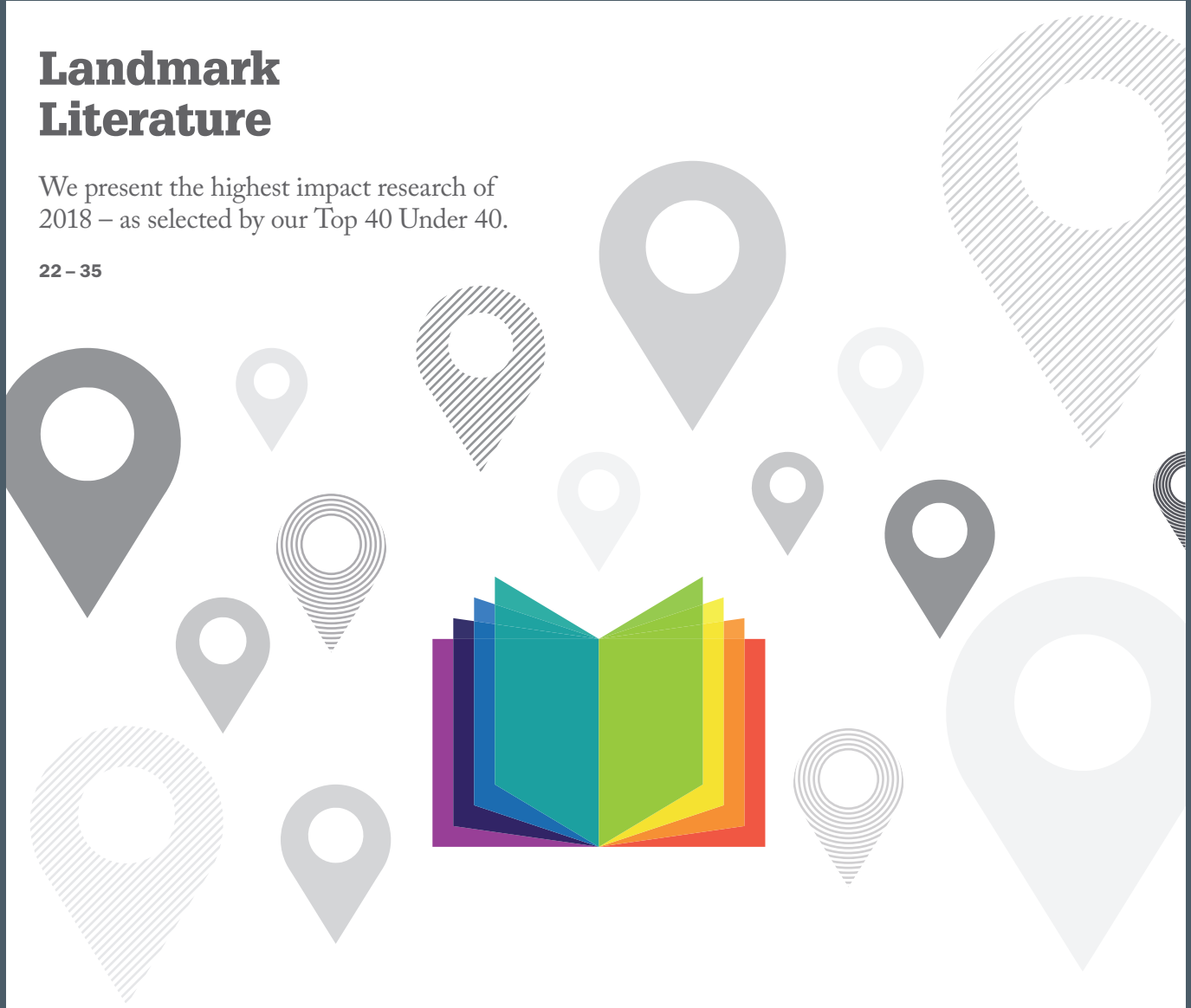
JANUARY 2019 # 72

the Analytical Scientist™

Landmark Literature

We present the highest impact research of 2018 – as selected by our Top 40 Under 40.



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1850
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1951
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1966
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1975
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1993
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SUPELCO

1995
Establishment of Merck KGaA and public listing

SigmaAldrich.com/Supelco

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

Lit. No. MK_AD2917EN 10/2018

Founders of Supelco

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

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

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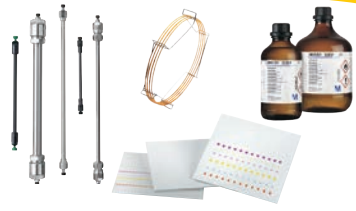

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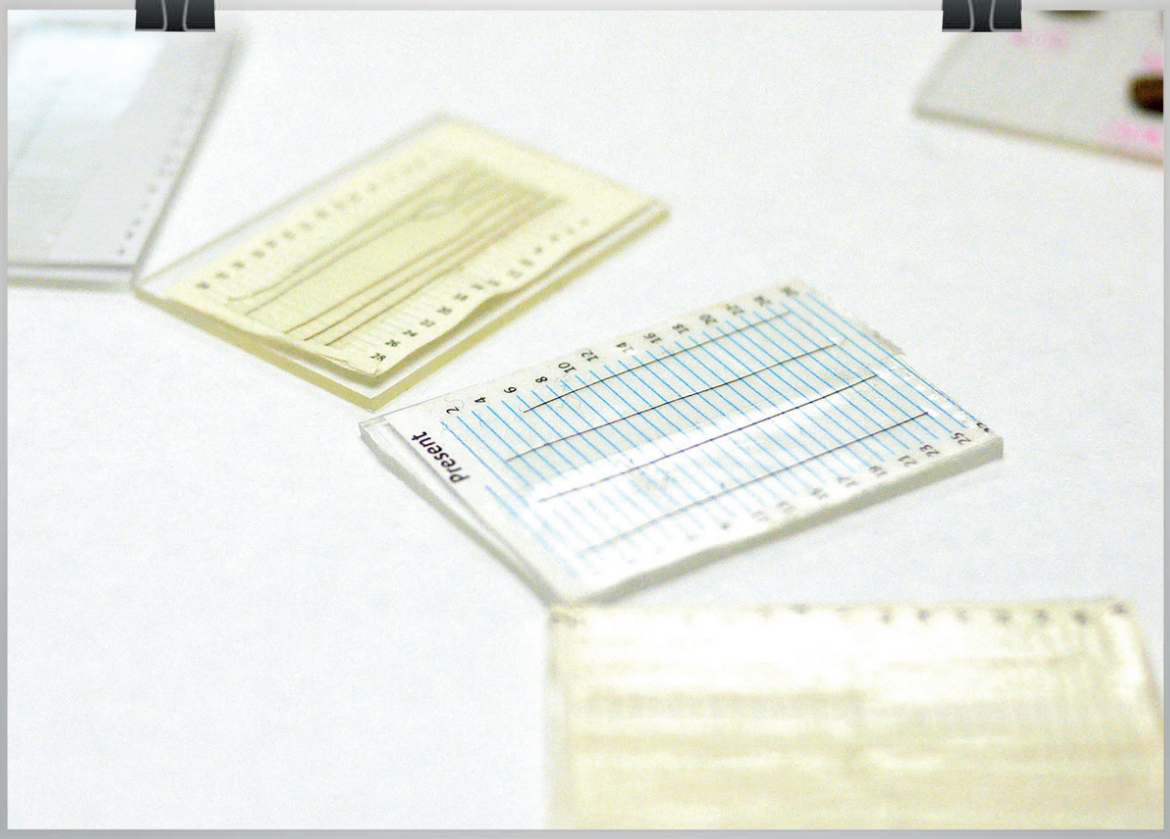

Deathly Metal

In 1994, a woman was deliberately poisoned with thallium, leaving her with lifelong neurological damage – and police were unable to establish who was responsible. Twenty years later, her family approached Richard Ash (the University of Maryland) in the hope that the lab's mass spec-based testing could provide some clues. Ash applied highly sensitive techniques developed for geological analysis to establish the timeline of the poisoning (1).

Reference - T Matsukawa et al., "Changes in thallium distribution in the scalp hair after an intoxication incident", Forensic Sci Int, 291, 230-233 (2018). DOI: 10.1016/j.forsciint.2018.08.019

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

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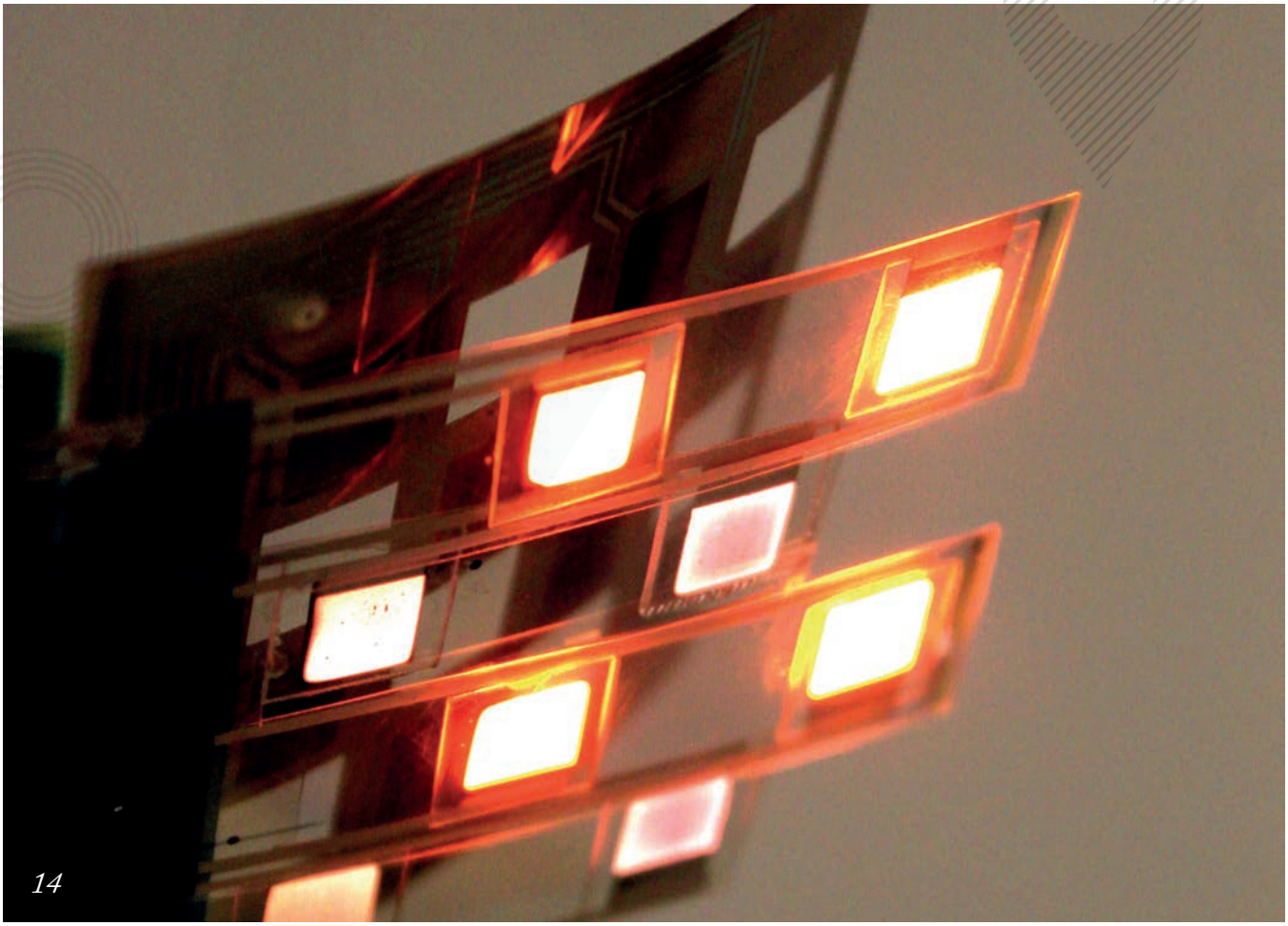

On The Cover

We're putting our experts' research highlights of 2018 on the map.

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In My View

Report

Features

Departments

Sitting Down With

the **Analytical Scientist**

ISSUE 72 - JANUARY 2019

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info@texerepublishing.com
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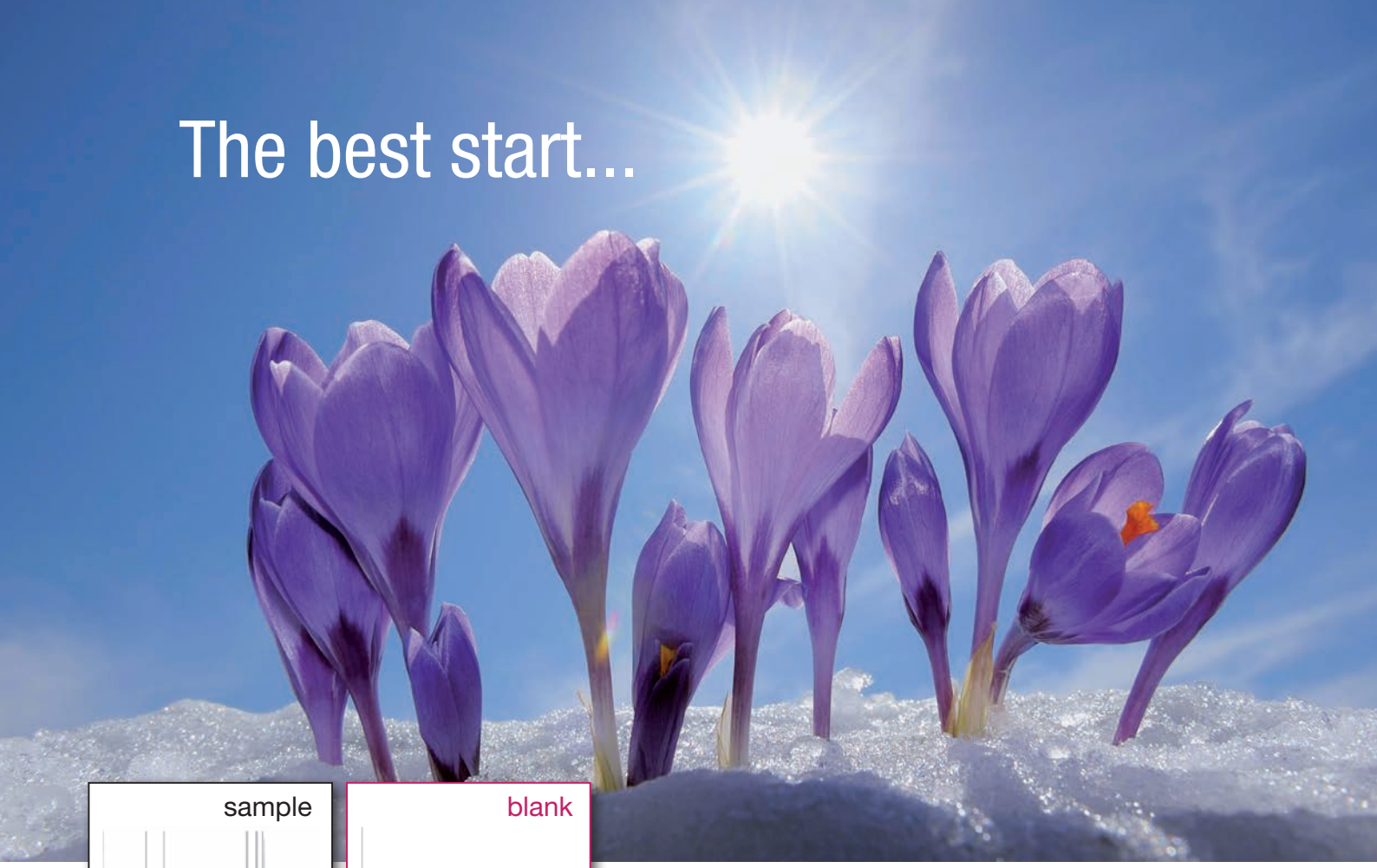

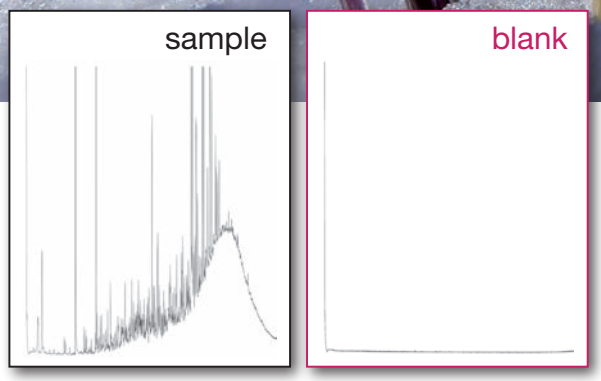

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The Lie of the Land

What can the research highlights of 2018 tell us about the hot topics of 2019?

