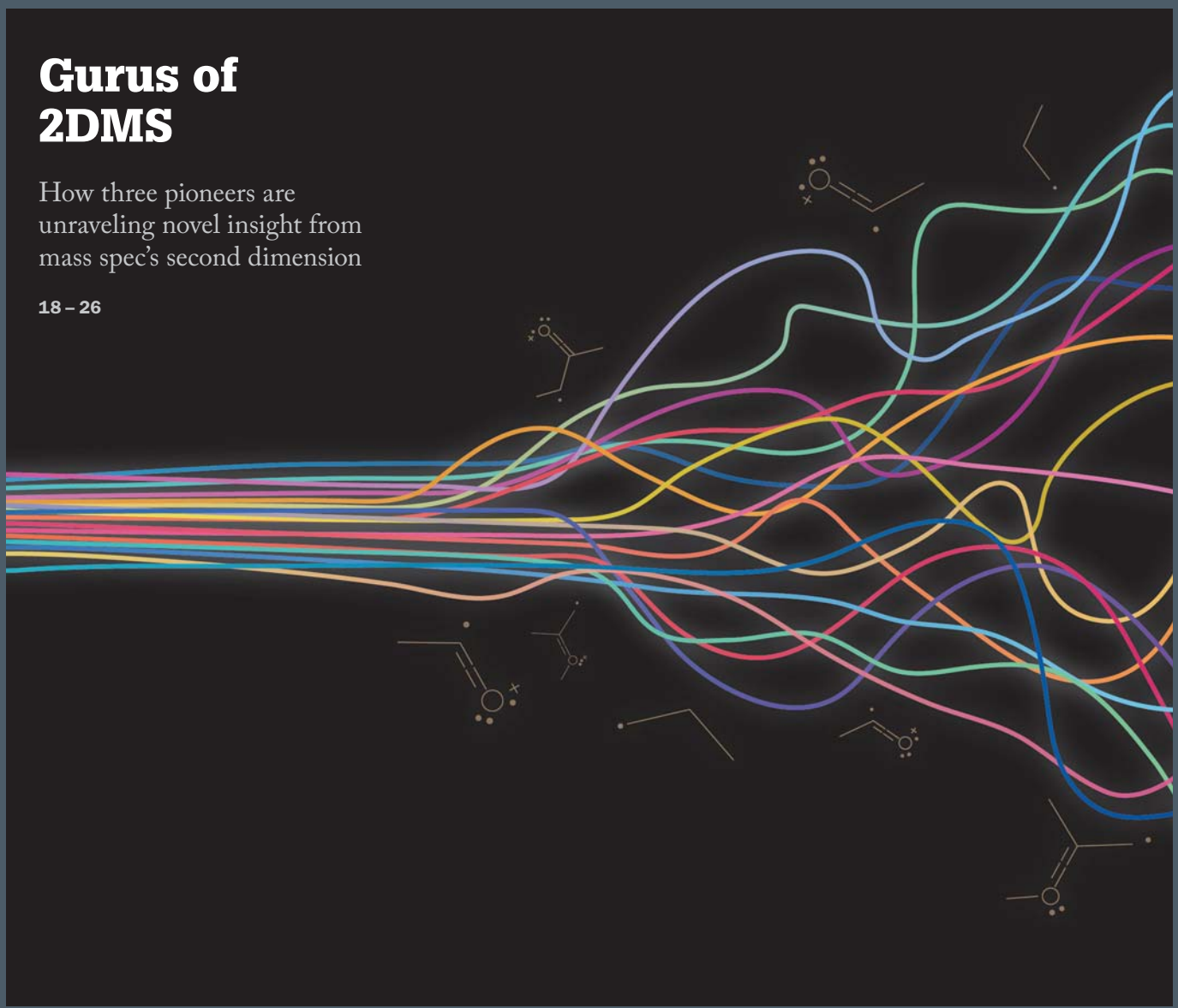
JANUARY/FEBRUARY 2020 # 84

the Analytical Scientist™

Gurus of 2DMS

How three pioneers are unraveling novel insight from mass spec's second dimension



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Dammit, Jim – I'm a Doctor, Not an Analytical Scientist!

The road to improved clinical decisions is paved with increasingly accessible information derived from increasingly complex data. Introducing the first 2020 Special Series: Advanced Clinical Analysis.

SPECIAL SERIES
Advanced Clinical Analysis

The journey shared by a patient and a medical professional begins with collecting information. Along the way, the clinician will have to make difficult decisions that may have a major impact on the patient's life. Those decisions will involve elements of uncertainty, complexity, high-risk, ethics...

Innovation across the breadth of analytical chemistry provides detailed molecular information on samples taken throughout the journey, increasingly impacting the decision-making process – and unraveling the molecular complexity of health and disease. Today's clinicians face a wealth of information to drive personalized treatment plans – but only once complex analytical data has been translated into something actionable.

Other revolutions on the horizon target the increase of (molecular) information density. Advanced in vivo imaging technologies, targeted bedside antibody-based assays, LC-MS in the clinical diagnostic lab, molecular pathology, and even whole genome screening – all these techniques generate more and more detailed molecular data in shorter and shorter timeframes.

As a result, we must make difficult decisions about data reduction for true clinical utility – what can be condensed or even lost? Other questions arise: how do we link an individual's data with population-based averages, personal behavior, and disease incidence? How should the combined data affect a personalized treatment plan? Many are looking for answers in artificial intelligence and machine learning. Radiomics has demonstrated that an algorithm can outperform a radiologist in finding small lesions on thousands of CT images… And similar approaches are being evaluated in the interpretation of histological images as well as infrared and mass spectra.

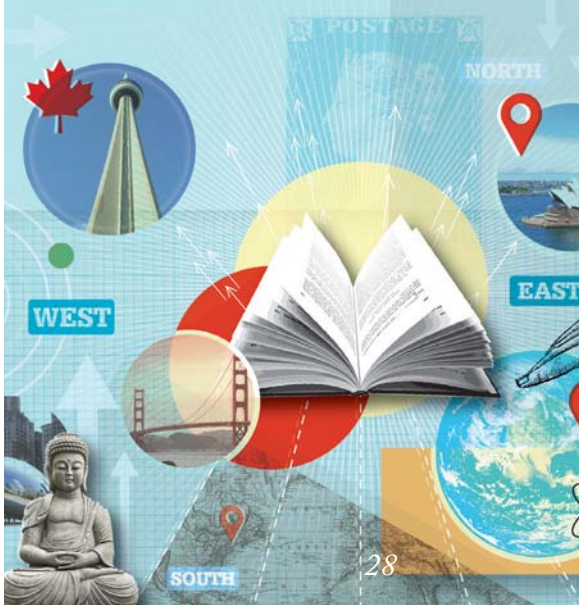
Analytical technologies can also play a role in the most time-critical decision-making processes; MS- and spectroscopy-based intraoperative diagnostics can provide immediate feedback to surgeons during tissue resection (see page 36). And perioperative molecular pathology with MS imaging provides pathologists with better cellular stratification.

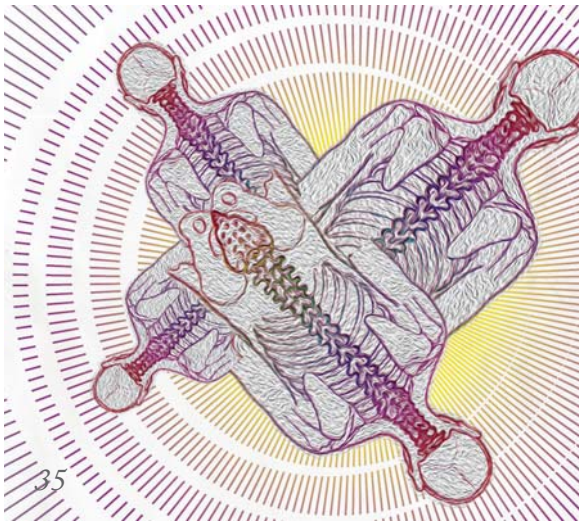
Undoubtedly, analytical innovations will improve patient outcomes. One could argue that the enthusiasm for new approaches indicates just how much uncertainty still exists in the clinical decision-making process. And that's why I'm delighted to kick off "Advanced Clinical Analysis" with this guest editorial.

I believe we are only at the beginning of personalized diagnostics based on multilevel analytical technologies. The best is yet to come.

Ron Heeren
Director, M4I, and Distinguished Professor, University of Maastricht, Netherlands

Contents



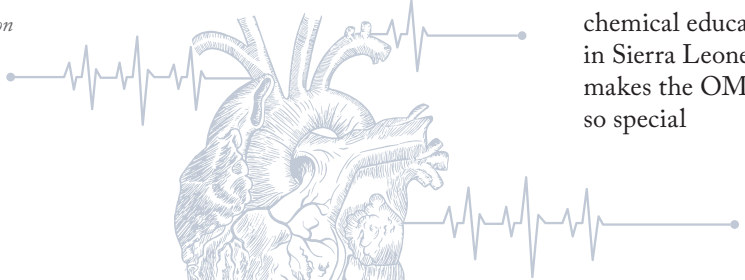


Upfront

In My View

On The Cover

The movement from 1D to 2DMS offers massive expansion of the chemical data we can acquire from samples



Features

The Spectroscopist Inside

Departments

Sitting Down With

the Analytical Scientist

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Upfront

Research
Innovation
Trends

Cretaceous Catastrophe

Was the Chicxulub asteroid solely responsible for dangerous changes in the prehistoric chemistry of our oceans?

The Cretaceous-Paleogene (K-Pg) mass extinction (perhaps more widely known as "the end of the dinosaurs") is almost exclusively attributed to the collision of the Chicxulub asteroid with Earth in popular culture. This collision – visible in the Chicxulub crater of modern-day Mexico – may not, however, be solely responsible for the extinction event that ensued. In fact, the contribution of other factors, such as volcanic activity – and resulting changes in ocean composition – remain poorly defined. Now, by analyzing ancient mollusk fossils, researchers have strengthened the hand of those arguing that the variable Earth's oceans were undergoing significant acidification and mineral saturation changes long before the infamous impact (1).

Ocean acidification, driven by CO_2 saturation, lowers the concentration of carbonates in seawater – a change that encourages numerous organisms (including mollusks) to alter the stable isotope composition of their mineralized tissues. Employing a double-spike method coupled with thermal ionization MS (2), the researchers quantified the calcium isotope ratio ($\delta^{44/40}Ca$) within mollusk shell samples spanning the K-Pg boundary. "We observed shifts in composition that were significantly larger than predicted," says Ben Linzmeier. Interestingly, these changes began hundreds of thousands of years prior to Chicxulub's impact. "This is a timescale consistent with changes in isotope fractionation driven by volcanism, rather than as result of shifts in the composition of the global ocean."

The likely culprit? The Deccan Traps – a large volcanic plateau in today's Central India, thought to have formed hundreds of years before Chicxulub ripped through our atmosphere. "The causes and consequences of mass extinctions are complex," says Linzmeier. "Our work supports a larger body of evidence that the combined effects of volcanism and bolide impact were responsible for the extent of the K-Pg event."

And though this is unlikely to offer much consolation to children's most beloved creatures, the research could have significant modern-day impact.

"Our findings could allow us to better predict how anthropogenic CO_2 will affect ocean geochemistry in the future," says Linzmeier. To this end, the team are looking towards mollusks grown in controlled conditions to expand our understanding of the relationship between the calcium isotope fractionation of their shells and the carbonate saturation state of the modern ocean.

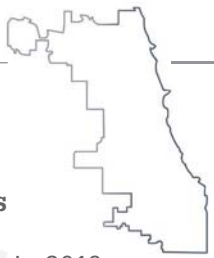
Reference

1. *B J Linzmeier et al., "Calcium isotope evidence for environmental variability before and across the Cretaceous–Paleogene mass extinction", Geology, 1, 34 (2020). DOI: 10.1130/G46431.*
2. *Lehn GO et al., "Precise analysis of Ca isotope ratios (δ44/40Ca) using an optimized 43Ca–42Ca double-spike MC-TIMS method", Int J Mass Spec, 351, 69 (2013). DOI: 10.1016/j.ijms.2013.06.013*

TIMELINE

Conference Highlights 2020

A flyby view of the key conferences for analytical aficionados in the months to come



PITTCON – Chicago, Illinois
March 1-5
>7,800 attendees in 2019
>2,000 technical presentations

Analytica – Munich, Germany
March 31-April 3
"The world's biggest industry gathering"
>1,000 exhibitions

BUSINESS IN BRIEF

Amplifying automation

Waters has announced its acquisition of Andrew Alliance – an innovator in specialty laboratory automation technology – broadening their product portfolio to include advanced robotics. The software from Andrew Alliance, which utilizes a cloud-native platform and modern interface, could improve laboratory workflow performance and repeatability.

Shine bright like an emerald

Emerald Scientific customers in North America can now take advantage of PerkinElmer's high-throughput instruments and regulation-compliant software for cannabis and hemp testing, following announcement of collaboration between the two companies. On top of gaining access to advanced LC-MS, GC-MS, high-performance LC and microwave sample separation systems, Perkin Elmer's services and consumables (chromatography columns, vials, preparation products and so on) will also be on offer.

Translating Success

Clarivate Analytics has signed an agreement to acquire Decision Resources Group (DRG; a healthcare data and analytics body) from Piramal Enterprises Limited for $950 million. The partnership will be well-positioned to support customers across the entire drug, device and medical technology lifecycle, from research to patient outcomes, in the ever-expanding market of life science analytics – currently worth $19 billion.

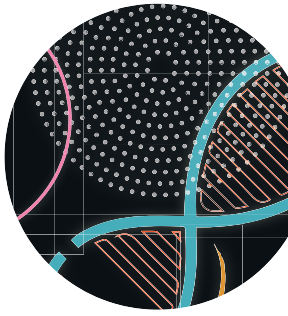
Dana Nessel

Don't mess with Michigan

Attorney general of Michigan, Dana Nessel, is suing 17 of the nation's biggest chemical manufacturers for $3 million over the production and "intentional hiding" of per- and polyfluoroalkyl substances (PFAS). Companies have been told to cease PFAS sales and offer compensation for any subsequent investigation, monitoring or removal required.

