmaceutical research (from development to quality control), as well as food and materials labs that use MS data for data-driven decisions. The instrument has a range of features to reduce downtime and improve productivity, including intelligent instrument tracking to ensure robust and reliable operation, and embedded sensors that quickly assess system configuration. Lab managers can plan routine maintenance in line with their lab's schedule to maximize effeiciency.

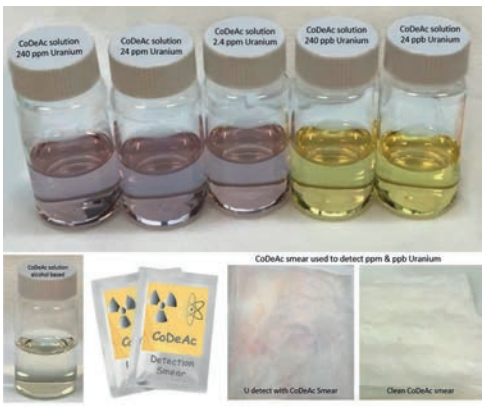
8

COLORIMETRIC DETECTION OF ACTINIDES (CODEAC)

A quick and easy way to detect dangerous actinides in the field

Produced by Idaho National Laboratory

First responders, radiation detection specialists, and nuclear operators need simple, rapid, and reliable field equipment to detect radionuclide contamination, but handheld detectors are inadequate for detecting alpha-emitting actinide species like uranium and plutonium. This newly developed, selective colorimetric technology can be used by response personnel to characterize actinides during field contamination events and everyday maintenance testing at nuclear facilities. CoDeAc technology presents a visual color change for uranium at ppm and ppb levels using a smear and solution system; this novel system will allow first responders to assess the magnitude, dimension and severity of radiological events on-site, thus helping on-scene coordinators to make decisions quickly. All in all, CoDeAc provides a practical alternative to collecting thousands of forensic grab samples that then require off-site laboratory analysis.



Potential impact

We must prepare for major nuclear incidents, regardless of their source (from reactor accidents to improvised device detonation). The colorimetric approach for actinide detection presented here allows for substantial time and cost savings over current methods, is easily and simply deployed in the field, and has no known industrial equivalent. The impressive detection levels of the CoDeAc detection method can be used for both maintenance checks and potential spills, meaning hazards can be identified early, protecting the public from future events.

7

HIGH-THROUGHPUT TD-SIFT-MS

Dream team: combining thermal desorption (TD) and real-time selected-ion flow-tube (SIFT)-MS

Produced by Syft Technologies and GERTSEL GmbH & Co.KG

The release of the TD-SIFT-MS marks the second automated SIFT-MS solution commercialized in recent years. The result of a collaborative effort between Syft Technologies and GERSTEL, TD-SIFT-MS speeds up sample throughput for TD tubes. The speed and selectivity of SIFT-MS is the result of multiple, rapidly switchable reagent ions, while the soft chemical ionization ensures sensitivity and precision. Coupling SIFT-MS with GERSTEL automation has allowed improvements in repeatability and sample throughput, combined with GERSTEL's Maestro software. In addition to controlling injection into the SIFT-MS instrument, the Maestro software's PrepAhead function allows for optimal sample scheduling, as well as temperature ramping and cooling steps, allowing throughput of up to 20 samples per hour.

Potential impact

The combination of high-performance TD and real-time SIFT-MS allows for simultaneous desorption and analysis, meaning more information can be extracted from temperature-resolved concentration profiles. This is particularly advantageous for studies of off-gassing because it allows for rapid, direct emission analysis during thermal extraction. In addition to enabling faster analysis of TD tubes, the high sensitivity of SIFT-MS enables shorter tube-loading times; SIFT-MS also allows for simple analysis of chromatographically-challenging compounds, such as aldehydes, as well as quantification of diverse compounds in one analysis. In short, the combination of TD and SIFT-MS saves time and has potential applications in studies of the environment, air quality, automobiles, breath, and material emissions.

THERMO SCIENTIFIC ORBITRAP EXPLORIS 480 MASS SPECTROMETER

A benchtop mass spectrometer to advance quantitative proteomics and translational research

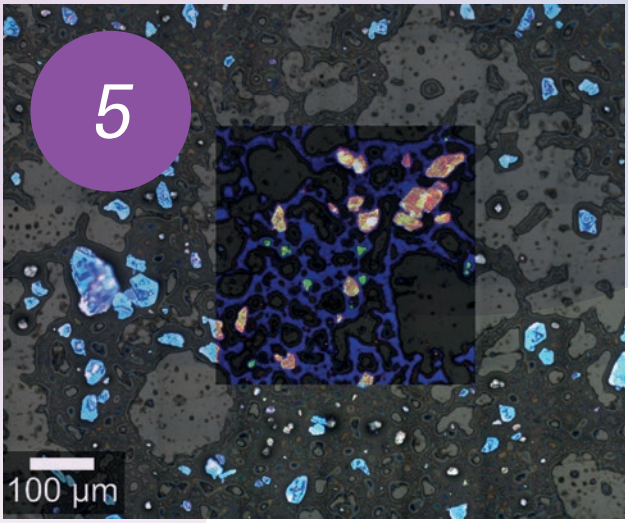
Produced by Thermo Fisher Scientific

6

The Thermo Scientific Orbitrap Exploris 480 mass spectrometer offers a compact, benchtop solution for advanced protein analysis, quantitative proteomics and small-molecule applications. The system addresses the need to support large-scale translational studies, delivering high-throughput protein identification and quantitation, and structural characterization of biotherapeutics and translational biomarkers. The use of intelligent data acquisition methods is designed to allow even inexperienced analysts to gain confident insights into compounds across a mass range of 40-6000 m/z. With a smaller footprint than previous generations, the new system takes up less laboratory space while maintaining high resolution, mass accuracy, and spectral quality. The company claim that combination with the Thermo Scientific FAIMS Pro Interface can increase the proteome coverage by a further 20 percent.

Potential impact

Scientists are using the instrument to rapidly assess the quality and safety of future therapeutic approaches, identify novel biomarkers, and further our understanding of the proteome. The need for flexible analytical instruments usable by analysts regardless of their experience will only grow as the analysis of protein-based therapeutics and discovery and validation of novel biomarkers become increasingly routine. This instrument helps biopharmaceutical scientists identify structural characteristics to determine whether a batch meets quality standards, while also supporting translational scientists to explore samples and target specific analytes when needed.



WITEC PARTICLESCOUT

Supporting microparticle analysis using automated Raman spectroscopy

Produced by WITec GmbH

ParticleScout is an advanced particle analysis tool for the WITec alpha300 confocal Raman microscope series that finds, classifies and identifies microparticles over even large sample areas. Measurements guided by automated routines proceed from sample overview to targeted investigations into physical properties and the chemical characterization of individual particles. ParticleScout capitalizes on the inherent advantages of Raman imaging to conduct fast, label-free and non-destructive chemical characterization. Focus stacking keeps differently sized particles in focus and the system has full integration with the TrueMatch Raman database management software.

Potential impact

Microplastics have permeated the environment and made headlines around the world, with some going as far as to describe the residual presence of microplastics in sediments as evidence of the "Anthropocene" epoch – the age in which human activity is the primary driver of environmental change. For the results of investigations of microplastic pollution to be regarded as conclusive, the particles must be detected, identified and quantified with great precision. What's more, for investigations to be comprehensive and have real-world significance, samples must also be measured in a practical amount of time; advanced optical and algorithmic techniques are necessary to expedite this process. ParticleScout fulfills the speed and precision requirements of these studies in a user-friendly format.