As we launch ourselves into 2019, we welcome the return of our annual "Landmark Literature" cover feature (see page 22). Once again, we asked the great and the good of analytical science – our esteemed Top 40 Under 40 Power List, in this case – to select the most eye-catching, high-impact research of the past year. The resulting commentaries not only make for an engaging read, but they also reflect many of the important trends shaping analytical science.

1. Proteomics rules the roost… for now Several of our contributors selected papers focusing on proteomic analyses. Powerful mass spectrometry (MS) techniques are helping us to map proteins – and their myriad proteoforms – better than ever before. On page 28, Andrea Gargano highlights native MS as an area of special interest. And he believes we can expect to see great progress in the near future. However, Anna Laura Capriotti hints on page 25 that the golden age of proteomics might be on the wane. With new technology allowing us to track events within cells in real time, Capriotti suggests that metabolomics will be an increasing focus.

2. Data, data, everywhere As instrumentation advances and the volume of data balloons, it is essential that software keeps pace. On page 30, Hiroshi Tsugawa is impressed by a new MS annotation program, while Anneli Kruve describes an approach to make sense of the huge amounts of data obtained from non-targeted screening experiments (page 34).

3. Better together The 16 papers selected by our experts cover a wide range of advances, but do the biggest steps forward result from combining multiple techniques. Consider the "Unified chromatography" highlighted by Caroline West on page 27 or the combination of sensor technologies championed by Jean-Francois Masson (page 33).

4. Another (manufacturing) dimension James Grinias' selection (page 26) showcases the increasing role of 3D printing in creating smaller and more affordable analytical devices – in this case, designed to identify biomarkers of preterm birth.

5. Analytical science must take the lead in reproducibility How do we move on from the "reproducibility crisis?" The paper selected by Juris Meija (page 34) puts analytical scientists front and center in efforts to increase confidence in research results. Robust, repeatable measurements are, after all, the raison d'etre of the field – so an increasing focus on reproducibility can only serve to increase the profile of measurement science everywhere.

Charlotte Barker
Editor

Upfront

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

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

In Cold Blood

Hundreds of environmental contaminants exist in polar bear serum

The polar bear is the top predator in a lengthy Arctic marine food chain. Pollutants become more concentrated with each link in the chain (a process known as biomagnification), which makes the bears a good place to look for emerging ocean pollutants.

"Recent scientific evidence suggests that there are unknown chemicals in polar bear blood serum that can disrupt natural hormone levels – and it was our objective to identify these substances," says Jonathan Martin, a Professor at Stockholm University. "We were concerned that the mixture of manmade chemicals in their bodies is negatively impacting the health of the bears."

The researchers removed major protein and phospholipid interferences from the polar bear serum, stirred the serum with small pieces of plastic (polyethersulfone) to concentrate a broad range of analytes, then used HPLC and ultrahigh resolution mass spectrometry to spectrally flag unknown organofluorine and organochlorine compounds. And the news wasn't good. Martin and his team discovered hundreds of new contaminants in all serum samples, including samples from two locations in the Canadian Arctic dating back to the 1980s. "More specifically, new classes of global pollutants were discovered, including several classes of persistent fluorinated acids. It is worrying that their concentrations appear to be increasing in the bears over time," says Martin.

The analyses also uncovered many new polychlorinated biphenyl (PCB) metabolites (containing hydroxyl, sulfate and/or methylsulfone moieties) – an unexpected finding: "PCBs are perhaps the most prolific of all environmental pollutants – and I thought we knew everything there was to know about them," says Martin.

To confirm their findings, the researchers conducted lab-based experiments to see if the same chemicals could be formed following PCB exposure in mice. "They were – and, what's more, we suspect that other organisms, including humans, are also exposed to most of these fluorinated and chlorinated chemicals," says Martin.

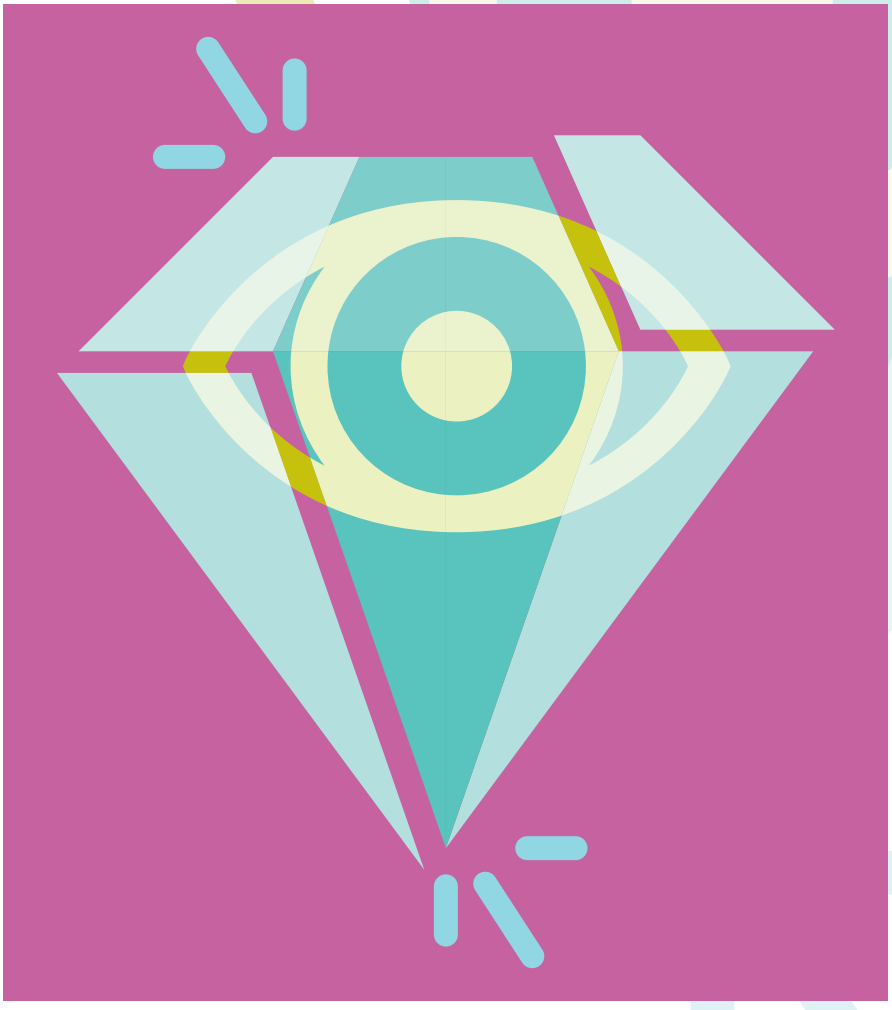
The emerging nature of these – and other (2) – fluorinated contaminants presents a challenge from an environmental control point of view; after all, as Martin notes, "The new fluorinated chemicals we detected are not banned under the Stockholm Convention on POPs […] some have argued that all classes of perfluoroalkyl substances should be banned, because most are highly persistent and can move long distances in oceans or air (3)."

References

1. *Y Liu et al., "Hundreds of unrecognized halogenated contaminants discovered in polar bear serum", Angew Chem Int Ed, [Epub ahead of print] (2018). DOI: 10.1002/anie.201809906*
2. *Y Liu et al., "Nontarget mass spectrometry reveals new perfluoroalkyl substances in fish from the Yangtze River and Tangxun Lake, China", Environ Sci Technol, 52, 5830–5840 (2018). DOI: 10.1021/acs.est.8b00779*
3. *A Blum et al., "The Madrid statement on poly- and perfluoroalkyl substances (PFASs), Environ Health Perspect 123, A107–A111 (2015). DOI: 10.1289/ehp.1509934*

Crystallins and Cataracts

Mass spectometry helps uncover the complex biochemistry behind cataract formation



Crystallins are a collection of structural proteins found in the lens of the eye that help to focus light onto the retina. Over our lifetimes they can accumulate damage, losing their native structure and fusing together to form aggregates – ultimately leading to the development of cataracts. But how does this happen – and how can we prevent the process?

Eugene Serebryany (Department of Chemistry and Chemical Biology, Harvard University, USA) has been studying these proteins for a number of years. "We need a non-surgical treatment for cataracts for the millions of people who can never benefit from surgery, but first it is necessary to understand what goes wrong with eye lens crystallins to cause the disease," he says.

Back in 2015, Serebryany discovered that wild-type (undamaged) crystallin promoted aggregation of the mutant version – without itself aggregating. "It had been known for some time that, in certain proteins, mutated molecules that fold into aberrant structures could template similar aberrant structures in the unmutated (wild-type) molecules of the same protein, leading to aggregation of both the mutant and the wild-type molecules," he says. "Our hypothesis then was that a similar phenomenon could exist in eye lens crystallins – so it was very surprising to discover the reverse."

His more recent research into the mechanism behind this phenomenon led him to another surprise (1). Using mass spectrometry, in vitro oxidation and mutational analysis, he and his Harvard–MIT team found that a process of oxidation-reduction was taking place between these crystallin protein molecules – disproving long-held theories that crystallins were inert.

"We have found that the crystallin proteins can pass disulfide bonds among themselves," Serebryany says. "If they land on a damaged protein molecule, they get stuck with the disulfide bond, trapped in a sticky non-native structure, and forced to aggregate. In this way, the disulfides do no great harm to the structurally sound crystallin molecules, and may in fact be protective, but they drive the structurally weakened molecules into aggregates that scatter light."

Serebryany believes the findings take us a couple of steps towards understanding the mechanisms behind what is likely the most common type of cataract, though notes that there is probably a second aggregation-promoting mechanism at work – something he and his team are now studying. "The more we learn about the biochemistry and biophysics of cataract formation, the wider the space of therapeutic possibilities will be."

Reference

1. *E Serebryany et al., "Dynamic disulfide exchange in crystalline protein in the human eye lens promotes cataract-associated aggregation", J Biol Chem, 293, 17997–18009 (2018). DOI: 10.1074/jbc.RA118.004551*

Credit: James Crall

Plight of the Bumblebee

A robotic tracking system highlights the negative effect of pesticides on bee colonies

The humble bumblebee just can't catch a break. Numbers have been on the decline in recent years, with at least one species facing extinction. Pesticides have been blamed for declining colony sizes – and a new study appears to offer answers as to why (1).

James Crall and a team at Harvard University used environmentally relevant concentrations (~6 ppb) of imidacloprid (a neonicotinoid pesticide) in artificial nectar to assess its impact on bumblebee colonies versus control colonies. By supergluing "BEEtags" (QR codes) onto the backs (specifically, the mesoscutum) of all bumblebees in all colonies, the team was able to use IR-sensitive cameras to track within-nest behavior.

The experimental design was fascinating, with many moving parts (including the bumblebees of 18 commercial colonies): camera gantries with Smoothieboard motion controllers, IR-LED arrays, and a Matlab computational pipeline. But despite the complexity of the core experiment, the authors did not skimp on analytical chemistry. The mean concentration of imidacloprid in dosed nectar was confirmed by LC-MS to be 5.34 ppb (+/- 0.29 SE). The authors also assessed whole-body imidacloprid concentrations after the experimental period from dosed and controlled colonies. Pesticide analysis will be familiar to a select group of readers – but have any of you needed to use the words bumblebee and bead beater in the same sentence?

The group discovered that imidacloprid had a "profound" effect on worker bees' social behavior – particularly at night: those exposed to the neonicotinoid spent less time taking care of the nest and nursing larvae, remaining on the periphery of the nest. It also impaired bees' ability to warm the nest and build insulating wax caps, affecting thermoregulation of the entire colony.

"This work […] opens up a new set of questions, not just about what the direct effects of pesticides are, but how those pesticides impair the ability of colonies to cope with other stressors," said Crall. "It changes both how we go about practically testing agrochemicals in general, but it points to specific questions about whether we might see stronger declines in certain environments […] we should be very, very concerned about how the ways in which we're changing the environment is undercutting and decimating insect populations."

Reference

1. *J Crall et al., "Neonicotinoid exposure disrupts nest behavior, social networks, and thermoregulation", Science, 362, 683–686 (2018). DOI: 10.1126/science.aat1598*

A Philadelphia Story

Our top presentation picks for Pittcon 2019

This year's Pittcon will be covering the hottest of topics, including epigenetics, automation, nanomaterials and cannabis analysis. It'll also be worth seeing the plenary lecture by Fenella France (Library of Congress), "Preserving and Revealing History – Challenges of a Cultural Heritage Scientist" for an insight into the multiple techniques used in the conservation field. Below are the sessions we'll be seeing – but come to our booth to say hello to The Analytical Science team!

