SEPTEMBER 2019 # 80

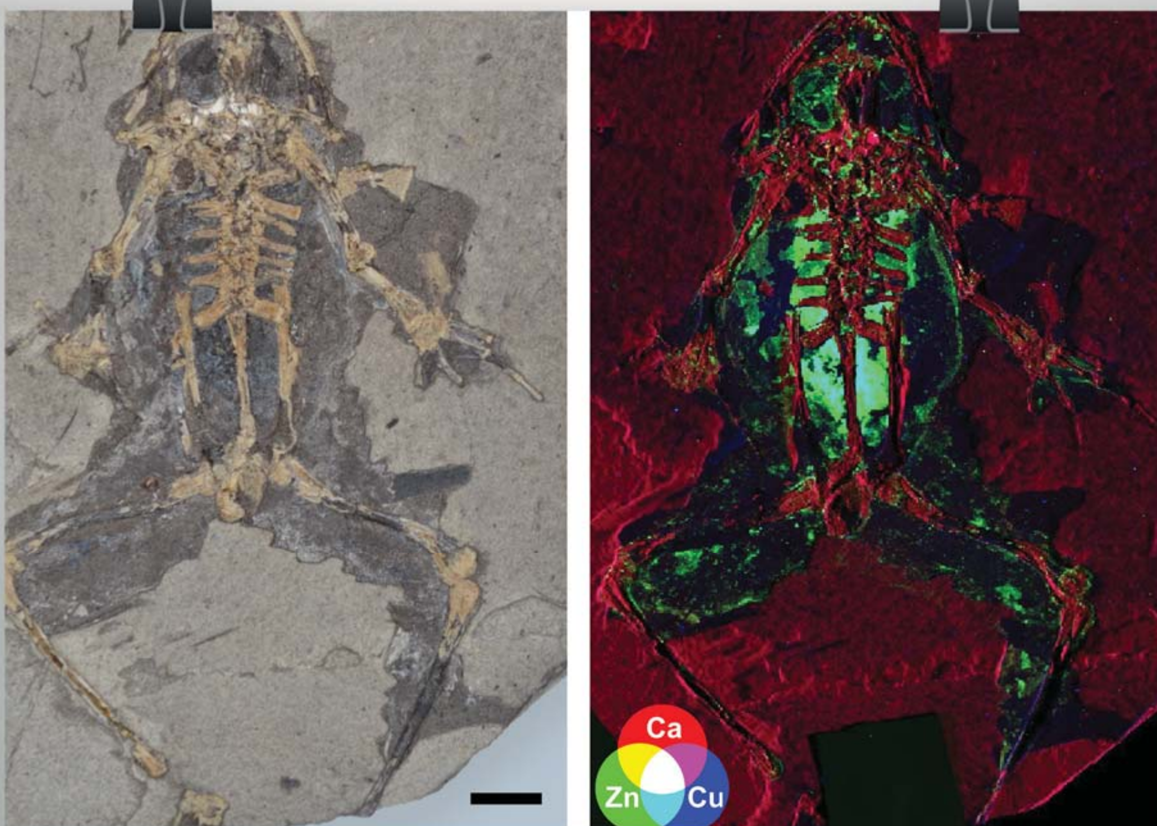
the Analytical Scientist™

Stories of the Dead

Turning back time by analyzing human remains.

20 – 28

Image of the Month



Ancient Amphibian Autopsy

A combination of scanning electron microscopy and synchrotron rapid-scanning X-ray fluorescence has revealed the most anatomically detailed structures of fossilized frogs to date. Fossilized melanosomes – the cellular repositories of the pigment melanin, in addition to a variety of different metal ions, proved to be the perfect biomarker.

Credit: Fossil photograph copyright the Natural History Museum, London. X-ray fluorescence map copyright Valentina Rossi.

Reference: V Rossi et al., "Tissue-specific geometry and chemistry of modern and fossilized melanosomes reveal internal anatomy of extinct vertebrates", Proc Natl Acad Sci USA, [Epub ahead of print] (2019). DOI: 10.1073/pnas.1820285116

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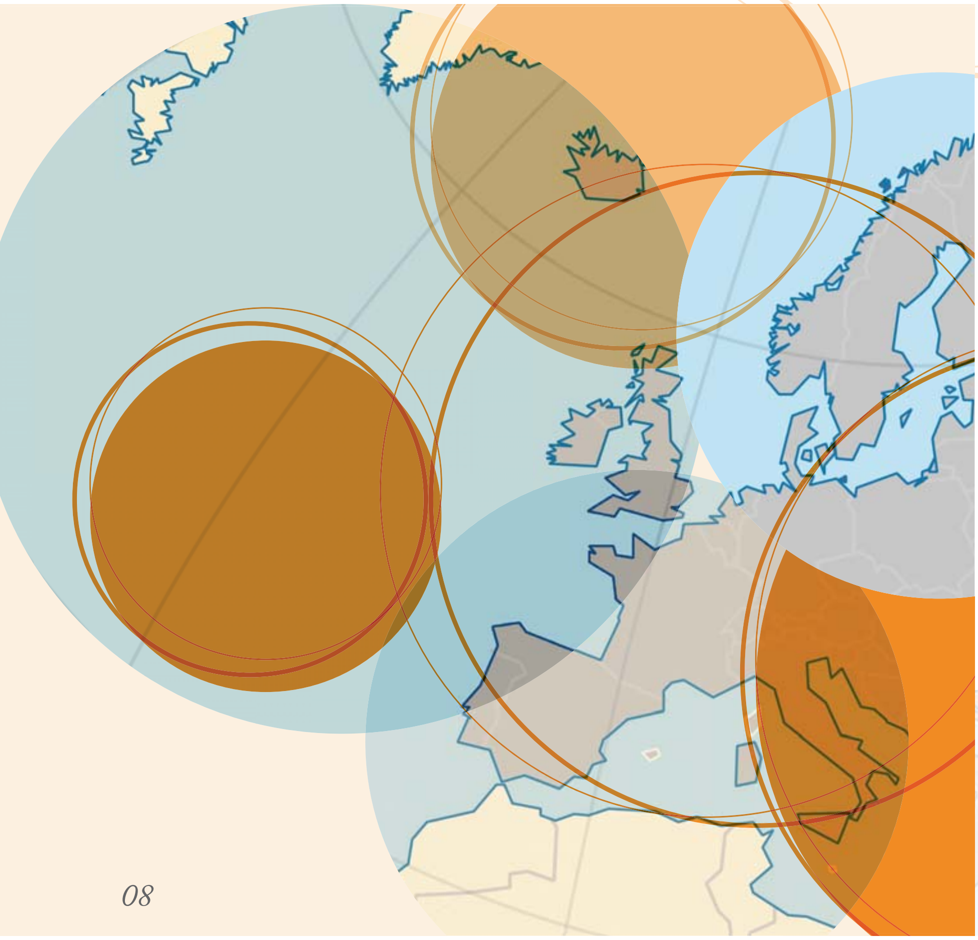
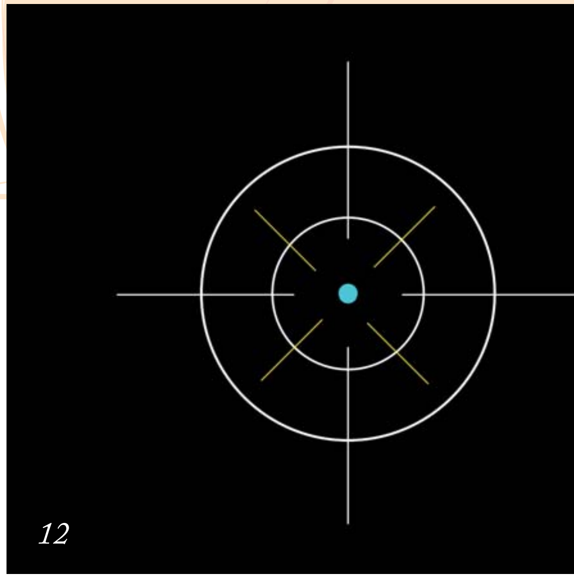
Contents





On The Cover

Skeletal remains preserved in the beachside chambers of Herculaneum following the Vesuvius eruption of 79 AD – provided by Pier Paolo Petrone (University of Naples "Federico II").

The Spectroscopist Inside

Reports

Sitting Down With

the **Analytical Scientist**

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Analytical Science Breaks Free

Testing is moving out of the lab and into the real world – bringing risk but also exciting potential.

The feature this month, which previews the exciting topics coming up at Recent Advances in Food Analysis (RAFA) 2019, contains some provocative comments from our expert panel – food for thought, if you'll forgive the pun.

All three panelists agree that the future of food safety and authenticity testing lies not in increasingly sophisticated lab tests, but in handheld devices (food scanners) that can be used in the warehouse, the supermarket, and even at home. With analytical devices becoming ever-smaller and more user-friendly, it's a trend that reaches further than food analysis.

But the move from lab to home comes with risks. I was particularly struck by Michel Nielen's thoughts on consumer-level testing:

"It's easy to imagine a future society in which everyone has the ability to conduct food analysis. I do not doubt that consumers would trust themselves in spite of the poor-quality device they might use to conduct it, and in whatever fashion they would apply it."

The consequences of unreliable at-home testing could be serious, says Nielen. Bad news travels fast in today's connected world and could have a damaging effect on public confidence in analytical measurements more generally. To that end, portable tests must be regulated as stringently (or even more so) than lab-based instruments, and allow for less-than-perfect conditions (and less-than-perfectly-trained operators).

Yes, there are risks, but the potential is exciting. For someone with food allergies, being able to test your food using smartphone-based technology would remove some stress from day-to-day life. But on a larger scale, the ability to collect data from thousands or millions of people brings a new meaning to Big Data and could revolutionize medical and environmental studies.

Ultimately, rapid, portable analytical testing could make everyone an analytical scientist – and, as far as I'm concerned, that is no bad thing!

Charlotte Barker
Editor

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

Bronze Age Bartering

Trace element and isotope analyses highlight metal trading practices in Bronze Age Scandinavia.

Cross-border trading in Europe has roots that far predate the political agreements governing these practices today. There is much evidence for this activity in the form of recent works using trace element and isotope analysis; now Heide Nørgaard and colleagues join the party using X-ray spectrometry (EDXRF) and multicollector-inductively coupled plasma MS.

Researchers applied these techniques to a collection of 210 metal objects from early Bronze Age (2000-1600 BCE) Denmark – a sample pool representing almost half the bronze artifacts available from this area at this time (1). "It's astonishing how rapidly trade growth took off in Scandinavia," says Heide Nørgaard, referencing a previous study conducted by Swedish archeologists (2). "From 2000 BC to 1600 BC, we see the volume of bronze rise from 60kg to 500kg." But where did all this bronze come from?

Fortunately, many of the samples had been processed during previous archeological work in the 1960s. The result? A glut of high-quality and well-preserved materials; a welcome change from the milligram quantities of material typically available for archeological analyses.

Using Danish artifacts stored at the Curt-Engelhorn Center in Mannheim, Germany, as well as from several other European museums, the team were able to uncover a complex network of trade spanning much of central and northern Europe. Given that the Bronze Age Danes inhabited an area devoid of natural ore, the team suggests such trade routes may represent the means by which these people obtained their tools.

Combining multiple analytical techniques proved key; whilst lead isotope ratios differ between ore deposits – in many respects acting as an isotopic "fingerprint" - they are not unique enough to distinguish between deposits with similar signatures. Here, EDXRF stepped up to the plate: "It's a superb technique because it's non-destructive and provides crucial information that allows us to precisely localize samples," says coinvestigator Ernst Pernicka. "In combination with isotope analysis and Heide's archaeological knowledge, trace element analysis has helped us to establish a complete overview of trading patterns in the early Bronze Age."

And it seems Bronze Age Danes liked to shop around… Early copper imports bore the signatures of ore from modern-day Slovakia, but the signatures of later items suggest that trade soon turned other sources in the eastern and southern Alps. Of course, copper is only one half of the jigsaw. Bronze also contains tin, but determining the provenance of this ore is proving far more complicated – and with no clear answer in sight. However, tin isotope ratios may provide a decisive clue (3). Unperturbed, Nørgaard says the team is not done yet: "We have a lot more data to analyze, and nearly 600 samples from the Middle Bronze Age to work with. That should tell us even more about European trading habits."

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The Analytical Scientist Innovation Awards 2019

Nominations are open for this year's TASIAs!

The Analytical Scientist Innovation Awards (TASIAs) return in 2019. The goal? To highlight the latest and greatest technology, instrumentation and software making waves throughout the analytical science community.

Nominations for The Innovation Awards are welcome from individuals, groups, or organizations.

To enter, please email matthew.hallam@texerepublishing.com (Subject line: 2019 Innovation Awards) with the following information:

- Name of innovation
- Launch date (must be after October 31, 2018)
- Brief description (~10 words)
- Detailed description (50-150 words)
- Potential impact (50-150 words)
- One image (if applicable)

The deadline for entries is October 24, 2019. All nominations will be put to a panel of experts, who will decide on the 15 top innovations of 2019. The panel's decision is final and no correspondence regarding their deliberations or the final list will be entered into.