Driving Drug Discovery Forward

ZebiAI Therapeutics and X-Chem have entered a strategic agreement to enable the validation of therapeutic targets and accelerate drug candidate discovery. X-Chem's proprietary DNA Encoded Library technology (DEX™) will support ZebiAi's quest to discover small molecules to support its Chemome Initiative, focused on the identification of probe molecules for novel targets, and drive drug candidate identification.



A Case of Identity

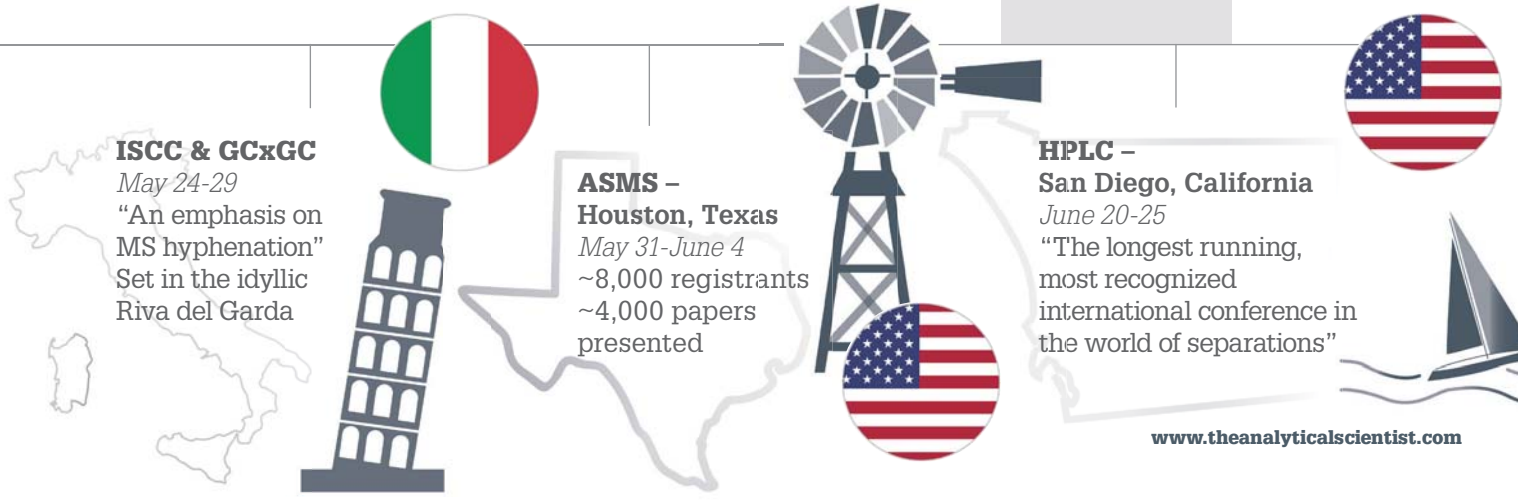
A new sequencing method promises to streamline the characterization of bacteria

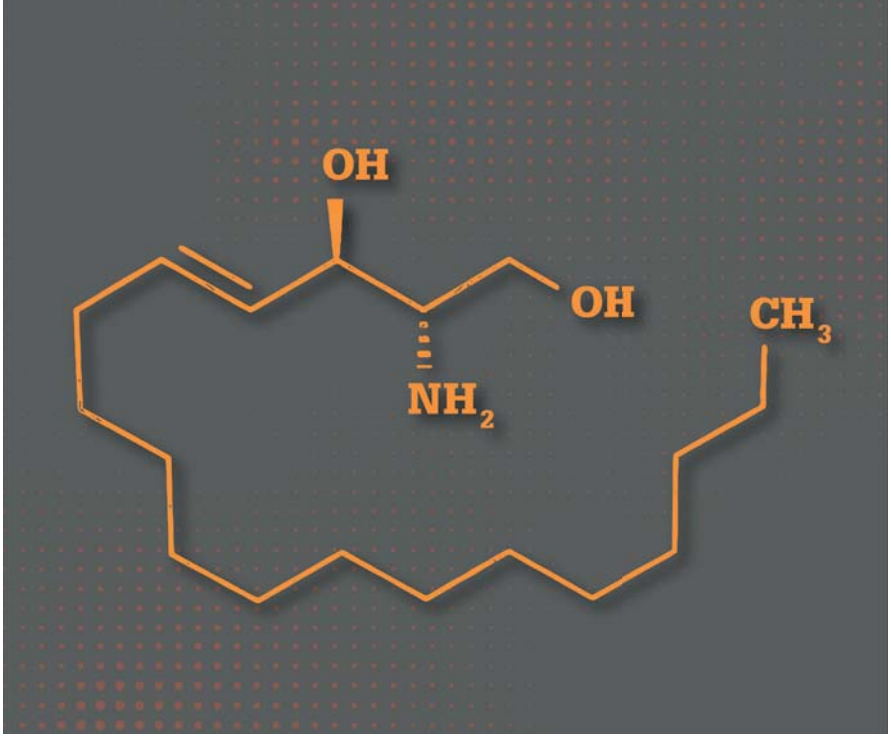
Bacterial typing at the species or strain level is not easy – fast methods lack accuracy, while complex MS technologies remain expensive and laborious. Lukasz Krych presents an alternative: ON-rep-seq – an approach targeting specific fragments of the bacterial genome (1). "We've developed a system that assigns each bacterium a genetic barcode," says Krych. "This allows us to run hundreds of samples simultaneously at reduced cost."

While early results have proven promising, Krych urges caution. "Further algorithm development and a user-friendly software package are needed," he says. "This technology is a reflection of advances in biotechnology, computer science, and nanotechnology in a single package." Pressing ahead, the team is collaborating with private companies and universities to provide real-world testing of their method.

Reference

1. *L Krych et al., "DNA enrichment and tagmentation method for species-level identification and strain-level differentiation using ON-rep-seq", Commun Biol, 2, 369 (2019). DOI: 10.1038/s42003-019-0617*





Lipid Locators

Could combining microarray and MALDI-MS technology improve lipid characterization?

A cross-border collaborative group has developed a microarray/MS-based method that promises simplified lipid profiling in tissues and cells (1). We sat down with two of the team – Gabriel Barreda-Gómez and José Andrés Fernández González – to find out more.

What was the inspiration for your work?

Our objective was to develop a novel method capable of determining the lipid phenotype of cells, tissues and organs. We're particularly interested in the brain, so we went in search of an approach that would allow us to identify specific cell subtypes in brain tissue, as well as determine their proportions and characterize the effect of cancer on the composition of their membranes.

How does the method work?

We make use of two complementary technologies: microarrays and matrix-assisted laser desorption/ionization (MALDI)-MS. The microarrays can hold membrane homogenates, lipid extracts or intact cells, spotted on the surface of a microscope slide using a piezoelectric robot to minimize the volume of sample required. We're then able to utilize MALDI-MS to generate our data because we use a sublimator to ensure each spot on the array is covered with a similar amount of matrix. Our approach also allows us to combine lipid profiling with other experiments, such as protein affinity or autoradiography, as the membrane proteins in our samples remain fully functional.

What are your aspirations?

The technology is well suited to the design of diagnostic tests based on lipid biomarkers. One possible application is tumor screening; the growth of malignant cells requires a great synthesis of new membranes so we would expect to see significant changes in the lipid fingerprint of a tissue, even in the early stages of cancer. We envisage our approach complementing the current gold standard (traditional histology) and hope it might go some way to reducing the growing pressure placed on hospital pathology departments

Reference

1. *R Fernandes et al., "Microarray and mass spectrometry–based methodology for lipid profiling of tissues and cell cultures", Anal Chem, 24, 15967 (2019). DOI: 10.1021/acs.analchem.9b04529*

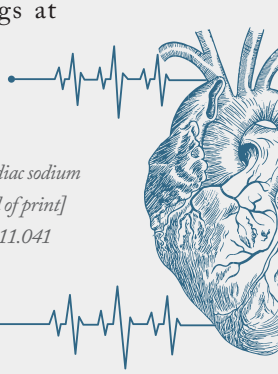
Got Rhythm?

An atomic view of cardiac arrhythmia

Dysfunction of voltage-gated sodium channel 1.5 (Nav1.5) can trigger life-threatening arrhythmias, but little is known about the structure and physiological function of these channels.

William Catterall and colleagues used cryo-electron microscopy to construct a complete model of Nav1.5's structure at a resolution of 3.5 Å (1). The result? A more comprehensive understanding of what makes the channels unique – namely, an unexpected glycosyl moiety and the loss of disulfide bonding capability at specific subsites – and advanced insight into mechanisms of voltage-dependent channel functions and sodium ion conduction. The team also investigated Nav1.5-antiarrhythmic drug interactions. "We've been able to characterize how flecainide – a commonly prescribed antiarrhythmic – specifically targets the central pore cavity of Nav1.5, physically blocking sodium permeation," says Catterall.

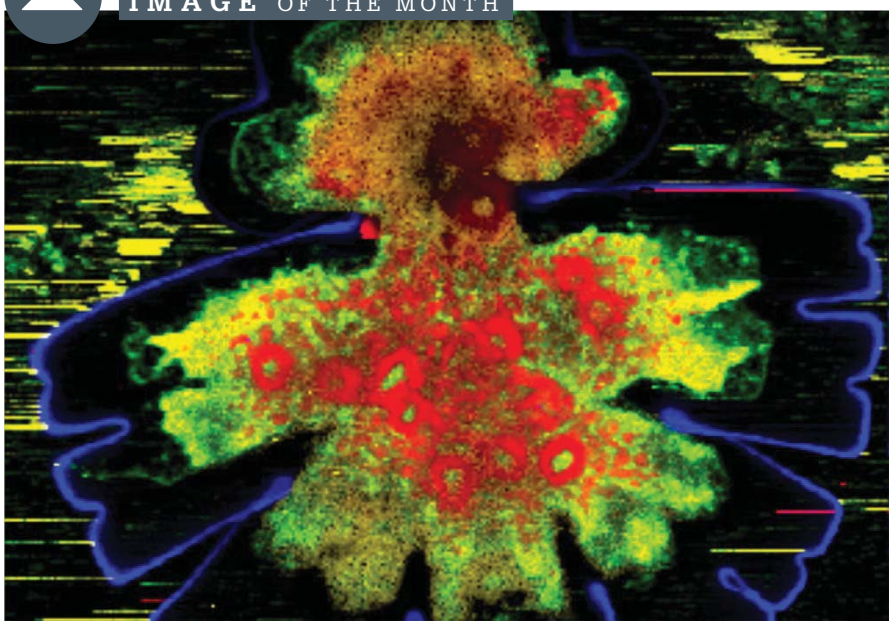
Looking ahead, the team plan to image multiple arrhythmic mutations and antiarrhythmic drugs at the atomic level to guide future drug design.



Reference

1. *D Jiang et al., "Structure of the cardiac sodium channel", Cell, 1, 122 [Epub ahead of print] (2020). DOI: 10.1016/j.cell.2019.11.041*

IMAGE OF THE MONTH



Doubling Up

Micrasterias denticulata is a green alga found in acidic-to-neutral fresh waters and sphagnum bogs. This confocal Raman micrograph shows the unicellular organism undergoing cell division; the cell wall is shown in blue, starch in red, and proteins, pectins and fats in green and yellow. The entire image width is a mere 160 µm.

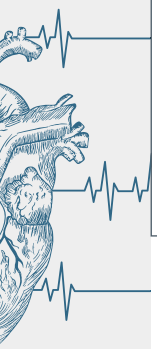
Credit: S Dr Notburga Gierlinger, BOKU; licensing information available at https://bit.ly/2R4bp2r

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

QUOTE OF THE MONTH

"Prediction: getting mass spectrometry to the standardized, streamlined place where DNA sequencing is right now would have at least 10X the effect that sequencing has had. It is such a cool piece of technology with endless applications."

Pablo Cordero (@tsuname) AI engineer, co-founder of RETINA-AI.



Agents of Destruction

A simple sensor to measure nerve agents in the field

Detecting organic compounds that disrupt the nervous system – whether used in chemical warfare or pesticides – is no easy task, but researchers at the University of Alberta have risen to the challenge with a spectroscopic approach that capitalizes on the quenching ability of nerve agents (1).

While both paraoxon and parathion easily quench the photoluminescence of silicon quantum dots, they are unable to quench green fluorescence protein. The result? A ratiometric sensor, capable of quantifying the concentration of nerve agent in a sample by its overall luminescence. "We've developed a rapid, straightforward, and cost-effective method to detect nitro-containing organophosphate nerve agents," say researchers Christopher Robidillo and Jonathan Veinot.

"We're now looking to expand the range of analytes we can study," they say. "Our dream? A simple system that can be implemented on-site and without training."