4

METLIN LOCAL

Tandem MS database of 500,000 standards for small molecule identification

Produced by Scripps Research

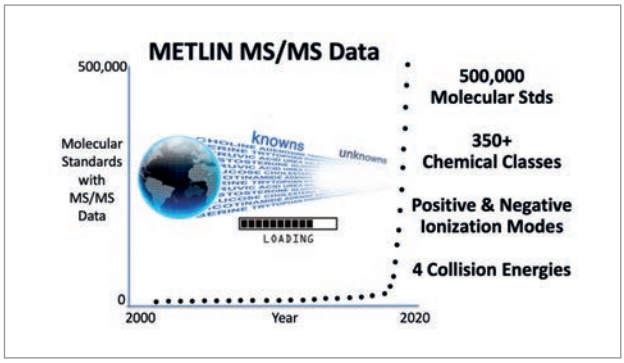
METLIN reached the milestone of 500,000 standards of tandem MS data in August 2019. The new downloadable version – METLIN Local – contains experimental data for each molecular standard in both positive and negative ionization modes generated at four different collision energies. Originally designed to facilitate the field of metabolomics, METLIN Local has now expanded into the broader field of small molecule chemical analysis, including organic chemistry, pharmaceuticals, toxicology, exposure research, and drugs of abuse.

Potential impact

METLIN Local will have far-reaching implications, firstly by increasing the ease and reliability of molecular identification exercises, but also by providing researchers with countless further opportunities to exploit the data. The dataset is 30-times larger than alternative standards databases and is a refined resource that has been widely used for over a decade. Beyond METLIN Local's obvious benefits for metabolite and chemical entity identification, it is also valuable for unknown identification through the implementation of Scripps Research original similarity searching technology.

Judge's verdict

"Modern LC-MS analyses allow us to obtain spectral information on hundreds of compounds in under an hour – this database is a great step forward in simplifying the painstaking identification process that follows."



THERMO SCIENTIFIC VERISPRAY PAPERSPRAY ION SOURCE

High-throughput direct sampling system for routine MS-based applications

Produced by Thermo Fisher Scientific

The Thermo Scientific VeriSpray PaperSpray ion source is a high-throughput direct sampling system that provides an alternative to complex chromatographic separation steps for numerous MS-based applications. Compatible with the latest generation of Thermo Scientific mass spectrometers, it simplifies sample preparation and enables faster results with reduced cost-per- test. With a disposable interface, the ion source eliminates complicated off-line sample preparation and chromatographic separation. Plus, unprocessed samples can be analyzed in a single step, with results in under two minutes. The system provides a complete sampling solution with an easy-to-operate interface designed to be accessible for all analysts, and the VeriPray PaperSpray ion source reduces solvent consumption and disposal, which should eliminate LC and GC maintenance costs and derivatization steps.

Potential impact

Life science labs using MS for routine applications, including drug analyte testing and drugs of abuse analysis, face a series of challenges that can cause backlogs of time-critical samples, such as reduced availability of skilled personnel, rising costs per test, and issues with instrument maintenance and downtime, resulting in significant pressure to increase throughput while reducing costs. The Thermo Scientific VeriSpray PaperSpray ion source replaces complex sample preparation and chromatographic separation steps with a simple sample blot on a single-use paper cartridge. The direct sampling strategy allows researchers to overcome the limitations associated with routine LC- and GC-MS-based strategies across applications, delivering results in under two minutes and improving productivity.

SELECT SERIES CYCLIC IMS

Novel cyclic ion mobility (cIM) technology integrated into a high-performance time-of-flight mass spectrometer

Produced by Waters

The SELECT SERIES Cyclic™ IMS integrates novel cIM technology into a next-generation time-of-flight mass spectrometer. The cIM region consists of a 98 cm path length, closed-loop traveling wave (TW)-enabled IM separator positioned orthogonally to the main ion optical axis; a key part of this geometry and its flexibility is the interface between the ion optical axis and the cIM, where a planar array of electrodes provides control over the TW direction and subsequent ion motion. On the other side of the array, ions are injected, ejected, stored and activated by ion guides, allowing ion mobility selection in a commercial instrument for the first time. The instrument also includes new ion optics, including the time-of-flight geometry, which provides MS resolution up to 100,000 m/z, a new detector and instrument control software.

Potential impact

The innovative cyclic device provides selectable, high-resolution ion mobility separations and provides experimental flexibility to IMSn experiments, alongside improved resolution – a key asset for assessing small molecules like oxidized lipids and oligosaccharides. Scientists are applying the technology to investigate unfolding curves for native proteins, isomeric compounds in petroleomics, and isobaric compounds in complex biological matrices – topics on which peer-reviewed publications making use of the device are already published.

1

SOLVERE CARBON SELECTIVE DETECTOR FOR HPLC

The world's first universal flame ionization detection (FID) for HPLC

Produced by Activated Research

The Solvere is an LC detector that produces a linear response to non-volatile organic compounds using FID and a novel separation-reaction method. The key innovation driving these capabilities is the use of a catalytic reactor to transform organic molecules and remove solvent from LC effluent streams, allowing improved linear range and high sensitivity to the universal detection of non-volatile carbon organics.

Potential impact

In the pharmaceutical industry, the Solvere has the potential to accelerate drug development processes while simultaneously supporting the production of cleaner and more advanced pharmaceuticals. Elsewhere (for example, in the research of fuel, renewables, food, and flavor), the Solvere will enable research endeavors across industry and academia alike.

Activated Research hopes that minimizing the need for calibration will facilitate research that was previously considered prohibitively expensive or practically impossible, with lasting impacts for the global scientific community, and for society as a whole. A current HPLC user in the drug discovery market said: "Activated Research's technology would be completely disruptive; it would change the paradigm of how pharmaceutical analysis is performed."

Judge's verdict

"Quantification of HPLC peaks of unknowns or of compounds for which no standards were available has resulted in numerous errors. Now every compound can be quantified, taking away subjective assumptions and large errors."

THE INNOVATORS

Top vendors share their most innovative technologies

CAMAG® HPTLC PRO

Fully automated sample analysis and evaluation system for routine quality control

With the launch of HPTLC PRO in September 2019, CAMAG has introduced nothing less than a revolution in analytical science: the world's first fully automated high-performance thin-layer chromatography (HPTLC) sample analysis and evaluation system, elevating HPTLC to the next level in routine analytics.

When employing HPTLC PRO, manual intervention is no longer required. Once the sample rack is loaded, the reagents are prepared, and the required analysis parameters are set in the visionCATS software, the system is ready and the user can start the fully automated HPTLC process with a single mouse-click. Consisting of modules for each step of the HPTLC process, the system loads an empty 20 x 10 cm HPTLC glass plate from the dedicated module and the built-in conveyor transports it from one module to the next. After analysis, the conveyor moves the plate back for storage.

Using patented technology, the HPTLC PRO System is capable of autonomously running analysis sequences involving

up to five HPTLC glass plates, allowing a throughput of up to 300 samples per day (15 to 20 plates per day).

The HPTLC PRO System produces reproducible and reliable results. New chamber geometry revolutionizes the development step as the gas phase can be actively circulated during development (conditioning), allowing the separation of target analytes to be further optimized.

Hyperspectral data with a range from 200–1000 nm are used to characterize and quantify all analytes. Substance confirmation by HPTLC-MS is likewise possible. All HPTLC steps are software controlled. The location of the plate is known at all times due to the specialized plate carrier, making the entire HPTLC analysis traceable and cGMP compliant. Full automation throughout the entire process makes the system highly efficient, while a significantly reduced solvent consumption keeps operating costs low. By employing HPTLC PRO, the already economical HPTLC technique becomes even more cost efficient when compared with other analytical systems.

The CAMAG® HPTLC PRO System will be launched sequentially over the next two years.

Explore the next dimension of high-performance thin-layer chromatography at www.camag.com/hptlc-pro

INFINITYLAB LC/MSD iQ

Widening MS accessibility and enhancing analytical productivity

The Agilent InfinityLab LC/MSD iQ is the newest and smartest mass-selective detector on the market today. The intuitive and compact instrument is the perfect partner for labs performing small molecule analysis in pharmaceutical drug discovery, development, quality assurance/quality control and academic, chemical and food labs that require mass spectral data to make key business decisions.