The winners will be announced in our December issue – in print and online.

To learn about last year's winners, go to tas.txp.to/TASIA2018.

A Call to AMS

Measurement science in the UK faces uncertainty: can CAMS lead the scientific rebellion?

Measurement science plays a key – yet often overlooked – role in research and innovation, and their translation into industry. From healthcare to consumer products, energy and environmental regulation, analytical science is ubiquitous – a hallmark of a modern and vibrant economy. Yet, when The Royal Society of Chemistry (RSC) and the Engineering and Physical Sciences Research Council (EPSRC) conducted landscaping reviews of the field (1) in 2015, the findings did not reflect the essentiality of this space.

The EPSRC makes clear the need to actively strengthen analytical sciences in the UK to maintain current standards. If not, adverse consequences will be felt across the entire UK science sector, owing to "disjointed infrastructure and lacking education programs." The solution? A "centralized organization, capable of propelling the field forward," says the EPSRC.

Enter stage right: the Community for Analytical Measurement Science (CAMS), an initiative designed to build on the foundations laid by the EPSRC's 2015 report. "Measurement science is a crucial enabler of multidisciplinary scientific research and innovation," says Melissa Hanna-Brown, Chair of the CAMS Executive Board. "Yet, it is apparent that there are major issues – notably the field's poor public profile, as well as a lack of proactivity regarding the implementation of emergent technologies across sectors. It is important we address these challenges to maintain one of the UK's biggest strengths – its leadership in science and innovation," she says. This June, after significant effort to unite the community, CAMS celebrated their highly anticipated launch at the RSC. Now, the hard work begins.

Their first line of attack: emergent technology. Measurement Scientists have an important role to play in the era of "Big Data," and, referencing a report by NASA (2), Hanna-Brown is keen to stress the importance of measurement science in challenging new areas; in particular, the seamless integration of analytical instruments with advanced computational modelling, predictive software and simulation tools: "Looking forward, we must improve on our existing abilities to produce and measure masses of high-quality data to fully understand our analytical limitations, and how these data can be applied to derive meaningful insight into problems."

Modern challenges require modern solutions. And education is no exception: "Many training materials – even those produced five or ten years ago – do not meet today's requirements," says Julian Braybrook, UK Government Chemist (Julian expands on the importance of education and collaboration in "Connecting the Dots," page 14). "In addition to supporting new studentships, postdoctoral positions and other academic posts, CAMS is working with a number of e-learning companies to produce the educational material demanded by today's workforce."

A consortium of UK universities – the CAMS Measurement Science Research Institute – is working to anchor these initiatives and facilitate analytical research under CAMS' leadership. Hanna-Brown is pleased with current progress and remains optimistic for the future: "The goal is to bring cohesiveness to the community – ensuring a sustainable pipeline of analytical measurement talent. By establishing a central, innovative core, we can drive progress in science, technology, and education."

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In the News...

Bitesize developments in analytical science.

The Tongue of Tomorrow

The trade of counterfeit alcohol is rife, and efforts to stifle it are struggling to keep up. Introducing the "artificial tongue" – a checkerboard arrangement of sub-microscopic gold and aluminum slices capable of distinguishing between beverages with over 99 percent accuracy. The metals demonstrate light absorption properties (plasmonic resonance) when submerged in liquid, and this resonance varies subtly when exposed to different drinks. Seemingly identical solutions can be differentiated with ease, providing a valuable tool for forensic scientists.

Read more: https://rsc.li/2YUfH2b

Don't Sweat it

Many medical tests are invasive in nature – taking blood, for example. A team from the University of California, Berkeley, want to bypass such procedures by using microfluidic sensors to measure the electrolytes and metabolites in sweat in real time; the approach should be helpful for monitoring dehydration and fatigue, but may find more far-reaching applications as research continues.

Read more: https://bit.ly/2OXOfge

Ditching the Labels

Surface-enhanced Raman spectroscopy can be used to detect DNA mutations without using labels, but technological limitations have thus far restricted its use to analyzing short sequences. The incorporation of dichloromethane (an interfacial agent) into standard protocols allows single-base mutations in double-stranded DNA to be detected at a resolution of 100 bases, potentially paving "a new avenue for highly selective DNA detection in clinical applications."

Read more: https://bit.ly/2YQ5XpL

Precision Excision

Two-photon laser microscopy reveals unique tumor tissue features that may improve oncological surgery.

Imaging technologies are invaluable in the operating theatre. Modern approaches allow surgeons to visualize cancerous tissue in real time; a reassuring addition for those holding the scalpel. There is, however, room for improvement; low spatial resolution means that smaller metastatic lesions may go unnoticed.

Thomas Schnelldorfer and colleagues have developed a new protocol capable of classifying tissue biopsies with an accuracy of 97.5 percent by combining two-photon laser scanning microscopy with advanced imaging and statistical software (1). "We've demonstrated that we can identify specific cellular and tissue-level features at the microscopic level – distances as small as 1/100,000 the width of a human hair," says Schnelldorfer.

But a small sample size – just 41 images – and numerous technical challenges mean the tool still has a way to go before it can be used on operating tables. "We need to evaluate a greater image sample from a more extended patient population," says Schnelldorfer. "In parallel, we also need to determine how to miniaturize these microscope modalities and integrate them into surgical instrumentation and procedures."

If the team is successful in these endeavors, the tool will give clinicians access to real-time information about the size and location of tumors with higher accuracy than ever before – an approach that will revolutionize the field, according to Schnelldorfer. "This method could profoundly augment sensitivity and specificity during operative determination of cancer metastasis," he says. "Fundamentally, this could drastically improve how we treat patients suffering from a wide range of tumors by allowing surgeons to remove a far larger proportion of tumor mass."

Reference

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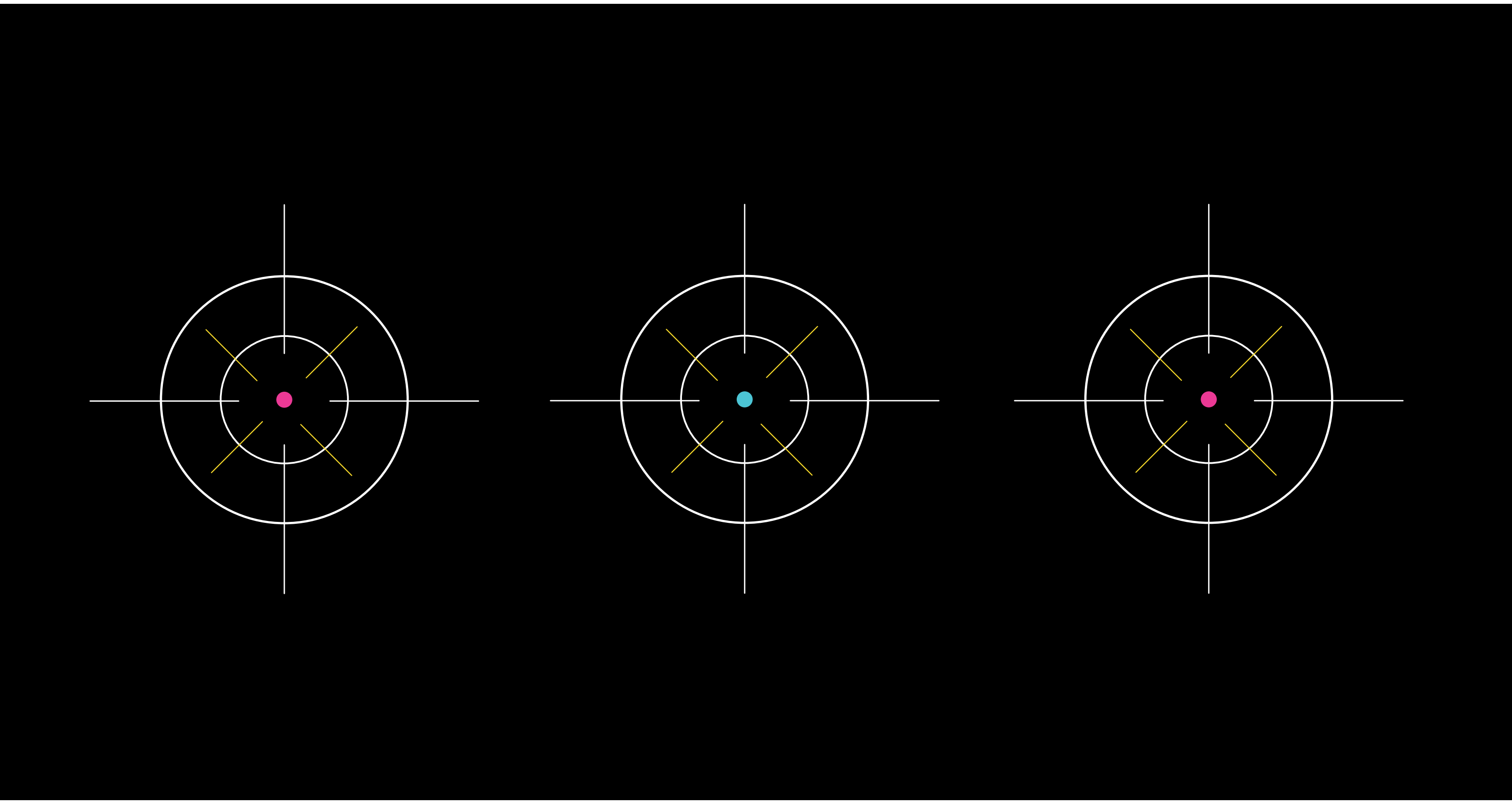

Resolution Revolution Realized

Breakthroughs in cryo-electron microscopy provide atomic-level protein information that may transform drug development.

Atomic-level structural resolution has driven major breakthroughs in drug development by gifting pharmacologists with ever-increasing knowledge of potential drug targets. Cryo-electron microscopy (cryo-EM) represents a valuable tool for extracting this information, rivalling classic techniques like X-ray crystallography and earning Jacques Dubochet, Joachim Frank and Richard Henderson the Nobel Prize in Chemistry in 2017 for their work laying the foundation for this technique in the high-resolution structural determination of biomolecules.

Zongli Li and colleagues recently took up this (admittedly rather chilly) torch, having determined the structure of the mouse transient receptor potential canonical subfamily member 5 (mTPRC5) (1) – a nonselective calcium cation channel – at an unprecedented level of detail: 2.8-Ångstroms. The key findings – a unique extracellular pore domain coupled a disulfide bond (2) – highlight mTRPC5 as the "black sheep" of the larger TRPC sub-family, and may explain the divergent physiological role of this channel. Li believes these findings give credence to the idea that human TRPC5 is a promising target for drug development – particularly for psychiatric disorders: "These channels are highly expressed in the brain – providing a promising pharmacological target ripe for exploration," he says.

Li is quick to pinpoint the success of the study on the "resolution revolution"- a movement over the last decade that has facilitated major improvements in cryo-EM technology. "The field really took off around 2013, with the first near-atomic resolution imaging of membrane proteins," Li says. "This was driven by major improvements in camera technology and data processing software, as well as better cryo-electron microscopes."

Against a backdrop of ongoing technological advancement, the team have wasted no time plotting their next steps. "We are talking to a couple of companies, exploring ways in which we might work together," says Li. "Unsurprisingly, due to TRPC5's role in disease, it is of considerable interest as a drug target." But before that tantalizing lead can be followed, Li concedes that the team will need to characterize the entire length of the protein: "To identify potential drugs, we need to fully understand the structural elements of the protein we are targeting with small molecules, irrespective of whether we intend to activate a channel or block it."

Looking ahead, Li is optimistic. "There is a real opportunity for those in academia, who have been crying out for years for improved technology, to really begin to understand macromolecules at an atomic scale," he says. "No doubt, this will provide vital new information that will prove crucial in treating diseases."

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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

Connecting the Dots

Bringing industry, government and policy together will supercharge the UK's analytical sector.

By Julian Braybrook, Director of Measurement Science for the National Measurement Laboratory at LGC, UK, and Government Chemist.

The establishment of the Community for Analytical Measurement Science (CAMS) (1) is a landmark moment for analytical science in the UK. If you look back over the past decade, there has been a significant shift in attitudes towards the "measurement" sciences – driven in part by the publication of two major reviews. The first, a landscaping exercise by the Royal Society of Chemistry (RSC) in 2015, was quickly followed by a report by the Engineering and Physical Science Research Council (EPSRC) (2). Both acknowledged the value of analytical science in the UK, but also highlighted that there is a significant gap between theory and practice.

The all-encompassing nature of analytical science is both a gift and a curse. The field's value is often overlooked. Many people describe measurement science as a utility – like electricity and water – which you may not fully appreciate because they are ubiquitous. It's only when they vanish that you recognize – in haste – their value. When everything is progressing well, people carry out their measurements without a care in the world; only when things go wrong do they pay more attention.

The challenge lies in tying together every aspect of analytical science to form an effective community structure – one that is coherent and impactful. Fortunately, the desire for such a system fits within the government's industrial strategy. The objective? To connect trade via a unified system of analysis, making it easier to move goods across borders. Global trade will prove imperative in a post-Brexit world because this approach can facilitate access to new markets, and make for more efficient regulatory compliance. The goal is to bring together various elements of analytical science, driving product development and new infrastructure investment to support our future.