Reference

1. *CJT Robidillo et al., "Ratiometric detection of nerve agents by coupling complementary properties of silicon-based quantum dots and green fluorescent protein", ACS Appl Mater Interfaces, 36, 33478 (2019). DOI: 10.1021/acsami.9b10996*

Pittcon In Our Sights

With Pittcon on the horizon, we offer our top picks from the program to streamline your time in Chicago

Pittcon is back – for many, a highly anticipated feature of the annual conference line-up. And this year's program is set to bring fresh gales to the windy city. With a program boasting top experts across the full spectrum of analytical sciences and the biggest vendors vying for your attention in the exhibition hall, you could easily find yourself conflicted as to where to spend your time. But fear not - The Analytical Scientist editorial team is here to highlight some of the key happenings for your consideration…

Awards and symposia

- Advanced Neuroanalytical Measurements: From Single Cells to Whole Organisms (Sunday PM)
- The Wallace H. Coulter Lecture (Monday PM)
- Pittsburgh Conference Achievement Award(Monday PM)
- IAEAC (International Association of Environmental Analytical Chemistry) – Thinking Outside of the Box: Analytical Approaches Towards the Grand Challenges (Tuesday AM)
- Coblentz Society – Williams Wright Award (Wednesday AM)

Oral sessions

- Bioanalytical Detection using Mass Spectrometry Testing (Sunday PM)
- Handheld and Standoff Detectors for Drugs and Explosives (Monday AM)
- Novel Applications of Microfluidics (Tuesday PM)
- Methods for Air Quality and Emissions Monitoring (Wednesday AM)
- Innovative Training for the Next Generation of Analytical Chemists (Thursday PM)

Organized contributed sessions

- National Institute of Justice – Advancements in the Analysis of Forensic Trace Evidence (Monday PM)
- An Update on Advances and Trends in Lab Automation Today (Tuesday AM)
- The LCGC Awards, Part II: Advancing the Frontiers of Separation Science (Wednesday AM)
- The Science Behind Cultural Heritage Materials: Preserving our Past (Wednesday AM)
- Applications of Microdialysis from A to Z (Thursday AM)

Networking

- Food Contact Materials – Yet Another Source of Contamination in Our Food (Monday AM)
- Industry-University Collaborations in Measurement Science: Collaborative Development of Enabling Technologies for Industry (Monday PM)
- Understanding The Nuances of Accreditation for Cannabis Testing Laboratories (Tuesday AM)
- Environmental Concerns for 2020 and Beyond: PFAS, Microplastics and More! (Wednesday AM)
- Leveraging Social Media and Modern Marketing Tools to Share Your Research and Solutions (Wednesday AM)

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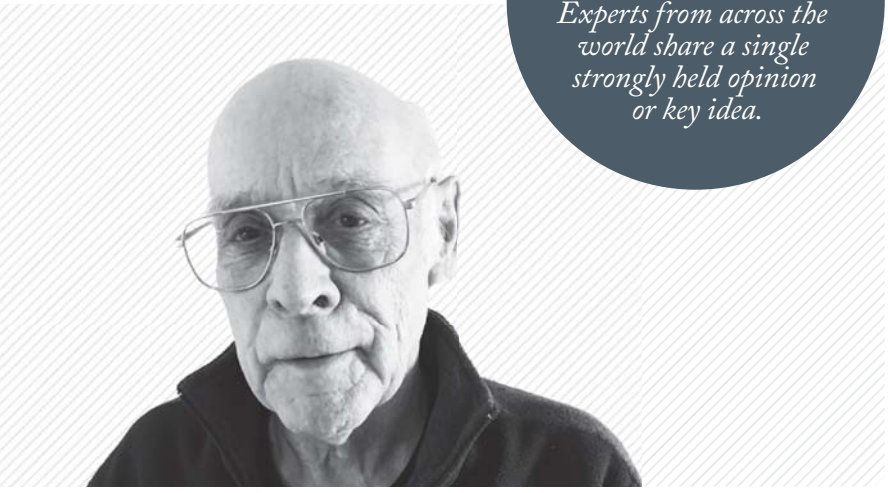
In My View

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

Biochar to Combat Climate Change

Chemists Without Borders is uniting minds to combat pressing issues across the world

By Ray Kronquist, President, Chemists Without Borders, San Jose, California, USA



I started working with Chemists Without Borders in 2014, and I've been President of the organization since 2016. Our mission? To solve humanitarian problems by mobilizing the resources and expertise of the global chemistry community and its networks.

We work with people around the globe to fulfil this mission. For example, one of our teams has three members in Australia, Switzerland and Argentina respectively – three points that couldn't be geographically further apart. Together, we work on numerous projects, focusing on issues from improving living conditions in less developed countries to combating global issues and scientific education. Scientists have a duty to further understand and improve the human condition, and I believe that many of us could make more active contributions to improving lives around the world. That is why I joined Chemists Without Borders.

A huge issue the world faces right now is climate change; we've burnt fossil fuels for over a century, greenhouse gas levels have climbed and temperatures have followed suit. In fact, the global temperature has risen by approximately 1 degree Celsius since the start of the industrial revolution. Though the rise may seem negligible, the climate is extremely sensitive to such changes – hence the sharp rise in storms, droughts, hurricanes and floods that we have witnessed these past few years.

Looming tipping points such as the melting of permafrost in the arctic, which would release large quantities of greenhouse gases, mean that we must find a solution quickly; we risk an irreversible global temperature increase that we may not survive. And though many groups have focused on political activism and the growth of green energy sources, I have focused my attention elsewhere: biochar.

Plants absorb carbon dioxide throughout their life and release it back into the atmosphere upon dying. The production of biochar – primarily carbon extracted from dead plants – can block this cycle, preventing carbon dioxide release and limiting eventual increases in atmospheric temperature. Around 200 companies are operating globally in this area already – analyzing and improving their biochar with techniques like Fourier-transform infrared spectroscopy and solid-state NMR – but our aim is to expand the industry further. Providing sales support to these companies could provide a much-needed push into the mainstream. Growth of this industry to a size at which it could process most of the world's dead plants could produce positive change.

"Looming tipping points such as the melting of permafrost in the arctic... mean that we must find a solution quickly; we risk an irreversible global temperature increase that we may not survive."

We're currently working with five biochar companies across America and Canada, and our next steps will be to build networks between these

businesses, farmers, and the US Department of Agriculture. These networks will be essential to open up communication with those who will benefit from using biochar for their specific soil and environmental conditions. In short, as in all areas of science, communication and collaboration will be key to our success.

To this end, we're constantly recruiting volunteers to support our cause, including students involved in crop and soil research, environmental science, agriculture, and even business. We are encouraging university professors in the relevant fields to design student research projects on biochar applications for masters' programs and PhD theses. These thesis projects could simultaneously solve the problems faced by biochar customers and grow the market. In short, the model offers a win-win-win-win: the student gets a thesis topic with mentoring from Chemists Without Borders and the biochar producer; the biochar producer improves their sales; the biochar purchaser gets the benefits from its use; and the world comes closer to a solution of the climate crisis.

"We're constantly recruiting volunteers to support our cause, including students involved in crop and soil research, environmental science, agriculture, and even business."

Many skills will be needed to communicate our message widely through the scientific and agricultural communities (marketing, social media, sales, engineering, and so on), and the more people we can recruit with expertise in these areas, the better. Bringing together such minds could enhance not only the reach of our climate change project, but also the numerous other projects in which Chemists Without Borders are involved.

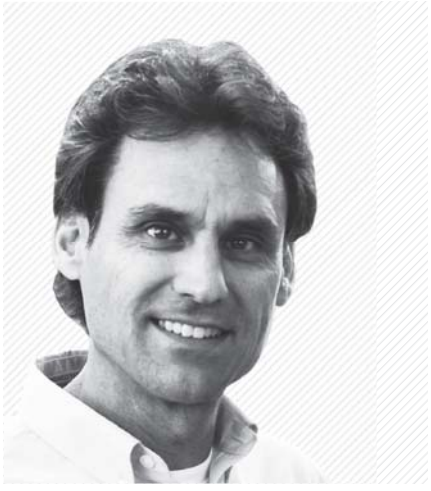
Consider this a call to arms. Whether your talents lie in laboratory work, communication through social media platforms or the running of successful business, we would love to hear from you. Analysts have molded the world we live in and continue to do so every day – why not help in extending this hand to the people and causes that would benefit from it most?

If you're interested in contributing to Chemists Without Borders, feel free to contact me at ray@kronquist.com.

And for further information, please see the following In My View articles from my colleagues Robert Kurkjian and A Bakarr Kanu. respectively.

Unpoisoning the Well

Bringing safe drinking water to Bangladesh is a tall order, but Chemists Without Borders are rising to the occasion



By Robert Kurkjian, Environmental Strategies International, Pasadena, California, USA

"The largest mass poisoning in history" – that's how the contamination of drinking water with arsenic in Bangladesh has been described. In fact, as many as 95 million people are chronically exposed to this danger in Southeast Asia. The outcomes of this poisoning? Long-term damage to health, ranging from respiratory disease to skin lesions and cancer. Needless to say, it's a huge problem – and one that I felt I could help address.

I have worked on dozens of international projects such as evaluating and remediating contaminated fish ponds resulting from untreated industrial and domestic waste discharges; assessing acid mine drainage; providing oversight of the investigation and demolition of bulk petroleum storage facilities in residential areas; evaluating water resources for drinking and irrigation; and redeveloping contaminated properties. Each project was a collaborative effort between international consultants and local scientists, governmental agencies, the general population, and non-government organizations (NGO's). I learned that information exchange and stakeholder outreach were an essential element and keys to project success.

About one year ago, I joined Chemists Without Borders, after seeing an article on their work in Chemical Engineering News. Given my 28-year background in environmental consulting and investigating chemical contaminants, I was up to the challenge. And the project certainly is challenging. Bangladesh (like many less economically developed countries) lacks resources and processes to deal with hazardous chemicals, which means that outreach and education targeting local government, NGO's, and residents lie on the frontier of our efforts to bring about sustainable improvement.

But the project also involves a lot of chemistry. For example, how do we test wells for arsenic? And how do we then remove it when it's present? Laboratory analysis is important, of course, but we're also able to use arsenic test strips (Hach, Colorado, USA) to test water samples for costs as low as $2.00 in the field. The test strips cost about $1.00 for each test, and we recruited nearby college students, whom we paid about $1.00 per well tested. We tested 320 wells in this community and found that a staggering two thirds of them were heavily contaminated – arsenic concentrations of more than 50 ppb. For context, the US EPA's drinking water maximum contaminant level is 10 ppb.

To solve the problem, our project entails two major components: first, the so-called "WASH" project, which is focused on providing water with low concentrations of arsenic (less than 10 ppb) or treating contaminated water, and providing improved sanitation and hygiene; and second, the introduction of a well-sharing program, which allows locals whose wells are contaminated to take water from a neighbor's safe well. Well sharing presents its own associated difficulties (overcome in part through education on water resources, toxicity of chemicals, etc.), but we plan to have families who take the safe water pay a small monthly fee. We will investigate other incentives, as well. A major part of the program at this first community will be the development of the policies that make the program acceptable to the community. Once that is done, we believe the model can be replicated across Bangladesh.

"We tested 320 wells in this community and found that a staggering two thirds of them were heavily contaminated – arsenic concentrations of more than 50 ppb."

This international work brings with it a sense of achievement so different to that found elsewhere in my professional life. Not only do we help people, but

we are constantly solving problems that we don't consider when working domestically – a great example being the need to consider logistics and the long-term sustainability of the solutions we provide in Bangladesh. If we provide a $50,000 water treatment system that subsequently breaks down or is at the end of its useful life, how would locals then acquire the parts needed maintain or to fix the system? You have to readjust your mindset to think within the parameters of the local community – and this expands to further considerations, such as cultural differences and their impact on the work.

All in all, it's truly rewarding to think that the project could be such a great success, and – if the model works in wider Bangladesh – it could be expanded to further geographies experiencing similar problems. And, the solutions in place aren't limited to arsenic – we could tackle other types of contaminants. Though this kind of work certainly isn't for everybody, anyone thinking about it should give it a go. Chemists Without Borders is a brilliant organization that's making a real difference, and we are always looking for an extra pair of hands to help drive our cause forward.

"A major part of the program at this first community will be the development of the policies that make the program acceptable to the community."

Robert Kurkjian, PhD is a volunteer with Chemists without Borders and an international environmental consultant and founder of Environmental Strategies International, a not-for-profit organization which performs environmental consulting and training worldwide. Robert has lived in New York City, Los Angeles, and Yerevan, Armenia and has traveled to more than 40 countries. He can be reached at robert@environmentalstrategies.org.

To Educate Is to Drive Change

Bringing scientific education to developing nations for a brighter and more collaborative future

By A Bakarr Kanu, Associate Professor, Winston-Salem State University, North Carolina, USA

I joined Chemists Without Borders because of their mission statement – it fits incredibly well with my personal goals regarding community development. In October 2015, I took over the Ongley-Myers Sierra Leone Chemistry Education Project (OMSLCEP), a name coined in honor of the two former leaders of the project (Lois Ongley and Rusty Myers, both of whom sadly passed away).

OMSLCEP seeks to provide chemistry education in developing nations that people can then apply to their daily lives and teach others. The ultimate aim? To allow them to make improvements in their own country. Sierra Leone remains the focus of these efforts at present; like many developing nations, Sierra Leone was subject to a civil war that caused great disruption to its educational infrastructure. And, although most students in the region retain a strong theoretical background in chemistry, they still lack a laboratory framework in which they can develop the associated practical skills.

And that's where we come in. We have developed a total of 16 laboratory activity kits ready for use in Sierra Leone – all of which are inexpensive, produced by green approaches, and tied to laboratories associated with the West African Examination Council (WEAC) curriculum. Students in Sierra Leone must pass the WEAC with at least four subject passes to transition to university – one of which must be chemistry. What's more, the kits do not require dedicated laboratory space for application, and they generate very little waste. And, as I mentioned briefly above, their use has focused largely on everyday Sierra Leone needs – for example, to purify water or focus on the chemistry of cement. In Sierra Leone, people build their own homes, making cement knowledge somewhat vital.

When asked what we need to continue our work, the answer will always be money - money and human resources, largely in the form of volunteers. On this front, we've secured significant external funding in the past (from the American Chemical Society Global Innovation Committee, the Department of Defense, the Defense Intelligence Agency, Hopevale Church in Michigan, and individual donors like Dr. Ronda Grosse), but we are waiting on a proposal from the USAID at present. I've also developed a study abroad class at my institution to allow undergraduate students to teach science in developing nations themselves. I think that such schemes represent a powerful tool to drive meaningful change in countries where scientific education may be lacking – and may well represent the future of education in science.

"When asked what we need to continue our work, the answer will always be money – money and human resources, largely in the form of volunteers."

Of course, meaningful change takes many forms. When it comes to OMSLCEP, we anticipate we will be able to provide not only essential support to communities that need them, but also enhance scientific talent, intellectual capital, student potential, global competitive ability, youth engagement in science, and female empowerment. In Sierra Leone, only 30 percent of those entering university following standard tests are female. Plus, as is the case with many of the Chemists Without Borders projects, we are also looking to expand; I anticipate similar projects in Ghana, Gambia, and other Spanish-speaking countries.