The LC/MSD iQ is specifically designed for chemists, chromatographers and new users striving for more certainty in their LC-based results. The new Auto Acquire mode sets up the acquisition details and simplifies the learning curve. The InfinityLab LC/MSD iQ incorporates instrument health tracking, utilizing embedded sensors to ensure robust and reliable operation, and reports system performance. In conjunction, an overall evaluation of the entire LC-MS system is completed with a system suitability check. With a drive toward maximizing lab productivity, early maintenance feedback features help lab managers plan routine maintenance in line with their lab's schedule.

The InfinityLab LC/MSD iQ resides beneath the LC system, saving valuable bench space. The versatile Agilent 1260 Infinity II Prime LC system is a perfect front end for your LC/MSD iQ system. This LC system has the highest functionality and operational convenience for analytical HPLC and UHPLC separations at pressures up to 800 bar with quaternary and ternary solvent mixing. The 1260 Infinity II Prime LC helps to achieve the highest separation performance in terms of accuracy and precision for utmost confidence in the results.

The 1260 Infinity II Prime LC has gradient and mixing performance equivalent to an Agilent 1260 Infinity II Binary LC system, provides quaternary and ternary solvent mixing, and offers functions like Agilent Intelligent System Emulation Technology (ISET) for perfect method transfer. Agilent BlendAssist enables automatic mobile phase blending by leveraging the Agilent 1290 Infinity II Quaternary Pump technology.

To accommodate flexibility in lab utilization and layout requirements, the Agilent InfinityLab Flex Bench MS enables mobility and modular mounting of all LC and LC/MSD iQ system components. Flexible access to all modules is combined with an integrated solution for waste management, and noise reduction to enhance the lab environment.

Learn more at www.agilent.com

MOBILE CONTROL: COLUMN TEST USER INTERFACE

Co-developed with a well-established LC column manufacturer

AUTOMATED QUALITY CONTROL OF LC COLUMNS

LC column test system for column manufacturers or contract laboratories

Quality control of analytical and preparative high-pressure LC (HPLC) columns – as well as fast protein LC (FPLC) columns – is a crucial step for column manufacturers and facilities that rely on LC, such as contract laboratories. Inspecting one column after another is work-intensive and time-consuming, making it an ideal target for automation. Once started, the automated column testing requires no further support. For overnight measurements, results are available the next morning. Alternatively, column tests can be performed continuously. Columns that have already been examined can be removed during the test process and exchanged for new, untested columns.

After the quality test, a test certificate displaying the column and method specifications, the chromatogram and the result table is generated for each column. The design and content of the column test report can be customized. An easily editable parameter list manages the specifications and test methods of several thousand columns, so that the right method for a column test can easily be chosen via the column specification; an intelligent search allows for quick selection of the desired column in the software. For a fast and intuitive operation, the column test option features an own user interface. The number of clicks to setup the test sequence has been reduced to a minimum.

The hardware and software are flexible, allowing different system layouts. Depending on the column specifications, a high-pressure, a biocompatible or a high-flow-rate system variant are available. Even the number of columns to be tested can be adapted depending on the size of the columns. The default system processes up to 8 columns, but, for smaller columns, a system layout for 16 columns is feasible. The basic system configuration consists of an isocratic pump, an autosampler, a column selection assistant and a variable single wavelength UV detector, as well as the software Mobile Control Chrom, including the column test option.

The LC Column Test System assures the quality of HPLC and FPLC columns at a minimum time and effort, and is recommended for users that test LC columns regularly. Therewith, it is tailor made for LC column manufacturers and every lab that is working with high throughput column testing.

For more information refer to www.knauer.net/columntestsystem

Gurus of CHEMOMETRICS

How can analytical scientists handle the data tsunami? We grill four champions of chemometrics on the progress – and pitfalls – of this rapidly evolving field

Introduced by Lutgarde Buydens, Professor of Analytical Chemistry, Dean Faculty of Science, Radboud University, Nijmegen, The Netherlands

In 2013, I penned a feature for The Analytical Scientist: "Towards Tsunami Resistant Chemometrics," drawing attention to a paradox at the heart of data science: traditional methods, regarded as the cornerstones of chemometrics, were not designed to handle the large volumes of data available today. New methods and strategies were urgently required to extract relevant chemical information from the data tsunami.

More than half a decade on, the data analysis landscape has changed tremendously. In computer science, deep learning and artificial intelligence methods have emerged, whilst in mathematics there is a growing interest in investigating the fundamentals of data science. Together, this progress can only further benefit the chemometric field.

This made me wonder: what is driving chemometricians, and how do they experience the field in relation to these developments? Asking some experienced chemometricians in key application areas such as food analysis, environmental science, metabolomics and industrial process analysis for their views on the field – and how they create value from analytical data, seemed a proper way to address this.

What spurred your interest in chemometrics?

David Wishart: I began my career as a structural biologist with a particular interest in protein structure. Over time, I drifted towards the study of drug design, quantitative structure–activity relationship models, and small-molecule therapeutics. I've always been interested in combining theory with practice: pairing mathematics and computer modeling with wet-bench biology and chemistry. In 2002, I joined the Department of Computer Science at the University of Alberta, where I began to explore machine learning and its applications. Since then, my interest in chemometrics has only continued to grow – driven by the enormous volumes of data produced in omics.

I now run a large experimental facility called The Metabolomics Innovation Centre, which serves as Canada's national metabolomics laboratory. The data we generate, coupled with that generated by many other metabolomics laboratories, is increasing year-on-year. Terabytes of data can easily be produced from a single metabolomics study. In addition to the sheer quantity of data collected, the size of individual metabolomic studies is also growing rapidly – it is not unusual to see 10,000 or even 100,000 subjects or samples being analyzed in some laboratories. This explosive growth is creating numerous data challenges.

Roma Tauler: We investigate environmental issues such as pollution, and the effects of environmental stressors on biological organisms at the omic level. My primary interests were solution chemistry and chemical speciation using electro-analytical and spectroscopic methods, which produced reams of multivariate data. This had driven me to employ chemometrics and multivariate data-analysis as part of my everyday workflow. Because chemometrics has always offered me the tools I need to solve particular problems, it seems only natural to want to contribute to the field's ongoing development.

Jeroen Jansen: I started my university studies in chemistry at a time when many believed that biochemistry was the answer to the world's woes. However, it is now clear that understanding life in its full complexity is a far greater challenge than anyone could have imagined. Developing molecular therapeutics or solving food poverty is no trivial task. While studying chemometrics, I recognized the important role that data could play in tackling these challenges; thus, I began pursuing projects that employ a variety of techniques, such as multivariate curve resolution (MCR) and ANOVA-simultaneous component analysis (ASCA), to unravel the vague and seemingly random patterns emerging from data tsunamis. Now, I focus on two areas in which chemometrics shows considerable promise: multivariate process monitoring to make industry more sustainable, and citizen science, to bring measurement to the people.

Harald Martens: I still remember how exceedingly dull and meaningless I found the mathematics and statistics courses during my university studies. It wasn't until I started my first job in 1972 that I learned to love modelling of multivariate chemical data – what later developed into "chemometrics": we generated too much data and extracted far too little information from it, so multivariate data modeling was a vital tool. I discovered first-hand how important it is to ensure that modeling is statistically valid, and that data is interpretable to those with different backgrounds and experiences. I've had to learn basic mathematics and statistics the hard way, and have come to love its power and practicality. Sitting through a mathematical proof for proof's sake is a sure-fire way to send me to sleep! For me, the purpose of mathematics is to facilitate data-modeling in order to better understand the world.

What impact is the data tsunami having on your field?

Tauler: There's no doubt that the data tsunami is one of the major driving forces behind the digital boom. In the chemical and analytical sciences, this is a consequence of more and better measurements and the digital information revolution. Deeper insights are now possible in many areas: for example, extraction of spatial in-vivo chemical information from hyperspectral imaging and video, the investigation and biochemical interpretation of the chemical changes in biological systems instigated by stress factors, and the extraction of chemical, environmental, and climate information from huge data repositories.