Part of that process will involve integrating data-rich technologies. Yet, that alone will not prove sufficient – translation is equally essential. Bridging the gap between a technology with potential and its point of use is really about the small details; it's about trying to remove as much error and uncertainty as possible. At the same time, a skilled workforce with the ability to apply these technologies will be key, which highlights a central role for education in achieving our goals.

With support from BEIS (Department of Business, Energy and Industrial Strategy) we've been developing e-learning materials with some pilot companies. This experiment is in response to the demand – particularly in industry – for access to faster and less formal education tools. At the same time, however, we also want to support more formal education; we're now offering studentships, postdoctoral positions and lectureships so that we can build a lasting legacy in this space and establish a concrete structure for career development. After all, we don't want to fund posts that last three or five years and have the trained professional leave afterwards.

CAMS will work to connect the analytical infrastructure so that research and innovation can be directed towards four themes: point-of-use technologies, analysis of complex mixtures and separations, instrumentation, and data analytics. In short, we want to unite analytical science of all forms across the UK.

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Making Sense of Metabolite Mixtures

Substructure analysis provides a means to decipher complex metabolic samples.

Justin J.J. van der Hooft, Bioinformatics Group, Wageningen University, Wageningen, the Netherlands.

Personalized medicine. Antibiotic discovery. Host-microbiome interactions. Plant breeding. What do these fields have in common? All have benefited from the realization that comprehensive small molecule profiles are essential to increase our knowledge of complex biological systems. Metabolites then represent key markers in such studies, and are often the end goal of analyses.

To study metabolites, scientists typically extract small molecules from biological systems and subject them to MS. In recent years, technological advances have supercharged this technique; we are now able to analyze huge numbers of different molecules and vital data for their structural elucidation, such as their so-called fragmentation spectra, are more easily obtained. Faster measurements mean more spectral data, and ongoing optimization in this space means we are able to collect more than ever before. Yet, despite our ability to obtain a wealth of high-quality spectral data from biological systems, a major challenge remains: translating this spectral data into structural information.

Metabolite annotation and identification represent major bottlenecks when performing such translations (1). The main challenges are the structural diversity of metabolites found in natural extracts and the (still) large number of completely novel molecules measured. For the latter, there are no reference data available – not even from structurally-related molecules. Therefore, it's not surprising to see such a focus on the linking of spectral data to structural information at both the Faraday Discussions on Challenges in analysis of complex natural mixtures (Edinburgh, UK, May 13-15, 2019) and the Metabolomics2019 meeting (The Hague, NL, June 24-27, 2019). Traditionally, structural information is obtained by matching experimental mass spectra with database spectra for reference molecules (2); however, in practice, only a few percent of spectra can then be structurally annotated.

It is my view that metabolome mining and annotation tools will prove to be a crucial toolkit for overcoming this data deluge. How? By translating spectral data into structural information and providing comprehensive yet detailed chemical overviews of natural extracts. These approaches are based on two principles: i) the usual presence of structurally-related molecules in natural extracts, and ii) the similar mass fragmentation spectra of molecules sharing similar structures. In silico approaches hope to extract chemical information from spectral data by finding and recording relationships between spectra, and matching candidate structures with shared building blocks from databases with these measured mass spectra.

Once spectral relationships are known, one can build networks in which structurally-related molecules are grouped into molecular families (3). My team and others have shown that comprehensive chemical pictures and unprecedented chemical details can be obtained from spectral data when applying metabolome mining and annotation tools to complex metabolite mixtures in such a way (4-7). Moreover, the outcomes of different analysis workflows can be integrated; for example, fragmentation spectra can also be mined for co-occurring mass peaks.

Inspired by text-mining algorithms, the MS2LDA tool was designed to locate the chemical imprints of molecular substructures in metabolomics data using topic modeling (8-10). Analogous to searching for trending topics in text documents based on co-occurring words, MS2LDA groups consist of molecules with co-occurring mass peaks that can be linked to relevant biochemical substructures. The MolNetEnhancer workflow (11), which includes the MS2LDA tool, allows researchers to integrate several mining and annotation tools to detect the presence or absence of target substructures within molecular families.

Substructure-based workflows enhance our understanding of chemical profiles – and the profiling process itself – in manifold ways, from grouping unknown chemicals and explaining chemical differences between samples to structural elucidation (12). Extracting chemical information from metabolomics profiles by such methods will then work to bridge metabolomics to the broader omics field in many areas – for example, in matching natural products to the biosynthetic gene clusters behind their production.

All in all, I believe that substructure analysis will play a key role in helping to decipher complex biological systems and the functional role that metabolites play within them. And I look forward to the bright future of this field.

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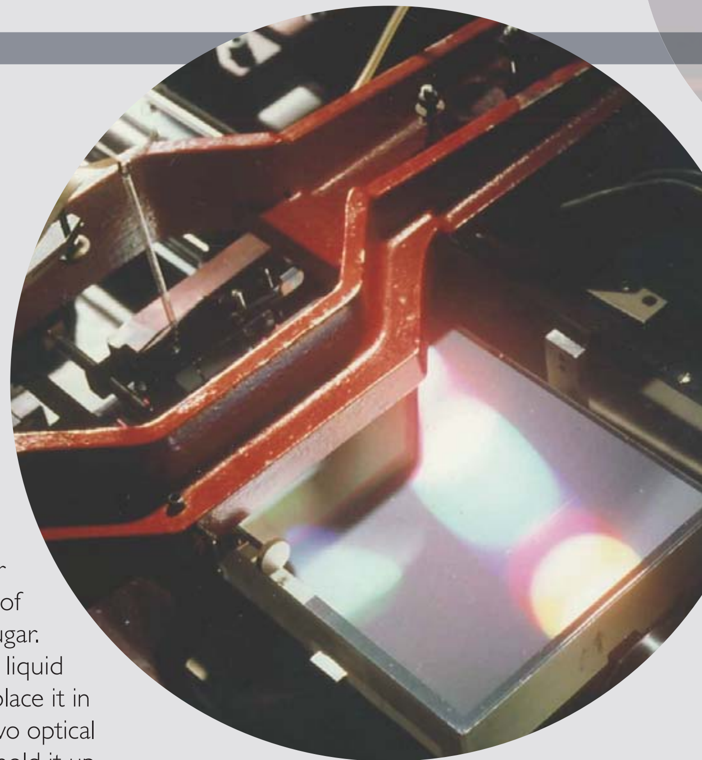
Celebrating 200 years of innovation at HORIBA Jobin Yvon.

By Sal Atzeni



After 25 years at HORIBA Jobin Yvon, the detailed molecular information we can obtain from light alone still amazes me every day. Today, our products are used everywhere from underground synchrotrons to outer space – but how did we get here?

The invention that saved a thousand ships

The story begins in the early 1800s with two Frenchmen – Augustin Fresnel and Jean-Baptiste Soleil – and a life-saving invention. Fresnel wanted to prevent shipwrecks by making lighthouse lamps more powerful. At that time, the lenses were heavy slabs of glass; Fresnel believed he could boost the beam with multiple segments of specially shaped echelon lenses. Eventually, he partnered with a glass-manufacturer, Soleil, who had developed processes for producing optics and lenses without defects. The combination of innovative design and precision manufacturing proved hugely successful, saving many sailors from a tragic end – and launching a new industry.

Fresnel and Soleil continued to refine their work on instruments that validated theories of light; in particular, the understanding of polarization. The company developed a small polarimetry instrument that was used for testing the chemical quality of products, such as wine and sugar. You could simply place your liquid sample into a cylindrical tube, place it in the instrument – which used two optical elements on either side – and hold it up to the window. The angle of light rotation showed how pure the product was – an amazing innovation at the time, and still used today (albeit with a laser in place of sunlight).

In the late 1890s to the early 1900s, the names of Amédée Jobin and Gustave Yvon appeared for the first time in the company's history. CEO Jobin, and his son-in-law Yvon, did for optics what Henry Ford did for cars – optimizing production processes to create the highest quality instruments. Their business philosophy is one we still adhere to today: serving niche markets with the highest performance, sensitivity and quality. In 1899, another great advance was developed – the Febry-Perot interferometer – which soon became the preferred high-resolution wavelength selection tool at the heart of key techniques, such as infrared spectroscopy. By the mid-1940s, the company had developed a plethora of optical instruments, including spectrometers and electrophotometers.

"At that time, the lenses were heavy slabs of glass; Fresnel believed he could boost the beam with multiple segments of specially shaped echelon lenses."

> *"Producing hundreds to thousands of perfectly parallel lines per millimeter is no mean feat, and required a specialized machine (the ruling engine)."*

'Grate' expectations

We all know you can use a prism to separate different colors of light into a spectrum, and up until the 1950s this was a common method for analyzing light. But there is another, better way – using a diffraction grating. In 1955, the Jobin Yvon group, now with over 100 employees, revolutionized a way to make light diffract off a hard surface engraved with closely spaced parallel lines using a stylus. Producing hundreds to thousands of perfectly parallel lines per millimeter is no mean feat, and required a specialized machine (the ruling engine). A new facility was set up in Longjumeau, well outside bustling Paris and built on top of solid bedrock, to keep vibrations to a minimum. Even today, gratings are at the heart of every optical instrument we make. Fast forward to the late 1960s, and the Jobin Yvon team had taken their technology to the next level by using hologram technology to etch the lines into substrates – essentially using optics to make even better optics!

In 1974, the company launched their first Raman spectrometer. Due to its non-destructive process that enabled researchers to observe and characterize a material's molecular composition and external structure, Raman instrumentation proved to be another huge hit for the company, with high-profile labs around the world investing in the technology.

The leadership of Michel Baudron and Gilbert Hayat during the 1980s and 1990s saw the company branching out into new applications, from life sciences to space missions. In 1997, the Jobin Yvon Group was acquired by HORIBA. While the large Japanese corporation already had their own instruments covering the top and bottom ends of the electromagnetic spectrum, they lacked certain core technologies in the middle. Jobin Yvon technologies filled that void.

The modern era

Our grating technologies have advanced to the point that we can create large gratings of up to meter-size, which are used for high energy physics experiments, such as recreating fusion conditions at the surface of the sun. The recent acquisition of an atomic force microscopy company enabled our Raman instruments to not only measure the Raman spectrum, but also detect each atom on the surface as it does so, providing extremely detailed surface information for semiconductors and other materials.

In 2018, we celebrated the opening of a 132,000 square foot optical spectroscopy center in New Jersey. The HORIBA Group keeps growing, but we retain the core goals set out by Jobin and Yvon over a century ago: to be the best.

To stay at the forefront of optical technology, we partner with bright people with great ideas, whether in industry, academia or elsewhere. We form collaborations, engage in joint ventures, and go all the way to mergers and acquisitions if we feel it can bring success. What's the common thread between our employees, collaborators and customers? Passion! When people really care about what they do, they keep on pushing forward, regardless of any failures along the way, or the challenges looming ahead. We believe the systems we are building will improve the human condition, and we will always go the extra mile to get there.

Sal Atzeni is Executive Vice President and General Manager/Chief Technology Officer at HORIBA Scientific, New Jersey, USA.

STORIES *of the* DEAD

HOW ANALYTICAL CHEMISTRY REFINES LIFE AFTER DEATH.

by Matthew Hallam

The history of our planet is both fascinating and complex, and humans are gifted with the ability to form a picture of its past by piecing together the evidence left behind by our predecessors. The clues take many forms, from galleons resting on the ocean bed to citadels standing high in the mountains and timeless relics proudly displayed in museums. Perhaps more informative than any of these (or all of them combined), however, are the human remains scattered across the globe.

The remains of ancient humans have ignited our imaginations for millennia, giving us a teasing taste of lives radically different to our own. Yet, it is only in the past century or so that we have developed the scientific means to delve deeper into the lives of our ancestors, from Neanderthals stalking their prey on the ancient planes of Europe to mass sacrifice atop the Aztec pyramids.

In honor of the ever-expanding role of analytical chemistry in archeological contexts, we decided to dig into three studies that underscore the capabilities of today's techniques – and shine a light on the researchers deciphering the stories of the dead. Welcome to the world's first (probably) scientifically-sound séance.

SECRETS *of the* PHARAOHS

Mummified remains stand the test of time – now chemists are looking to the canopic jars of ancient Egypt to find out why.

By Lana Brockbals, Department of Forensic Pharmacology and Toxicology, Zurich Institute of Forensic Medicine, University of Zurich, Zurich, Switzerland.

My PhD research at the Zurich Institute of Forensic Medicine focuses on mechanisms underlying the postmortem redistribution of centrally acting drugs; a phenomenon that leads to altered drug concentrations after death and poses difficulty for case interpretations in forensic toxicology. I apply this largely to determining the cause and manner of death for human remains admitted to our institute, where we conduct our studies with a time-span between death and medico-legal examination of three days or less. It wasn't long, however, before I found myself studying remains somewhat older than this… A few thousand years older, in fact.