If you're interested in lending a helping hand in any way, feel free to contact me at bakarrkanu@chemistswithoutborders.org. It's always a pleasure to expand our network, and I look forward to hearing from anybody who wants to be a part of it.

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

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

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

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

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

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

Looking forward to meeting you in astonishing Riva del Garda!

44TH INTERNATIONAL SYMPOSIUM ON CAPILLARY CHROMATOGRAPHY

AND

THE 17TH GC×GC SYMPOSIUM

Chroma leont

GURUS OF 2DMS

Advances in our ability to crunch data continue to lay the foundations for the rise of multidimensional MS in mainstream analytics. But what exactly is 2DMS – and how can the technique transform the field?

Two-dimensional techniques are shifting the landscape of analytical science – ramping up levels of data acquisition and offering unparalleled insights into the phenomena we investigate. Our thirst for "more" – especially when analyzing highly complex samples – has driven us out of the first dimension in multiple techniques; 2D NMR spectroscopy has been around for decades, and various flavors of multidimensional chromatography have proven utility in a range of applications. But now, it's time for the spotlight to shift. Prepare to enter a new dimension – of MS.

HOW EXACTLY DOES 2DMS WORK?

MARIA: Ions rotate with a frequency that depends on their mass-to-charge ratio in a magnetic field. This rotation – dubbed "cyclotron motion" – is measured in a high-vacuum, high-magnetic-field cell, such as the ion cyclotron resonance (ICR) cell of a Fourier-transform-ICR (FT-ICR) mass spectrometer, and the signal is transformed first to obtain the frequencies, and then the mass-to-charge ratios. In 2DMS, ion radii in the ICR cell are modulated according to their mass-to-charge ratios using a pulse sequence developed by Tino Gäumann and Geoffrey Bodenhausen in the 1980s and inspired by 2D NMR. Because the fragmentation efficiencies of each precursor ion depends on its radius, the abundance of fragment ions also depends on precursor ion radius, which in turn depends on the mass-to-charge ratio; this establishes a correlation between precursor ions and their fragments, which, after a double Fourier transformation, can be mapped on a 2D mass spectrum.

2D mass spectra contain not just the mass spectrum of the analytes from the sample (shown by the autocorrelation line on Figure 1) like a traditional mass spectrum, but also the fragmentation pattern of every precursor ion (the fragment ion scan), the precursor pattern of every fragment ion (the precursor ion scan), and neutral loss and dissociation lines that can be used to find classes of ions in the sample that fragment in identical ways – indicative of similar structures (protein forms with different post-translational modifications, for example).

"2DMS ALLOWS US TO MEASURE ALL THE FRAGMENTS FROM PRECURSORS SIMULTANEOUSLY."

PETER: In MS, the user first measures the masses of molecules and then performs what is called an MS/MS or Tandem MS study, in which molecules of interest are first isolated, then fragmented (by collisions with neutrals, photons, or electrons), and then a mass spectrum is measured of those fragments. To analyze everything in the sample requires sequentially isolating each precursor molecule, fragmenting it, and measuring the spectrum of the fragments from each precursor.

As Maria says, 2DMS allows us to measure all fragments from all precursors simultaneously. This is done by use of a signal coding trick, whereby the precursors are each modulated in and out of a fragmentation "zone." Because the fragments are only created inside that "zone," the fragments also modulate in their intensities according to the modulation frequency of the precursor. Thus, we know exactly which fragment is derived from which precursor in a complex mixture. 2DMS is therefore particularly useful for complex mixtures, or mixtures that are difficult to separate. Good examples include polymeric samples, proteomics samples and very complex mixtures like lignin, biofuels, and petroleum – we are currently focusing on such analyses in my lab.

WHY HAS THIS TECHNIQUE LAGGED BEHIND OTHERS HISTORICALLY, AND WHY IS THIS CHANGING NOW?

PETER: 2DMS is actually an "old" technique in that it was initially demonstrated in 1987 (1), but was subsequently ignored for many years due to computational limitations – we simply couldn't process the volume of data produced. In 1990, a 2-megabyte Fourier transform would take about 30 minutes, but around 1000-4000 of these calculations are needed to produce a 2D mass spectrum. By 1998, the CPU of a standard desktop PC could perform these calculations in half a second – though it would take a lot longer to

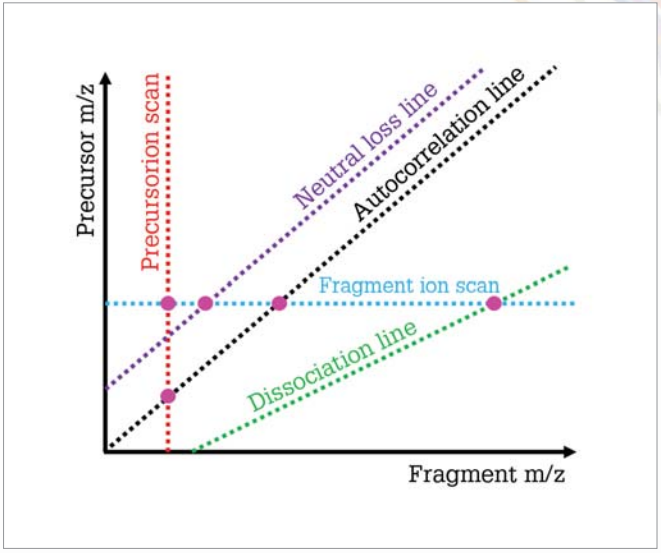


Figure 1. Generic 2D mass spectrum

transfer the data from hard disks into RAM. Continuous improvements in computational capability from then until now (Moore's Law estimates that computing power doubles every two years) mean that we can use cluster computers to parallelize the Fourier transform and data analysis, or simply use a maxed-out desktop PC with 256 gigabytes of RAM and multiple cores for data processing. 2DMS is now a credible approach for conducting analyses in a standard MS lab.

We have also developed a new way to conduct 2DMS analyzes on a linear ion trap, making the approach amenable to standard quadrupole time-of-flight mass spectrometers. Maria, Christopher Wootton and I then commercialized this success by setting up a startup company called Verdel Instruments with the University of Warwick.

DALTON: We weren't the first group to use 2DMS, but it had previously been compatible only with FT-ICR platforms. Peter (as you can probably tell from the above!) has been a key driver of the technique, having conducted pioneering research for several years. His work developing a method for 2DMS analysis on FT-ICR instruments laid the foundation for my research in the area, which represented a significant change in thinking about how 2DMS could be conducted. 2DMS on the FT-ICR consists of a series of scans from which the tandem MS data domain can be reconstructed (which takes hours), while the technology developed by Graham, Lucas and myself uses one scan, taking around one second to complete. Of course, the resolution of the FT-ICR is significantly higher, but we trade resolution for instrument runtime.

THE GURUS

Peter O'Connor

"I'm a Fourier-transform ion cyclotron resonance (FT-ICR) mass spectrometrist, and Associate professor at Boston University School of Medicine and Professor of Chemistry at the University of Warwick. Our work has focused on bringing 2DMS to the analytical mainstream, with the hope of developing routine applications in chemistry and biology."

Dalton Snyder

"I was lucky enough to conduct research under Arlen Kauffman during my undergraduate studies. Arlen introduced me to Graham's work on ambient ionization and molecular imaging, and I eventually became an "Astonite" myself, developing novel ion trap methods for miniature and portable mass spectrometers."

Maria van Agthoven

"I've worked on several 2DMS projects in labs from Florida State University to the Université de Lille Sciences et Technologies and the University of Warwick. Now, I'm based at the University of Innsbruck, Austria, where I'm continuing this work. The hope? That 2DMS will one day become as commonplace as other analytical techniques."

2DMS – MEETING A GREAT NEED

"Many pressing issues in science and technology have at their heart the question of molecular composition. Most real samples are complex mixtures and most real problems call for quick decisions based on molecular information. This statement is as true of the trace residues on the fingers of a passenger boarding an aircraft as it is of the spatial distribution of complex phospholipids in the brain tissue of a glioma patient as it is of the bacterial composition of lettuce in the quick-pick line. An argument can be made that the greatest need in technology is for near-instantaneous chemical identification tools. Ion traps fitted with ambient ionization sources and performing 2D MS/MS scans come close to answering this challenge. The near future for 2D MS/MS must be focused on utilization of the existing capabilities in solving real problems."

Graham Cooks, Henry Bohn Hass Distinguished Professor of Chemistry in the Aston Laboratory of Mass Spectrometry, Purdue University

"2DMS IS STILL IN ITS INFANCY WITH RESPECT TO TECHNICAL APPLICATIONS, BUT THERE ARE SOME CLEAR AREAS WHERE IT WILL HAVE AN ADVANTAGE OVER ALTERNATIVE METHODS."

HOW DOES 2DMS FIT INTO YOUR RESEARCH?

MARIA: I learned about FT-ICR MS during my first postdoc at Florida State University, and was hired by Christian Rolando to enable 2DMS on a Bruker instrument in 2009. We showed that 2DMS was viable with laser-based and electron-based fragmentation methods and we optimized the pulse sequence parameters for maximal signal-to-noise ratio, after which I moved to the University of Warwick to work alongside Peter O'Connor. At my current institute – the University of Innsbruck – I work on top-down RNA and histone analysis. We study these molecules because they are often subject to post-translational molecular modification, and thus are difficult to separate with chromatographic approaches.

In this space, I particularly focus on the development of quantification techniques in 2DMS, based on the neutral loss lines and dissociation lines demonstrated. Data analysis techniques will be invaluable in 2DMS research due to the sheer volume of data produced. Some of the analytical information present in 2D mass spectra cannot be obtained with any other method. Precursor and fragment ions are correlated not only through precursor mass:charge ratios, but also through precursor charge state. Information

on fragmentation mechanisms can also be uncovered by analyzing the harmonics present in the spectra.

DALTON: The initial applications that we looked at for 2DMS were relevant to our collaborators at NASA and FLIR. With FLIR, we focused on the detection of opioids (largely fentanyls) and other nefarious substances to demonstrate forensic utility. With NASA, we used 2DMS for the detection of amino acids and other small organics – molecules that we hope to find on Mars (or elsewhere) one day. Regarding the latter application, the hope is that NASA will be able to send a 2DMS-equipped ion trap to Mars or extraterrestrial icy moons to deduce the organic chemical makeup of a rock or ice sample, from which they could infer the past existence of or present suitability for life.

The limitations imposed by miniature mass spectrometers in terms of size, power, weight, and sample consumption were the main factors underscoring our research. Initially, we developed precursor and neutral loss scans (2, 3) as efficient means of sorting through complex chemical mixtures using a simple yet sensitive portable ion trap mass spectrometer. These methods were thought either impossible or problematic on anything but a bulky, power-hungry multiple analyzer instruments like the triple quad. 2DMS is an extension of our prior work, wherein all possible precursor scans, neutral loss scans, and product ion scans are conducted in a single run. This approach allows us to probe mixtures and obtain structural information on virtually every compound in the sample quickly (minimizing power consumption) and with minimal sample consumption.

WHAT IS THE CURRENT STATE OF 2DMS?

PETER: 2DMS is still in its infancy with respect to technical applications, but there are some clear areas where it will have an advantage over alternative methods. Proteomics is an interesting case that my team has been exploring in detail – inspired by the potential for 2DMS to explore complex protein mixtures, as showcased by the "Uncoiling Collagen" paper from Simon and colleagues in 2016 (4). The team used 2DMS to obtain data on trypsin digests of collagen cleanly and clearly using FT-ICR MS and a blind, unoptimized method. We have continued this work by proceeding onto more complex bulk proteomics experiments. On this front, we've obtained many interesting, unpublished results that are making their way out of the lab… But you'll have to wait

"I THINK WE'LL SEE INCREASED USE OF 2DMS IN THE FT-ICR MS COMMUNITY IN THE NEXT 5–10 YEARS"

until those are published! As a sneak preview, they involve 2DMS for whole protein analysis, polymers, pesticides, and – of course – proteomics.

DALTON: The technology is still fairly niche at the moment. Our technology, for example, has only been developed in the last couple of years, so it has much room to grow and evolve – hopefully leading to improved performance metrics, such as mass spectral resolution, sensitivity, and speed. I would say the biggest developments in the field to date are the initial conception of 2DMS on the FT-ICR by Pfändler and colleagues (1), optimization of the pulse sequence and data analysis technologies by the Rolando group, and our initial conception of 2DMS on quadrupole ion traps. At the moment, 2DMS on quadrupole ion traps is capable of near-unit precursor ion resolution (up to ~120 product ion resolution, variable with mass-to-charge) and a limit of detection that compares quite favorably with ion trap full scan mode.

MARIA: Today, 2DMS can be used for data-independent analysis in research laboratories for tandem mass spectrometry experiments without ion isolation. The pulse sequence can be optimized on any FT-ICR mass spectrometer, denoising

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"I WOULD ALSO HOPE TO SEE MORE RESEARCHERS GETTING INVOLVED IN INSTRUMENT DEVELOPMENT FOR 2DMS TECHNOLOGIES."

algorithms enable easy data analysis and interpretation, and Marc-André Delsuc and his group have even developed an open-source program package for data processing, visualization, and analysis. So far, 2DMS has been used for bottom-up and top-down proteomics, polymer analysis, and small molecule analysis. But I believe the best is yet to come.

WHAT CHALLENGES DOES THE FIELD FACE MOVING FORWARD?

MARIA: I think we'll see increased use of 2DMS in the FT-ICR MS community in the next 5–10 years, particularly for quantification studies in top-down and bottom-up proteomics. The methods developed for 2D FT-ICR MS can then be transferred to 2DMS on a linear ion trap with time-of-flight mass analyzers as they reach the market. These instruments will be cheaper and faster (albeit with lower performance in terms of resolution and mass accuracy), and will be potentially coupled with chromatographic techniques. Once we can use 2DMS to separate analytes by chromatographic time, mass-to-charge ratio, and charge state in a fully multiplexed way that does not involve loss of sample through isolation, we will have overcome a major analytical barrier. In short, I anticipate that 2DMS will allow us to extract more information from highly complex samples – perhaps even by several orders of magnitude – in the years to come.