The amount of data acquired by these studies is enormous. This raises a number of interesting challenges, impacting everything from data preparation and pre-treatment, to interpretation and pattern recognition.

Wishart: The tsunami of metabolomic data has brought with it both opportunities and challenges. The good news is that more data means more "training" and "testing" datasets available for

various analytical or machine-learning techniques. Some of the most useful datasets will be those compiled for reference metabolites, which can be used to develop prediction or classification software. These tools will be particularly useful in identifying the tens of thousands of still unknown, or unidentifiable metabolites in the human metabolome – the so-called "dark matter" of the metabolome

However, simply storing and retrieving such large amounts of data in a suitable manner is itself a significant challenge, let alone the difficulties in analysis, standardization, and interpretation of the data. Furthermore, most metabolomic data derived from biological studies are highly variable, both in quality and type. As a result, its interpretation can produce widely different results; relatively few studies, even if carried out in identical conditions, produce similar outcomes. This generates confusion and doubt in end-users, who question the utility of this whole approach. Of course, this isn't a new problem: in the past, similar issues have beset other branches of the omics science. Overcoming this challenge will necessitate the development of standardized protocols for data analysis, better handling of false-discovery rates, increased community training, and a greater focus on collecting or creating reference standards.

Jansen: My work covers a broad spectrum, though those with the most potential for impact and innovation are industrial process control and citizen science. Experimental design has proven itself essential for understanding systems biology: we now use these same ideas to systematically explore data from large industrial processes. This provides a wealth of new information about these large, man-made systems.

We've quickly learned that the calibration of new, handheld sensors for citizen science requires fundamental knowledge about experimental design to ensure robust and dependable data. The challenge? Making it possible for end-users of these technologies, who are not trained analytical chemists, to operate them effectively. This is no simple task; developing methods that are complex enough to deliver the information we need but also intuitive enough to be used by non-experts is a careful juggling act.

Martens: Humanity is faced with a number of serious challenges: climate change, a loss of biodiversity, human poverty, the spread of new diseases, migration crises, and war. The huge data sets we're generating – if handled correctly – give us the tools to better understand and tackle these problems. But then our data modelling also needs to respect the laws of physics and the explicit and tacit knowledge that

THE ROUNDTABLE

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humanity already has. If instead we handle it wrongly with lots of black box machine learning, the combination of the data tsunami and hyped unexplained artificial intelligence will lead to societal dementia.

How can we adapt to the incoming data tsunami?

Jansen: What is required is closer cooperation between quantitative modelers and the end-users, improving industrial sustainability and empowering citizens to take control of their lives based on quantitative evidence.

Chemometrics should take on the role of "translator"; bringing together the knowledge floating around on factory floors and inside tech-savvy living rooms with that gained through big-data approaches. It should not become a science of servitude, but rather empower us to produce novel, data-analysis-backed solutions with real-life value to society. Bringing the end-user on board early to co-create the solution makes adoption easier, no matter how abstract the chemometric methods employed.

To have any kind of impact, we chemometricians can never work alone. Luckily, collaboration is in our blood; talking to any of my colleagues reveals collaborations across a broad spectrum of professions, from the hospital to the industrial plant. Having built these relationships, it's key that we now move from collaboration to co-creation. Using MCR, almost all chemical knowledge can be translated into mathematical models with appropriate constraints: we can code any kind of experimental design into ASCA to extract only the most relevant information from our data.

Tauler: Since its humble beginnings in the 1980s, progress in chemometrics has been intimately linked to the increasing power of computers, analytical instrumentation, and measurement science. The goal of chemometrics is to extract chemical information from measurements via computational means; thus, it is a field well prepared to handle big data challenges. The tools developed in the last few years are already being implemented in new processes. Methods developed in chemometrics, together with the explosion of statistics and machine learning, have proven key to generating, extracting and interpreting useful information from the data tsunami.

The results can already be seen in real-world applications. The implementation of powerful, multivariate calibration and resolution methods to allow better monitoring, modeling and control of chemical processes has resulted in improved classification, quality, and pattern recognition of industrial and food products. New challenges and perspectives have arisen as society evolves, with a focus on health and the environment now at the forefront.

> "To have any kind of impact, we chemometricians can never work alone."

Wishart: To its credit, the metabolomics community has risen to the challenge. The creation of two databases – MetaboLights and the Metabolomics Workbench – has resulted in open-access archival resources for metabolomic data deposition, particularly for biological studies. Unfortunately, the development of resources capable of depositing and storing chemical data still lags behind. The creation of open-access tools for standardizing data analysis and data interpretation is well underway; indeed, developing open-access, web-enabled software tools, and hardware resources has been a major priority for my laboratory for over a decade.

Comprehensive, web-enabled databases have allowed our lab to obtain the chemical and metabolic data needed for appropriate training and testing of novel machine learning approaches. By ensuring our data are freely available on the web, we also help other scientists to develop new, or related, applications. Database construction is a win–win, both for our lab and for the broader metabolomics community.

We have developed a large number of web-enabled databases or web-servers to aid in standardization. These include the Human Metabolome Database (HMDB), MetaboAnalyst, Bayesil, ClassyFire, and others. The HMDB, which has collected information on over 100,000 human metabolites, has helped the metabolomics community to conduct consistent compound identification, compound annotation, and spectral deconvolution.

Tauler: One of the main challenges associated with analytical measurement is limited sensitivity and selectivity; although

progress in the development of analytical measures has been enormous, the number of chemical species under study is near infinite. Thus, the goal of having one analytical measurement for every chemical species is unattainable. What we measure is always a mixture of species, and only part of what is measured relates to our interest.

There are different ways to increase the selectivity of analytical measurements, and one of the most powerful is using chemometrics. As well as broadening the extent and power of analytical measurement, chemometrics also allows for the discovery and interpretation of the latent (hidden) multivariate or multifactor structure and response of chemical systems. These latent variables reveal the complex behavior of the analyzed systems – especially those in natural systems. This would not be possible using traditional means of analysis, even if your target has been very well characterized.

Martens: We need to deploy mathematical models to properly handle big data. While purely mechanistic models may be good for simple systems, this traditional approach to modeling is inadequate when faced with real-world complexity. We do understand most of the laws of nature, but not how they combine with each other in concrete situations. The real world must form an integral part of our modelling processes, by combining massive streams of multichannel measurements to update the relevance of our models based on feed-back.

What have been **your biggest successes** to date?

Jansen: For us, the cornerstone of our success has been co-creation. When we began working with process engineers and operators at a large chemical factory we dusted off Path-PLS – an almost forgotten analytical methodology (but still widely used in the social sciences). The chemical company had a clearly-stated challenge in their process, that they themselves – employing their own knowledge – had already broken down into manageable questions. Together, we filled in the pathways between the different unit operations, which proved very valuable. The resulting model was much more informative – and far more predictive – once we had incorporated information from the end-user.

I think this is reflective of a wider trend: with the emergence of the data tsunami, people are far more data-conscious. This is making conversations with non-chemometricians much easier for us.

Martens: The on-the-fly-processing algorithm for ever-lasting chemometric model-building that we developed in the 1990s is now having a significant impact in industry and shipping – allowing users to handle very big data streams without being overwhelmed or alienated.

Analysis of ever-lasting streams of high-dimensional measurements can be likened to the full sound of a symphony orchestra in a concert hall. We prime our mathematical models with prior knowledge about "what music to expect" (the laws of physics, prior observations, and so on) before opening the metaphorical data flood gates. From the ensuing tsunami, we estimate parameters and variables, often via mathematical metamodels. Following this theory-driven approach, we start the data-driven model. We listen critically to the unmodelled residuals, to discover unexpected but clear "rhythms" and "harmonies" that we quantify and display for interpretation and practical use. Finally, we check for possible "arrhythmia" and "disharmony" – data sticking out from the random background noise. Based on this, we can then correct our initial models, whilst extending or improving our understanding of the processes. This entire process forms a rational, interpretable base for deep learning in technical systems.