Canopic jars were used to hold the viscera (stomach, intestines, liver and lungs) of those deemed worthy of mummification in ancient Egypt and, in contrast to the mummies themselves, are very poorly studied. That's one of the reasons why joining the "Canopic Jar Project," alongside my PhD supervisor Thomas Kraemer, was so exciting – there are so many questions to be explored! The project is headed by Frank Rühli, Head of the Institute of Evolutionary Medicine at the University of Zurich, and aims to fill the knowledge void with significant genetic, medical, Egyptological and chemical evidence.

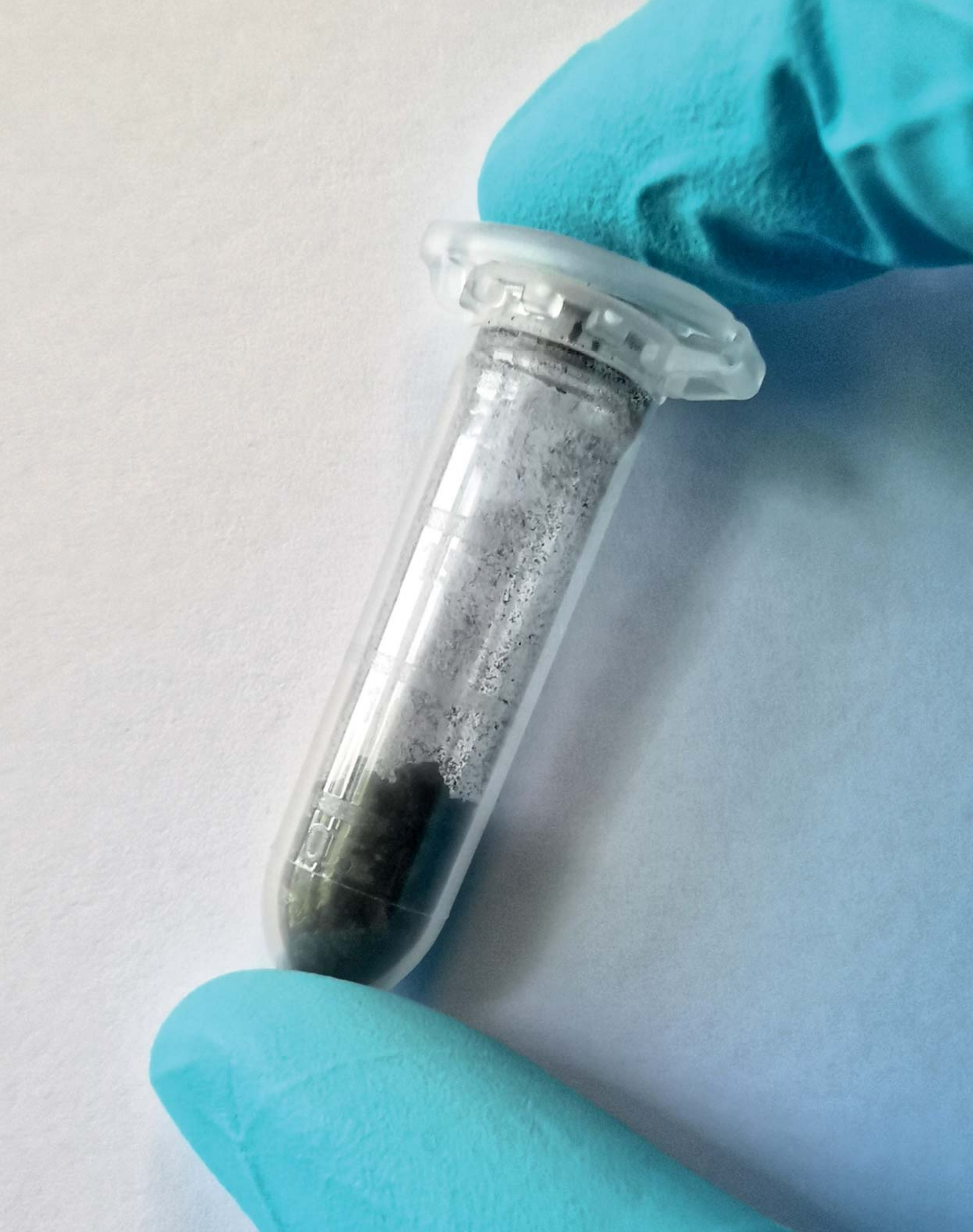
With this goal in mind, our lab adopted a metabolomics-like screening approach, using GC-high resolution MS, to analyze both canopic jar and mummy samples that date from approximately 2686 BCE to 395 AD through stylistic examination and radiocarbon dating (1). What made our approach novel was the use of an untargeted approach, which enabled the successful chemical differentiation of the mummy and canopic jar samples by statistical means. Many previous examinations had performed targeted examinations, which – in most cases – were based on our existing knowledge of mummies and thus excluded many potentially important chemical species. Our approach – on the other hand – utilized all the chemical information gathered through untargeted analysis to feed statistical tests (principal component analysis and partial least squares-discriminant analysis), allowing for the differentiation of mummy and canopic jar samples; this could support the classification of samples of unknown origin in the future, and could even be used to determine the age of samples.

There was initial concern, however, regarding the contents of the jars; at first glance, we were convinced there might not be an adequate amount of sample suitable for chemical characterization. Thankfully, our suspicions were dispelled when a parallel study used computerized tomography imaging to identify hyperdense structures with organ-specific morphology in a subset of the jars. We proceeded with a highly sensitive, universal method, using methanol as our extraction solvent and conducting a two-step derivatization of methoximation and silylation to ensure volatility among a large number of analytes. This approach enabled us to exercise a reproducible, and hence reliable, sample preparation protocol for these valuable samples.

> "Our approach identified numerous compounds detected in earlier studies, including terpenoids, fatty acids and beeswax."

Our approach identified numerous compounds detected in earlier studies, including terpenoids, fatty acids and beeswax. Interestingly, the beeswax we identified was associated mostly with samples dating from the late to third intermediate period, demonstrating a potential increase in the use of this material for embalming in the later dynasties of ancient Egypt. The terpenoids were then difficult to attribute to a specific botanical source because of their variable occurrence in numerous plant extracts, but we eventually suggested the presence of corniferous resin through the presence of cuparene (a constituent of resin, wood and wood extracts) and longiborneol (found in cedar, juniper and pine resins), along with additional plant materials.

We also detected various polycyclic aromatic hydrocarbons – organic compounds generated predominantly during the incomplete combustion of organic materials. The discovery of levoglucosenone and levoglucosan, both of which are formed by the pyrolysis of carbohydrates, such as starch and cellulose, suggest some thermal degradation of the bodies – a finding that may add strength to previous claims that melted resin was



likely used to fill the chest and abdominal cavities during the mummification process; however, we also cannot discount the possibility that they might be external contaminants. In fact, all such studies face the significant challenge of distinguishing between endogenous chemicals and external contaminants that may have accumulated at any point over thousands of years.

We also successfully identified a number of substances that – to our knowledge – had not been discussed in previous literature on this topic, including aniseed constituents, salicylic acid, chamazuelene and jacobine. These compounds are all thought to have had medical significance in ancient Egypt; aniseed, for example, was cultivated at this time to alleviate pains and treat stomach disturbance, and the anti-inflammatory effects of salicylic acid (aspirin) are documented in medical documents of this culture, such as the Ebers papyrus (dated to circa 1550 BCE).

A single analytical system is unable to detect all possible exogenous and endogenous analytes, so further untargeted screening using methods like LC-high resolution MS represents a key next step for these studies. Such an approach will cover an even broader spectrum of substances, increasing our ability to identify novel chemical constituents of embalming fluids. Coupled with new analytical advances that lend themselves towards data of increasingly high resolution, we expect an increased ability to identify currently unknown peaks in the near future.

I will definitely continue analyzing human remains in my career – not only because it is currently the focus of my PhD, but also because this space poses so many important questions to analytical chemists. Providing answers to these questions will allow us to dig deeper into the history of crucial civilizations, such as the ancient Egyptians, while streamlining the future progress of our field as a whole.

Reference

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The VICTIMS *of* VESUVIUS

The 79 AD Vesuvius eruption is perhaps the most famous volcanic event in history, but how exactly did its victims meet their ends?

By Pier Paolo Petrone, Laboratory of Human Osteobiology and Forensic Anthropology, Department of Advanced Biomedical Sciences, Azienda Ospedaliera Universitaria, University of Naples "Federico II," Naples, Italy.

Vesuvius has erupted numerous times during its 20,000 years of volcanic activity – many have been explosive, and some absolutely catastrophic. The "Pumices of Avellino" (4000 BCE) completely devastated the Campanian plain, leading to the abandonment of the surrounding area for centuries, and the infamous Plinian eruption of 79 AD led to the complete devastation and burying of the ancient cities of Pompeii and Herculaneum (1).

The horror of the eruption engulfing Pompeii and Herculaneum is difficult to imagine; apocalyptic scenes of superheated gas blasting through the streets and ash raining from a sun-blocked sky. The death toll remains unknown to this day, but several hundred human bodies have been recovered by researchers. These bodies – along with the cities themselves – are perfectly preserved in calcified ash, providing a unique opportunity for us to study how these people were killed by the infamous event.

I capitalized on this opportunity in 2018, when I began the next phase of an ongoing study of skeletal remains from the beach of Herculaneum (2). Naturally, we started with bioarcheological and taphonomic features of the remains, and were astonished to find numerous skulls not only charred, but exploded – indicative of exposure to extreme temperatures. What's more, bones demonstrated charring and fractures with sharp edges (typical of cremated bones). This was a previously undocumented finding, which – alongside laboratory heating experiments and findings of bone structure microcracking – suggested exposure to temperatures circa 500 °C.

"This high iron content could not be ascribed purely to volcanic ash or other volcanic products, which suggests another source entirely."

We next set out to conduct multi-element analysis of encrusted mineral residues on the bones by inductively coupled plasma-MS (ICP-MS). These residues ranged in color from light red to black, and impregnated the ash-filled intercranial cavities of the bodies and their ash-bed casings – but what are they? And what could they tell us about a disaster that happened almost two millennia ago?

What we found was an extremely high amount of iron in the red incrustations detected in both cranial and postcranial bones, as well as in the ash inside the skulls and the ash-bed. This high iron content could not be ascribed purely to volcanic ash or other volcanic products, which suggests another source entirely. Coupled with negative results obtained when analyzing the ash alone, we were forced to consider the possibility that this iron may have had an endogenous source: the victims' own evaporating body fluids.

To assess this possibility, we investigated the potential presence of heme-containing protein in the residues by means of trypsin digestion and subsequent LC-MS/MS, and found that no tissue proteins were present at detectable levels. We were, however, able to identify alpha-1(I) and alpha-2(I) – reliable peptides from human collagen – most likely originating from within the bones. This finding led us to believe that there was a good reason we could not identify heme-containing proteins with ICP-MS; only proteins protected by the inorganic bone were able to survive the unbearable temperatures of the eruption.

Raman microspectroscopy was, however, able to identify potential products of heme protein degradation among samples. The presence of hematite, an iron oxide, found both alone and in combination with other iron oxides across a subset of samples was a valuable clue; anhydrous metal oxides are an expected product of heme degradation above temperatures of 400 °C. The coexistence of non-crystalline iron oxides and amorphous carbon (attributed to potential organic combustion) in single samples also suggested a human body source for these iron-containing compounds.

Overall, we concluded that these people met their end instantaneously, and death was followed by the rapid vaporization of body fluids and soft tissues. This theory is backed up by all facets of our experiment discussed thus far, but maybe more so by the haunting 'life-like' stances of the victims – the product of extraordinarily well-preserved

skeletal joints in three-dimensional space, which can only be explained by sudden death and the rapid replacement of flesh by ash. The absence of 'pugilistic' poses – the result of rapid protein denaturation and muscle contraction in extreme heat – among the bodies at Herculaneum also suggests that the muscles of these people disappeared more quickly than they could contract, adding further weight to our hypothesis of instant vaporization.

Our study of these bodies is ongoing, and is now providing evidence far beyond our initial expectations. The next steps will be to compare the findings with further remains from more recent volcanic sites, and also to conduct DNA analyses to determine the family relationships and geographical origins of the victims. The evidence accumulated thus far has allowed us to propose alternative hypotheses for the mechanism by which a number of Vesuvius' victims met their untimely demise, and yet so many questions remain unanswered (for now).

The city of Naples has a population of roughly three million and sits just 15 kilometers from Mount Vesuvius – to this day considered one of the most dangerous volcanoes in the world. Many smaller towns and villages also pepper the land surrounding the crater, making the land around Vesuvius the most populous volcanic region on the planet.

Vesuvius has exhibited minor eruptions at regular intervals since the burying of Pompeii and Herculaneum in 79 AD – the last occurring in 1944. Many factors would dictate the strength of a future event, but knowledge is power; and studies like ours are fundamental for understanding the events surrounding Vesuvius' eruption. The more we understand the course that such an eruption might follow, the more equipped we will be to deal with it. The ultimate goal is to understand how me might protect resident populations from the same fate as the bodies at Herculaneum – and I think that's a noble cause.