DALTON: The truth is that we have little idea what the future holds for 2DMS. And that's the exciting thing about this research! In the next several years, I imagine we will see new versions of the technology emerging with improved resolution, sensitivity, and scan speed. Perhaps someone will think of clever ways to do 2DMS on quadrupoles or time-of-flight instruments, too. I expect further interest from those involved in the development of new portable and miniature mass spectrometers and perhaps 2DMS will end up as a key feature of the next generation of devices!-

I would also hope to see more researchers getting involved in instrument development for 2DMS technologies. So far, the community has only covered two types of spectrometer (quadrupole ion traps and FT-ICRs), so there are many more to go. I certainly imagine new methods of 2DMS emerging as more clever graduate students get involved in the subject, and I look forward to seeing this happen.

PETER: The technical limitations of 2DMS are mostly well understood, but there's a persistent problem in calibration of the vertical axis that remains. This problem is related to the timing of the detection electronics and is annoying to define. For this reason, every publication to date has had to use internal calibration of the vertical axis, but we believe that some relatively simple modification to the electronics will eliminate this calibration problem and allow robust, external calibration of the vertical axis of 2DMS data.

Beyond this calibration problem, the main technical problem remains processing the data obtained. We are developing the software to do the 2D Fourier Transform (routine), the denoising (tricky and under development), peak picking (challenging, but conceptually straightforward), and the assignment of masses from the resulting peak lists to important chemical features (an ongoing and probably perpetual struggle). Still, if we can push most of the technical problems towards being software problems, many more individuals can become engaged in the solution – and that can only be a good thing for the field.

References

1. *Pfändler et al., "Two-dimensional fourier transform ion cyclotron resonance mass spectrometry", Chem Phys Lett, 138, 195 (1987). DOI: 10.1016/0009-2614(87)80367-6*
2. *Snyder DT et al., "Single analyzer precursor ion scans in a linear quadrupole ion trap using orthogonal double resonance excitation", J Am Soc Mass Spectrom, 28, 1929 (2017) DOI: 10.1007/s13361-017-1707-y*
3. *Snyder DT et al., "Implementation of precursor and neutral loss scans on a miniature ion trap mass spectrometer and performance comparison to a benchtop linear ion trap", J Am Soc Mass Spectrom, 29, 1355 (2018). DOI: 10.1007/s13361-018-1922-1*
4. *Simon HJ et al., "Uncoiling collagen: a multidimensional mass spectrometry study", Analyst, 141, 157 (2016). DOI: 10.1039/c5an01757b*

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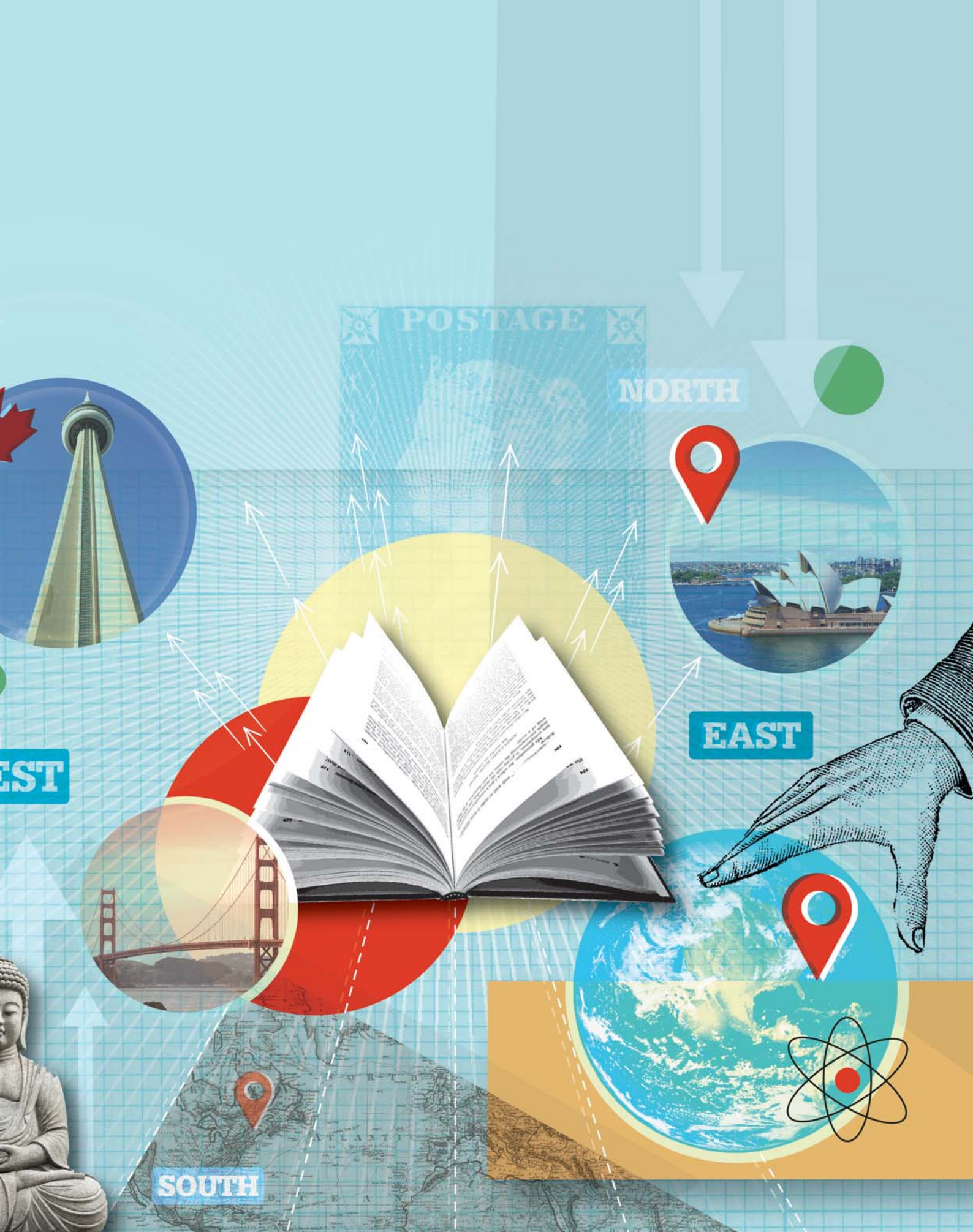
Landmark Literature

Every year, the analytical community takes significant steps towards increased speed, sensitivity, accuracy, accessibility, and more. Here, our experts each share one particular 2019 paper that, for them, really stood out from the crowd.

2019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LESS IS MORE

By Norman Dovichi, Grace-Rupley Professor of Chemistry and Biochemistry, University of Notre Dame, Indiana, USA

Landmark paper: Z Liu et al, "Stable isotopic labelling and nontarget identification of nanogram/liter amino contaminants in water", Anal Chem, 91, 13213 (2019). DOI: 10.1021/acs.analchem.9b03642

Analytical chemists have worked for decades to develop technology that detects and identifies very low concentrates and quantities of analyte. This effort is driven, in part, by the need to identify trace-level environmental contaminants. Many such contaminants are pharmaceuticals and pesticides discarded into sewage, which can be toxic to aquatic species at even very low concentrations. These contaminants often contain amines.

Liu and colleagues report the detection and quantitation of ppt (picomolar) concentrated amino-containing compounds in environmental waters. The team used formaldehyde to isotopically label the amines, which allows quantitation by comparison of intensities for the light-isotope-labeled standards and heavy-isotope-labeled analyte. Labeling also enhanced solid-phase extraction of these trace-level components. Once concentrated by solid-phase extraction, conventional LC-MS completed Liu's analysis platform. The authors report detection of thousands of MS features from the analysis of single liter aliquots of environmental water – some compounds were identified at the hundred picomolar level.

However, this work highlights one important challenge in trace-level analysis. Although trace-level components can be detected as features in mass spectra, identification of those features is extremely difficult; Liu tentatively identified only 154 compounds from the thousands of features that they detected. This challenge of identifying features present at very low levels is not only important in environmental analysis – as demonstrated in this work – but is also a common challenge in metabolomic analysis, where feature generation is easy but feature identification is much more difficult.

POWERFUL PREPARATION

By Gongke Li, Professor and Director of the Institute of Analytical Sciences, School of Chemistry, Sun Yat-sen University, China

Landmark papers: P Nanthasurasak et al, "In-transit electroextraction of small-molecule pharmaceuticals from blood", Angewandte Chemie, 58, 3790 (2019)

Y Yu, "Ultrasensitive determination of rare modified cytosines based on novel hydrazine labelling reagents", Anal Chem, 91, 13047 (2019)

Sample preparation is a critical step in complex sample analysis that impacts the selectivity, speed, and accuracy of analytical results. The goal: separation and enrichment. From chaos to order, separation and enrichment are entropy reduction procedures that cannot happen spontaneously. On account of consuming over two thirds of analysis time, sample preparation becomes the bottleneck issue in many labs.

Interesting in-transit sample preparation was carried out by Nanthasurasak and colleagues, in which a clinical sample was prepared during transport to the laboratory using a portable device and electroextraction method. Benefiting from both device miniaturization and a multistep integration strategy, this work provides a potential time-saving approach to processing samples.

In another paper by Yu and colleagues, the coffee ring effect was combined with surface-enhanced Raman spectroscopy for rapid, in situ sample preparation and analysis. Without sampling and sample transfer processes, in situ approaches are advantageous as they examine the real status and concentration of target analytes, especially in medical diagnosis, environmental monitoring, food safety, and forensics. Acquiring enough information on the target analyte from the sample matrix within a minimum period of time is one of the greatest goals of our field.

Both of these papers feed into this goal, demonstrating the development of sample preparation towards fast, automation, low-cost, and eco-friendly.

EXTRA DIMENSIONS OF DRUG KNOWLEDGE

By Kelly Zhang, Principal Scientist and Associate Director, Research and Early Development, Genentech, USA

Landmark paper: A Goyon et al, "Streamlined characterization of an antibody–drug conjugate by two-dimensional and four-dimensional liquid chromatography/mass spectrometry", Anal Chem, 91, 14896 (2019). DOI: 10.1021/acs.analchem.9b02454

The cover story on Analytical Chemistry in December by my colleagues Alex Goyon and Cinzia Stella at Genentech in collaboration with the University of Geneva, is one of my favorite papers in the field of analytical chemistry from 2019.

It was truly exciting to see multidimensional separation (in this case 4DLC-MS) being used in biopharmaceutics. The outcome? Significantly improved working efficiency. The reported online automated approach is much faster than the traditional offline approach, which would have required the researchers to conduct several separate and time-consuming manual methods. The reported approach reduced the antibody–drug conjugate characterization time from weeks to days – an impressive feat.

The streamlined 4D (SEC-reduction-digestion-RPHPLC) method can simultaneously measure several critical quality attributes: aggregation, average drug-to-antibody ratio, and post-translational modifications by online peptide mapping after trypsin digestion – all in a single analysis. Peptide mapping of the size species may help to identify specific peptides involved in aggregate formation, and could help to guide antibody reengineering efforts in early stages of production.

I think it's also important to note how this work bridges the disconnect between academic research and real-world applications.

THE TRUTH ABOUT TRANSFUSIONS

By Catherine Fenselau, Distinguished University Professor Emeritus, University of Maryland, USA

Landmark paper: L Chen L and RB van Breemen, "Validation of a sensitive UHPLC-MS/MS method for cytochrome P450 probe substrates caffeine, tolbutamide, dextromethorphan, and alprazolam in human serum reveals drug contamination of serum used for research", J Pharm Biomed Anal, 179 (2020). DOI: 10.1016/j.jpba.2019.112983

Researchers at Oregon State and the Linus Pauling Institute identified and reported the widespread presence of caffeine, alprazolam (an anti-anxiety medicine) and dextromethorphan (an over-the-counter cough suppressant) in samples of "pure" human serum. Rigorous measurements were mad using stable, isotope-labeled internal standards and ultrahigh-pressure (UHP)LC-MS/MS. Eighteen samples of human serum from North American sources were tested. All contained caffeine levels as high as 250 ng/mL; alpraxolam was also detected in 13 lots, and dextromethorphan in 8.

Two individual donors had to be recruited to abstain from caffeinated foods and beverages to complete the research. Quoting EurekAlert: "If you ever need a blood transfusion, your odds of also receiving caffeine, cough medicine and an anti-anxiety drug are pretty good."

FRONTLINE FOODOMICS

By Alejandro Cifuentes, Laboratory of Foodomics, Institute of Food Science Research, Spanish National Research Council, Madrid, Spain

Landmark paper: Barabási A et al, "The unmapped chemical complexity of our diet," Nat Food (2019). DOI:10.1038/s43016-019-0005-1

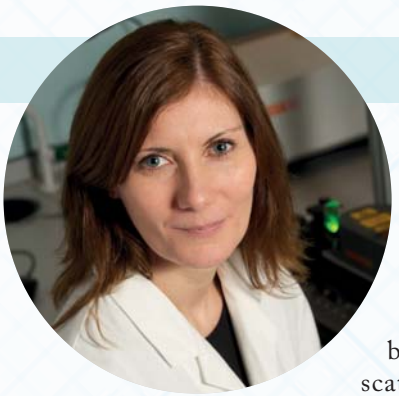
This is one of the first papers published in the inauguration of a new journal called "Nature Food." The paper was published on December 2019 and, as indicated online, the journal will be open for submissions from January 2020; the unveiling of this new journal from the prestigious Nature group is exciting news for people working on food science (like myself). In this article, the authors highlighted that only 150 nutritional components are tracked in food composition tables – about 0.5 percent of the 26,625 chemical compounds documented in food. This, of course, provides a very poor representation of this complex issue and may be responsible for many irreproducible results.

As may be expected, the researchers found a wealth of information about food composition scattered across multiple publications that has not been collected in any relevant database. According to the authors, the use of new high-throughput tools to scan the scientific literature could set the stage for an in-depth and systematic understanding of the ways in which our food affects our health. The paper also touches on other issues in the food and health binomial, and – although it uses the concept of the "foodome" in a somewhat peculiar way (already defined in a SCI journal in 2017) – it provides an interesting perspective on a complex issue that is well worth the read.