Symposia

- Analytical Chemistry and ANYL: New Measurement Tools for Characterizing Individual Cells (March 17)
- Novel Approaches to Undergraduate Chromatography Education (March 18)
- Next Generation Analytical Tools for Investigating Waste to Energy Systems (March 19)
- Micro and Nanotechnologies for Next Generation Precision Medicine (March 20)
- Whole Genome Sequencing: Current Instrumentation, Impact, and Application in the Food Safety Arena (March 21)

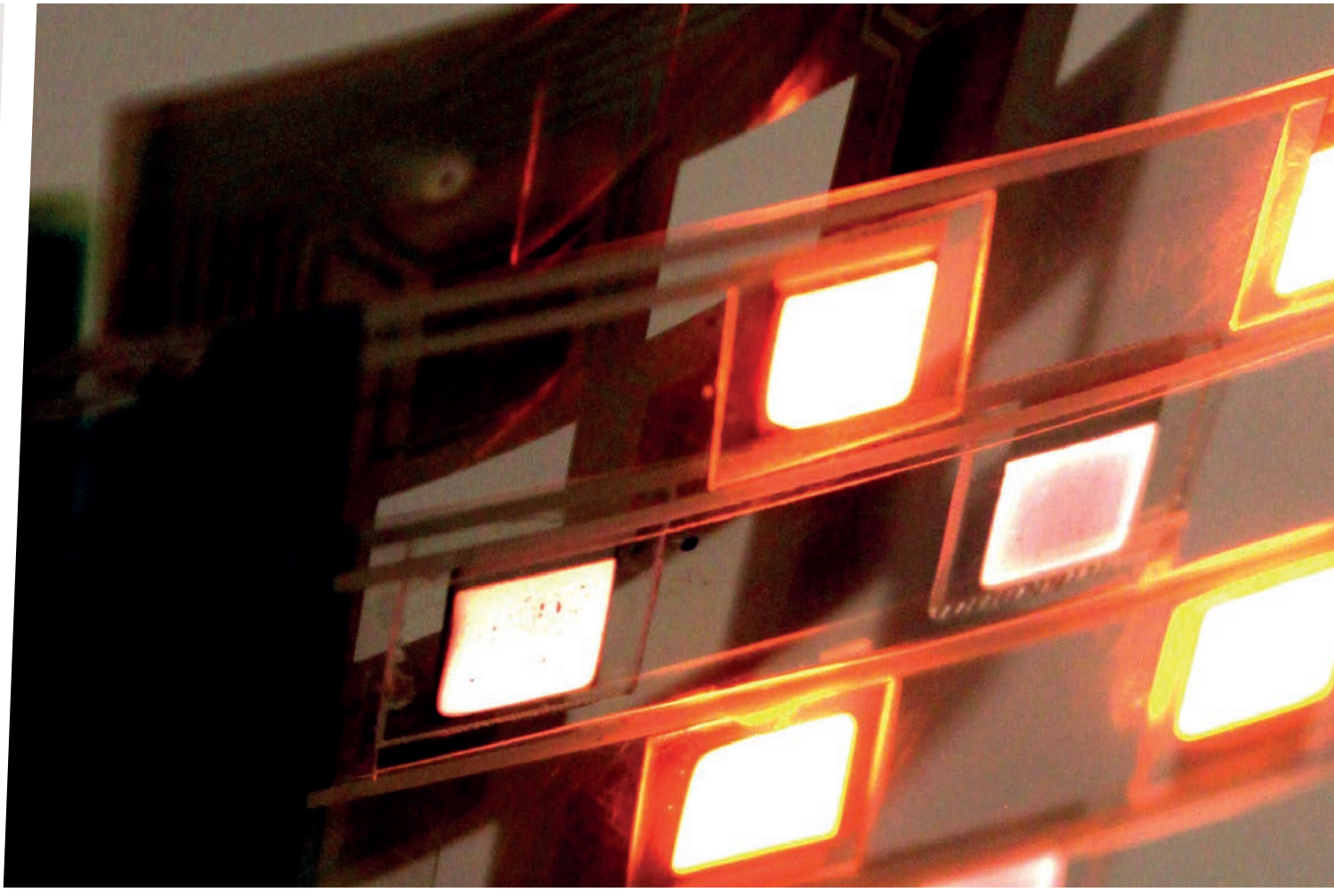
Oral Sessions

- From Bits to Bytes: Data Processing in the 21st Century (March 18)
- Neurochemistry: Voltammetry (March 19)
- Overcoming Challenges and Streamlining Cannabis Contaminant Testing (March 20)
- 'Omics: From A-Z and Every Application in Between (March 21)

Organized Contributed Sessions

- Emerging Leaders in Separation Science (March 19)
- NIJ (National Institute of Justice) – Advancements in the Analysis of Forensic Evidence (March 20)
- Analytical Testing of Antibody-Drug Conjugates in Pharmaceutical Development (March 21)

Pittcon 2019 will be held March 16–21 at Pennsylvania Convention Center, Philadelphia, USA: www.pittcon.org



A Flexible Friend

Blood-oxygen sensors get bendy

What?
A flexible 3D-printed sensor array that can determine oxygen saturation in blood in real-time, providing an "early warning signal" for hypoxemia (oxygen deficiency in arterial blood).

How?
Comprising organic light-emitting diodes and photo-diodes, the sensor passes two wavelengths of light through the body. Oxygen-rich blood absorbs more infrared light, while blood below the patient's oxygen baseline will absorb more red light.

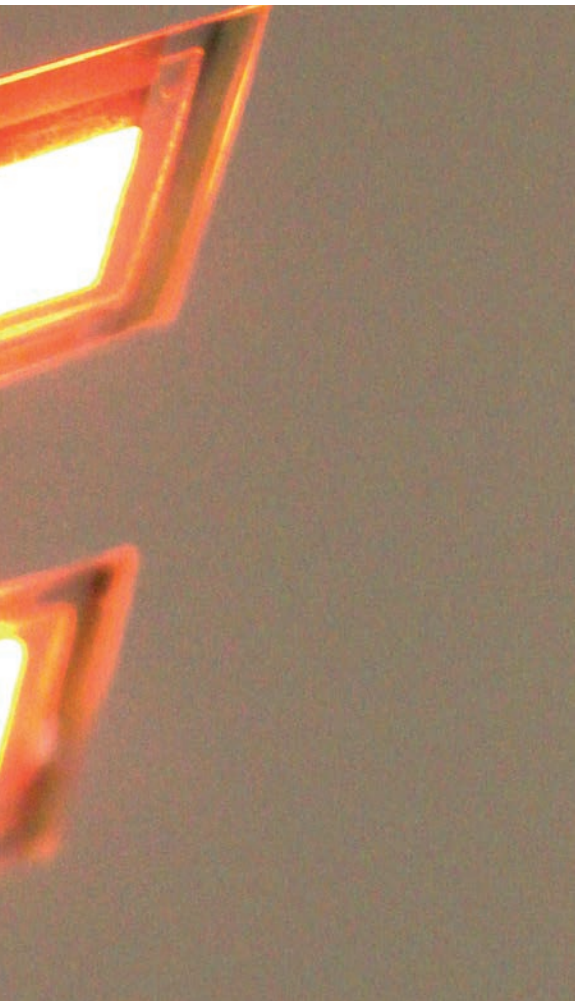
Why?
The researchers wanted to devise a lightweight alternative to the bulky finger-clip sensors that are used currently. The flexibility of the array also means it can be placed in various locations on the body, increasing the potential applications.

Who?
The research was conducted by a team at University of California, Berkeley. It was supported by Cambridge Display Technology Limited and by Intel Corporation via Semiconductor Research Corporation.

What next?
The researchers believe the sensor can be used to assess wound healing, as well as conditions such as sleep apnea and diabetes.

Reference

1. *Y Khan et al., "A flexible organic reflectance oximeter array", Proc Natl Acad Sci USA, 115 [Epub before print] (2018). DOI: 10.1073/pnas.1813053115*



Diagnostics and Discovery

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

Products and launches

- Shimadzu has released a UHPLC system, "Nexere Bio," aimed in particular at the pharmaceutical field.
- Bruker has launched INVENIO, a compact FTIR spectrometer.

- Analytik Jena has announced the launch of its new ICP-OES range – the PlasmaQuant PQ 9000 series – which aims to simplify the analysis of complex sample matrices.

Collaborations and company updates

- Bruker and Mestrelan have joined forces to develop chemistry software that processes spectroscopic data in pharmaceutical, biotechnology and chemical applications.
- InterVenn BioSciences has raised $9.4m in funding for a mass spectrometry-based AI platform that it hopes will improve diagnostics for ovarian cancer.
- PerkinElmer has appointed Prahlad Singh (pictured) onto its board of directors. Singh, who joined the company in 2014, will take responsibility for the Discovery and Analytical Solutions division.

For links to original press releases, visit the online version of this article at: tas.txp.to/0119/BUSINESS.

In My View

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

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

Contact the editors at charlotte.barker @texerepublishing.com

Helping Microplastics Float to the Top

The keynote speech at SciX 2018 – exploring the analytical challenges of microplastics – highlighted the importance of scientific conferences in keeping analytical science relevant to the wider world.

By Karen Esmonde-White, Senior Marcom Specialist, Kaiser Optical Systems, Inc., and SciX 2018 Program Chair, Ann Arbor, Michigan, USA.

One of my roles as the SciX 2018 program chair is to develop themes and drive awareness of contemporary issues. Last year, I chose to give special focus to analytical chemistry's role in addressing the impact of microplastics – an area currently garnering significant attention in both environmental circles and the popular press.

Recent reports by the BBC and National Geographic have amplified concerns expressed in the scientific literature about the biological and environmental impacts of microplastics in marine ecosystems. Analytical science plays a critical role in addressing this burgeoning problem; identifying the chemical composition of microplastics is fundamental to understanding and predicting environmental effects, including bioaccumulation and natural- and bacteria-mediated degradation, as well as developing strategies for remediation. As an event with a reputation for cross-disciplinary research, SciX was the perfect forum to bring together environmental researchers and analytical scientists to raise awareness and discuss solutions to this emerging problem.

"I feel that the success of the microplastics sessions shows the important (perhaps crucial) role that conferences play in raising awareness of pressing issues."

There were two technical sessions on "Analysis of Microplastics," anchored by an outstanding and informative keynote address by Matthew Savoca of the NOAA Southwest Fisheries Science Center and Hopkins Marine

Station at Stanford University. Matthew's compelling talk outlined the challenges of identifying microplastic debris, understanding how marine wildlife interacts with microplastics, and supporting and encouraging the efforts of citizen–scientists. SciX is known for its networking opportunities, and I was especially pleased to see strong interest in developing collaborations and partnerships between the microplastics and analytical sciences communities, which included scientists from the US, Canada, Australia and Japan.

"One of the reasons why the SciX conference continues to grow is because the program dynamically adapts each year to introduce new ideas and concepts to the community."

I feel that the success of the microplastics sessions shows the important (perhaps crucial) role that conferences play in raising awareness of pressing issues – and, most importantly, what we as analytical scientists can do to mitigate these issues. It is because of the collaborative atmosphere at conferences that we can continue to have an impact not only on each other's research, but also – as in this case – on the wider world. In 2018, in addition to the microplastic sessions, SciX featured 130 sessions covering all fields of analytical chemistry, including nearly 1,000 oral and poster presenters. Program highlights included special sessions to celebrate the 60th anniversary of the Society for Applied Spectroscopy, emerging biopharmaceutical applications, nanomaterials, automation and food security.

The name "SciX" is short for "Scientific Exchange" – and the kinds of knowledge exchange and relationship-building displayed at these sessions make the conference valuable to scientists across academic, industrial, and government settings. In fact, one of the reasons why the SciX conference continues to grow is because the program dynamically adapts each year to introduce new ideas and concepts to the community. SciX contributes to conferees' continuing education; they learn something new that can be taken back to their

laboratory. Of course, it's a mutually beneficial exchange: the conference can only maintain its vibrant atmosphere by attracting a range of scientists from different analytical disciplines. FACSS was especially pleased to welcome the 2018 LIBS conference, and the AES Electrophoresis Society and The Coblentz Society annual meetings.

True to the collaborative nature of SciX, I could not have developed these sessions alone. Special thanks are due to Ian Lewis and Heather Juzwa, 2019 Pittcon Program Chair, for their help in coordinating funding for these sessions, and thus allowing us to bring together top speakers in the field. I also want to thank the Pittcon organization for their ongoing support of topics in analytical chemistry presented at SciX. I am already looking forward to 2019's SciX, in Palm Springs, California – and all the hot topics that will be discussed among our community.

A Day to Remember

Doesn't chromatography – or at least analytical chemistry – deserve a place among the days of international celebration?

By Victoria Samanidou, Department of Chemistry, Aristotle University of Thessaloniki, Greece.

Several official annual international days are established by resolutions of the United Nations or other agencies, such as UNESCO, UNEP and WHO. Often the chief aim of these "days" is to raise awareness of international issues, but that is not always the case. Sometimes, they exist to remind us of past events that deserve to be honored. Whatever the special day, activities and celebrations take place all over the world to shine a spotlight on everything from nature to scientific achievements to world heritage (1).

However, I could not find an International Day related to chemistry. National celebrations exist – some of them taking place over a week. For example, National Chemistry Week in the US, organized by the American Chemical Society (ACS), was celebrated October 21–27 in 2018, and encouraged ACS members and other science enthusiasts to raise awareness of chemistry at the local level, promoting the importance of chemistry in everyday life (2). In 2019, it will take place October 22-26 (https://www.acs.org/content/acs/en/education/outreach/ncw/themes.html). The Royal Chemical Society (RSC) also celebrates Chemistry Week (in 2019, it will take place (date TBC); once again, it's an annual celebration of the chemical sciences that aims to share the passion of chemists with the public. Similarly, the Chemical Institute of Canada hosts an annual National Chemistry Week (date TBC) that celebrates the chemical sciences in all provinces and territories in Canada. In 2018, it connected a multi-age audience with the "magic" of chemistry through experiments, games, demonstrations, lectures, exhibitions and much more (4). In Greece, since 1995, we have celebrated the National Day of Chemistry on the March 11 but, in fact, events take place over several days, either in schools or organized by the Association of Greek Chemists in various divisions in Greece (5,6).

"All of these events represent excellent opportunities to organize events and activities that connect chemistry with local people and communities."

All of these events represent excellent opportunities to organize events and activities that connect chemistry with local people and communities. And they can also go a long way to eliminating what I call "chemophobia." Indeed, non-scientists tend to adjust their attitudes to chemical sciences, as they realize – in an accessible way – that chemistry is present and part of their everyday lives (3). But these celebrations and events need not be limited to chemistry as a whole – couldn't they be extended to

"The term chromatography – from the Greek words chroma (color) and graphein (writing) – wasn't used until 1906."

more specific annual days?

What about "Chromatography Day" as an idea?!

All analytical chemists are aware of the significance of this separation science – introduced by the "father of chromatography," Russian botanist Mikhail Semyonovich Tsvet. But does it deserve its own international day?

Well, thanks to the thorough work of many researchers, huge advances have been reported, and several types of chromatography have been applied to determine countless analytes in almost any kind of matrix. And it is worth noting that twelve Nobel Chemistry awards (up until 1972) have been given to scientists whose research was largely based on chromatographic methods (7,8). The number of chromatography applications has grown dramatically over the past fifty years, and this is due both to the development of new chromatographic techniques and to the increasing demand for novel, sensitive and more effective methods for the separation and identification of complex mixtures. Gas chromatography, liquid chromatography and supercritical fluid chromatography, hyphenated with high sophisticated detectors, have given rise to numerous breakthrough publications that have ultimately given rise to invaluable tools in the hands of medical doctors, veterinarians, food scientists, biologists, geologists… The list goes on and on.