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You Are WHAT YOU EAT

Stable isotope analysis highlights the longevity of Mediterranean diet staples – and the travel habits of the people who consumed them long ago.

By Cristina Barrocas Dias, HERCULES Laboratory & Chemistry Department, University of Évora, Évora, Portugal.

The way we eat is related not only to available resources, but also gender, socioeconomic factors and religious beliefs. Our tissues record traces of our food choices and mobility, and this information can be recovered from an individual's skeleton millennia after death by studying stable isotopic compositions (1).

Our first attempt to use isotopic analysis investigated fat residues recovered from archaeological sherds (broken pieces of pottery). Palmitic and stearic fatty acids are widely widespread in nature, but their stable carbon isotopic composition ($^{13}C/^{12}C$ ratio) depends on their biosynthesis, meaning different $^{13}\delta C$ values are observed between different organisms, and even between parts of the organism from which the acids originate. Thus, GC-isotopic ratio MS (GC-IRMS) enables the differentiation of ruminant, pork, marine and equine fats, and can also distinguish between those sourced from dairy and adipose fats.

This first attempt was a failure, as the sherds we were working on had only trace amounts of organic material. The south of Portugal has a climate that hinders organic residue preservation, and the sherds had also been stored for decades in plastic bags, which ruined our chromatograms due to phthalate contamination. Tip: beware the danger of storage conditions when it comes to your archaeological samples!

> "Despite this failure, my interest and curiosity about the application of stable isotopic analysis to archaeological materials took me in another direction."

Despite this failure, my interest and curiosity about the application of stable isotopic analysis to archaeological materials took me in another direction. Paleodiet studies rely mostly on isotopic ratios of $^{13}\delta Ccol$, $^{15}\delta N$ and $^{34}\delta S$ in bone collagen, which are measured using elemental analyzer isotopic ratio MS (EA-IRMS). Our lab acquired an EA-IRMS instrument in 2013, along with two postdoc researchers who knew how to use it. I had been reading about the subject for a few years and was excited to make a start, but we weren't quite there yet…

Studying the diet and mobility of ancient populations focuses on osteological remains and is very much an interdisciplinary field, with several essential contributors: archaeologists (for approximate dating, social and economic contexts), anthropologists (for sex, age at death, and dental and health status information), zooarcheologists and archeobotanists (for the identification of animals and plants potentially used as food products), and analytical chemists (for radiocarbon dating and stable isotopic data measurements). When studying the mobility of an individual's remains, it's also advantageous to work alongside a geologist or geochemist to assist with comparisons between the strontium isotopic ratios ($^{87}\delta Sr$), which are measured in the teeth and skeleton of the individual, and in the local geology. $^{87}\delta Sr$ is not measured by IRMS, but by thermal ionization MS or multi-collector ICP-MS, which tends to require even larger teams.

Mobility can also be studied by analyzing $^{18}\delta O$ in apatite phosphate and carbonate in bone or enamel (less prone to diagenesis). The $^{18}\delta O$ values can be correlated with the isotopic values of local water, which in turn are dependent on climatic and geographic factors. Though $^{18}\delta O$ in apatite phosphate can be measured by EA-IRMS after elaborate sample preparation, $^{18}\delta O$ in apatite carbonate is measured using a Kiel interface, in which the carbonate fraction of the apatite reacts with phosphoric acid prior to the IRMS. Along with the $^{18}\delta O$ values from carbonate, these analyses give the $^{13}\delta Cap$, which can be used in combination with the $^{13}\delta Ccol$ as a proxy to investigate the consumption of fish products.

In recent years, our lab has

collaborated with colleagues from universities in Coimbra, Aveiro, Lisbon and Algarve to collect information on the diet and mobility of populations living in southern Portugal from the Neolithic, Chalcolithic, Late Antiquity and Medieval periods (2). Such studies provide insight into the daily lives of ancient people in this region – one of the most western places in Europe. We found that these populations relied heavily on cereals and pulses, with small amounts of meat and fish from low trophic levels. This diet represents the foundation of the Mediterranean diet that is still eaten today. The studied populations were also quite mobile, even in Pre-Historic times, as is clear from the agreement between the available analytical data and archaeological information on the number of foreign traded goods recovered in the region.

Paleodietary reconstructions based on isotopic ratio collagen bulk analysis are limited by the unavailability to us of the whole range of foods eaten by prehistoric human; for example, plant foods are typically lacking and can have very different $^{15}\delta N$ values according to the use of different soil manuring practices. Coupled with the fact that fish and C4 plant ingestion are easily confused and can mask one another, it's clear there are a number of hurdles to overcome in paleodietary reconstructions. The latter can be solved by the use of bulk $^{34}\delta S$ sulfur, but relatively large amounts of collagen need to be available for analysis because of the small amount of sulfur-containing amino acids in human bone collagen.

Paleodiet studies have more recently evolved towards the measurement of carbon and nitrogen isotopic ratios in individual amino acids within purified collagen. This approach has shown promise for elucidating dietary behaviors in complex socioeconomic and environmental contexts, but requires the hydrolysis of collagen and subsequent separation of the individual amino acids prior to their conversion into CO_2 or N_2 for IRMS. The separation can be done by LC or GC, but amino acid derivatization is required for GC separations. We have just acquired a GC-IRMS instrument, and look forward to tackling more questions on paleodiet with this sensitive approach.

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iQ Test

In July, we told the development story behind the new Agilent InfinityLab LC/MSD iQ, which aims to bring accessible LC-MS to routine analyses. The innovative instrument addresses some of the key barriers to adoption of MS – ease of use, downtime and cost. But what do end users make of the potential? We spoke with Phil Anderson, Principal Scientist at Cambrex, to find out why the small-molecule contract development organization is investing in LC/MSD iQ.

What is the most rewarding aspect of your job?

I find the most satisfaction in helping less experienced colleagues learn how to approach and solve the analytical challenges we encounter every day. I'm constantly motivated in my role by the "fun" that comes with constant opportunities to learn new things; in the development environment we are in, we are always looking at new chemistry, and unexpected things happen all the time. It's always exciting to find something previously unencountered, and it's challenging too because I'm kept on my toes by the need to do work more quickly and with reduced resource.

What challenges do you face in your LC-MS analyses?

Besides the usual analytical challenges relating to limits of detection, specificity and repeatability, the biggest issue is generating relatively simple LC-MS methods that can be executed successfully by non-specialized analytical development and quality control (QC)colleagues and collaborators. We also face the additional hurdle of developing methods in a compressed timeframe, so that we can avoid delays in the drug pipeline.

Is it becoming more important that analyses can be done by non-specialists? Why?

The number and complexity of analyses utilized by QC constantly increases due to expanding regulatory expectations. Highly experienced analytical chemists are a limited commodity, and it is critical to our success that we expand the impact of complex analytical instruments as broadly as possible. As previously described, the LC/MSD iQ should simplify analysis for non-MS specialists, and reduce the training required to successfully execute these analyses.

How do you plan to apply the LC/MSD iQ in your lab?

We use unit-resolution single-stage LC-MS for a number of problems; for example, potential genotoxic impurity methods, cleaning verification (especially for poorly UV-absorbing analytes), assays of non-UV absorbing impurities in intermediates and active pharmaceutical ingredients, and impurity tracking during method development.

What advantages will the new technology provide compared with existing instrumentation?

There are two big winners in our view: first, the simplified dashboard approach to assessing the health and operational status of the instrument (Instrument Health Tracking); second, the two-tiered method control system (Auto Acquire and Advanced Acquire).

The dashboard will be particularly good at letting analysts – especially those who are not subject-matter experts – know if the instrument is operating properly. A correctly operating instrument is essential for analyses conducted in a good manufacturing practice (GMP) environment. The proactive instrument health tracking for planned maintenance will also be very useful in predicting service periods. Maximizing the uptime of instruments is vital to meeting deadlines – and for busy contract development and manufacturing organizations, that's a constant endeavor!

Two-tiered instrument control is also valuable – by allowing full-parameter access for method developers, the best instrument performance for any method will be accessible. For routine analysis, especially by non-specialists, the simpler operation interface is likely to be more suitable.

How does the new technology address some of your core challenges?

We believe it will simplify analysis for

"The LC/MSD iQ should simplify analysis for non-MS specialists, and reduce the training required to successfully execute these analyses."

non-MS specialists – and also reduce the time it takes to train non-specialist analysts to successfully execute these tasks. In short, it's really all about making MS more accessible.

It should also support us in maximizing instrument uptime and minimizing unplanned downtime by allowing for better monitoring of instrument performance. This, in turn, should enable better scheduling of preventative maintenance, as noted earlier.

What other applications can you see for the LC/MSD iQ?

I foresee a number of useful applications in other areas of pharmaceutical development and manufacture. For example, it could prove invaluable in the assay of small-molecule, non-UV-absorbing raw and starting materials, reagents, and intermediates, including impurity and identity analysis. Similarly, I would expect to see the instrument used in routine identification of biomolecule raw and starting materials, reagents, and intermediates for use in GMP processes.

Why would LC/MSD iQ be particularly suitable for these applications?

These are all analyses that would typically be done in a QC environment, and the operational accessibility of this instrument to a wide variety of analysts is critical to efficient analysis in such labs. The design and control strategy of the instrument should also help in maximizing instrument uptime, and minimizing unplanned downtime by allowing for better monitoring of the instrument performance. This should enable better scheduling of preventative maintenance.

What advance in technology would really change how you work?

Scientifically: broader ionization coverage for MS with regards to molecule polarity. Practically: compliance and data integrity support for a broader array of instrumentation. The greatest practical necessity is for more streamlined data reduction and analysis tools; we can generate huge amounts of data relatively quickly – the time-consuming component is converting that data into information and subsequently into knowledge.

How important is it for your team to stay up to date with the latest instrumentation?

Although we don't always have the very latest instrumentation, we must remain close to the state-of-the-art from a competitive standpoint. There will always be a need for certain pieces of equipment in different client situations with regards to the time and resource involved, and the need for a lower limit of detection or higher precision. Clients frequently approach us due to our unique capabilities and expertise that is not available in other labs, and we typically leverage that into additional work in further areas.

What other technology are you investing in?

Our top priority is adding more MS capability and redundancy. Specifically, adding quadrupole time-of-flight will allow us to carry out high-resolution MS/MS for better impurity identification and structural elucidation. We are also aiming for redundancy in our triple-quad capability, interfacing GC with high-resolution MS via atmospheric pressure chemical ionization, and inductively coupled plasma with high-resolution MS to reduce interferences from polyatomic ions. Looking further ahead, we may look at adding ion mobility to LC-MS and matrix-assisted laser desorption/ionization for polymer and biomolecule ID.

Profile of an Early Adopter

I have a PhD in analytical chemistry from Indiana University, USA, and have worked in pharmaceutical chemistry, manufacturing and control for 27 years, primarily dealing with small molecule drugs. I've worked across the pharmaceutical industry – from big pharma to start-ups and contract companies.

I lead a small specialty analytical chemistry group in a pharmaceutical contract development organization. We support projects from pre-clinical to commercial release, most of which are in early development, such as in Phase I or IIa studies. We conduct analyses for both research and GMP purposes, employing mostly LC-MS, GC-MS and nuclear magnetic resonance.