Tauler: We've conducted significant work using multivariate curve resolution-alternating least squares (MCR-ALS) to investigate equilibrium and kinetic reaction-based chemical systems using spectroscopic methods. The MCR-ALS soft-modeling approach competed favorably with other traditional, hard-modeling parameter estimation data-fitting methods. Implementing hybrid hard-soft modeling has allowed us to extend the range of chemical systems we can analyze as well as expanding the range of data-sets we can cover. MCR-ALS has been extended to the analysis of very complex multiway and multiset data structures. Recent applications have also seen it applied in omics and hyperspectral imaging.

What are your goals for the future?

Jansen: We want to further implement and refine novel chemometric methods incorporating industrial knowledge and resources. While we've already gained good insights into how to create better data analysis solutions with lasting value to the end-user, the greater challenge will be engaging the measuring citizen to the same degree. Understanding the relations between human behavior and our measurement and prediction innovations, is likely to prove critical.

"The greater challenge will be engaging the measuring citizen to the same degree"

Martens: I hope to continue developing professional software that can bridge the math gap in society. I also want to combine different pragmatic mathematical sciences, particularly chemometrics, control theory and cognitive science. Of course, I also want to use more advanced tools for mathematics, statistics, and computer science – but only when needed, and without losing the real-world connection.

Moreover, I want to continue the work that my colleagues and I have done to develop continuous chemometric- and cybernetics-based machine learning tools for ordinary people to use in their daily work. We need even better ways to summarize, compress, quantify and understand the essence of real-world data without being overwhelmed by numbers, caught up in mechanistic oversimplifications, fooled by good-looking p-values. or alienated by black-box descriptions.

Tauler: In the next few years, we want to develop better approaches to ascertain the reliability of MCR solutions, in order to consolidate their general use. New data-fusion strategies and analyses are also needed, for instance in multimodal hyperspectral imaging data analysis or in multi-omic data analysis.

Wishart: Our focus over the next 2–3 years will be to utilize machine-learning technology to develop software to more accurately predict MS/MS and NMR spectra of small molecules. In tandem, we hope to develop algorithms capable of predicting biologically feasible compounds or chemical biotransformations. These tools will allow us to more easily identify new or unknown compounds using "in-silico metabolomics." We are also keen to construct ontologies and pathway databases that can be used to better annotate metabolites and aid their biological interpretation.

Solutions

Real analytical problems
Collaborative expertise
Novel applications

Record Breakers

A challenging analysis led to a new method able to extract more unique chemical compositions than ever before from a single petroleum sample – and it could have applications in biology and beyond.

By Diana Catalina Palacio Lozano and Mark P. Barrow, Department of Chemistry, University of Warwick, Coventry, UK

The problem

For many years we struggled to analyze the maltenes components of a truly non-distillable fraction from a particular heavy petroleum sample. Along with our collaborators, we applied a variety of sample preparation and ionization approaches, but they all proved unsuccessful. The issue was – of course – the complexity of the sample.

As analytical science evolves, we must improve our experimental and data processing capabilities in order to characterize increasingly complex samples. Thus, if we are to continue to answer important questions across analytical applications, innovative new approaches are needed.

Background

Petroleum is one of nature's most complex organic mixtures; hundreds of thousands of compositions can lie within an observed mass range, with hundreds of unique compositions per nominal mass. And, as Mieczyslaw Boduszynski states, truly non-distillable residues are by some way the most difficult fraction of such samples to analyze, due to the broad range of molecular weights present, the heteroatomic nature of the compounds, and general low volatility (1).

Luckily, the Barrow Group had expansive experience in Fourier transform ion cyclotron resonance (FT-ICR) MS – instruments which offer the very highest resolving power and mass accuracy. As a result, FT-ICR MS instruments are able to separate molecular species with very small mass differences (including compositions that differ by less than the mass of an electron), and can subsequently assign peaks to each with a high level of confidence. However, it is also widely understood that the resolving power of this technique is inversely proportional to the mass-to-charge ratio (m/z). So, for a given m/z range, the resolving power drops as the m/z rises, which is precisely where there can be a greater number of elemental compositions per nominal mass. This means that peaks become more difficult to resolve at the higher end of a given m/z range, and compositions at the upper end of the range may be missed.

What's more, the collision cell and ion cyclotron resonance (ICR) cell trap a limited number of ions – typically in the range of millions – but a minimum number of ions (roughly 100) of the same m/z must be present to detect the signal and record a peak. These two parameters determine the peak capacity of a single mass spectrum, typically meaning instruments are limited to tens of thousands of peaks using traditional methods. Increasing the ion population in the instrument also leads to undesirable space-charge effects, reducing resolving power and mass accuracy. These factors underpin the difficulties experienced when dealing with highly complex samples and presented us with a challenge that we could not refuse to face head on.

The solution

Introducing operation at constant ultrahigh resolution (OCULAR), our approach using a combination of custom experiments and data processing techniques.

Operating FT-ICR MS at constant ultrahigh resolution has set a new world record for the number of unique compositional assignments derived from a single sample – 244,779, to be exact (2); a considerable advance on the previous record of 126,264 compositions set in 2017 (3). The breakthrough? The use of a modified stitching method incorporating a mass filter to selectively accumulate ions for successive m/z windows of constant ultrahigh resolution per window, and a custom algorithm for processing and stitching the data, ensuring a final mass

spectrum with constant resolving power across the desired m/z range. The result: data with several orders of magnitude more peaks than the tens of thousands allowed by traditional broadband FT-ICR experiments.

Determination of the number of windows to incorporate constituted a key consideration in planning the stitching method, owing to the known link between resolving power and window width; more complex samples spanning a wide m/z range will require the acquisition of a larger number of narrower segments. To achieve our record analysis of the non-distillable fraction with ultrahigh resolving power and part-per-billion mass accuracy, we divided the data set into 65 windows, each with an m/z width of 24.

"Petroleum is one of nature's most complex organic mixtures."

The next step was to "phase" the data (producing absorption mode mass spectra) and calibrate the mass spectra, followed by use of Rhapso (4) – a novel algorithm for automated stitching, named after a character from Greek mythology suspected to have been a seamstress. Rhapso trims each segment at highest and lowest m/z to prevent including peaks outside of the isolated window, giving reduced-width segments. The corrected, reduced-width segments spanning the entire m/z range of interest were then combined to give the fully stitched mass spectrum, from which data analysis could be performed and unique molecular compositions were assigned.

As conventional sources deplete, petroleum companies are exploring heavier sources of crude oil and the truly non-distillable fractions of crude oil (with a boiling point over 687 °C) could contain high-value products that are important targets for analysis. Approximately 80 percent of the compositions we assigned had an unknown boiling point above this value, including individual molecules with up to 114 carbon atoms and up to 51 double bond equivalents, spanning many heteroatom classes.

OCULAR is the only documented method to date able to obtain these results, and was performed using a 12 T FT-ICR MS instrument – the FT-ICR instruments with the very strongest magnetic fields currently available use 15 T or 21 T. We anticipate that the use of OCULAR with even higher magnetic fields and newer instrument hardware would further improve the performance of this approach, leading to a higher dynamic range and mass accuracy with reduced noise and enhanced peak positions.

Beyond the solution

We have demonstrated that OCULAR, in combination with FT-ICR MS, is effective for the characterization of heavy petroleum, but we anticipate it will also prove useful in the analysis of complex environmental samples (including weathered heavy petroleum). The growth of metabolomics, which considers many thousands of analytes within a single sample, also provides testament to the need for such approaches, and there is an emerging need for the development of even more advanced tools to combat the associated challenges.