The method was first described on December 30, 1901 at the XI Physicians and Physicians Conference in St. Petersburg, so that date might be a good choice for an international Chromatography Day. That said, the term chromatography – from the Greek words chroma (color) and graphein (writing) – wasn't used until 1906… Any additional recommendations? Please do let The Analytical Scientist editors know (edit@theanalyticalscientist.com).

OK – I'll admit that a special day set aside for chromatography may be a little ambitious at this stage. And besides, doesn't our highly significant field – and those within it – deserve to be celebrated every day of the year?

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Your Efficiency Challenge – Part IV

In the latest installment of our series "Your Efficiency Challenge", we explore how you can get more from the tools you use every day. Using results of our reader survey on efficiency in liquid chromatography and a series of lively roundtable discussions, we continue the conversation on efficiency – this time with a focus on instrumentation and software.

Guru of Instrument Efficiency

Adrian Dunn draws on his 25 years in GSK's analytical chemistry division to offer his six top tips on boosting instrument and software efficiency.

1. Ease of use is key. Nowadays, many laboratory scientists using LC are not analytical scientists by training. We need to get these non-experts using the equipment more efficiently by improving workflows, making software easier to use, and cutting the time taken at all stages. I'd like to see the intelligence and the experience of analytical chemists distilled into the software, so that users no longer have to be experts. The ideal would be to do everything within one package. We're not there yet, but we're heading that way. Even troubleshooting could be automated to some extent, with instrument software suggesting potential causes for unusual results.

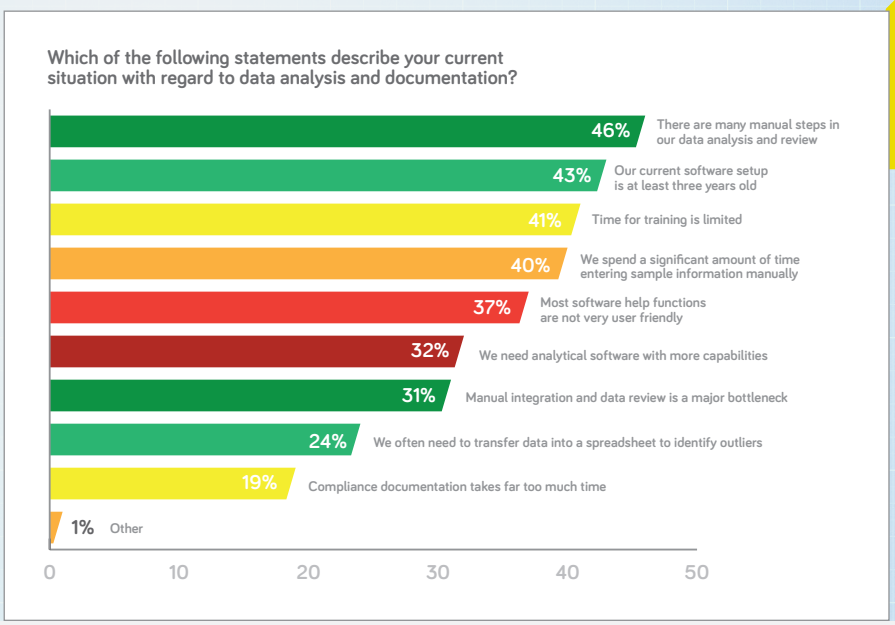
2. Robustness underpins efficiency. You've got to be able to rely on your results, and trust that they won't change from one run to the next. You also need your instrumentation to work efficiently to avoid downtime.

3. Find time for training. When it comes to implementing new software, 41 percent of respondents in a survey of 1,200 LC users reported not having enough time for training. To me that's a false economy. If you have software that's capable of doing your data analysis, why wouldn't you learn to use it and save time down the line? You may lose a day in training but, if you save three weeks over the year as a result, it's well worth it. This is true of instrumentation too – there are often lots of ways of saving yourself time and effort that you can easily find by studying the manual or asking an engineer.

4. Sometimes, it's about getting the basics right. If your instrument is not performing as you'd like, start by testing the simple, inexpensive parts of your system. For example, check you're using the right column chemistry, solvents and consumables.

5. Prevention is better than cure. One way to minimize downtime is to carry out regular system suitability testing, so you can spot problems early.

6. The most efficient way isn't always the fastest. I define efficiency by how useful your results are, balanced against the input required. If you spend an extra hour or two to get a better result it's not necessarily inefficient. You have to ask yourself: is it more efficient to save time but only complete 90 percent of a project, or spend a little more time and complete 100 percent?



Eye on the Future

Agilent's Stéphane Dubant shares what's new in instrument and software efficiency – and the developments coming down the line.

Software

There are already some interesting software applications that can guide you to the optimal method for your sample. At present, you need to have a good level of understanding to be able to use the software – if you ask the wrong question, you will get the wrong answer. I predict in future we may have more intelligent software that can define the inputs that are needed and all the parameters that should be studied, so that we are less reliant on human input.

Automation

Automation is a big trend in industries such as biopharmaceutical manufacturing. The ideal is a line that takes a sample from your reactor to your instrument automatically every few minutes and confirms that all parameters are within acceptable limits. If a problem occurs, production is halted automatically and staff are alerted.

Sample handling

Using barcodes to track samples is still rare amongst the labs I visit, but I believe that as we start to see off-the-shelf systems becoming available, we will see greater uptake of this type of tracking system.

Troubleshooting

Already, a lot of instrument software offers some hardware failure identification, and will alert you to problems with pump pressure, potential leaks, blockages, and so on. But once you get into chromatographic issues, such as peak distortion, it's still largely down to experience – again, that's something that may change as software grows increasingly sophisticated.

Final thoughts

Regardless of how technology advances, it's important to keep things simple. For example, if you have a choice of mobile phases, use the simplest that is fit for purpose – it will be much more robust. And don't be afraid to try an entirely different approach, rather than persevere with a technique that is simply not suitable.

The Road to Improved Efficiency

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

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

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Landmark Literature

2018

Every year, we ask experts from across the analytical sciences to select one eye-catching article from the past 12 months. Here, the rising stars from our Top 40 Under 40 Power List pick their top papers of 2018 – and tell us why.

Phosphate to the Rescue

By Michael Witting, Research Scientist, Research Unit Analytical BioGeoChemistry, Helmholtz Zentrum München, Neuherberg, Germany.

Landmark paper: JL Spalding et al., "Trace phosphate improves ZIC–pHILIC peak shape, sensitivity, and coverage for untargeted metabolomics", J Proteome Res, 17, 3537–3546 (2018).

When I first used HILIC separation during my studies, I remember the satisfaction of achieving near-Gaussian peaks of polar substances that could not usually be analyzed by reversed-phase techniques. However, to achieve those nice curves we used phosphate buffers in the millimolar range with UV detection.

When I later moved into the metabolomics field, which employs mass spectrometric detection, I had to say goodbye to phosphate-based buffers – and to nice peak shapes in HILIC. The polar part of the metabolome is still a major analytical challenge. Using specific columns and solvent systems, it's possible to optimize chromatographic conditions for one or two classes of metabolites, but the comprehensive analysis of "all" metabolites is still a distant dream. Indeed, it is hard to see how we will ever achieve complete metabolome coverage in a single method – and analyzing several hundreds or thousands of samples using different methods, each optimized for a few metabolites, is not feasible in terms of time or sample amount.

In their paper, Spalding and colleagues showed that traces of phosphate improve metabolite separation on a zwitterionic column. In a series of experiments, they demonstrate that the addition of ammonium phosphate to either the mobile phase or injected sample improves the chromatographic peak shape. They conclude that the high charge density of the phosphate anion helps to shield strong electrostatic interactions, which otherwise would lead to asymmetric and distorted peaks. Using the optimized method – with phosphate added to the sample solvent – the authors were able to detect metabolite features with a higher sensitivity and increase their coverage of the polar metabolome.

This paper proves once again that analytical chemistry is not just a tool for doing metabolomics, but central to the whole approach. Certainly, more time must be spent on developing better and faster methods, if we are to achieve full metabolome coverage.

Mirror Image

By M Farooq Wahab, Research Engineering Scientist-V, Department of Chemistry & Biochemistry, University of Texas at Arlington, USA.

Landmark paper: K Banerjee-Ghosh et al., "Separation of enantiomers by their enantiospecific interaction with achiral magnetic substrates." Science, 360.6395, 1331–1334 (2018).

In the 19th century, Max Planck's supervisor advised him not to pursue physics because "almost everything is already discovered, and all that remains is to fill a few holes" – a few short years later, quantum physics opened up a new world. Like the physicists of old, some analytical chemists feel that we have achieved everything we can in separation science, but the paper I have chosen as my landmark breaks the mold by showing separation of enantiomers using achiral magnetic substrates and magnets. Coincidently, the project is a collaboration of the Max Planck's Institute, IBM and two institutes from Israel.

Classically, we separate enantiomers by introducing them in a chiral environment, where spatial effects retard one of the enantiomers in a fluid carrier; as a result, one of the enantiomer elutes later than the other. The authors of this paper added a new dimension to liquid chromatography by showing that enantiomers also interact differently with magnetized materials. If the magnetic dipole is pointing up, one enantiomer adsorbs on the surface, and if the direction is reversed, the other enantiomer adsorbs faster. In the case of racemic [Cya-(Ala-Aib)5-CO2H], where Cya is cystamine, Ala is alanine, and Aib is aminoisobutyric acid, the adsorbent surface (gold layered upon magnetic materials) preferred the L enantiomer when the magnetic field was up, while D-enantiomer was favored when it was down. The study attributes this discrimination to a spin-specific interaction, but not by the magnetic field itself. The beauty of this work is that the method is generic and in future we may no longer require costly, specific chiral columns.

This paper proves once again that analytical chemistry is not just a tool for doing metabolomics, but central to the whole approach. Certainly, more time must be spent on developing better and faster methods, if we are to achieve full metabolome coverage.

Proteomic Renaissance

By Anna Laura Capriotti, Associate Professor, Department of Chemistry, University La Sapienza, Roma, Italy.

Landmark paper: EN McCool et al., "Deep top-down proteomics using capillary zone electrophoresis tandem mass spectrometry: identification of 5700 proteoforms from the Escherichia coli proteome", Anal Chem, 90, 5529–5533 (2018).

"Bottom-up proteomics provides indirect information, based on the analysis of peptides, which does not provide complete sequence coverage and hinders quantitative analysis."

In the last two decades, proteomics has begun to overtake genomics in the study of biological systems. Bottom-up proteomics now allows the identification of thousands of proteins; nevertheless, some believe the golden age of proteomics might be fading with the advent of new omics technologies, such as metabolomics, which shed new light on what is happening within living organisms in real time. Bottom-up proteomics provides indirect information, based on the analysis of peptides, which does not provide complete sequence coverage and hinders quantitative analysis. Developing new top-down strategies to accomplish direct comprehensive protein analysis presents a formidable but not insurmountable technological challenge – and it would hugely benefit the biomedical community. Top-down proteomics gives access to the identifications of proteoforms – with a variety of sequence variations, splice isoforms, and over 400 known posttranslational modifications.

My chosen landmark paper deals with the identification of proteoforms in a model system, Escherichia coli, using an orthogonal multidimensional separation platform that couples size-exclusion chromatography and reversed-phase liquid chromatography-based protein prefractionation with capillary zone electrophoresis tandem mass spectrometry. The authors obtained the largest bacterial top-down proteomics data set reported to date, identifying 5,700 proteoforms from the E. coli proteome, with a tenfold improvement compared with a previous study from 2017. It begs the question – how many proteoforms exist in nature? We currently do not know, although the advent of innovative strategies for proteoform identification may bring answers in the near future.

A Third Dimension in Diagnostic Medicine

By James Grinias, Assistant Professor, Department of Chemistry & Biochemistry, Rowan University, Glassboro, New Jersey, USA.

Landmark paper: EK Parker et al., "3D printed microfluidic devices with immunoaffinity monoliths for extraction of preterm birth biomarkers", Anal Bioanal Chem, In Press (2018).

One of the fastest growing areas in analytical chemistry is the use of 3D printing to facilitate lower-cost separation methods. Several research teams across the world have been working in this subfield, and one that I have closely watched is the collaboration between the Woolley and Nordin groups at Brigham Young University. These groups have recently printed microfluidic chips with feature sizes well under 100 µm, achievable only after building their own digital light processor-stereolithography (DLP-SLA) 3D printer and formulating unique printer resins. This new platform has since been used to generate printed channels, valves, pumps, and myriad other parts that would be necessary for a fully integrated microfluidic total analysis system.

In the report featured here, the groups applied this new fabrication technology to a medical issue that the Woolley group has previously studied with microchip electrophoresis – the clinical diagnosis of preterm birth (PTB). As a new father, it is not long ago that I worried about the health of my own baby during his development, which made me take special notice of this paper – tragically, PTB complications lead to over one million infant deaths annually. In an effort to improve the diagnosis of PTB and prevent severe complications, the team developed a new point-of-care testing device, which features an integrated monolithic extraction bed for the isolation of PTB biomarkers from human blood serum. The ability to generate a functionalized monolith for sample trapping directly in a 3D printed device opens a wide range of possibilities towards low-cost analytical devices that require a separation step. Although the authors admit that this is just the first step towards a fully integrated system, it is an important one that may eventually lead to clinical measurements that significantly reduce the infant mortality rate due to PTB.

"In an effort to improve the diagnosis of PTB and prevent severe complications, the team developed a new point-of-care testing device, which features an integrated monolithic extraction bed for the isolation of PTB biomarkers from human blood serum."

God of **Small Things**

By Matthew Baker, Reader in Chemistry, Department of Pure and Applied Chemistry, University of Strathclyde, UK.
Landmark paper: TJ Huffman et al., "Infrared spectroscopy below the diffraction limit using an optical probe", Proc SPIE, 10657, Next Generation Spectroscopic Technologies XI, 106570O (2018).

Infrared spectroscopy is currently undergoing a prolific stage in terms of new technologies. This paper describes "a new technique to collect infrared hyperspectral images below the IR diffraction limit. Optically Sensed photo thermal InfraRed Imaging micro-Spectroscopy (OSIRIS) permits the construction of infrared images on a resolution limited by the wavelength of the probe beam. The technique, named after the ancient Egyptian god of the underworld, is incredibly exciting for the future of imaging spectroscopy and in particular for uncovering new biology. The developments described in the paper suggest that contrast resolutions below 100 nm may be possible. And that opens up many new options for image analysis via infrared, including previously unattainable subcellular resolutions and structures, and even viral analysis.

Breaking Barriers

By Caroline West, Associate Professor, Institut de Chimie Organique et Analytique, University of Orleans, ICOA, CNRS UMR 7311, France.
Landmark paper: V Desfontaine et al., "Applicability of supercritical fluid chromatography–mass spectrometry to metabolomics. I – Optimization of separation conditions for the simultaneous analysis of hydrophilic and lipophilic substances", J Chromatogr A, 1562, 96–107 (2018).