TODAY'S MENU: SOUND SCIENCE

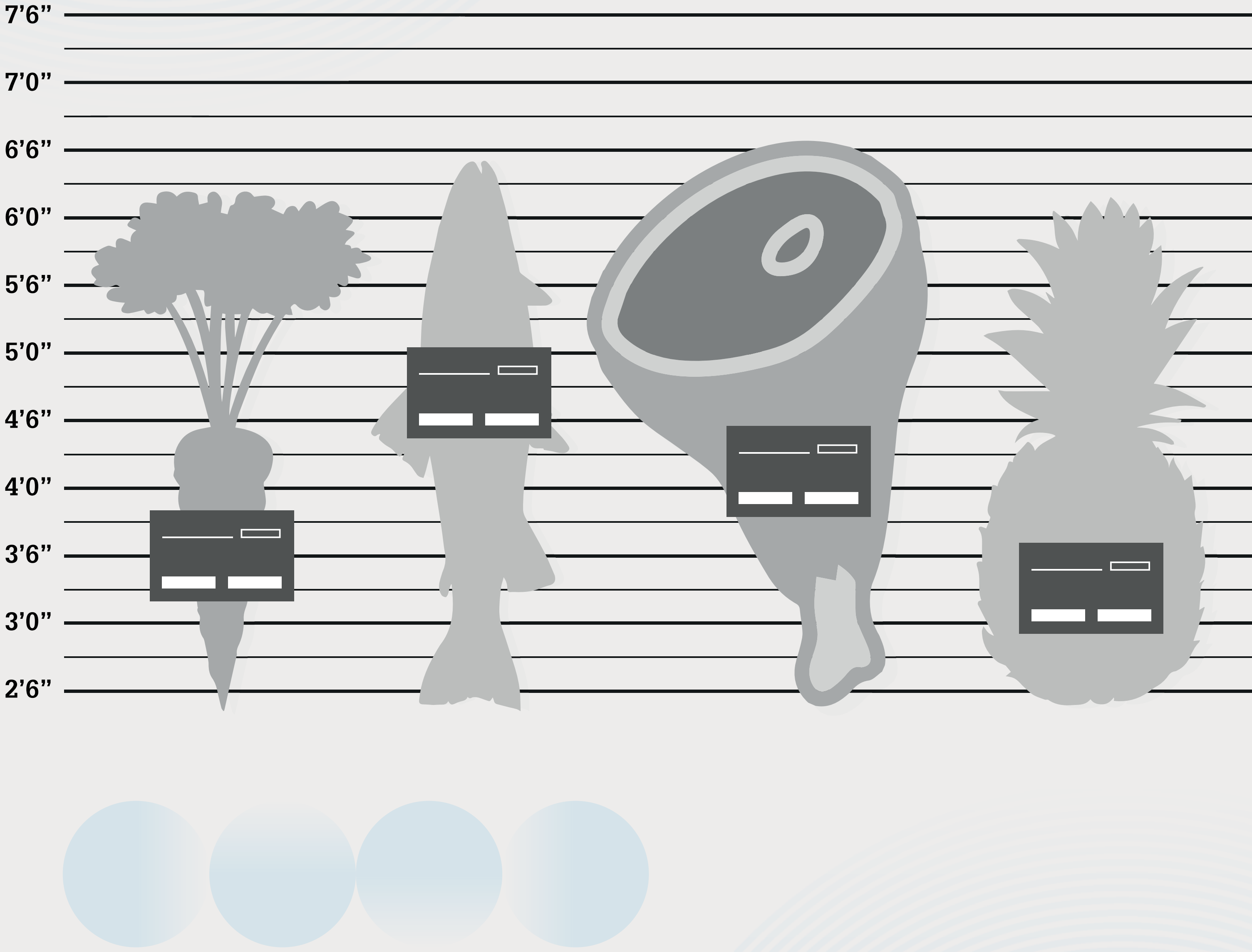
To ready you for RAFA 2019, we find out what's hot in food analysis with Michel Nielen, Hans-Gerd Janssen and Chris Elliott.

What breakthroughs have had – or will have – a key role in food authenticity?

Michel Nielen: Modern chromatography-MS approaches are perhaps most applied in the detection of food contaminants, from pesticides to antibiotics and natural toxins. These processes make use of the latest column technology, and have played a central role in the expansion of full-scan accurate mass MS techniques; this latter technology, coupled with advanced chemometrics tools, enables food profiling to detect authenticity and fraud issues. Human biomonitoring studies have also emerged in recent years to assess the bodily exposure related to these contaminants.

Hans-Gerd Janssen: Our food is safer and of higher quality than ever before, and we owe this largely to advances in analytical chemistry – both in terms of emerging methods for food monitoring and cooperation with experts involved with food processing, chemistry, and production. As Michel mentions above, tools that allow scientists to monitor regulated compounds – including pesticides and process contaminants – are key, and are in a constant state of improvement with regards to their speed and reliability. In fact, MS instrumentation has advanced to the point that researchers are now able to monitor more unique compounds in a single sample than ever before. Coupled with improving resolution and the integration of -omics, there are a number of reasons that our ability to analyze food is improving so noticeably.

Michel Nielen: The historical dominancy of GC- and LC-MS in food analysis is due, at least in part, to legislation dictating that such evidence be provided through these techniques. Sooner or later, though, I would expect novel enabling technologies to be integrated into these regulations; this is why RAFA has always focused both on emerging analytical technologies and inventive food analysis workflows.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Between holding a special chair for analytical chemistry at Wageningen University, having acted as president for the Dutch Society of Mass Spectrometry and playing the role of principal scientist for WFSR, **Michel Nielen** *has held many prestigious positions. Today, having been cited over 8,000 times for his work in numerous analytical technologies, Michel acts as both an executive board member for TI-COAST (a Dutch public-private analytics body) and coordinator of the EU Marie Curie Innovative Training Network FoodSmartphone, a PhD program focused on the research and development of handheld food analyzers. The production of such handheld devices represents a primary research focus for Nielen, who believes they will improve food safety by facilitating the collation of geographically tagged food quality data by stakeholders throughout the food chain, including consumers.*

Hans-Gerd Janssen *is perhaps best known for his comprehensive chromatography workflows, designed to give high-resolution molecular information from complex samples, such as food and cosmetics. During his time at the University of Amsterdam and as Science Leader for Unilever Research Vlaardingen, Janssen has contributed to hundreds of studies, and recently received a groundbreaking grant from VUV Analytics for the application of vacuum ultraviolet detection to transform the study of mineral oil saturated and aromatic hydrocarbons in consumer products. The goal? To continue innovating our analytical capabilities to unravel the identity of molecules in samples and understand the behaviors and capabilities of these molecules in real-world contexts.*

Chris Elliott *is the founder of the Institute for Global Food Security at Queen's University, Belfast, and Director of the ASSET Technology Centre. He currently coordinates the flagship Horizon2020 project – a collaborative effort to tackle food safety issues involving 16 European and 17 Chinese partners – and played a central role in the QSAFFE study of contaminant issues across Europe. What's more, he led the UK government's food system review in response to the 2013 horsemeat scandal, is an elected Fellow of the Royal Society of Chemistry, Royal Society of Biology and the Institute of Food Science and Technology, and co-founded the International Drug Residue School of Nante, France. It's clear to see why he was awarded the OBE – among numerous other awards – for his extraordinary contributions to this field.*

Given the large variety of food matrices and their inherent heterogeneity, sample preparation is also a topic of considerable interest at RAFA – and beyond.

RAFA 2019 will showcase major developments in portable, rapid and non-invasive instruments, often referred to as "food scanners," which are expected to facilitate a massive increase in the number of food samples we're able to test. Optical spectroscopy (such as hyperspectral UV scanners covering visible and near-infrared wavelengths with image recognition) is a great example, and is experiencing a resurgence in food studies due to successful instrument miniaturization, the availability of advanced chemometric data handling tools, wireless data communication and 'Big Data' compatibility – in many cases, ordinary smartphones will provide a readout system. What's more, major developments in biochemical assays, such as strip tests, lateral flow devices, and biosensors will be showcased at the meeting, as will advances in portable MS – though these tend to move more slowly in food analysis than other fields.

What will your presentation at RAFA 2019 focus on?

Michel Nielen: For me, the message to convey at RAFA is clear: within the next decade, food inspectors, farmers, retailers, and even consumers, will be demanding the ability to test food themselves. To this end, I anticipate that rapid, smartphone based technologies with built-in and remote quality assessment features will supersede laborious laboratory practices – delayed action due to analytical limitations will not be acceptable. These events will trigger a paradigm shift: labs will move from dealing with high numbers of compliant samples to fewer, more interesting samples that have been identified as suspicious. Such a shift may even provide an opportunity to pinpoint completely new food contaminants and metabolites.

Chris Elliott: Food integrity is a multifaceted field that I summarize using seven key principles: that the food we eat is safe, authentic and nutritious, is produced to the highest ethical standards and in a sustainable way, and that we respect our planet and those who work in the global food supply system throughout production. Of course, each principle is faced with a number of challenges, and many of these have wide-reaching implications... A full risk assessment will be required to fully understand what challenges we will face in ensuring safe food against a backdrop of climate change and growing levels of organized crime penetrating the food industry.

No food commodity or ingredient is safe from adulteration, and new cases of food fraud seem to be reported on a near-weekly basis. There are those who will always seek to find new ways to cheat the system for their own profit, and current reports of fraud in the rice trade are particularly worrying. Sadly, such cases should almost be expected - as the most consumed food worldwide with associated complex supply chains, the rice trade is ripe for exploitation.

Scientists play a major role in detecting food fraud using applicable analytical technologies, but there is no "one size fits all" technique for every problem we face. The development of a "toolbox of techniques" that exploits different measurement technologies is an ongoing process. Yet, analysis alone cannot eliminate food fraud completely; testing programs must be part of much broader control measures that incorporate robust audits and excellent tracking and tracing systems.

Our efforts should be directed towards developing the capabilities to undertake field-based testing for food fraud. Innovations in sensor technologies, smartphone-based analysis and portable MS are exciting new avenues for exploration – no doubt, all of these instruments will find their place in the larger technical toolbox of the future.

> **"No food commodity or ingredient is safe from adulteration, and new cases of food fraud seem to be reported on a near-weekly basis."**

Michel Nielen: Realizing the visions discussed by Chris and I will require the miniaturization of tandem MS, as optical and biochemical food scanners are already developing rapidly. The high numbers of regulated pesticides and antibiotics in complex food matrices and the relatively low legal limits will require analytical selectivity and sensitivity currently unavailable in portable MS; once developed, however, portable triple quadrupole MS may be adopted relatively quickly because of similarities with current laboratory workflows and regulatory requirements.

What challenges are shaping the field today?

Chris Elliott: It depends what part of the world you herald from! In Europe, we all remember the horsemeat scandal of 2013; in China, it is the 2008 melamine scandal that has left its mark, resulting in a loss of trust among the Chinese population regarding their national food system. Such cases have led to a shift away from classic targeted methods of analysis to untargeted methods, which has been possible largely due to advances in chemometrics. These developments (often referred to as 'food fingerprinting' methods) mean that the detection of food adulteration is much more likely, no matter what substances the fraudsters uses.

Of course, we can all do better to tackle this problem… But it is clear that being able to detect and stamp out food fraud has an enormously positive effect on society; not only does it prevent consumers from exposure to fraud, but it also helps ensure their safety.

Our changing climate, characterized by rising temperatures and issues with water sustainability, poses the greatest threat to the integrity of the global food supply system. We may well suffer multiple food safety and fraud issues as a result, will potentially need to use more agrichemicals to control pests, and will face greater challenges from natural contaminants, such as fungal and plant toxins.

Michel Nielen: Food analysis is an ever-evolving field, but the aforementioned 'classical' contaminants, as well as natural toxins, remain areas of enormous interest. In contrast to pesticides and antibiotic residues, which present as a priori, known substances, natural toxins present a very different challenge; their abundance and chemical diversity, coupled with a lack of purified standards (and associated internal standards), present many levels of complexity.

The focus of analytical scientists working on these toxins was initially well defined – mainly mycotoxins and a few shellfish toxins. Nowadays, however, it is important to also consider plant and bacterial toxins. Advances in method development have been boosted by scandals as discussed above, among others. These developments have relied on both non-profiling technologies and advanced data mining tools, both of which have advanced considerably in recent years.

Hans-Gerd Janssen: These are all very valid points, and alongside these developments we are also witnessing a major shift in consumer behavior. Food must be available anywhere and at all times; in addition, it must be free of e-numbers, natural – or vegan – in origin, sustainably produced and sustainably packed, and incorporating increasingly desirable ingredients. Meeting this demand will require faster product development, as well as studies into new natural ingredients, natural preservatives, and new ways of inhibiting lipid oxidation. And that will require analytical support and measurement that goes beyond simple data production – we need to generate new knowledge.

Every change to a recipe, processing methods or packaging can have consequences for the quality and safety of products. The answer? Analytical chemistry. Our field provides the tools to detect these differences and assess their subsequent impact, essentially forming the basis of our entire understanding of the topic.

And yet, despite progress, we still face many challenges. For instance, we lack the proper instrumentation to ensure food authenticity... How can we prove that organic food is indeed organic, or vegan food vegan? Many of the measurements needed to answer such questions require well-equipped laboratories with trained experts and state-of-the-art equipment.

Rather than spending time, effort, and resources developing even more advanced laboratory instruments, we need to turn our attention elsewhere. There is a clear need for small, easy-to-use instruments that employ selective chemistries; in an ideal world, as Michel suggested earlier, consumers should be able to perform these measurements themselves.

Michel Nielen: Another food contaminant we are becoming increasingly aware of is microplastics – little is known about their effects, both in terms of human health and the environment; we need better analytical methods for their detection in food matrices. The same holds true for non-intended added substances (NIAS), which migrate from packaging into foods. As society continues to grapple with ensuring the circulation and recycling of materials, this will inevitably cause further NIAS contamination.

Hans-Gerd Janssen: Society faces enormous challenges. Feeding an ever-growing population sustainably will require new sources of raw materials – each of which will require characterization. At the same time, we face issues with food waste; one third of food produced is wasted instead of consumed. It would seem that myself, Michel and Chris are all aligned in thinking that we need to develop the tools to rapidly assess food quality and safety in the supermarket and at home. In many cases, we already know the appropriate chemical markers. For example, histamine is a marker for fish freshness, and hexanal is a marker for fouling lipids. Moving forwards, we require further advances in the tools used to measure these molecules so that we can do so with increased selectivity and sensitivity.

What broader challenges face the field of food integrity today?

Chris Elliott: We are lacking systems and frameworks that would ease collaboration between governments and the food industry. The sharing of important and confidential information also remains a massive challenge – only in the UK have the correct systems been put in place to facilitate this, and this was only as a direct response to the horsemeat scandal. Then there is the problem of priorities. Though many governments realize that food fraud is an issue, they are unable – or unwilling – to invest in the types of systems required to protect their citizens from this menace, and the organized crime underlying it.