NEW MODELS FOR NANOPARTICLES

By Karen Faulds, Head of Bionanotechnology and Analytical Chemistry, University of Strathclyde, UK

Landmark paper: H Arami et al, "Nanomedicine for spontaneous brain tumors: a companion clinical trial", ACS Nano, 13, 2858 (2019).



The understanding of the mechanism of uptake and distribution of nanoparticles within tumors by enhanced permeation and retention (EPR) is critical for the future use of untargeted nanoparticles as imaging and therapeutic agents. The EPR effect relies on the tendency for nanoparticles to accumulate in tumors over healthy tissue; however, the majority of animal studies use mouse models – subject to some scrutiny regarding their ability to accurately represent spontaneous human tumors. In particular, mouse models of brain cancer involve the intracranial implantation of human tumor cells, which generally results in more homogenous tumors with altered invasiveness when compared with spontaneously occurring tumors in humans. Rodents also have much higher resting heart rates than humans, which impacts the pharmacokinetics and circulation stability of nanoparticles.

This paper from Ghambhir and colleagues details a study of EPR uptake and the distribution of silica-coated gold nanoparticles in canines with spontaneous brain tumors using surface-enhanced Raman scattering, scanning electron microscopy, inductively coupled plasma MS, magnetic resonance imaging and histology. Four different companion canines with spontaneous brain tumors (differing in pathology and grade) were recruited. The results show that the EPR effect was still valid in these spontaneous canine tumors, but the heterogeneity of the naturally occurring canine tumors resulted in variability in the EPR effect and non-homogenous uptake of nanoparticles into the tumors versus the homogeneous tumors of mouse models.

This really important paper enhances our understanding of the uptake and fate of nanoparticles in spontaneous cancers, which is necessary knowledge if nanoparticle approaches are to be used for diagnostic and therapeutic applications in humans in the future.

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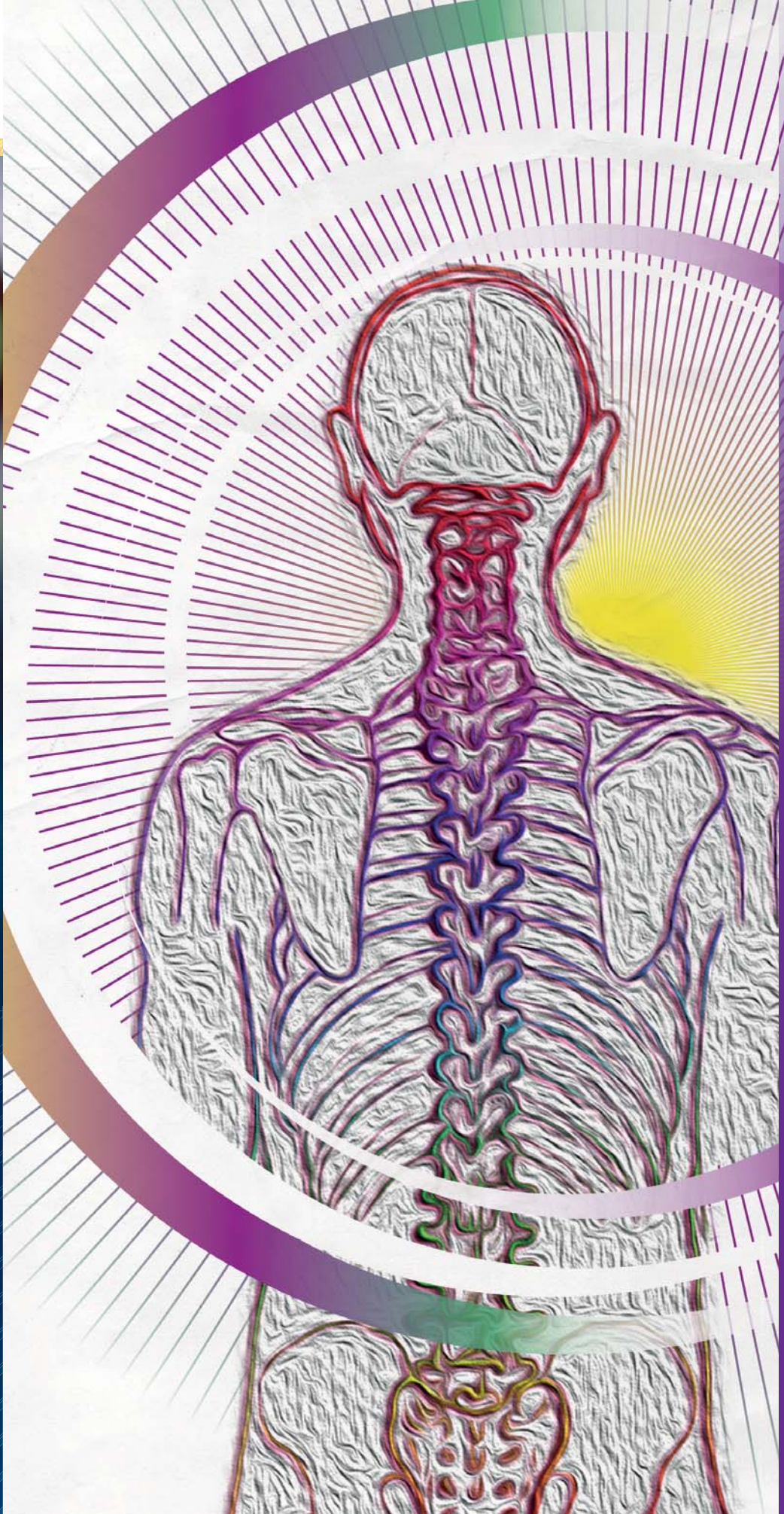

the Spectroscopist

INSIDE

SPECIAL SERIES
Advanced Clinical Analysis

Operation Spectroscopy

In the quest to improve patient outcomes, collaborations between surgeons and spectroscopists are leading the charge with real-time measurements that could take some of the guesswork out of surgery

A recurring theme in the analytical sciences is the movement of techniques out of the lab and into the field. In past issues of The Analytical Scientist, we have put the spotlight on spectroscopic guns to extract information from ancient art, portable GC-MS systems for the rapid identification of hazardous chemicals at fire scenes, and portable analyzers to ensure quality of consumer products at all phases of production. But perhaps the most exciting stage of all is the operating theater.

Already, patients going under the knife may come under the scrutiny of advanced analytical instruments – all in the name of improved treatment and outcomes. These efforts are visible in success stories like the iKnife (a surgical instrument that identifies cancerous cells by rapid evaporative ionization MS intraoperatively) and MasSpec Pen (a similar tool using ambient ionization MS). Arguably less publicized, however, is the expanding role of spectroscopic approaches in this space.

Do spectroscopic approaches have the potential to change the way we operate? In what areas will they make the biggest impact? And what will these changes mean for the way analysts and clinicians collaborate? We spoke to two specialists – one surgeon and one spectroscopist – to answer some of the key questions.

Spectroscopy at the cutting edge

Spectroscopy isn't new to the clinic. Even well-established practices like cervical cancer screening may make use of an electrical impedance spectroscopy (EIS) rod to differentiate between healthy, premalignant and malignant tissues based on their respective resistance and capacitance properties. And increasingly, we are seeing spectroscopy applied in more challenging clinical scenarios, including during surgical procedures.

"Spectroscopic techniques have been used in intraoperative contexts for a number of years now," says Alba Alfonso-García (Project Scientist in Photonics at the University of California, Davis). "Fluorescence lifetime imaging (FLIm), Raman, near-infrared (NIRS) and diffuse reflectance spectroscopy – as well as many others – have all been utilized for such purposes."

The applications for spectroscopic analyses during surgery are varied. For example, studies have shown a benefit for perioperative NIRS monitoring of the tissue oxygenation index – which predicts the occurrence of ischemic intolerance and cerebral hyperperfusion (adverse events with significant patient morbidity) – during carotid artery stenting (1). NIRS has also shown potential as a predictor for shunt requirements during carotid endarterectomy by tracking cerebral oxygenation to predict cerebral ischemia (defined by insufficient blood flow to the brain) (2). And it's not just human surgeons who benefit. Robot-assisted surgery – in which spectroscopic approaches represent a potentially powerful tool for defining target tissues – is becoming increasingly widespread (3).

In oncology, promising results in both animal models and excised tissues (alongside key instrumental advances) has allowed studies to progress into the clinic, with a number of human trials underway (4,5). But, as Saba Balasubramanian (Honorary Professor in Surgical Oncology at the University of Sheffield) explains: "Spectroscopic approaches are currently applied only in early-phase clinical trials in oncology, and remain relatively novel in the operating theatre."

Despite numerous challenges, both Alfonso-García and Balasubramanian are determined to continue evaluating the utility of spectroscopic techniques as a regular part of the surgical toolkit.

A guiding light?

Alfonso-García's research focuses on identifying and highlighting tumor tissue during resection surgery. "Being able to identify tumors in situ – without the need to treat patients with external labels – means that spectroscopic techniques are minimally invasive and thus very promising," she says.

Her group, led by Laura Marcu, has developed a number of approaches that use fluorescence lifetime spectroscopy to diagnose and guide the removal of tumors. The rationale? To remove the subjectivity involved in resecting tissue on the basis of visual inspection during surgery. While the current gold-standard imaging approaches (magnetic resonance imaging and positron emission tomography-computerized tomography, for instance) are helpful in guiding tumor resection surgeries, they are carried out pre-surgery and cannot highlight potential tissue changes caused by drift or swelling during procedures, explains Alfonso-García.

Balasubramanian echoes the need for real-time information. "The current approach for differentiating the parathyroid glands (each of which is approximately the size of a grain of rice) from normal thyroid tissue relies largely on surgeon experience and judgment – more objective approaches are needed," he says. Inadvertent damage to parathyroid glands during thyroid surgery can lead to post-surgical

Meet Our Contributors

The Surgeon: Saba Balasubramania

"My interests lie in the surgical management of primary hyperparathyroidism and thyroid disease – using novel technologies and evidence-based approaches to achieve the best possible outcomes for patients. I am an Honorary Professor at the University of Sheffield, and have been conducting this work since 2010. I have also acted as Principal Investigator on a number of animal and clinical studies in this space, and am currently Chief Investigator on a project exploring the clinical utility of near-infrared fluorescent imaging in thyroid surgery. The aim? To enable the real-time differentiation of the thyroid and parathyroid glands and reduce human error in the operating theatre."

The Spectroscopist: Alba Alfonso-García

"When training as a physicist, I soon realized that a number of the tools developed in physics and chemistry labs could be applied by biologists and doctors. That's when I decided to join Laura Marcu's team, drawn in by her unique expertise in translating imaging tools into the clinic. Now I work as a Project Scientist at the University of California, Davis, developing optical imaging tools for biomedical applications. My team uses fluorescence lifetime imaging for disease diagnosis, including the detection of tumor margins during neurosurgery."

hypoparathyroidism – a condition associated with a variety of distressing symptoms, ranging from muscle cramps to seizures and cardiac disturbances, that can negatively impact quality of life.

In order to reduce such errors, Balasubramanian and colleagues applied EIS to differentiate between thyroid and parathyroid tissues in 56 patients in a Phase I clinical study – the first of its kind (6). The department's previous work using rabbit models had provided proof of principle but as with all first-in-human trials, but there was no guarantee the animal findings would translate successfully to humans. To the team's delight, the technology – which used a handheld device with disposable, single-use sensor covers comprising four gold electrodes arranged in a square across a diameter of 5.5 mm – demonstrated good sensitivity and specificity when handled by two consultant endocrine surgeons.

Alfonso-García's team has enjoyed similar success, in this case using FLIm instruments integrated with surgical microscopes to provide real-time modification of the surgical field of view and provide diagnostic information to surgeons (Figure 1) (7). "This provides surgeons with an extra dimension of information based on tissue structural organization and metabolism, in

Theater of Applications

Exploring innovative intraoperative spectroscopy approaches

Gleaning Glioma

Genetic tumor classification is central to guiding personalized therapy in clinics; for example, In the case of glioma, the presence of isocitrate dehydrogenase mutations guides surgical decisions. By coupling Raman spectroscopy of fresh tissue from neurosurgical theaters with immunohistochemical confirmation and genetic sequencing techniques (with subsequent principal component analysis), researchers from Oxford, UK, have demonstrated the applicability of Raman in rapid intraoperative glioma classification (1). When choosing between three genetic subtypes, a sensitivity of 79-94 percent and specificity of 90-100 percent was achieved. The mean time taken for data collection was 9.5 minutes.

Duct Identification

Researchers successfully applied near-infrared fluorescence imaging with indocyanine green dye to visualize remnant cystic and bile ducts, guiding surgery to alleviate post-cholecystectomy syndrome (prolonged pain following gall bladder removal), in a 36-year-old woman who initially presented with acute biliary pancreatitis (2). Intraoperative duct visualization was feasible with no complications and took less time than standard intraoperative radiographic cholangiography. The team concluded that the technology could be applied to reduce the operation time during difficult, robot-assisted procedures, owing to the rapid and simple detection of the biliary tract – allowing remnant cystic ducts to subsequently be removed.

Reference

1. *Livermore LJ et al., "Rapid intraoperative molecular genetic classification of gliomas using Raman spectroscopy", Neurooncol Adv, 1, vdz008 (2019). DOI: 10.1093/noajnl/vdz008*
2. *van Manen L et al., "Intraoperative detection the remnant cstic duct during robot-assisted surgery using near-infrared fluorescence imaging: a case report", BMC Surg, 19, 104 (2019). DOI: 10.1186/s12893-019-0567-8*

addition to the preoperative information and visual cues already available to them," says Alfonso-García. "The main benefit for patients is that these measurements are innocuous – the probe doesn't touch the body and there is no discomfort involved. Other imaging techniques, by contrast, tend to use ingested or injected contrast agents or ionizing radiation." But it's the ability for surgeons to respond to real-time data and so improve surgical outcomes that will drive these approaches out of the laboratory and into the clinic.