In the age of ever-increasing sample complexity, we also expect to see OCULAR used for discerning the contents of biological samples. MS has

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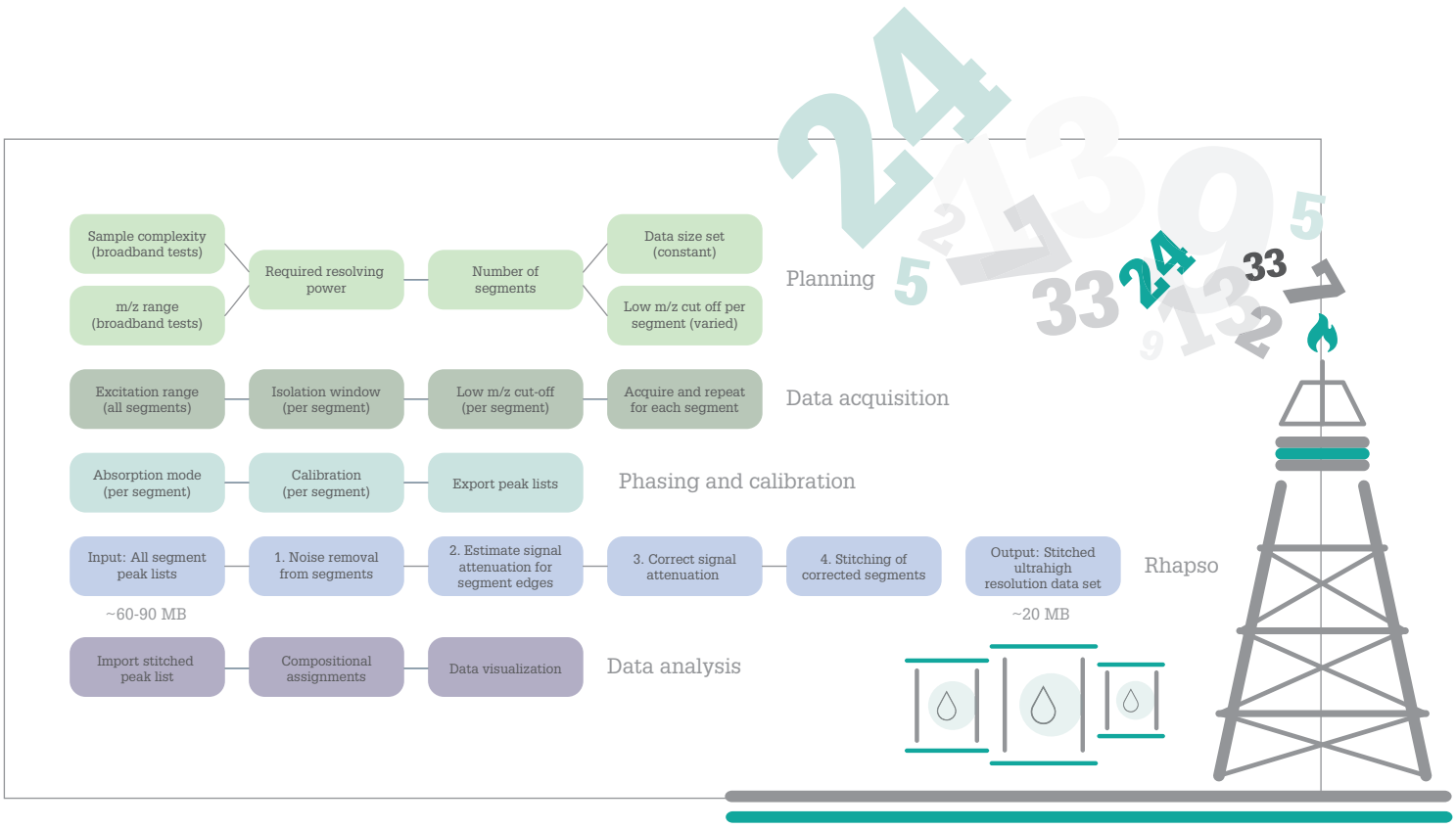
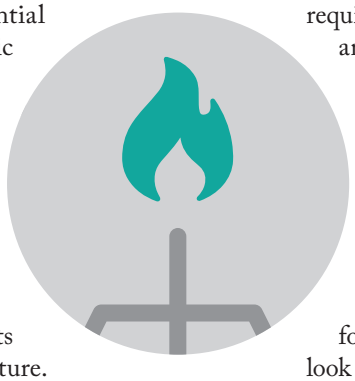


found applications throughout modern studies of biology and medicine, from biomolecule–drug interactions to ecology and biodiversity. In these contexts, the dynamic range examined can be particularly critical; for example, a defined range may be necessary to follow species of relatively low abundance. Plus, in the case of isotopic-labeling experiments, peak resolution for complex spectra is essential for analysis of the isotopic fine structure.

In terms of our own work, we have a few ideas…. We won't give away all the details just yet – suffice to say you should expect to see further applications and method developments hitting journals in the future. Of course, there are a number of factors that will support advances with the method, including the use of more modern ICR cells – like the "dynamically harmonized Fourier transform ion cyclotron resonance cell" or "ParaCell" – and the development of new instrument control software to boost performance and improve speed.



Speaking more broadly, the main challenges we face are the increased complexity of heavier fractions of crude oil and non-conventional sources of crude oil (such as bitumen), the requirement for advanced data analysis and visualization, and the separation of isomeric contributions, known for their influence on physical characteristics and toxicity. Thus, the developments needed to propel this research forward are many, but we look forward to the challenges.

We hope to see OCULAR used by a wide range of research groups across numerous fields in the future – not just for petroleum research. Given the analytical insight bestowed by the technique, we anticipate applications in a range of areas, where increasing interest will also drive accessibility.

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Evolved Gas Analysis and Multi-Step Pyrolysis: Two Powerful Tools for Polymer Analysis

Evolved Gas Analysis (EGA) in conjunction with multi-step pyrolysis (MSP) can provide ample separation to yield well-resolved chemical information

Introduction

The plastics and rubber industry play a significant role in bringing us to the modern age, which emphasizes the balance between life convenience and environmental sustainability. From the very beginning of this industry, four different categories of additives were incorporated into the products as stabilizers, plasticizers, lubricants and flame retardants, to either enhance the physical performance of the finished product or assist the manufacturing process. A vast number of chemical species, whose molecular weight varies from 200 to 1000 Da with a wide range of boiling points, are being used nowadays. These additives become a challenge in the quality control process. A single step pyrolysis GC/MS analysis often produces cluttered chromatograms. Evolved Gas Analysis (EGA) in conjunction with Multi-step pyrolysis (MSP) can address this challenge effectively. EGA provides thermal information which can be used to select appropriate MSP thermal extraction temperatures. Each thermally sliced chromatogram will provide ample separation to yield well-resolved chemical information.

Experimental Setup

A vinyl transparency sheet, underwent EGA at 50°C per minute from 50°C to 800°C. This temperature ramp up rate is 2.5 times faster than the traditional thermal gravimetric analysis (TGA). Approximately 100µg of vinyl polymer was added to the Drop-In-Sample Chamber (DISC) tube in a CDS 6150 Pyroprobe, before entering into a GC/MS system.

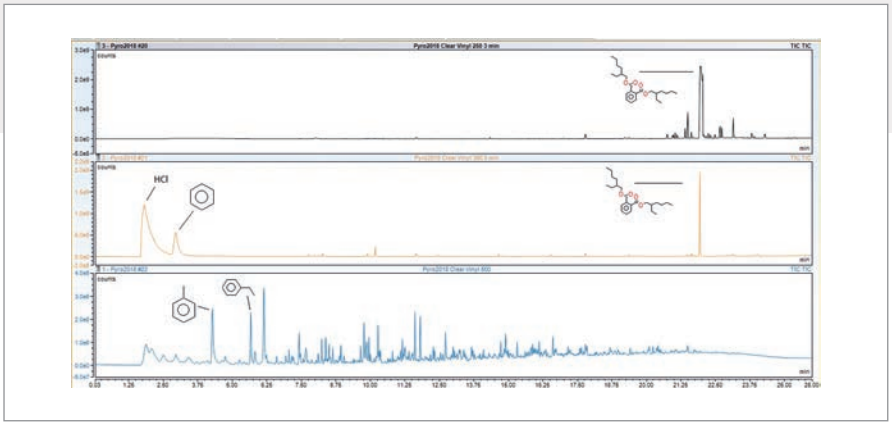


Figure 1.