Michel Nielen: There is a lack of trust surrounding measurement science and its communication. "Measuring is knowing" – but only if we can trust the validity of the data and the officials and scientists communicating it. It's easy to imagine a future society in which everyone has the ability to conduct food analysis. I do not doubt that consumers would trust themselves in spite of the poor-quality device they might use to conduct it, and in whatever fashion they would apply it. Nevertheless, the ability to immediately communicate unreliable test results on social media could also have serious consequences; blaming and shaming the food industry or government food testing administrations. The consequence? A decline in trust in analytical measurements – irrespective of how, when and why a test has been performed. We must work together to ensure these tests are validated, have built-in quality assessment and control features, and are communicated fairly. Only then can we protect the public while maintaining current faith in analytical measurements.

the Spectroscopist

INSIDE

Read My LIBS

Mayo Villagrán Muniz discusses the importance of Latin America's conference season in 2019 – and the wonders of laser-induced breakdown spectroscopy.

What's the focus of your work?

My group at the National Autonomous University of Mexico (UNAM) studies the interaction of nanosecond laser pulses with a given target using optical, electrical and acoustic techniques. In Mexico, we pioneered the use of laser-induced breakdown spectroscopy (LIBS) – one of the most powerful methods available to characterize light-matter interactions. Our lab is called "Photophysics and Thin Films," owing to the potential to obtain thin films when using pulsed laser deposition. We've also used the laser-induced breakdown mechanism to simulate and study physical processes that are difficult to study in situ – such as stellar explosions and lightning.

There are many laboratories at UNAM that provide a diverse range of physical and chemical analytical techniques; our institute, the Institute of Applied Sciences and Technology (ICAT), is a key example, but we also have access to the Spectroscopic Characterization University Laboratory and the Environmental Nanotechnology University Laboratory. In our lab, we specialized in optical emission techniques and photoacoustic techniques. Simply put, we "see and hear" matter responding to excitation with nanosecond laser pulses. At the moment, we are applying this to the production, functionalization, and characterization of nanoparticles for medical applications.

Where is LIBS best applied?

There are many areas where LIBS is useful; geologists, for example, need to make frequent measurements in situ, but fluorescence X-ray guns are expensive, require periodic calibration and are incapable of detecting light elements. As an alternative, we are building a portable LIBS system for soil analysis, dubbed the LIBS gun. In doing so, we are trying to overcome the challenge of an inherent matrix effect by furthering our basic research into LIBS itself. This is typical of the work in ICAT – we conduct basic research to solve an existing problem, and then we develop technologies that can be used in instruments with transferable applications.

What's the importance of the first Latin American Meeting on LIBS (LAMLIBS)?

Some groups in Brazil started working on LIBS as early as the 1990s, but it wasn't until the turn of the millennium that the technique really started to gain traction. Now, there are groups from at least a dozen Latin American countries working with this technique – some focus on fundamentals and general applications, and others are working to solve specific challenges of their region. The monitoring of polluted water, characterization of prehispanic species with archeological value, and removal of prickly pear spines for consumption are just a few examples of such challenges.

In Latin America, the relationship between academia and industry is just beginning to flourish, and I believe that LIBS will play a crucial role in this coming together because of its practicality.

How does the LIBS research focus in Mexico differ from the rest of the world?

LIBS embodies a practical solution to issues across a range of applications, and these applications do not differ too much between Mexico and the rest of the world. We simply want to use the congress as an opportunity to promote the usefulness of the technique. But there are also issues specific to Latin America, such as the analysis of regional soils in archeological contexts; in such cases, we must adapt the protocols used elsewhere or work to produce our own. This research requires trained personnel, which was a key consideration in deciding to organize the conference – to make the field known, to drive developments, and to enthuse the next generation of LIBS researchers, technicians and industry professionals.

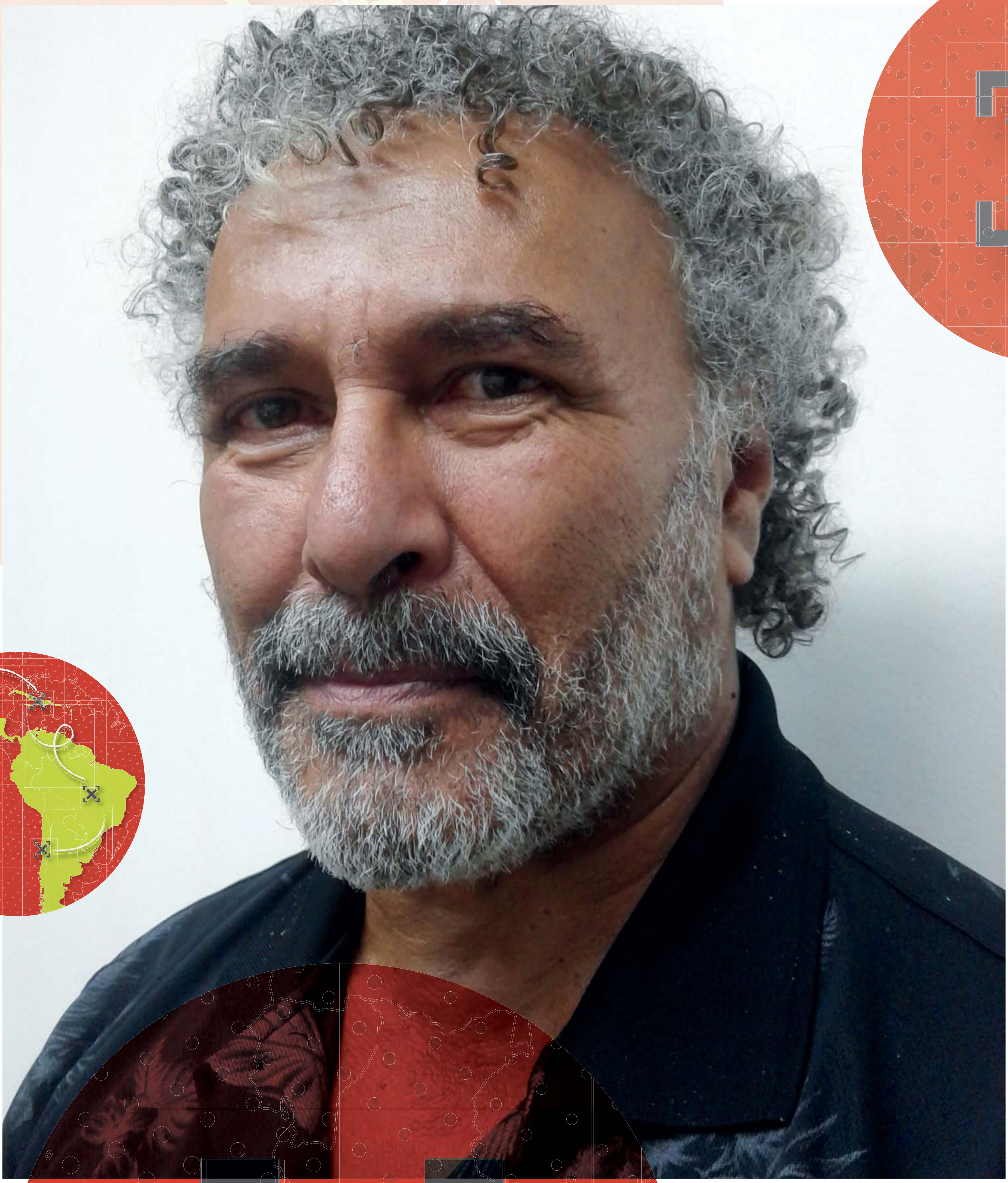
What were the most interesting developments shared at the CSI and LIBS conferences?

The goal of both events was to promote new collaboration and reinforce partnerships that already exist, so that we may take full advantage of the natural resources available to us in Latin America and address socioeconomic changes in the region. The shield of our institution displays a two-headed bird, which represents the Mexican eagle and the Andean condor, safeguarding a map of Latin America from the northern border of Mexico to Cape Horn, reflecting the unification of all Iberian–American countries. This shield embodies the spirit of camaraderie that we live by in Mexico, and this is something we try to highlight by promoting scientific development in our brother countries through LAMLIBS. It was great to see students, young scientists and academics from Latin American and Caribbean universities alike seize the opportunity to share the stage with renowned scientists – and the world – at both of the events.

Tell us a bit about how LAMLIBS came about – and your hopes for the future.

For years, Latin American LIBS researchers have had to meet at optics conferences. We capitalized on these conferences by organizing workshops and promoting student exchanges in LIBS, but decided to organize an individual conference while at RIAO in Chile (2016). We were given this opportunity in 2017, quickly acting to obtain the venue for CSI and organize LAMLIBS. The hope is that we will meet again in another Latin American country a couple of years from now – we can't ask for much more than that!

The next CSI (CSI XLII) will be held in 2021 in Gijón, Spain.



At One with the Elements

Promethium was discovered almost 75 years ago, but only now are spectroscopic approaches unveiling key properties of this rare element.

The periodic table might have reached the ripe old age of 150 this year, but there are still a number of key questions hiding within Mendeleev's iconic chart. Only in 2019 have we confirmed the ionization potential of promethium (element number 61 of 118 known elements) – with that gap filled, all elements up to lawrencium (element 103) have now had their atomic properties experimentally determined. We spoke to Ulli Köster (Institut Laue-Langevin, Grenoble, France), a nuclear physicist-come-chemist and contributor to the study, to find out more.

Tell us about the promethium project.

The study can be split into three main parts: (1) nuclear transmutation to produce promethium, (2) purifying the promethium, and (3) spectroscopic analysis. We used enriched and pre-purified neodymium-146 as a precursor and irradiated it in our institute's high-flux reactor, then shipped it to the Paul Scherrer Institute in Switzerland for chemical separation of the promethium fraction. The promethium was next passed to Mainz University in Germany to obtain its atomic spectrum, from which we were able to determine the ionization potential of the element using a combination of laser spectroscopy and mass separation, effectively tripling our knowledge of atomic levels in this element.

Why has this part of the periodic table been missing for so long?

As a scientific community, we're still in the process of measuring elemental ionization potentials. The super-heavy elements at the top of the periodic table, for example, have only been synthesized for the first time very recently and are still produced in meager quantities – a few atoms an hour, or in some cases a month. As a result, it's difficult to obtain big enough samples for spectroscopic analysis. Promethium is obviously less exotic, but still isn't readily available due to the radioactivity of its isotopes. Analysis is also complicated by the element's complex atomic spectrum, but advances in atomic spectroscopy are constantly enabling new breakthroughs; for example, we now we now use titanium sapphire lasers, which facilitates the scanning of wide frequency regions more easily than was previously possible.

For what applications will this knowledge of promethium be used?

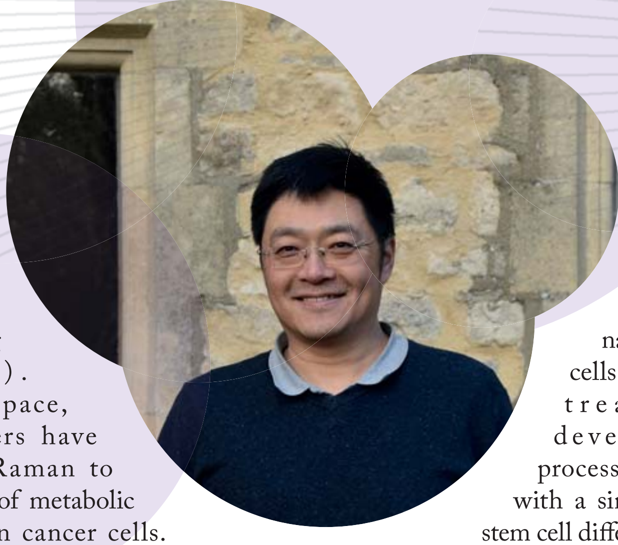
Promethium isotopes have various applications. An interesting feature of promethium-147 is that it has a half-life of 2.6 years, and one can amass a relatively large amount of it using high-flux neutron irradiations. Due to the considerable energy released by its beta decay, it could be used to produce a nuclear battery, transforming this energy into electricity – such a battery can operate under harsh conditions, so could be used to power satellites or probes used in challenging geophysical environments. Promethium-147 prepared in our experiment is also being used to study one of its nuclear properties, the neutron capture cross-section, which is important for nuclear astrophysics, and the method of producing high activities of pure radionuclides has applications in nuclear medicine, namely in cancer treatment.

How important was collaboration in this work?

The Institut Laue-Langevin is involved in a huge collaborative network with involvement in many interesting projects with teams from all over the world. The institute is an established European research center operated by its three founding countries (France, Germany and UK) to provide instrument access to scientists of its 10 member countries; we're essentially a service laboratory with around 1,600 users a year, and our main role is providing neutron beams for neutron scattering experiments and various other neutron applications. In the current study, we produced promethium by bombarding neodymium-146 with neutrons, and collaborated with centers in both Switzerland and Germany for the subsequent steps.

What's next for your group?