Other successes from the UCD lab include real-time guidance during robotic oral cancer surgery, assessment of radiation-induced necrotic changes in the brain, and automated breast cancer detection in resected specimens.

Spectroscopy and surgery: a match made in heaven?

The research is certainly promising - but how close are we to seeing these techniques in everyday use by surgeons? Speaking of his success in the application of EIS to (para)thyroid differentiation, Balasubramanian was quick to highlight the limited spread of these techniques at present. "Right now, these methods are being used only in clinical trials," he says. "As we know, these studies are often limited to the ivory towers or Centers of Excellence." Indeed, Alfonso-García highlights that her FLIm method to guide neurosurgeons is currently only conducted at the high-tech University of California Medical Center in Sacramento. The team is working on cloning the device and establishing partnerships with more universities and institutes. But, for now, it remains – in Alfonso-García's words – "a clinical research approach."

The first step towards moving either of these approaches into regular clinical practice will be to demonstrate utility in a wider cohort of patients. For Alfonso-García's team, this effort is characterized by identifying numerous cases in which the approach is effective and subsequently applying advanced data analysis techniques to classify future measurements as healthy versus not. In the case of the acquisition of very large amounts of data, even more nuanced distinctions between tissue types or degrees of malignancy may even be possible. Movement into additional therapy areas such as head and neck and breast cancers is also currently underway.

"Improvements in augmented and mixed reality hardware (in the form of headsets that augment the visible tissue landscape or a modified display on a screen) will also be of benefit to advance these approaches and make them more user-friendly," says Alfonso-García. "In addition, full-field systems (three-dimensional measurement systems that capture the entire field of view)

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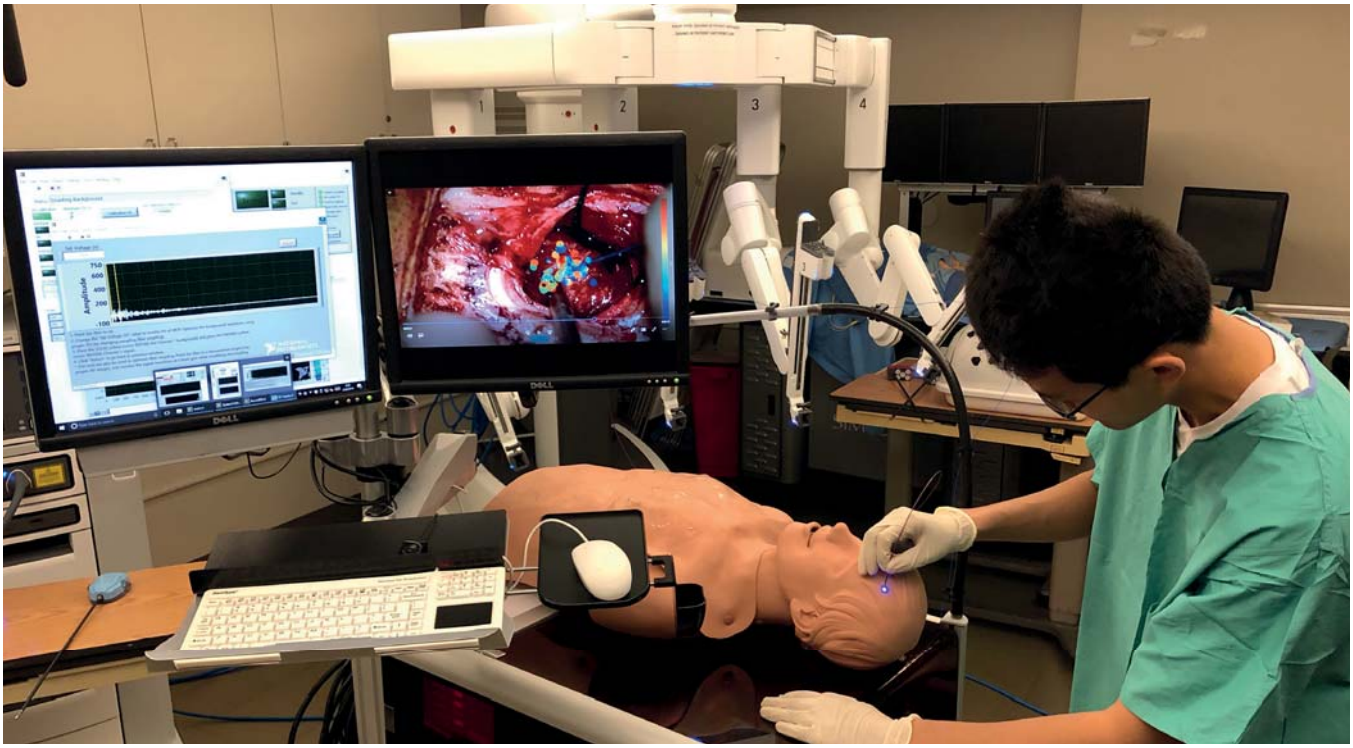

Figure 1. Graduate student Tianchen Sun (Marcu Laboratory, UC Davis) testing the FLIm instrument on the training suit of the UC Davis Medical Center

may support certain applications by providing a complementary method to the "painting" approach that we currently have, based on point measurements. Similarly, advances in data analysis techniques (including machine learning and other artificial intelligence approaches) will provide more refined and sophisticated data interpretation and visualization schemes."

Balasubramanian's team is concentrating on the more traditional route to the clinic. Following their successful Phase I trial in fluorescent imaging, they have secured funding to proceed to Phase II and III trials. With regards to their electrical impedance device, a number of changes are required to optimize the instrument for use in the operating room. Namely, the surface area of the sensor tip will need to be reduced and measurement acquisition will be modified to occur in real-time.

The other necessary ingredient to bring these approaches into routine use? Collaboration, according to our contributors. As in all areas of scientific research, well-organized collaborative efforts will lead to faster progress, says Balasubramanian: "Do we identify a clinical problem and then try to identify analytical techniques to solve it, or do we begin with the technology and look for clinical applications? Cross-disciplinary teams are needed to bridge these two approaches and lead the way in the field."

References

1. *Terakado et al., "Effectiveness of near-infrared spectroscopy (NIRO-200NX, Pulse Mode) for risk management in carotid artery stenting", World Neurosurg, 131, e425 (2019). DOI: 10.1016/j.wneu.2019.07.184*
2. *Jonsson M et al., "Near infrared spectroscopy as a predictor for shunt requirement during carotid endarterectomy", Eur J Vasc Endovasc Surg, 53, 783 (2017). DOI: 10.1016/j.ejvs.2017.02.033*
3. *Gorpas D et al., "Autofluorescence lifetime augmented reality as a means for real-time robotic surgery guidance in human patients", Sci Rep, 9, 1187 (2019). DOI: 10.1038/s41598-018-37237-8*
4. *Livermore LJ et al., "Rapid intraoperative molecular genetic classification of gliomas using Raman spectroscopy", Neurooncol Adv, 1, vdz008 (2019). DOI: 10.1093/noajnl/vdz008*
5. *Eissa A et al., "'Real-time' assessment of surgical margins during radical prostatectomy: state-of-the-art", Clin Genitourin Cancer, S1558 (2019). DOI: 10.1016/j.clgc.2019.07.012*
6. *Hillary SL et al., "Use of electrical impedance spectroscopy for intraoperative tissue differentiation during thyroid and parathyroid surgery", World J Surg, 44, 479 (2020). DOI: 10.1007/s00268-019-05169-7*
7. *Alfonso-Garcia A et al., "Real-time augmented reality for delineation of surgical margins during neurosurgery using autofluorescence lifetime contrast", J Biophotonics, 13, e201900108 (2020). DOI: 10.1002/jbio.201900108*

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Entrepreneurship is a skill, and we need to start teaching it

By Ali Salehi-Reyhani, Lecturer in Chemistry and Innovation, Department of Chemistry, King's College London, UK

The UK government's Industrial Strategy sets out ambitious targets to "boost productivity and earning power" across the nation and position the UK as a center of innovation. Contribution to global challenges requires innovative minds and there is nowhere better to drive bottom-up initiatives than the university campus; however, innovation and entrepreneurship have been somewhat neglected in British universities. As educators, we have an important part to play in producing the entrepreneurs Britain will need to adapt and thrive in a changing global economy.

Multi-national organizations like Google, Apple, and Microsoft believe that open, collaborative styles of working are particularly conducive to productivity and innovation – so much so that they are rebranding their R&D hubs as "campuses." Universities, by their very nature, operate on the frontiers of current knowledge, and provide a supportive, collegiate environment to nurture grand ideas.

Seizing opportunities, learning from mistakes, and seeking funding are as much a part of the job description of an academic as they are that of a dynamic entrepreneur, and here at King's College we're developing new teaching and research programmes to develop an entrepreneurial mindset in students. Our vision is that by 2029 everyone will have the opportunity to make entrepreneurship a part of their DNA. It's incredibly ambitious for such a large institution, but we consider it absolutely necessary to ensure the ongoing success of the university - and, ultimately, the nation.

King's College is home to a wide-ranging support network: acceleration programmes, maker spaces with university-wide remits, workshops, co-working spaces, mentorship programmes, and investor networks.

"As educators, we have an important part to play in producing the entrepreneurs Britain will need to adapt and thrive in a changing global economy."

Coupled with our central London location, we are in the best position to offer world-class opportunities for our students.

My own contribution to our mission is creating a lecture series – "Innovation & Entrepreneurship" – delivered to undergraduate chemistry students in their final year, developed first at Imperial

and now at King's. The course aims to teach a wide-range of entrepreneurial skills and concepts, such as ideation, intellectual property, funding landscapes, and proposal pitching. It's hard to get everything across in one course, so instead we provide the basics before delving deeper through discussion. A series of interactive lectures and guest seminars from investors, entrepreneurs, start-ups, academics, and CEOs is designed to inspire and motivate students to consider starting their own ventures. Students also acquire and build-upon their existing skills to help them in their future endeavors – be they in industry, business, or academia.

"Seizing opportunities, learning from mistakes, and seeking funding are as much a part of the job description of an academic as they are that of a dynamic entrepreneur."

Over the years, I've focused our topics through the lens of chemistry. Students get to see the other side of the academics delivering their lectures; in today's ecosystem, entrepreneurship is a given, rather than a rarity. That was not the case decades ago, when limited resources and a culture that frowned upon such activities acted as significant barriers to progress.

Our first guest lecture was delivered by Bruno Cotta – then Director of Enterprise at Imperial College. It was a watershed moment for many of our students, highlighting the seriousness with which student-driven entrepreneurship was being taken. Entrepreneurship is a multi-faceted concept – much more than simply starting a business, it's about innovative ideas.

We've been fortunate to have been graced by many memorable guests since the inception of the course. Here are just a few standout examples:

- Dominic Falcao, Founder and Director of Deep Science Ventures (a London-based incubator supporting scientists building their own companies with a particular focus on global challenges) presented a lecture on: "What is a good idea?" Students were encouraged to think about their ideas as a set of hypotheses and set about devising careful tests to prove or disprove them.
- Phil Parsons shared his very personal journey, including many of the obstacles he faced at a much more challenging time to become

an academic entrepreneur. Founder and Director of Cookson Chemicals (Tocris Cookson), he has gone on to found Pareon Chemicals, and won numerous awards during his career.

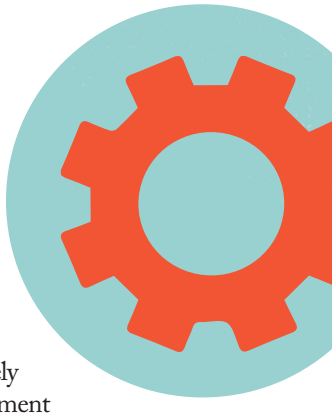
- Executive Director of the Commercialization Office at Imperial College London, Govind Pindoria's lecture explored the machinations of those sitting on the other side of the table. He laid bare his experiences in helping to scale up science ventures and was unflinchingly honest about what investors are looking for – and what ultimately succeeds or fails.

The course presents a chemistry-focused view of the market: physical chemists, synthetic chemists, chemical biologists, and experts in diagnostics and nanotechnology are invited to talk about their start-ups. Crucially, they reveal how they've overcome the challenge of conducting world-leading science alongside commercial ventures. It's eye-opening for the students, who typically experience science through the narrow lens of academia.

Students are given 6 weeks to work in a team to develop a new idea from scratch and pitch to their entire year group. During this time, I mentor each team, from ideation, to fleshing out a business outline, and finally developing a pitch. Students are examined on their ability via a formal presentation, their response to a judging panel and audience questions, clarity of their proposal, and their defense of it under scrutiny. It's a high-stakes assessment that must be passed. To enhance the learning experience, the judging panel – which is made up of real-world entrepreneurs – are reminded to "keep the gloves off." They act as though they are working on a real-world example, providing direct feedback.

The university has been pleasantly surprised by the quality of ideas emerging from younger generations, and appreciate the value entrepreneurship adds to a student's education. Seeing this ability grow organically in our students is incredibly encouraging, and I am certain it will make them more successful in the long term.

Two rather interesting examples have sprung from members of my own research group. While doing his PhD in single-cell proteomics, Stelios Chatzimichail founded BioNet, a project dedicated to developing a biodegradable polymer to replace the plastic netting currently used in the farming industry to bail hay. Similarly, Pashiini Supramaniam, who applies our microfluidic technology to better understand artificial cell synthesis, is part of the QuickCount team – an organization developing technology that can indicate the presence of bacterial infection in under 1 minute from a fingerpick of blood. Both are members of interdisciplinary teams – managing their own research projects (including budgets and grants) alongside ambitious and intensive PhDs. Having engaged in projects of their own, I can see first-hand how much more productive and engaged they are in their work. Plus, their CVs are incredibly competitive – reading more like that of junior faculty members than PhD students.



My own academic career has benefited hugely from my involvement in a technology spin-out, through which I've learnt how to deliver scientific innovation commercially and drive impact. I received no formal training – my knowledge was gained the hard way through experience – and I know first-hand how valuable the course is.