Supercritical fluid chromatography (SFC) was long regarded as a UCO (unknown chromatographic object) by many chromatographers. It was thought to be complicated, unpractical, inappropriate to many application fields, and many other inaccurate qualifying adjectives. But times are changing. With the advent of modern instruments, many newcomers to the field bring with them a different view of the possibilities of SFC. Rather than limiting the technique to chiral prep-scale separations of pharmaceutical compounds with low or moderate polarity, they have adopted it for achiral analyses in a variety of applications that were previously mostly unknown to SFC. The prominence of the technique has risen greatly in natural products and environmental analysis, but the greatest change has been in the field of bioanalysis. Only ten years ago, SFC was hardly ever applied to biological samples like urine or plasma – now it is one of the dominant applications. The facilitated hyphenation of SFC to mass spectrometry is certainly a major contributor to this increased popularity, but the recent realization that SFC can work for polar species has also played a part. To allow these analyses, different mobile phase compositions must be adopted, comprising not only the most common pressurized carbon dioxide and alcohol co-solvents, but also small quantities of water and significant concentrations of salts to favor analyte solubility. In addition, the proportions of CO_2 and co-solvent were previously always in favor of CO_2, because of the invisible (nonexistent) barrier of 50:50 that few SFC chromatographers dared to cross. Now, it is better understood that larger proportions of co-solvent can be used. In the course of a gradient program, spanning the full composition range from 100 percent CO_2 to 100 percent solvent is entirely feasible. This is unifying SFC and HPLC in a single analysis, and may be termed "unified chromatography".

The paper I have selected is emblematic of these changing trends. It explores the feasibility of metabolomic analyses with unified chromatography hyphenated to mass spectrometry. In comparison to the most commonly used reversed-phase (RPLC) or hydrophilic interaction (HILIC) liquid chromatographic methods, the proposed method is able to analyze both lipophilic and hydrophilic metabolites within a single chromatographic analysis. With a careful selection of stationary phase and mobile phase to overcome the constraints of such a wide composition gradient, a 7-minute program allowed the elution and detection of 88 percent of metabolites (comprising a wide diversity of structures and polarities). Perfection is not possible in this world, and a portion of the detected metabolites still had unsatisfying peak shapes, but the potential of this method as a viable complement to existing LC methods is certain. Applicability to real samples remains to be demonstrated, but nonetheless I congratulate the authors on this fundamental work.

Going **Native**

By Andrea Gargano, Tenure Track Assistant Professor, Centre for Analytical Science Amsterdam, van't Hoff Institute for Molecular Science, Amsterdam, the Netherlands.

Landmark paper: T Wohlschlager et al., "Native mass spectrometry combined with enzymatic dissection unravels glycoform heterogeneity of biopharmaceuticals", Nat Commun, 9, 1–9 (2018).

"The work of Therese Wohlschlager captured my attention both for the complexity of the sample analyzed and the elegance of its sample preparation approach."

For my landmark paper of 2018, I have chosen a research article that I believe expresses the impressive development of analytical chemistry research in mass spectrometry (MS) of proteins.

The infusion of purified proteins in water-based (volatile) buffer solution using electrospray ionization mass spectrometry (native MS) was pioneered in 1990. Its maturation through the years has extended the mass range of MS of biomolecules (enabling measurements over 1 MDa), shining a light on the heterogeneity of large proteins (for example, distribution in phosphorylated and glycosylated forms) as well as their noncovalent interactions (protein complexes).

The work of Therese Wohlschlager captured my attention both for the complexity of the sample analyzed and the elegance of its sample preparation approach. In their manuscript, they performed native MS measurement of the therapeutic fusion protein etanercept. This biopharmaceutical is a large protein (with a theoretical mass of about 102 kDa) and highly heterogeneous, with multiple sites of glycosylation (adding up to 30 kDa).

The authors observed over 100 glycoforms of etanercept, combining native MS of the intact protein with measurements from different enzymatic dissection procedures of the samples to selectively cleave sugar residues (for example, sialic acid), sites of glycosylation (N or O glycans) or portions of the protein (TNFR and Fc domain). The integration of the results allowed the authors to assign a large proportion of the masses observed. The article reveals the complexity of new biotherapeutics, underlying the analytical challenge of their characterization. However, native MS measurements are mostly limited to static nanoflow infusion experiments of (highly) purified proteins (with a few exceptions). To extend native MS to the study of large biomolecules in complex mixtures and matrices, there is a need for (native) separation science methodology hyphenated with native MS. I believe that this is an area where we will see significant developments in the next few years.

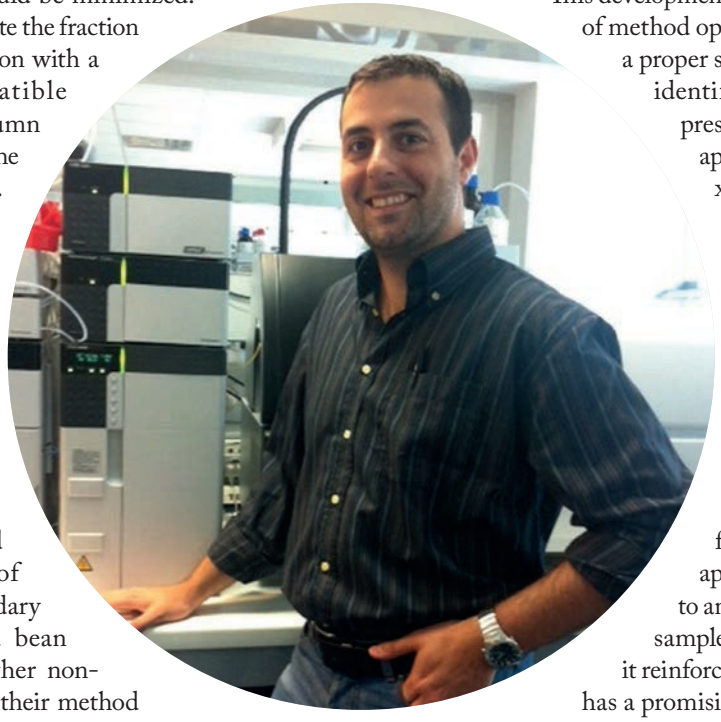
Wake Up and Smell the LC×LC

By Francesco Cacciola, Associate Professor of Food Chemistry, Department BIOMORF, University of Messina, Italy.

Landmark paper: S Toro-Uribe et al., "Characterization of secondary metabolites from green cocoa beans using focusing-modulated comprehensive two-dimensional liquid chromatography coupled to tandem mass spectrometry", Anal Chim Acta, 1036, 204-213 (2018).

"This development demonstrates the importance of method optimization in food analysis, as a proper separation aids the subsequent identification of the components present in the sample."

The analysis of complex food samples is challenging, but on-line comprehensive two-dimensional liquid chromatography is proving a very useful tool. Although the applications of LC×LC expand every year, there are still problems that need to be resolved, especially when it comes to coupling different separation mechanisms. To allow a more robust coupling between non-correlated separation mechanisms, the extent of the solvent strength mismatch between them should be minimized. An effective approach is to dilute the fraction eluting from the first dimension with a second dimension-compatible solvent, while a trapping column is employed simultaneously at the interface to avoid analyte losses.



Although theoretically simple, the optimization of this kind of approach is tricky (like almost everything related to method development in LC×LC!). The paper by Herrero and colleagues describes the development of an actively modulated on-line LC×LC method coupled to MS for the analysis of procyanidins and other secondary metabolites in green cocoa bean samples. Compared with other non-focusing modulation set-ups, their method allowed significant increases on resolving power and peak capacity. The proposed method demonstrates orthogonality reaching 66 percent of the available 2D space and a corrected peak capacity (accounting for the effects of first-dimension undersampling, band broadening and orthogonality) of 580. This development demonstrates the importance of method optimization in food analysis, as a proper separation aids the subsequent identification of the components present in the sample. Using this approach, the authors identified xanthines, flavan-3-ols and oligomeric procyanidins. Plus, it should be noted that the use of state-of-the-art instruments both at the separation and at the detection level (high-resolution MS) could even further improve the obtained results. This methodology compares favorably to more conventional approaches previously employed to analyze procyanidins in complex samples. Perhaps more importantly, it reinforces our conviction that LC×LC has a promising future in food analysis.

De-Bugging Mass Spec Data

By Hiroshi Tsugawa, Researcher, RIKEN Center for Sustainable Resource Science, Yokohama, Kanagawa, Japan.
Landmark paper: H Mohimani et al., "Dereplication of microbial metabolites through database search of mass spectra", Nat Comm, 9, 4035 (2018).

Advances in computational mass spectrometry are essential to grasp the diversity of metabolomes in living organisms. Metabolite annotation is straightforward when an authentic standard compound is available; however, the coverage (<5 percent) of mass spectral libraries is far removed from the structural diversity found in biological samples. To increase the coverage of metabolic profiling in biology, we need a standard-free annotation pipeline.

In natural product chemistry, "dereplication" (identifying known natural products in a biological sample) is an essential process to accelerate novel antibiotic discovery from natural sources without repeating time-consuming identification processes. Liquid chromatography coupled with high-resolution tandem mass spectrometry (LC-MS/MS) is a popular platform for high-throughput screening of natural products, but informatics methods for small molecule dereplication remain immature.

The dereplicator+ program described in my chosen paper facilitates the process by using the GNPS (global natural products social molecular network) mass spectra repository. It incorporates the algorithm for estimating false discovery rate (FDR), which helps to control false positive identifications in an automated annotation workflow using MS-based metabolomics platforms. The authors provide the program as a user-friendly web-application and command line application (http://cab.spbu.ru/software/dereplicator-plus/). The platform not only facilitates natural product replication but also increases the number of characterized metabolites in mass spectrometry-based metabolomics approaches – an important step forward.

Breaking Dogma

By Mikhail Savitski, Team Leader and Head of Proteomics Core Facility, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany.
Landmark paper: CM Potel et al., "Widespread bacterial protein histidine phosphorylation revealed by mass spectrometry-based proteomics", Nat Methods, 15, 187–190 (2018).

Protein phosphorylation is widely regarded as the most influential protein modification in life sciences, particularly for its effects on cellular signaling. Over the past 15 years, mass spectrometry-based proteomics has made tremendous progress in identifying serine, threonine, and tyrosine phosphorylation on a proteome-wide scale. Yet, it has long been known that phosphorylation can also occur on histidine in bacteria, and more recently the presence of this histidine phosphorylation was proven in human cells by antibody-based methods.

However, strategies for detecting histidine phosphorylation from complex mixtures using mass spectrometry have so far been lacking, due to the prevailing dogma that histidine phosphorylation would be lost upon sample preparation because of the acidic conditions necessary for phospho-peptide enrichment.

Potel and colleagues have challenged this assumption and shown that mild acidic conditions are not as detrimental to histidine phosphorylation as previously thought. The resulting sample preparation strategy, in combination with mass spectrometry, enabled the first sensitive proteome-wide mapping of histidine phosphorylation in E. coli.

The results are very exciting, and demonstrate that there are over an order of magnitude more phospho-histidine sites than previously thought in this organism, which opens several exciting avenues of research. Which proteins are responsible for these novel histidine sites? What exactly is their function? Could inhibition of histidine phosphorylation be exploited for antibiotics development? Furthermore, these technological developments will enable mapping of histidine phosphorylation in other organisms and will likely lead to new advances in biology.

Acid **Test**

By Sergio C. Nanita, Principal Investigator, DuPont Industrial Biosciences, Wilmington, Delaware, USA.

Landmark paper: JJ Hsiao et al., "Improved LC/MS methods for the analysis of metal-sensitive analytes using medronic acid as a mobile phase additive", Anal Chem, 90, 9457–9464 (2018).

"I expect that this approach will be adopted quickly for metabolomics, proteomics, and other analytical methods where reliable measurements of phosphorylated species are challenging."

Over the past few decades, there have been many advances in chromatography instruments and mass spectrometers, leading to the powerful LC-MS methods available today. Yet, rugged methods for the analysis of "metal-sensitive" compounds are still frustratingly lacking. We have known for a long time that certain compounds, such as phosphorylated metabolites, phosphorylated peptides and carboxylic acids, can form analyte/metal complexes during LC-MS analysis, which can be detrimental to method sensitivity and reproducibility. In some cases, analyte/metal complex formation makes LC-MS analysis unreliable or impractical.

A recent article by Jordy Hsiao and colleagues caught my attention because it addresses the above-mentioned problem in a simple and practical way. The authors demonstrated that LC-MS analysis of phosphorylated metabolites, phosphorylated peptides, carboxylic acids and other metal-sensitive compounds can be improved significantly by adding a "sacrificial ligand" to the mobile phase at trace levels. The task of this mobile phase additive is to bind to any available metal throughout the LC-MS system, so that the analytes do not. The authors tested pyrophosphoric acid, EDTA and medronic acid as additives; medronic acid added to the mobile phase as a metal complexation agent at micromolar concentrations was the ligand of choice reported in the paper. I expect that this approach will be adopted quickly for metabolomics, proteomics, and other analytical methods where reliable measurements of phosphorylated species are challenging. The paper also discusses the use of new HILIC-type stationary phases, which provide improved capability for the analysis of ionic compounds, and represent excellent options for methods employing medronic acid as mobile phase additive.

Who Watches the Watchmen?

By Ken Broeckhoven, Associate Professor, Department of Chemical Engineering, Vrije Universiteit Brussel, Brussels, Belgium.

Landmark paper: PK Dasgupta et al., "Flow-cell-induced dispersion in flow-through absorbance detection systems: true column effluent peak variance", Anal Chem, 90, 2063–2069 (2018).

"I firmly believe that this study will be a reference for further work on detector dispersion in LC – one of the most important contributors to extra-column dispersion."

Over the last year, our group has spent a lot of time and effort trying to elucidate the different contributions to extra-column band broadening, so this article was of great interest to me. The article starts with a comprehensive history of absorbance detection in LC, and a discussion of its technical limitations from a sensitivity and extra-column perspective. The authors then propose a novel method to determine the overall contribution of the detector to the dispersion of a chromatographic band. Their methodology consists of diverting a part of the eluent to waste prior to the detector. By extrapolating measurements at different split ratios towards zero flow to – and thus zero residence time in – the detector, they obtain the true efficiency of the band before the detector. In a second series of experiments, they use a modified detector to vary the path length and thus detection cell volume, to disentangle the dispersion contributions from the cell in- and outlet and from the detection cell itself. The article highlights some very important aspects of detector cell-induced band broadening, the first being that the flow cell dispersion is flow rate dependent (except for very long cells), which is often overlooked. A second important aspect is that, for a detector with cell volume (Vcell), the volumetric dispersion should not (as is almost always assumed) lie in between $Vcell^2/12$ (perfect plug flow) and $Vcell^2$ (perfect mixing in cell), as poorly swept regions might result in a value equaling a multiple of $Vcell^2$ – the traditional "perfect mixer" terminology to describe the detector contribution is poorly chosen. Finally, for short path lengths, the dispersion in the inlet/outlet zones influence each other and make up the majority of the flow cell dispersion, rather than its detection cell volume. I firmly believe that this study will be a reference for further work on detector dispersion in LC – one of the most important contributors to extra-column dispersion.

Two Sensors Are Better Than One

By Jean-Francois Masson, Professor of Chemistry, Université de Montréal, Canada.