We are working on various other isotopes, including some for cancer therapy; for example, lutetium-177, which is the current gold-standard for targeted radionuclide therapy. Our ability to produce high-purity radioactive samples through neutron capture is generating a lot of interest, and we're also collaborating with the ISOLDE and MEDICIS facilities at CERN in Geneva, where complementary neutron-deficient isotopes are produced by high-energy proton beams.



There's Something About RamanFest

RamanFest is a valuable platform for researchers, but what makes the event – and the technique – so special?

By Wei Huang, Synthetic Biology & Single Cell Biotechnology, University of Oxford, Oxford, UK.

RamanFest is a relatively new to the conference scene; we celebrated its seventh birthday this year in Oxford, UK. Yet, I would say it is already an established international meeting, attracting world-leading minds to partake in discussions at exciting venues from China to Boston to France. The topic on everybody's lips? Raman spectroscopy, with presentations on a range of topics in accordance with a select theme each year.

With the help of Dr Simon FitzGerald, we had two themes for 2019: i) health and life sciences, and ii) advanced materials and technologies. In line with the first theme, we invited key speakers including Adrian Harris – one of the world's most cited cancer research scientists – and Michael Wagner – a leading figure in the microbiology community – to discuss cancer research, microbiology, single-cell analysis and the analytical technologies underlying all these incredible applications.

One such application that was presented quite widely was Raman activated cell sorting (RACS) – an important label-free technology that may eventually replace more traditional fluorescence-based sorting methods, such as fluorescent-activated cell sorting (FACS). In this space, researchers have applied Raman to the study of metabolic changes in cancer cells. Such developments made up a significant portion of the conference program for 2019, but many more exciting developments were also presented. The conference saw a great focus – for example – on advances in the reproducibility of tip- and surface-enhanced Raman spectroscopy (TERS and SERS, respectively), which has enabled in depth analysis of graphene, as well as various catalysts and two-dimensional materials.

My talk focused on single-cell microspectroscopy – research that goes all the way back to 2004, when my team conducted Raman analysis of single bacterial cells to observe the Raman shift due to stable isotope ^{13}C incorporation and differentiate distinct species. We soon took this a step further when we realized that a stable isotope probing technique could be combined with Raman scattering to investigate the metabolism of single cells and related physiological changes. In essence, we were beginning to use Raman spectra of single cells as a phenotypic fingerprinting device.

In the modern age of molecular biology, we are able to link these cellular phenotypes to their underlying genetic code, which can then be expanded to inform us about the physiology and functions of tissues, organs and entire physiological systems. Though we cannot physically observe the relationship between these genetic elements and higher system functioning, Raman-based spectroscopic analysis of single cells can act to fill this void in a number of ways – not just for studying basic human biology, but also to investigate disease (for example, to understand the heterogeneous nature of cancer cells and improve treatments), developmental processes beginning with a single cell, and stem cell differentiation.

The applications of this technique reach far beyond the study of higher organisms though; for example, over 90 percent of naturally occurring microorganisms cannot yet be cultured in laboratories. These same microbes may play key roles in natural processes that we are unaware of, and, by applying single cell biological analysis, we can elucidate potential roles of these difficult-to-study organisms without the need for mass cell culture. What's more, this method can also be applied where the study of multicellular prokaryotic systems is warranted, allowing us to gain insight into processes such as carbon dioxide capture in oceans, and nitrogen and carbon cycling on land.

In fact, Raman-activated cell sorting has already been used to analyze the human microbiome – a highly complex microbial community that has far-reaching effects on our mental health and wider metabolic activity. In my mind, this provides valuable proof-of-concept for this technique, and I expect to see the number of studies that rely on these technologies mushroom in the coming years.

Accordingly, with the help of Horiba Jobin Yvon IBH Ltd., RamanFest will return each year to bring together the community involved with this valuable technique, allowing us to stay abreast of the latest developments, to pool our collective knowledge, and to discuss the next steps to keep our momentum going. In 2020, RamanFest will be held in Irvine (California, USA) and I'm sure will showcase even more exciting developments in Raman technology.

SciX: High Expectations

What should we be looking forward to ahead of SciX 2019? We asked three key faculty members to find out for ourselves.

Christopher Harrison
Associate Professor, Analytical and Bioanalytical Chemistry, San Diego State University, San Diego, California, USA.

I'm delighted to be attending this year's SciX conference in Palm Springs, California. The event is just the right size, which means you can attend plenty of great presentations and meet peers (some old friends, some new) working on exciting and novel research ideas. I'm especially looking forward to the sessions on electro-kinetic separations organized by the AES Electrophoresis Society. What's more, the keynote lecture on the role of artificial intelligence in analytical chemistry by Rohit Bhargava and the discussion on the role of women in this field with Rina Dukor are sure to be fascinating.

There's going to be a special poster session organized by the two major public universities of California in honor of this being the first SciX hosted in the state. Such a welcoming atmosphere is endemic to SciX, with the large number of social activities providing plenty of opportunity for networking. As a result, I don't think I've ever returned home from a SciX with the impression I've missed anything important.

For 2019, I'll have the privilege of acting as co-chair for the AES Mid-Career Award Symposium Honoring Chris Easley. The session will consist of five speakers, four of whom are thematically aligned with Chris' work: Charles Henry, Michael Roper (last year's award winner), Scott Martin, and Robbyn Anand. The symposium will finish with a final presentation from the recipient of the AES Blue Fingers Award – a young scientist recognized for publishing an outstanding paper.

And, last but not least, as the Local Chair of AES, I've been involved in the organization of the Wednesday night gala event – an offsite tour of a Palm Springs wind farm – and the route for the SciX bicycle ride. Ultimately, it is our goal to make the conference as open and welcoming as possible.

Greg Klunder
Chemist, Materials Science Division, Lawrence Livermore National Laboratory, Livermore, California, USA.

I'm always excited by the developments presented at SciX; with sessions that focus both on both analytical fundamentals and their application, the meeting provides a platform for new ideas that can be integrated into countless different projects. Like Chris, I'm particularly looking forward to the talk on the role of artificial intelligence in understanding and interpreting the large amounts of data obtained with novel technologies – I imagine this session will be a popular one.

The Forensics and Security component of this year's conference will focus on applications, and there will be related sessions across technical areas, making this a well-represented topic. Betsy Yakes has also done a great job organizing the Food Forensics session, which will deal with some very topical issues. In addition, we've also added an Environmental Forensics session (organized by Mark Cejas) that will address techniques for fingerprinting crude oil and petroleum products.

The 2019 program also has an emphasis on isotope analysis – a predominant component of nuclear forensics. Though the identification of isotopic signatures is of great importance, there is growing demand for additional physical and chemical information from samples. And that requires the incorporation of many analytical techniques with more conventional forensic analysis to provide a more comprehensive understanding of the specimens in question.

I've been attending SciX for over 30 years because of the welcoming community and quality science. There is much to be learned from the various talks and posters, but it is in conversation with the other attendees that new ideas are often brought to life.

Mary Kate Donais
Professor of Chemistry, Saint Anselm College, Manchester, New Hampshire, USA.

As someone who teaches at a small college, I have a limited travel budget, but SciX is the one conference that I choose to attend every year because it's so valuable to me as an archeological researcher. The meeting plays host to the best combination of science, exhibits, networking and social opportunities, and I'm always interested to hear about the diversity of measurement techniques and artifact types featuring in studies all over the world, with a wide range of art, archeology, and anthropology covered in the program. The forensic and chemometric sessions will also be fantastic to listen to, as these are areas that I use in my everyday teaching and research.

I'll be presenting a talk on X-ray fluorescence (XRF) and laser-induced breakdown spectroscopy (LIBS) for the study of archaeological ceramics from an Etruscan excavation site in Italy. The study involved comparing various figures of merit for the portable analysis of pottery by XRF and LIBS, but the talk will also explore our efforts to establish limits of detection.

I'm also the Awards Chair for 2019 – a "training job," if you like, in preparation for my appointment as Program Chair for SciX 2020! I've been organizing sessions at the conference for about 10 years, but there is something special about the Awards role – and interacting directly with this year's recipients has been very rewarding. I'm excited to learn about these award-winning scientists' work, and to meet any awardees I don't already know.

Detection of Polymer Impurities in Recycled Plastics Using Chemometric Analysis of ATR Spectroscopy

Learn how the Specac Quest can be used to quickly identify impurities in your plastic materials.

As concern grows over the amount of waste we send to landfill, demand for the ability to recycle has increased - particularly for plastic waste. Separating different types of polymers is essential to ensure the recycled product is suitable for reuse. Although every effort is made to ensure a pure recycled plastic is obtained, contamination is inevitable and therefore methods are required to quantify impurities. Here we have used FTIR spectroscopy coupled chemometric analysis to analyze polypropylene (PP) impurities in polyethylene (PE).

Chemometrics is the application of statistical tools to the measurement of chemical properties [1]. One of these tools is Partial Least Squares (PLS) analysis, a method to find the fundamental relationship between two related matrices. In our case the first matrix is comprised of the ATR-FTIR spectra, whilst the second matrix is the sample composition data. A model is first constructed using spectra of known composition. The model is validated against further spectra of known composition and once validated can then be applied to swiftly determine the composition of unknown real-world samples.

Below: The new Quest Flow-thru Cell

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Technology

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The Father of Foodomics

Sitting Down With… Alejandro Cifuentes, Laboratory of Foodomics, Institute of Food Science Research, Spanish National Research Council, Madrid, Spain.

You coined the term foodomics – why?

Food scientists have always found themselves in the second lane, so to speak – behind those involved in biotech, pharmacology and clinical studies. When a new instrument is developed, for example, it is always applied first in these areas – and this is also where the most money lies. I simply wanted to show fellow food scientists that we can use the same analytical approaches to solve important challenges in our own field, including metabolomics, genomics, transcriptomics and so on. Many people are interested in this field; in fact, we have a joint research institute with a team from the Chinese Academy of Agricultural Sciences and work with many other high caliber groups.

What keeps you busy?

I am a research professor at the Institute of Food Science Research of the National Research Council of Spain, for whom I also act as head of the Laboratory of Foodomics and Director of the Platform of Metabolomics. I also participate on editorial boards for 13 journals – acting as Editor on two of these – and have a constant flux of PhD students. A good portion of my time is spent seeking funding for the lab group, but this is not a worry at the minute thanks to financial support from some of our larger projects and collaborations. Interestingly, I'm also working as editor-in-chief of a new encyclopedia devoted to comprehensive foodomics – it will have around 200 chapters in total and should be complete around the end of next year!

Which of these roles do you particularly enjoy?

The greatest role for me is as a professor. Our lab always has about 20 PhD students from around the world; the only thing we ask is that they stay a minimum of six months. What's more, many come with PhD grants, which eliminates the need for us to source funding (a rather difficult process in Spain these days). I love helping the students evolve as scientists, and also watching them experience new things and develop lasting friendships; I feel this very much captures the more human side of our field. Of course, all of this transpires in the international language of science – broken English!

What are you currently working on?

We have been focusing on green strategies to obtain bioactive compounds from food waste, with a primary focus on research in colon cancer. In this context, food waste refers to byproducts of consumption, such as fruit peels or stones, which would often be discarded; our team wants to maximize the uses of such produce. We obtained good results in vitro and in preclinical mouse models of colon cancer, but translating this into the clinic has been tough. So, we decided to look at the use of food waste products to tackle another healthcare issue beside cancer, and we are now getting some great results in Alzheimer's disease. Of course, Alzheimer's is a tricky therapy area because the etiology of the disease is still up for debate; it's unclear whether amyloid beta plaques are a result of the illness or a cause, for example. Fortunately, I enjoy a challenge.

How do you go about identifying clinically useful compounds from food waste?

We try to go step by step, and tend to reach a bottleneck in our ability to screen compounds from food waste for clinical activity in vitro and in vivo because of the need for advanced analytical methods combined with high computer processing power. In the case of Alzheimer's, such screening efforts might focus on the activity of a given food waste compound against acetyl cholinesterase, for example, but screening could also work by identifying specific compounds with desirable activity (such as anti-inflammatory properties or redox balancing) and the ability to cross the blood–brain barrier. The furthest point we have reached so far with these compounds is clinical assays in diabetic children; we were monitoring how antioxidants from a given food could impact not only diabetes, but also secondary effects relating to diabetes (such as high oxidation levels). Our results were interesting, but failed to show clinical promise; metabolomics studies highlighted interesting pathway differences between treated and untreated diabetic children, but significant differences between these groups (for example, in protein glycosylation levels) were not observed in the clinic.

Are there any developments that would be particularly useful for foodomic studies?

There are many things to be done. For instance, many deficiencies persist in the -omics. We are able to generate a huge amount of data, but often we are not able to extract all of the useful biological information from these datasets. It would be helpful if we had a tool able to integrate data from proteomics, metabolomics and transcriptomics – at the moment, we take a much more "homemade" approach to this problem. What's more, a large number of compounds in the metabolomics datasets also remain unidentified, so developments in existing databases would also be a fantastic step forward. Then, in terms of instrumentation, advances are needed in areas such as the interface between capillary electrophoresis and MS. This is a difficult task, though – it's certainly not equal to GC-MS or LC-MS just yet.