Pyroprobe

Initial:	50°C
Final:	800°C
Ramp Rate:	50°C per minute
DISC Interface:	300°C
Transfer Line:	300°C
Valve Oven:	300°C

GC-MS

Column:	fused silica (1m x 0.10mm)
Carrier:	Helium 1.25mL/min, 75:1 split
Oven:	isothermal 300°C
Ion Source:	230°C
Mass Range:	35-600amu

Results

Figure 1, which displays the EGA from the transparency sheet, including a Total Ion Chromatogram (TIC), and Extracted Ion Chromatograms (EIC) has 3 defined regions of thermal outgassing. These peak regions occur at 250°C, 350°C, and 500°C. The first region is contributed by semi-volatiles (m/z=149) from phthalate plasticizers desorbed from the vinyl. The second and third regions are from material decomposition. The second region has an abundance of m/z=36 with a top match for HCl. This represents the first step of polyvinyl chloride pyrolysis, removal of the chlorine side group. The last region has multiple masses associated with it; m/z=91, 106, and 115 indicate aromatics, and represent the stabilization of the remaining polymer chain.

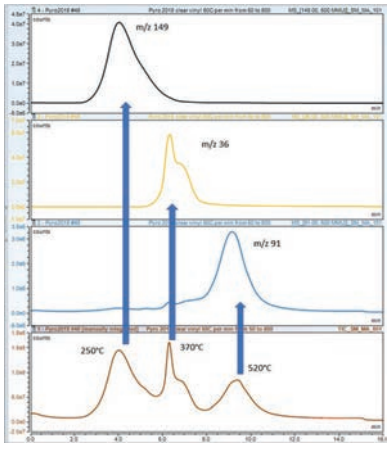
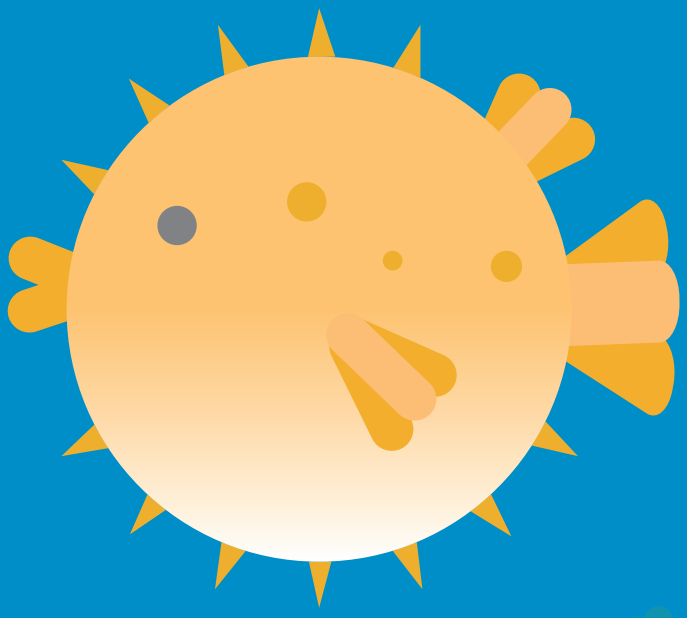


Figure 2.

After obtaining the EGA information, 250°C, 350°C, and 500°C were chosen to separate semi-volatiles and polymeric components for GC-MS analysis. Dioctyl phthalate (Figure 2) was identified in the 250°C thermal slice. At 400°C, dioctyl phthalate is still extracting as the vinyl breaks down, releasing HCl. At 500°C, the remaining portion of the vinyl are stabilized to aromatics.

Conclusion

Evolved Gas Analysis (EGA) in conjunction with multi-step pyrolysis can be used to effectively determine multi-step pyrolysis parameters, simplifying chromatography results of complex polymeric matrices.



Precision Analysis for Pufferfish Poison

Direct rapid analysis of tetrodotoxin contained in fugu using DPiMS™-8060

Fugu (pufferfish) is considered a high-quality food fish in Japan, and is now consumed in other countries as well. Even though it is widely known that certain parts and species of fugu contain the deadly poison tetrodotoxin (TTX, also called fugu poison), incidents of fugu poisoning occur frequently due to careless control. Thus, a quick and simple method to detect TTX from fugu is needed, not only for sites involved in good hygiene and quality control, but also for general consumers.

This article introduces such as TTX analysis method using the new Shimadzu DPiMS-8060 mass spectrometer (Figure. 1), which combines probe electrospray ionization (PESI) with a tandem-type mass spectrometer. We also present a rapid method for TTX analysis free of pretreatment. This method is applicable not only to the liver and ovaries of poisonous fugu, which are widely known to contain TTX, but also to the skin and muscles, which may contain TTX depending on the species.

TTX standard sample measurement

As a standard sample, TTX (FUJIFILM Wako Pure Chemical Corporation) was prepared in 50 percent ethanol solution, and 10 µL of the sample solution was injected in the dedicated liquid sample plate of the DPiMS-8060 for measurement.

A product ion scan was carried out, conditions which enable confirmation of the characteristic fragment ion of TTX (m/z 162.1) were studied, and the conditions shown in Table 1 were applied. Results obtained from the product ion scan and from 1, 5, 25, 50, 100 and 300 ng/mL of the TTX standard sample were prepared. The samples were measured under multiple reaction monitoring conditions and a calibration curve was prepared.

Collision Energy	*-30 V*
MRM Transition	m/z : 320.2 > 162.1 (Monitoring conducted using proton adduct as precursor ion.)
Survey Event : Product	m/z : 100-370
Ion Scan MS Range	
Scan Speed	5,000 u/sec
Event Time	0.06 sec
Desolvation Line	250 °C
Heat Block	50 °C
Polarity	Positive
Acquisition time	0.5 min

Table 1. TTX analysis conditions for DPiMS-8060.

Figure 1. DPiMS-8060.

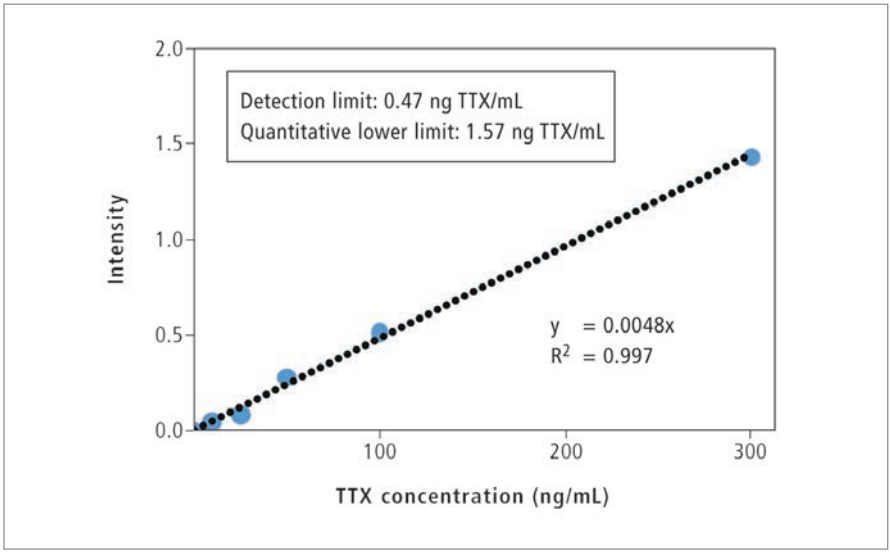


Figure 2. Calibration curve of the TTX standard sample.

The detection limit and quantitative lower limit of TTX were calculated, and calibration curves were produced (Figure. 2).