To students, my message is simple: you came to university to change the world – so get out there and do it! To institutes I say the following: recognize that you are sitting on enormous, often untapped potential – academics and their ideas are one of our most valuable assets. To make the most of it, you must encourage your faculty to embrace entrepreneurship. Together, students and academics can work together to the benefit of society as a whole.

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

Evolved gas analysis and multi-step pyrolysis performed on a vinyl polymer

Karen Sam

A vast number of chemical species are being used as polymer additives. These additives can become a major challenge in the quality control process. A single-step pyrolysis GC/MS analysis often produces cluttered chromatograms without adequate separation between residual solvents, pyrolysis fragments, contaminants, and additives. Evolved Gas Analysis (EGA) in conjunction with multi-step pyrolysis can address this challenge. EGA provides thermal information which can be used to select appropriate multi-step temperatures. Each thermally sliced chromatogram will provide ample separation to yield well-resolved information.

A transparency sheet, 100µg, was added to a Drop-In-Sample Chamber (DISC) tube and analyzed with a CDS 6150 Pyroprobe connected to a GC/MS containing a fused silica column. The sheet underwent EGA at 50°C per minute from 50°C to 800°C, sending vapors directly to the MS detector. This temperature ramp up rate is 2.5 times faster than traditional thermal gravimetric analysis (TGA).

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

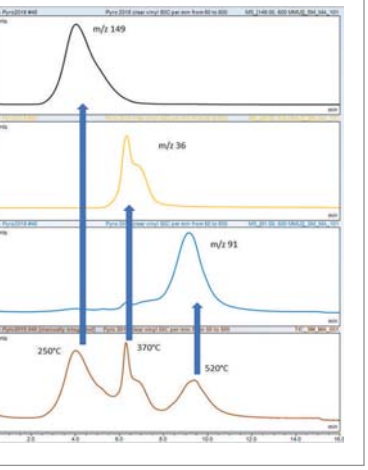


Figure 1. EGA plot of clear vinyl TIC (bottom), and EICs.

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

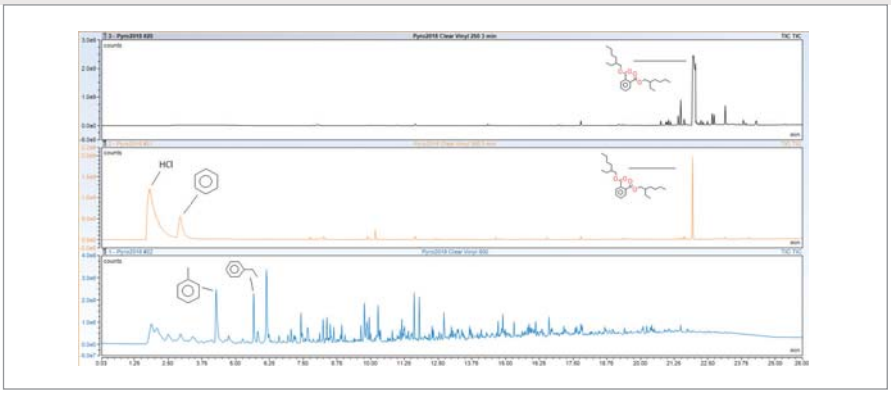


Figure 2. Clear Vinyl at 250°C (top), 350°C(middle) and 500°C (bottom).

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

Experimental Setup

Pyroprobe Setpoints:

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

GC-MS

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

Contact name: Carol Byrd
Contact Phone Number: 610.932.3636

Analysis of Therapeutic Oligonucleotides by UHPSEC-MALS

The oligonucleotide therapeutics field has seen remarkable progress over the last few years and oligonucleotides are increasingly recognized as potential therapeutic agents for a variety of diseases. Ultra-high performance size-exclusion chromatography can be used to analyze size heterogeneity of oligonucleotides

A new application note describes the ability of size-exclusion chromatography to discriminate oligonucleotides differing by one base in length when using UHPLC or UHPLC-MALS. For this purpose, a new silica gel-based phase, TSKgel UP-SW2000, with a pore size of 12.5 nm was applied, which is also perfectly suited for the analysis of smaller proteins and peptide aggregates.

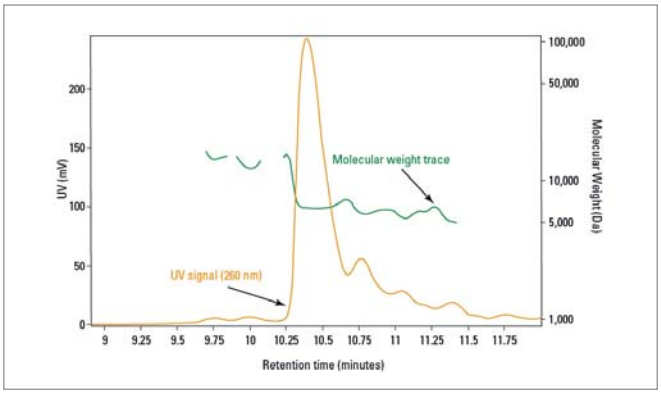


Figure 1: SEC UV trace and molecular weight distribution of a unpurified 20-mer

Chromatographic Conditions:
Column: TSKgel UP-SW2000 (2 µm, 4.6 x 300 mm);Detection: UV @ 260 nm & MALS; Sample: 20mer oligonucleotide with MW= 6141 Da

Read the full application note at http://bit.ly/UHPSEC-MALS

(Full product page: bit.ly/UP-SW2000)

WEBINAR

Panel discussion: the pros and pros of HRMS implementation in routine quantitative analysis

March 12, 2020, 9am GMT

Over decades, triple-quadrupole MS (TQMS) and high-resolution MS (HRMS) have served different purposes in testing laboratories. However, now that boundary-breaking advancements of HRMS are enabling both quantitative and qualitative analyses, scientists are urged to rethink how HRMS should be positioned to maximize laboratory output and value. This free panel discussion welcomes the expert panelists to provide insights into the use of HRMS across a variety of fields, namely food safety, forensics and clinical research. The discussion will feature how HRMS compares with TQMS, main drivers for implementation, common challenges and opinions on what the future holds.

Learning Objectives

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Speakers

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Director, European Union Reference Laboratory for Pesticide Residues in Fruit & Vegetables (EURL-FV), Universidad de Almeria, Spain

Dr. Adam Cawley
Science Manager, Australian Racing Forensic Laboratory, Racing NSW, Australia

Dr. Kelvin Goh
Research Fellow III, Dept. of Pharmacy, Singapore General Hospital, Singapore

Dr. Atsuhiko 'Ash' Toyama
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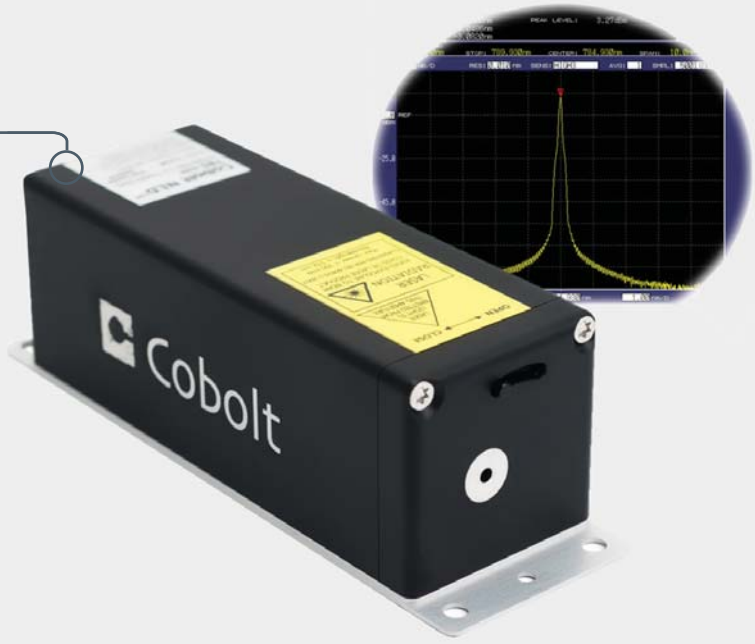
Spotlight on... Technology

Robust 785 nm lasers for Raman by Cobolt

HÜBNER Photonics, a leading supplier of all laser wavelengths to Raman, introduces the Cobolt 08-NLDM 785 nm, with enhanced spectral purity. HÜBNER Photonics now offers the widest selection of Cobolt lasers for Raman spectroscopy and all with the same footprint. Run your system or experiment knowing the laser is dependable.
https://bit.ly/2OnLAK4



A State-of-Art Thermal Injection System for GC/MS

The 6200 Pyroprobe is the 6th generation pyrolyzer from CDS Analytical. Built on the revolutionary Drop-In-Sample-Chamber (DISC), it is a versatile thermal injection system with reproducibility at 1.5% RSD for Pyrolysis up to 1300°C, Dynamic Headspace, Thermal Desorption and Thermal Slicing. Newly added Photoprobe for weather degradation study.
https://www.cdsanalytical.compyrolysis-6200

Fully automated thermal desorption instrument

TD100-xr is a fully-automated analytical TD instrument that combines with any GC(MS) for the automated detection of VOCs and SVOCs in various matrices. It offers reduced running costs by cryogen-free cooling, increased sample security through automated splitting and re-collection, and lower analyte detection limits with backflush trapping and sample stacking.
http://chem.markes.com/TAS/TD100-xr

WITec ParticleScout: Detect, Classify & Identify Particles with Raman Imaging

WITec's ParticleScout is an advanced analytical tool for the alpha300 Raman microscope series that surveys, classifies and identifies particles over even large sample areas. Automated routines sort particles, acquire their Raman spectra and generate detailed reports. Microparticles are of ever-increasing interest in environmental science, cosmetics, packaging and many other fields.
www.witec.de/products/accessories/particlescout

Making MS Matter

Sitting Down With…
Pieter Dorrestein, Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, the University of California at San Diego, USA.

How do you decide where to focus your attention?

I pursue what I think will have an impact – throughout my career I've pivoted numerous times, something uncommon in academia. During my third year as an assistant professor, I moved from top-down MS to work on understanding the functional role of small molecules using microbial imaging MS. People tried to discourage me; yet, it was the resulting microbial paper that set me apart and led to my being recommended for tenure. In 2012, I shifted once again, redirecting my focus towards molecular networking and, more recently, repository-wide MS data analysis. And my team and I certainly haven't finished; if something impactful arises in the future, we won't hesitate to change direction again.

You're a noted critic of enclosed MS data libraries. Why?

The MS and natural product communities that discover new molecules have certainly done themselves no favors by creating closed environments for reference libraries, and failing to make data (and knowledge about the data) publicly accessible in uniform computer-readable formats akin to the gene sequencing community. I believe that published data, code or scripts should be publicly available unless a specific disclosure is provided to explain why this is not possible, especially if the work is taxpayer-funded. It is odd to me that analysis is generally still conducted one data set at a time, rather than in the context of cumulative knowledge. Slow, inefficient, and incomplete systems are the result. Our mission to generate data, capture knowledge and make this knowledge accessible is likely why our GNPS infrastructure and the associated tools such as MASST and ReDU are currently getting 200,000 accessions each month. In 2016, we could annotate less than two percent of data in an untargeted MS experiment; today, that number has climbed to five percent and is growing quickly. Imagine if it was closer to 50 percent – how much more capable would MS be? And what type of applications would we have?

One day, MS will be incorporated into smartphones, allowing consumers to conduct analysis in real-time. When will that happen? It will depend on whether the community makes an effort to organize itself; if it does not, I fear that progress will continue at a snail's pace.

Who were your most influential mentors?

Bill Gerwick has been an informal but influential mentor since I joined the University of California, San Diego. He engaged me by bringing me along on collection trips, and promoted a truly holistic approach to science. His ethos was clear: to develop well-rounded scientists who are truly engaged with the entire scientific process, rather than just focused on the lab bench, and have interests outside their work (in my case rock climbing, hiking and mountain biking). After all, we must be inquisitive about our surroundings if we are to generate new ideas rather than simply regurgitating those of others.

Would you say younger scientists face increasing pressure to succeed?

There's a lot of confusion, particularly among younger scientists and post-docs, regarding the importance of maintaining a work–life balance. The suggestion – often propagated on social media – that you need to work 80 hours a week to earn a Nobel Prize is harmful and unhelpful. To be successful, you need to conduct good science, but if you prepare well ahead of time and you are focused and efficient in your work, then the hours worked become less important. It's what you deliver that counts. Sacrificing your health and hobbies is no way to do that.

Of course, social media can also be a force for good in science: it drives exposure to different opinions, which dispels the risk of "bubble-thinking" within your lab. Through Twitter, I've learned a lot about the bottlenecks other scientists are facing in MS, and this has actually instigated many exciting collaborations.

How do you keep such a large lab group flourishing?

My door is always open – it doesn't matter how busy I am. Some people take advantage of it – I might see them 10 or 20 times a week – while others pop in once or twice a month. It really depends on the needs and interests of the individual – we are all unique. Every Friday we conduct "efficiency meetings" – we discuss issues with instrumentation and any lab challenges we are facing, which ensures that technical knowledge is disseminated throughout the entire group. In addition, we try to foster a dynamic working environment by holding joint meetings with Rob Knights' group – this exposes our team to high-level microbial science, while exposing Rob's group to high-level MS.

What does the future hold for you?

We want to be able to extract the maximum amount of chemical information from any data set – not only all the annotations, but also substructure information and relevance of the molecules in biology – in a matter of seconds. To get there, we'll need standardization of data reporting, inclusion of more MS methodologies such as GC-MS, imaging, and others – all needing new algorithmic learning strategies that include crowd-sourced analysis, machine learning, artificial intelligence, but also simpler network relationship modeling to improve the general connectivity of MS data. The development of tools is driven by real applications. Right now, we're pushing heavily to understand the role that microbiomes play in human, plant, personal care, food and ocean health – and through that work we are gaining a better appreciation of the limitations of current infrastructure. The ultimate goal? To develop a system that functions as efficiently and as speedily as a Google search.

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- Evaporative concentration (mVAP)
- Agitation, quickMIX
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