Landmark paper: J Shu et al., "Plasmonic enhancement coupling with defect-engineered TiO2-x: A mode for sensitive photoelectrochemical biosensing", Anal Chem, 90, 2425-2429 (2018).

"I find it refreshing to see that the combination of two hot fields in biosensing, namely plasmonics and electrochemical sensing, can lead to further advancement."

Chemical and biological sensors rely on sensitive materials that convert a detection event into a physical signal, mainly relying on the electrical, optical, piezoelectric or mass sensing properties of the transducer. The field relies on sensors of increasing performance for detecting lower concentrations of analytes, but the basic principles governing them have not changed much in the past decade. Hence, advances in sensing performance have more often come from employing new biochemical schemes rather than fundamental advances in transducer technology. The opportunity still exists to further improve sensors by combining sensing technologies in new forms of transducers. To be truly advantageous, this combination must yield a response that is better than the individual components. This is exactly what has been accomplished in my landmark paper by Tang and coworkers at Fuzhou University, China.

Based on photoelectrochemical principles, they have devised a sensing platform that benefits from the plasmonic effect of AuNP and the photoelectric response of TiO2. When an analyte joins the two together, for example, strands of DNA, the hot electrons generated by the AuNP under visible light irradiation significantly increases the photocurrent of TiO2. In the absence of the analyte, the photocurrent was low. The novelty lies in the synergic effect between the defect-engineered TiO2-x substrate and AuNP as a new sensing modality. This new sensing modality was shown to be very sensitive to DNA with a detection range from 1 pM to 10 nM. While this range is achievable by other biosensing methods, the measurement of lower photocurrent than was achieved in this article is foreseeable, and therefore holds the promise of further improvement in the performance of the sensor.

I find it refreshing to see that the combination of two hot fields in biosensing, namely plasmonics and electrochemical sensing, can lead to further advancement in sensing and I am hopeful that this will lead to other significant advances in the field.

Priority Paper

By Anneli Kruve, Humboldt Fellow, Institute of Chemistry and Biochemistry, Freie Universität Berlin, Germany.

Landmark paper: MM Plassmann et al., "Nontarget time trend screening in human blood", Environ Sci Technol Lett, 5, 335–340 (2018).

LC-HRMS is used extensively for identifying (possibly toxic) compounds that humans are exposed to in their daily lives. In spite of the great potential, it is still hard to make sense of the huge amounts of data obtained from non-targeted screening experiments. One of the most crucial problems is that current technology does not yet allow automatic annotation of all the features found in LC-HRMS analysis, which makes the prioritization of the relevant features highly important. An obvious solution would be to focus on the most prominent features; however, the intensity of the peaks in mass spectrum does not correlate to the concentration of the compound because of the vastly different ionization efficiency of different compounds. Additionally, high-intensity peaks in the mass spectrum may lack biological significance.

My choice for a landmark paper describes the first human blood exposome study to include a significant time series. They propose using time series analysis as a tool to prioritize features, as increasing intensities in the time series analysis may refer to bioaccumulating compounds or to compounds to that we are increasingly exposed to. They analyzed human blood samples from 1983 to 2015. By focusing on the time series they were able to narrow important features down from 14,460 to 716. Finally, some of the substances were confirmed with the aid of standard substances.

The current shortcoming of this approach is that time series samples are rarely available and results obtained today and five years ago, in Tokyo and New York, on Orbitrap and ToF instruments, with and without LC separation, are not directly comparable. Still, this paper demonstrates the vast possibilities of uncovering time trend screening with non-targeted screening and hopefully we will see a major breakthrough in routine time trend analysis soon.

Once More, With Feeling

By Juris Meija, Research Officer, Metrology, National Research Council Canada, Ottawa, Canada.

Landmark paper: AL Plant et al., "How measurement science can improve confidence in research results", PLoS Biology, 16, e2004299 (2018).

Most of us have heard stories regarding the inability of scientists to replicate the studies of others. This "reproducibility crisis" is a serious problem in all fields because most scientists tend to overestimate their confidence. In the 1990s, for example, contemporary determinations of the gravitational constant were in severe disagreement, the half-life estimate of technetium-97 isotope has doubled between the 2003 and 2012, and the primary international standard of arsenobetaine was revised by 20 percent a decade ago after errors were revealed from an interlaboratory comparison. These powerful examples show that chemists cannot simply ignore the reproducibility crisis.

Reproducibility is the business of metrologists and my chosen article by Anne Plant and her NIST coworkers provides fresh guidance on how practices of measurement science can improve confidence in the conclusions of many research studies. This article reminds us to consider principles of metrology in our daily work; for example, evaluate the robustness of the data, look for any possible sources of uncertainty, and pay attention to potential systematic biases.

Tracking **TB**

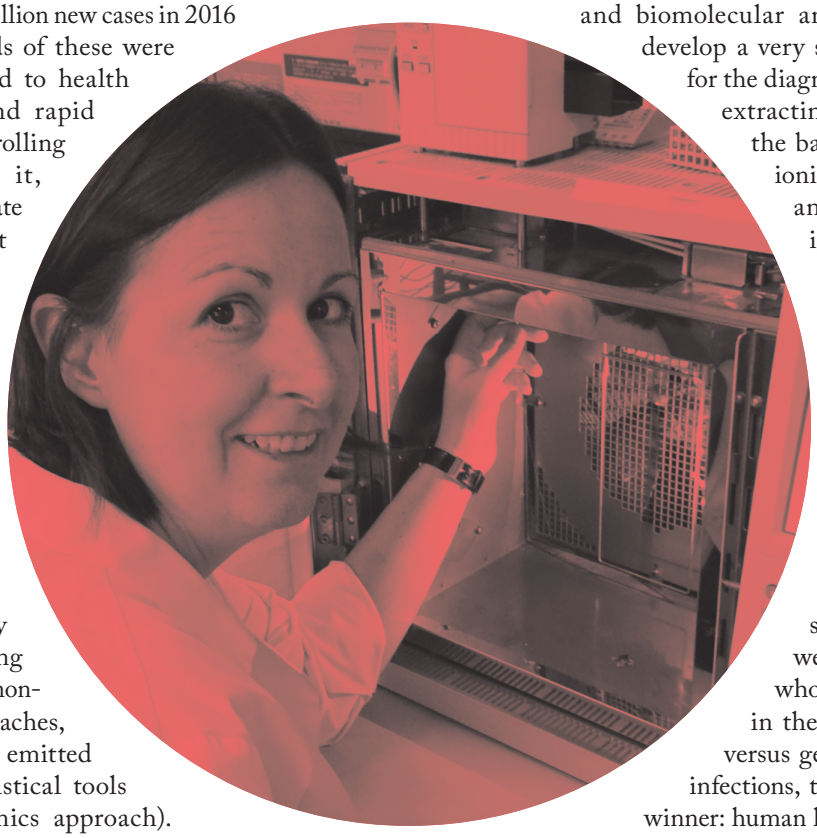
By Cecilia Cagliero, Assistant Professor, Department of Drug Science and Technology, University of Turin, Italy.

Landmark paper: M Varona et al., "Solid-phase microextraction of DNA from mycobacteria in artificial sputum samples to enable visual detection using isothermal amplification", Anal Chem, 90, 6922–6928 (2018).

"Both genomic and metabolomic approaches are being explored for diagnostics, with both showing significant strengths and weaknesses."

Reading literature and attending conferences in 2018, I was impressed by the number of studies dealing with the development of new analytical methods for the diagnosis of infections that are no longer major threats in Western countries.

Infections are still the main killers in developing countries. Just looking at tuberculosis, the WHO estimated around 10.4 million new cases in 2016 but less than two-thirds of these were diagnosed and reported to health authorities. Proper and rapid diagnosis is key to controlling infection – without it, efforts to provide adequate and prompt treatment are useless. Tests for developing world settings should not only be highly sensitive and specific, but also affordable, rapid and adoptable in-field by workers with minimal training (point-of-care assays).



The past year saw a number of very interesting studies dealing with the development of non-invasive sampling approaches, analysis of the volatiles emitted by pathogens and statistical tools (applying a metabolomics approach).

However, I was most impressed with the paper by Varona and colleagues, who combine their knowledge in varying analytical fields (the authors' specialisms range from sample preparation to ionic liquid chemistry and biomolecular analytical chemistry) to develop a very simple and reliable tool for the diagnosis of mycobacteria. By extracting genomic DNA from the bacteria with a polymeric ionic liquid SPME approach and analyzing it with an isothermal nucleic acid amplification method coupled with visual detection, the authors developed an approach suitable for point-of-care application.

Both genomic and metabolomic approaches are being explored for diagnostics, with both showing significant strengths and weaknesses. Regardless of who comes out the winner in the battle of metabolomics versus genomics for diagnosis of infections, there will be one definite winner: human health and wellbeing.

(Practically) Perfect PREDICTIONS

Chromatography method development is a time-consuming trial-and-error process. Is there an easier way?

By Paul Haddad

When a separation scientist is asked to develop a new separation method for a group of target compounds, there are many decisions to make. What type of separation will I use (reversed-phase LC, hydrophilic interaction liquid chromatography, ion-exchange)? What stationary and mobile phase? What about the precise separation conditions?

The usual first step in answering these questions is to consult the literature in the hope of finding conditions under which at least some of your target compounds can be separated. If the literature is silent, the scientist must examine the structures of the target compounds and then rely on prior training and intuition to deduce the approach most likely to be successful. Normally what follows is a trial-and-error process, where different chromatographic conditions are explored until eventually the desired separation method is developed. As many readers will know from experience, this can take a great deal of time and effort.

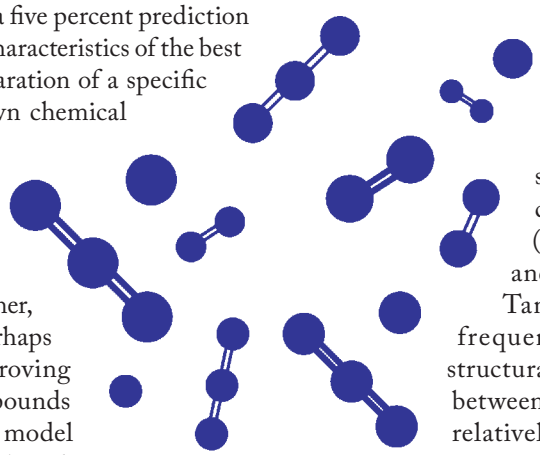
For the past five years, my team has been working on a project that seeks to put method development onto a more objective and structured scientific footing. By examining retention databases of numerous compounds under different chromatographic methodologies and conditions, we can derive a mathematical "quantitative structure–retention relationship" (QSRR) that links some "molecular descriptors" (characteristics) of the database molecules with their retention behavior. The descriptors may be physico-chemical properties calculated from the structure (such as hydrophobicity, polarity, partition coefficient, and so on) or theoretical properties calculated using molecular modeling – a task that can be facilitated by molecular modeling software; for example, Dragon or Volsurf+. Such software packages use high-level computational chemistry theory to compute a large number of parameters from all aspects of a molecule's structure.

The endgame? To develop a QSRR that can accurately predict the retention behavior of completely new compounds. The project runs across a team of five researchers (two postdoctoral fellows and three PhD students) at the Australian Centre for Research on Separation Science (ACROSS) at the University of Tasmania, supported by industrial collaborators. . Funding was provided jointly by the Australian Research Council (ARC) and a number of industrial partners.

It's complicated

We use the term "Holy Grail" to describe the goal of accelerated and reliable method development based only on chemical structures because it could potentially create a seismic shift in the way separation methods are developed. After all, chromatography is an exceedingly complex process that is governed by many experimental variables and, as a such, has long been considered an experimental discipline. Indeed, most separation scientists assume that its complexity prevents us from predicting retention behavior based on chemical structure. However, if one accepts a five percent error, the prediction of retention moves from theory into the realms of feasibility. Of course, a five percent error is too high if you wish to come up with the final optimal details of a new method – the best column, the precise mobile phase composition, the best flow-rate, and so on. However, chromatographic method development can be considered a two-step process, consisting of "scoping" and "optimization." Scoping involves defining the broad characteristics of the separation, such as the type of chromatographic method, the type of stationary phase, the nature of the mobile phase, and perhaps even the approximate mobile phase composition. By contrast, the optimization phase involves finding the precise details of the method. Here, we are using QSRR only for scoping, where a five percent prediction error is sufficient to predict the broad characteristics of the best chromatographic method for the separation of a specific group of target molecules with known chemical structures. Final optimization of the chromatographic method will always involve detailed experimentation.

Of course, QSRR is not new – it has been applied previously by several research groups around the world – rather, the novelty in our approach (and perhaps the key to our success) lies in improving the manner in which the best compounds to derive the QSRR mathematical model are selected from the compounds listed in the database.



Relationship building

It has been a steep learning curve but by bringing together talented people with complementary skills covering chromatography and molecular modeling, we have made excellent progress. Indeed, we have all been pleasantly surprised with how accurately we can predict retention times from chemical structure. The key breakthroughs were the decisions to focus on local modeling rather than global, and to use concepts of structural and chromatographic similarity to select the best database compounds to train the QSRR model.

Allow me to briefly explain some of the terminology and how we came to our decisions.

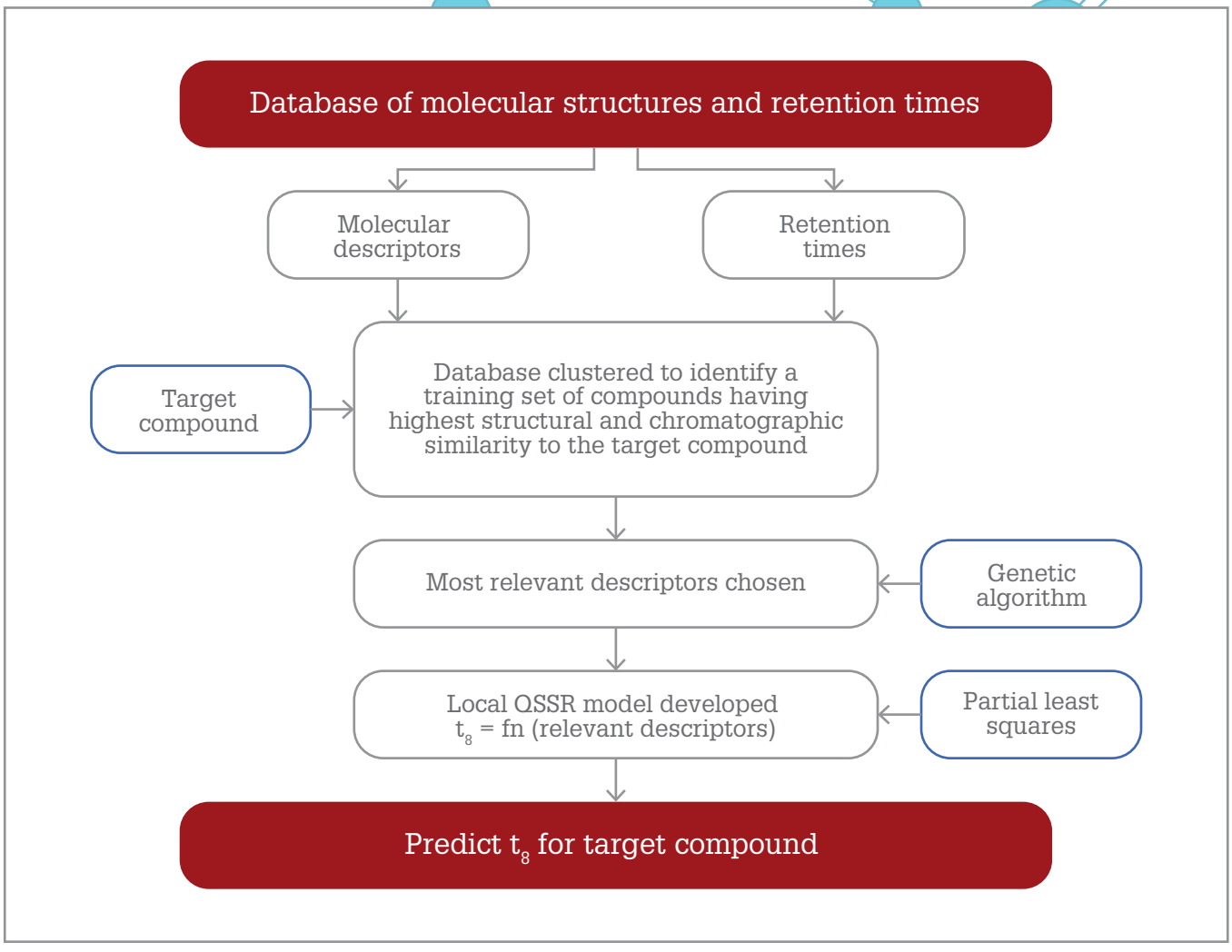
First, QSRR models can be global or local: a global model is when one QSRR mathematical model is derived for all compounds in the database (put another way, all retention time predictions are made from the same global equation). By contrast, a local modeling approach gives each compound its own mathematical model equation. Predictably (no pun intended), the latter approach is more time consuming, but also much more accurate.