Detection of TTX in fugu

Real samples approximately (~3mm^2) were taken from the muscle, skin, liver and ovary of the fine-patterned puffer *(Takifugu poecilonotus)*, a poisonous fugu species. The samples were inserted in the dedicated biological sample plate of the DPiMS-8060, 35 µL of the 50 percent ethanol solution was dripped on top, and a product ion scan was conducted. Fragment ions of TTX were detected in all of the tissues. We also observed differences in sensitivity between respective tissues of the fish, suggesting that TTX concentration can be measured simply across these compartments without pretreatment using the DPiMS-8060.

Conclusion

Analysis of a standard sample of TTX demonstrates the ability to conduct high-sensitivity analyses simply using the Shimadzu DPiMS-8060; we were able to conduct these studies without pretreatment, which is a necessary step when studying this high-polarity substance by LC-MS.

The DPiMS-8060 may become an effective analytical method in the field of inspections for protection of food safety.

The samples used here were provided by Prof. Yuji Nagashima of Niigata Agro-Food University.

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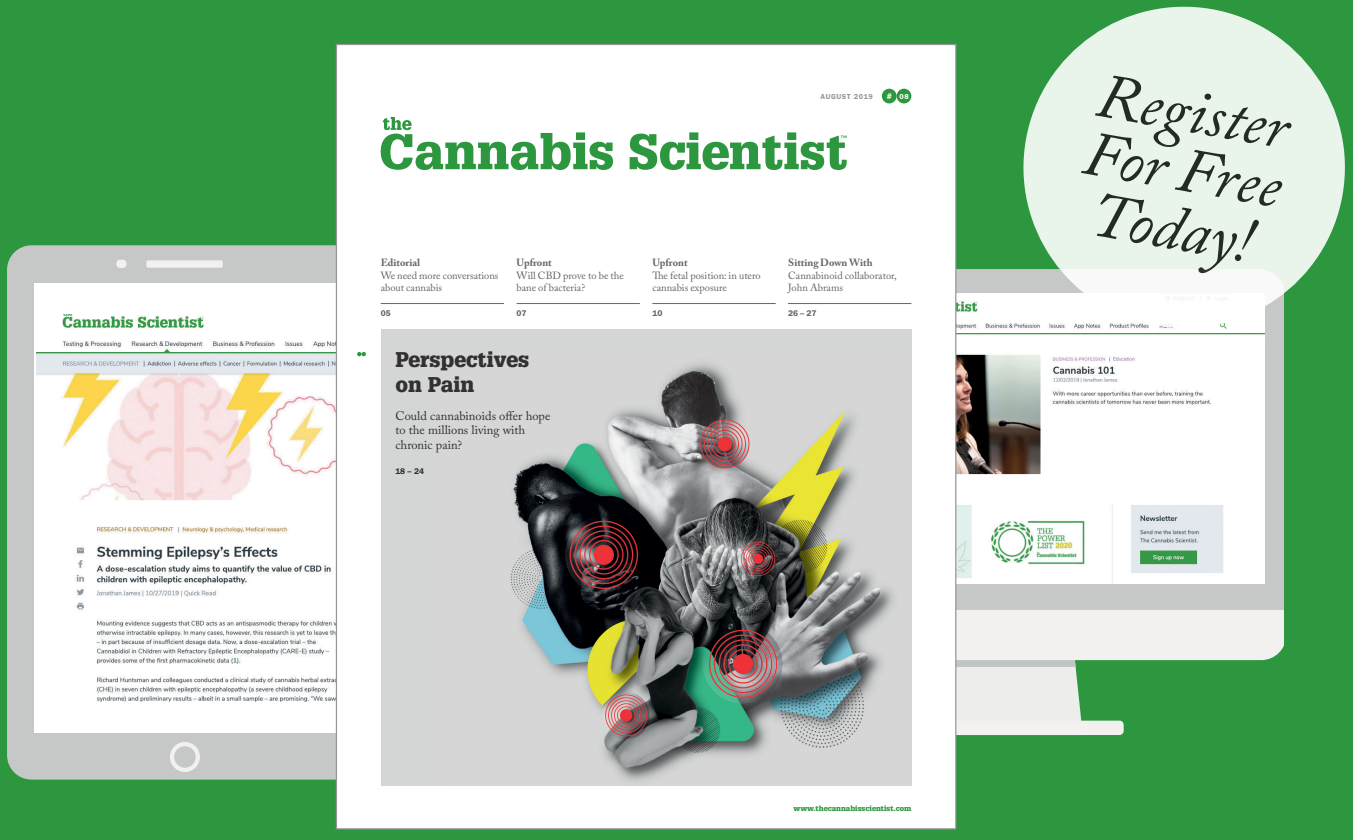

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Leading by Example

Sitting Down With…
Livia Eberlin, Assistant Professor, Department of Chemistry, The University of Texas at Austin, Texas, USA.

You're perhaps best known for developing the MasSpec Pen. Care to tell us more?

It's a handheld MS device capable of detecting cancer. The pen comprises a tip containing three channels that meet at a reservoir where a solvent droplet – typically water – is formed and interacts with a sample such as a tissue to extract molecules – lipids, metabolites, and proteins – from the sample. A tubing system then transports the droplet from the tip of the pen to the mass spectrometer for analysis. The whole process is automated – incorporating microcontrollers to ensure precise control of the operational steps. Plus, the system is biocompatible and safe to use in human patients.

We've analyzed over 800 tissue samples – mostly surgical biopsies acquired from tissue banks and analyzed in my laboratory – and we are now conducting a clinical study with over 100 patients to determine how well our device works during surgery in vivo and in freshly excised tissues. So far, so good: we are able to obtain complex and diagnostic molecular information from these samples. The next step is to continue testing and improving our methods for real-time disease diagnosis.

What is your current focus?

Pushing towards proper validation and testing of the MasSpec Pen in surgical use, as well as exploring other applications and technologies in health related research. I'm particularly excited by an ongoing project to improve the preoperative diagnosis of suspicious thyroid nodules. Is it benign or malignant? Using metabolic information from MS imaging, we can better determine whether a patient will benefit from surgery or not. We're now looking to validate this finding in a multicenter study using a greater number of samples. Plus, we are running a number of other projects designed to assess the efficacy of personalized treatment modalities, such as immunotherapy.

Who was your most important mentor?

My PhD supervisor, Graham Cooks, had a really big influence on my career – he helped me to define what I was really passionate about. A lot of my work is influenced by him; in particular, I try to carry on his vision by challenging my team to think creatively.

A personal connection is key. In days gone by, your PhD supervisor was often considered a superior figure you barely saw or spoke to – there was an element of fear. Taking inspiration from Graham, I try to be as open as possible; I aspire to be a mentor with a connection tailored to each individual student. Ultimately, it's a supervisor's responsibility to prepare their students for a successful career. It's vital that the student loves their project as much as you do; the last thing you want is a PhD student who is miserable, working on something that they really have no interest in or passion for. Once you find your passion, you don't need to be pushed – the effort comes naturally.

Does being a young woman in science present unique challenges?

On a personal level, I've not really experienced much pushback for being young and female; instead, most of the prejudice I've faced has been because I'm Latino. To be honest, that has only driven me to prove myself more. That said, I have felt a lack of women with children (I have three) as role models in senior academic positions. We have the same number of men and women receiving PhDs – yet we lose many of those women at higher professional levels.

I've been very fortunate. I gained a fellowship from L'Oreal, which has helped me overcome many challenges.

"It's vital that the student loves their project as much as you do; the last thing you want is a PhD student who is miserable, working on something that they really have no interest in or passion for."

Through that process I developed an interest in mentoring, and providing the support necessary to encourage women to stick with science. I'm keen to connect young researchers with mentors in the field, who can support and encourage those facing adversity.

What has been the proudest moment of your career?

The MacArthur Fellowship I received last year was really special – and completely unexpected! I was told they seek 20 or 30 letters of recommendation, and to know that so many people wrote in support of my career and my research was a massive honor. I feel extremely blessed to be able to work in this field, pursuing projects in the area of application that I love. Of course, it does come with a huge sense of responsibility – I am driven to continue striving for excellence and repaying the faith others have shown in me. I look forward to many more proud moments in the future.

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