Choosing the best database compounds to train the QSRR model is both important and complex. Intuitively, one would expect that, if you wished to develop a local QSRR model for a target compound, then the best results should be obtained using only "training" compounds that are "similar" to the target compound, rather than using all the database compounds to train the QSRR. There are two types of similarity that are relevant to this clustering approach. The first is structural similarity and the second is chromatographic similarity.

As the name suggests, structural similarity can be calculated by comparing structural elements (functional groups, carbon chains, and so on) between molecules. The Tanimoto Similarity Index (T) is a frequently used parameter to calculate structural similarity and provides a number between 0 and 1 to describe similarity. It is relatively straightforward to calculate the pairwise T value between a target compound and all the database compounds and to then cluster only those compounds in the database for which T exceeds a chosen value (0.7, for example).

Chromatographic similarity clustering refers to finding those compounds in the database that show similar chromatographic behavior to the target compound.

Figure 1. QSRR approach.



"It has been a steep learning curve but by bringing together talented people with complementary skills covering chromatography and molecular modeling, we have made excellent progress."

Typically, this means those compounds in the database that have similar retention times to the target compound. This type of clustering is paradoxical because to find the chromatographically similar compounds in the database, one needs to know the retention time of the target compound. Of course, this retention time is unknown and is exactly what the QSRR process is trying to predict!

Fortunately, we have discovered clustering tools that first use the Tanimoto Similarity Index but then also identify a surrogate compound (instead of the target compound itself) to use for subsequent chromatographic similarity clustering. Such a "dual" clustering approach has been shown to reduce prediction errors by up to a factor of 10 compared with no database clustering.

The QSRR approach we have developed is summarized in Figure 1.

"The application areas are unlimited. Perhaps the most obvious application lies in the pharmaceutical sector, where chromatographic separations are a lynchpin of successful drug development."

We start with a database of compounds with known structures and known retention times under specific chromatographic conditions. The aim is to have i) the largest database possible and ii) for that database to contain compounds with a wide structural and chromatographic diversity, so that, when clustering takes place, there will be sufficient compounds in the cluster to form a good training set. Molecular descriptors are then calculated for each database compound to give an array of descriptors with a matching retention time. The target compound is selected and the database is subjected to dual clustering to find a training set comprising the compounds with the highest structural and chromatographic similarity to the target. If the number of descriptors calculated for each database compound is large (Dragon software calculates up to 6,000 descriptors) a genetic algorithm is used to find those descriptors that are most relevant to the prediction of retention times. Next the QSRR model is developed to

provide an equation relating retention time to the relevant descriptors using an appropriate statistical tool, such as partial least squares regression. Finally, the model is then used to predict the retention time of the target compound by inserting the values of the relevant descriptors into the QSRR equation.

Who will benefit?

The application areas are unlimited. Perhaps the most obvious application lies in the pharmaceutical sector, where chromatographic separations are a lynchpin of successful drug development from early drug discovery through to final quality control of a manufactured drug product.

Consider the situation where an early drug discovery team has identified a target molecule to treat a specific disease. Drug synthesis modeling software has suggested three different synthesis routes that might be used to make the target molecule and has also suggested the range of impurities that are likely to be generated with each synthetic route. If the drug development chemists could use the QSRR approach to predict the retention times of the target molecule and the associated impurities from each synthesis route they could predict whether separation difficulties (separation of impurities from each other or from the target molecule) are likely to emerge in later stages of drug development, especially in quality control, and avoid those routes of synthesis.

Another good example lies in the area of non-targeted metabolomics. Here, metabolite screens are used to identify a target metabolite peak in that might be related to a particular disease. Mass spectroscopic analysis of the target peak might suggest multiple candidate chemical structures for the metabolite and the only way to eliminate false positives amongst the suggested candidates is to measure their retention times to see if they are eluted at the same retention time as the target metabolite peak. Using the QSRR approach the retention times of the suggested candidates can be predicted and false positives can be eliminated.

Manufacturers of chromatographic instruments and columns could also reap the benefits of retention prediction; customers often ask, "What is the best column and mobile phase for me to use for my particular separation?" QSRR would allow the in-silico screening of multiple stationary and mobile phases to come up with a logical selection of the best conditions.

It should come as no surprise then that the industrial partners sponsoring this research comprise a major pharmaceutical company (Pfizer Inc), a major scientific instrument manufacturer (Thermo Fisher Scientific) and a well-known developer of chromatography software (LCResources)! Each one of these partners has played a vital role, such as identifying scenarios for the application of QSRR modeling, the provision of databases of retention times of compounds, assistance with software, and provision of columns for testing of predictions. It has been a genuinely collaborative project.

What's next?

We have now completed the proof-of-concept phase of the project. We have shown that the QSRR approach – when applied with suitable database clustering methods – allows the prediction of retention times with an error of under 5 percent in reversed-phase LC, HILIC and ion-exchange chromatography. We have demonstrated applications in HILIC method development, early-stage pharmaceutical product development and non-targeted metabolomics.

However, we have been somewhat limited by the size of available retention databases, typically 150 compounds. Limited size means limited compound diversity, which sometimes leaves us unable to identify sufficiently large enough number of "similar" compounds for the training set for some target compounds. The next stage of the project will be to compile larger and more structurally diverse databases. Here, we will likely look to crowdsourcing or the establishment of a consortium of interested industrial partners (such as a group of pharmaceutical companies) who would be willing to share retention data. The larger the final database the better, provided that the retention data are reliable. With a big enough database, the sky's the limit.

Paul Haddad is Emeritus Distinguished Professor at the University of Tasmania, Sandy Bay, Australia.

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Music to Enjoy Science Lectures By

The use of songs in the auditorium can make learning more engaging and facts easier to remember – and it ramps up the fun factor for students and teacher alike.

By Roy Goodacre

Music touches all our lives. It can conjure a memory or feeling more strongly than almost anything else. The links between music and memory are visceral and – whether reminding you of your first kiss or your first concert – last a lifetime.

Even as I write, I'm smiling as I remember the songs I listened to before going out on a Saturday night in my student days, which included "She Sells Sanctuary" by The Cult. Later in the evening I could be found dancing to Billy Idol's rendition of "Mony Mony" – I could pogo quite well back then!

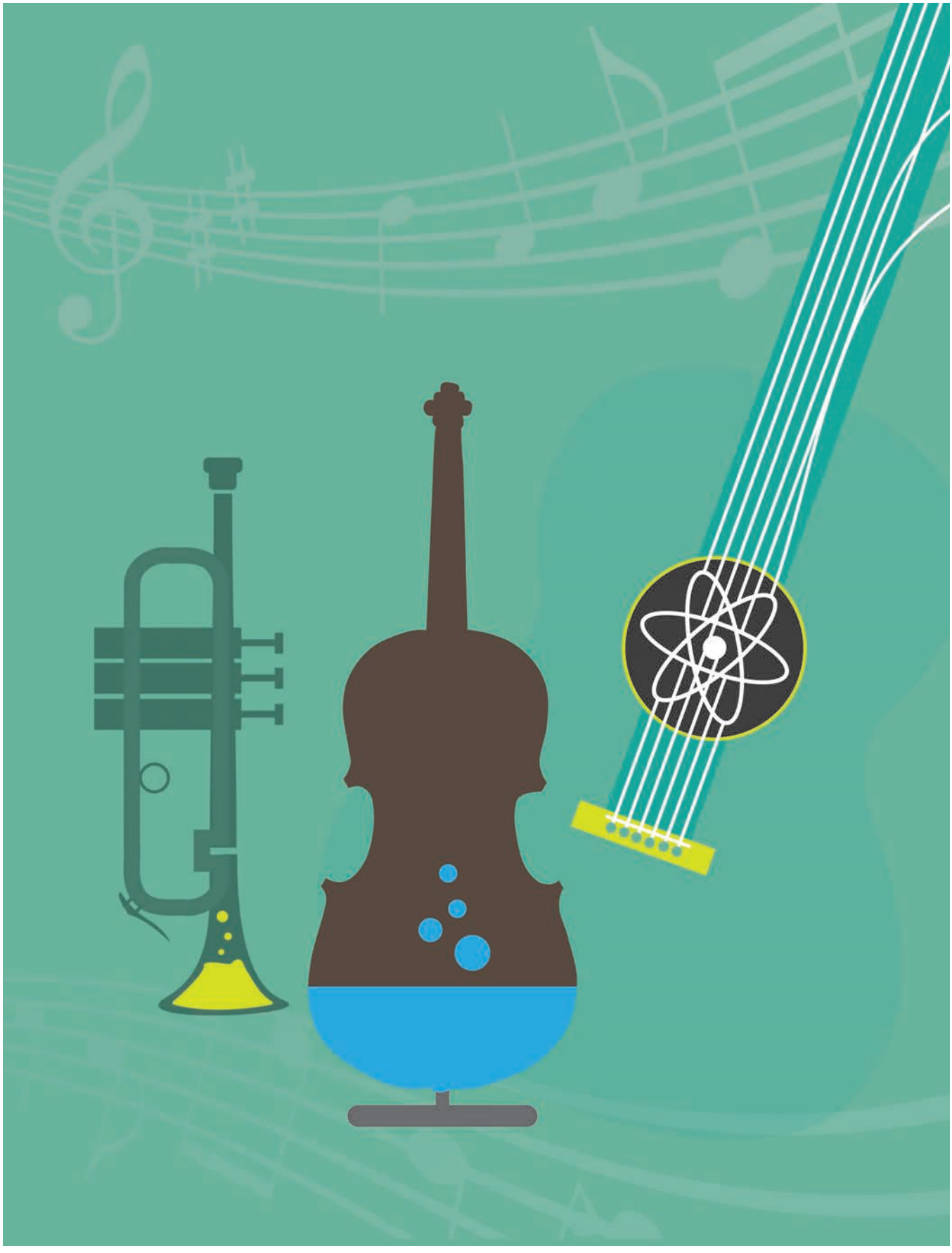
Another very strong song–memory association was formed in 1993, when my wife was pregnant with our daughter. Vanessa Williams' "Save the Best for Last" had been released the year before, and was playing constantly on Atlantic 252, a long-wave radio station we played in the car. Now, whenever I hear that song I am reminded of the birth of my daughter, and of my family becoming complete. The lyrics end with "You went and saved the best for last" – most poignant.

But music isn't just entwined with my personal life – it finds its way into my scientific memories too. One of my most striking musical associations related to science was during a visit to a chicken-processing plant at Sun Valley Foods Ltd 18 years ago. At the time, they processed 935,000 chickens per year, and I was investigating the possibilities of using infrared spectroscopy as a rapid tool to detect food spoilage; a method that we subsequently showed was indeed possible (1). I was told to wear ear defenders: whilst the machinery was below European sound limits, the music was on so loud it broke the legal limit. Now every time I hear "You Get What You Give" by the New Radicals, I see chickens floating above my head. I'm sure readers will have many similar song–memory links.

I first realized the potential for music in education during my high school exams. I used to play music from my favorite bands on my Sony Walkman (younger readers might have to look that up), which helped me cram. I remember thinking that if only the musical lyrics had contained facts, I'd have done much better…

"One of my most striking musical associations related to science was during a visit to a chicken-processing plant."

A couple of years ago, I was reminded of the power of music and memory when I heard my friend and colleague Colin Campbell (School of Chemistry, University of Edinburgh) using music in an after-dinner lecture during the annual Infrared and Raman Discussion Group Christmas meetings (also known as the Infrared and Raman Drinking Group).



Song title	*Artist*	*Science message(s)*
Raman spectroscopy		
Good Vibrations	Beach Boys	Used to remind people that Raman (and infrared) are based on molecular vibrations
The King of Rock 'n' Roll	Prefab Sprout	Summary of bond movements (sort of)
Mr Blue Sky	ELO: Electric Light Orchestra	Associates the fact that Rayleigh light scattering is wavelength dependent
Blue Eyes	Elton John	Highlights that Rayleigh light scattering is the reason that some people have blue eyes
Gold	Spandau Ballet	Highlights gold as a metal used for surface-enhanced Raman scattering (SERS)
Maxwell Silver Hammer	The Beatles	Highlights that silver is used a lot, perhaps dominates, SERS experiments
Silver Machine	Hawkwind	Another song that may be used as an alternative to highlight Ag-based SERS
God Gave Rock and Roll to You	Argent	Perhaps a more obscure one for SERS performed with silver nanoparticles.
Fluorescent Adolescent	Artic Monkeys	For biological systems the Raman signal can be affected by fluorescence
Ring of Fire	Johnny Cash	UV resonance Raman spectroscopy at 244 nm (i.e., in the deep UV) may burn and damage the sample during analysis
Applications of Raman and Infrared Spectroscopy		
Littlest Things	Lily Allen	Raman can be used to analyze individual bacterial cells – these prokaryotes really are small with dimensions in the order of 1 µm and weight about 1 pg
Do They Know it's Christmas	Band Aid	Infrared and Raman are used in food security – especially in terms of assessing food spoilage and food waste
Harvest For The World	The Christians	An alternative for the above; if the audience is (ahem) older
Art for Art's Sake or Money	10cc or Pink Floyd	Raman is used to assess the authenticity or otherwise of artwork. Here I like to highlight that a Marc Chagall painting bought in 1992 for £100,000 was tested with Raman spectroscopy and shown to be fake and thus destroyed.

Table 1. Songs I've used in undergraduate lectures, with the learning points.

"Music acts as a brain 'reset.' Most lectures are 50 minutes long, and I think lecturers sometimes forget that 50 minutes is a long time."

Within a memorable talk on surface-enhanced Raman scattering, which he was developing for the measurement of the redox potential in situ within cells (2), Colin captivated the audience by using musical quizzes. I borrowed (perhaps "stole" would be more accurate) his idea for use in undergraduate teaching, with three main reasons in mind.

The first reason is to punctuate scientific points. For example, when discussing Rayleigh light scattering I play "Mr Blue Sky" by the Electric Light Orchestra. This happy song associates the fact that light scattering is wavelength dependent. According to Lord Rayleigh, the intensity (I) of light scattering approximates to be inversely proportional to the wavelength of light to the power of 4 (i.e., $I = 1/\lambda 4$) and thus light scattering is ca. five times more effective for 400 nm (blue light) than 600 nm (red light). This can then be followed with a discussion on why certain people have blue eyes – also due

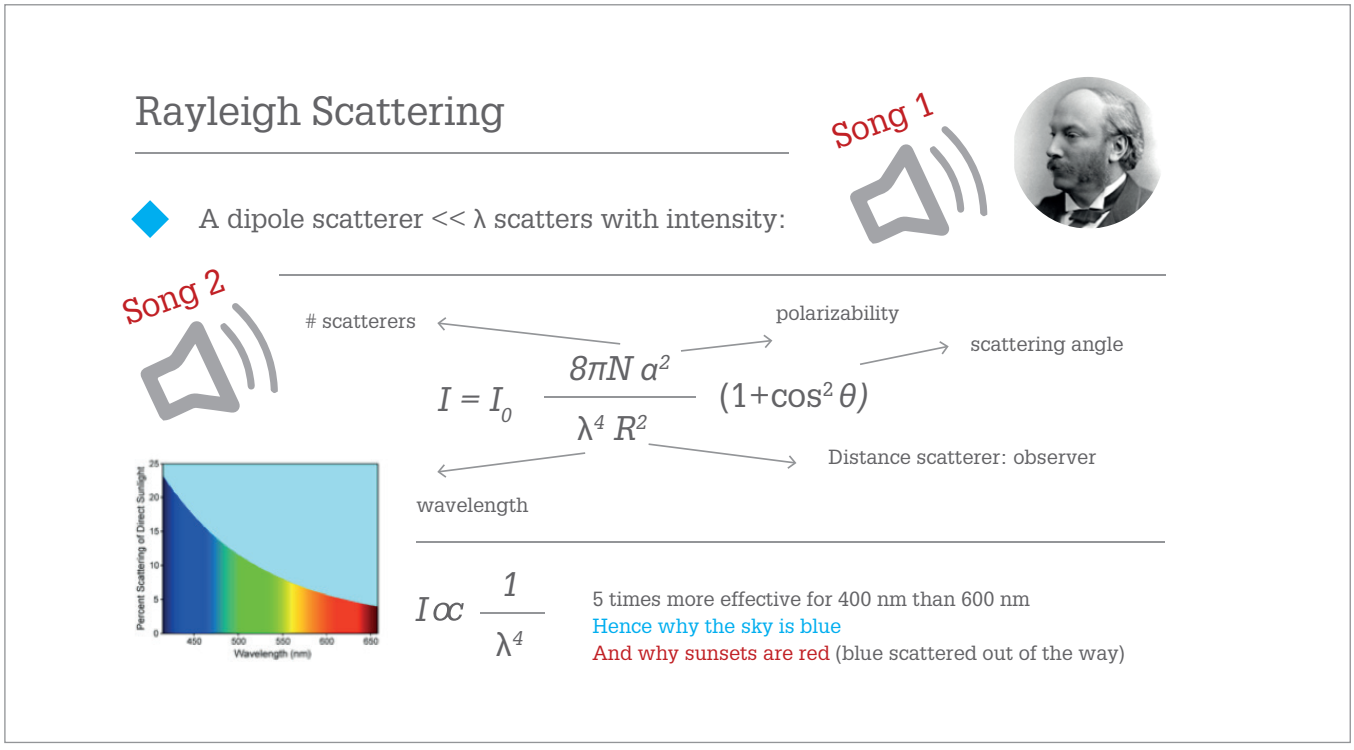
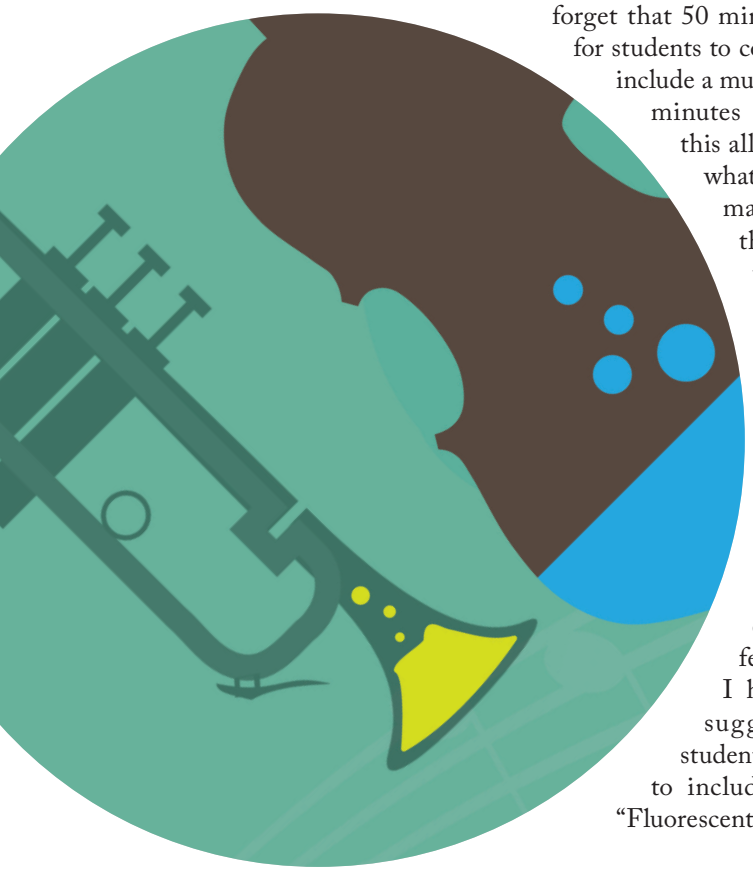


Figure 1. Slide introducing Rayleigh scattering. This highlights the Rayleigh equation and its approximation, along with explanation as to why the sky is blue, and two songs to help reinforce learning. Song 1 is "Mr Blue Sky" by the Electric Light Orchestra and Song 2 is "Blue Eyes" by Elton John. The significance of these songs is highlighted in Table 1.

Q: What aspect of the lecturer's approach to teaching best helped your learning?
Good explanations of content. The music was good as a quick break from thinking about the material and was entertaining.
The random musical snippets gave a nice break from solid lecturing while still being (albeit from my perspective, tangentially) relevant to the topic of discussion.
Engaging delivery, I liked the music :)
The musical challenges were very good! I liked learning about a technique that is used so extensively, and Roy's delivery of the content was enjoyable and funny.
He tried to make it interesting, included relevant topics to make it relatable and included random music to try and keep spirits up.
The use of music made what could have been a very dry unit entertaining.

Table 2. Highlights from feedback received after using music in undergraduate lectures.



to Rayleigh light scattering by proteins in the eye (which I accompany with "Blue Eyes" by Elton John). Table 1 highlights some songs, artists, and the science associations that I have used in lectures on Raman spectroscopy. Also included are a few songs that I have used to help people remember areas that Raman (and infrared) spectroscopy is applied within.

The second reason is that it's fun and increases student interaction. It allows the class to play name that tune, with prizes given to the first person to get the song title correct, and another for naming the right artist. (I recommend spherical chocolates – maximum accuracy when throwing to a worthy recipient!)

The third reason? Music acts as a brain "reset." Most lectures are 50 minutes long, and I think lecturers sometimes forget that 50 minutes is a long time for students to concentrate. I tend to include a music quiz about 20-25 minutes into a lecture, and this allows one to break up what may be quite dense material, lengthening the attention span of the students.

The feedback from my students has been very positive, with one saying "The use of music made what could have been a very dry unit entertaining." Table 2 contains other anonymous feedback I received. I have also received suggestions from the students of potential songs to include – which is why "Fluorescent Adolescent" by the Arctic Monkeys now features in lectures (science message: for biological systems, the Raman signal can be affected by fluorescence).

The use of music for scientific learning is not new. In 1982, Harold Baum published a delightful book entitled "The Biochemists' Songbook" (3). Music also features in research projects; there have been some relatively recent developments of turning protein sequences into Protein Music (4). And Howard Shapiro often used lyrics in talks when reporting his studies on flow cytometry – my favorite being "There's No Business Like Flow Business" (5).

Music and science are both relevant and ubiquitous. I hope that some of you may consider incorporating music into teaching and research. It's not only fun and memorable for the audience – it's also highly enjoyable to develop a scientifically inspired playlist.

Roy Goodacre is Professor of Biological Chemistry at the Department of Biochemistry, Institute of Integrative Biology, University of Liverpool, Liverpool, UK. His research interests are in mass spectrometry-based metabolomics, Raman spectroscopy and SERS.

Google Scholar: https://goo.gl/CVQRuy
Find Roy on Twitter: @roygoodacre

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3. *http://bit.ly/2C50Vtu*
4. *http://bit.ly/2C4dPaV*
5. *http://bit.ly/2C3KhtX*

Direct Analysis of Intact Proteins Using the Advion Touch Express™

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Touch Express OPSI coupled to the expression CMS provides fast benchtop analysis of intact proteins. Here, 2 µL of myoglobin (horse) at a concentration of 1 mg/mL in 10 mM ammonium acetate was used and deposited directly at the open port by pipette tip.

Following sample analysis, a charge deconvolution feature within Advion Data Express software automatically calculated the uncharged protein mass from the characteristic multiply-charged spectrum envelope obtained from ESI of biomolecules. The full mass spectra and the deconvolved, uncharged mass for myoglobin is shown in Figure 1.

A total of 14 multiply charged ions of myoglobin were detected with charge state ranging from +9 to +22 (Figure 1A). The uncharged mass of myoglobin is calculated to be 16,951.2 (Figure 1B), within 1 Da of the theoretical mass, 16,950.5.

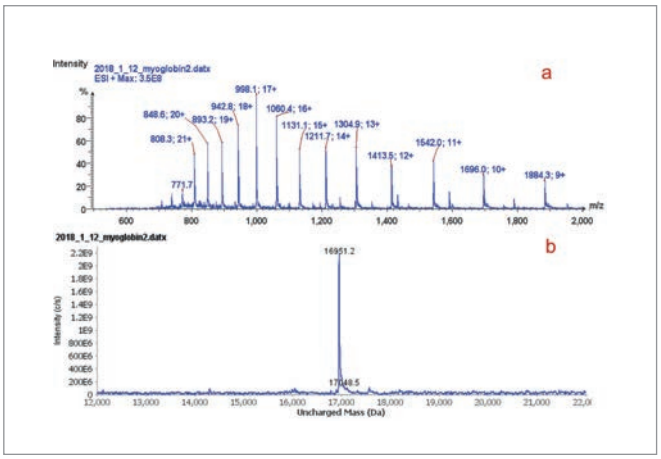

Figure 1

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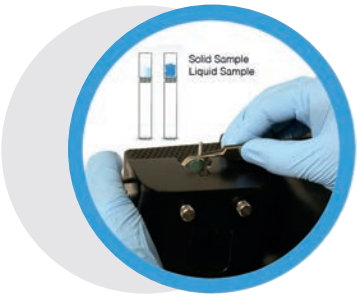

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The Raman Wizard

Sitting Down With…
Ian Lewis, Director of Marketing, Kaiser Optical Systems, Inc. – An Endress+Hauser Company, Ann Arbor, Michigan, USA.

What was your route into spectroscopy?

I got my PhD and Bachelor's degree at the University of Bradford in the UK, where I worked with polymer scientist Tony Johnson, and Howell Edwards – a Raman spectroscopist. My PhD was initially focused on polymers and their characterization, but I ended up concentrating more on spectroscopy. I then did my postdoc at the University of Idaho with Peter Griffiths, an infrared/vibrational spectroscopist. He was mostly known for his (and his group's) work on FTIR at the time, and was starting to do experimental work with Raman.

Any especially enjoyable projects?

During my PhD, I used a very expensive Raman FTIR system to look at the degradation of antique children's cellulose triacetate dolls. It was probably one of the most famous pieces of work I ever did – the story got picked up by The Times (UK), The Boston Globe and The Chicago Tribune, and was on British TV at one point. I remember them including pictures of beheaded dolls stuck in spectrometers!

What were you looking for?

A lady doll collector asked us to help determine what was happening to a set of her dolls – she said they were getting "sick" and didn't look the same. The same phenomenon was seen in dolls of the same era around the world. Using spectroscopy, we worked out that they were made of cellulose triacetate, and were undergoing the same degradation you'd expect with old movie films. The dolls had iron hooks embedded in each of the main components, with elastic bands between the hooks. We believed that the iron was helping catalyze the degradation of these bands and the acetic acid was making the dolls smell and corrode, leaking brown fluid from eyes and joints. It was like an infectious disease for old plastic dolls…

Ultimately, you choose to go into industry rather than continue in academia – why?

In 1994 Peter Griffiths and another academic, Ray Vonwandruska, had a successful grant application from the Federal Aviation Administration for detecting explosives in airports. I was working with a couple of different Raman companies to support that. At the end of the first year, our grant was stopped. The letter said something along the lines of: "There is no such threat to the US aviation system." (It's ironic – now you walk into airports worldwide and you see scanners being used with spectroscopy, quite often Raman.) My wife was expecting our second baby, so we decided that we needed a better way to support a small family and I made a swap to industry. I was hired by Kaiser as a Laser Spectroscopy Specialist, then I became Research Products Manager, then Marketing Manager, and now I'm Director of Marketing. The current role covers marketing communications as well as product management.

Where is Raman at right now?

People are spending a lot of time and research money looking into even smaller areas, like tip-enhanced spectroscopy or at ways of boosting the signal level with surface enhanced Raman spectroscopy – because they have identified that Raman can characterize materials they are interested in but not at the concentration levels or optical volume they need. At the same time, you see Raman moving beyond the lab into airports and clinics, with handheld devices being given to first responders to look at threats in the field.

How did you become involved with Federation of Analytical Chemistry and Spectroscopy Societies (FACSS)?

Back when I was in Idaho, I went to the 1995 FACSS meeting and suggested ideas for Raman sessions. From then on, I organized sessions annually until I ended up arranging the whole Raman program. I was asked to serve on the Coblentz Society board, then to be the Program Chair for the FACSS conference in Memphis (2007). From there, I served additional roles within FACSS, including as their Governing Board Chair in 2012 and 2013, and I was involved with the changing of its name to SciX.

Why is FACSS important?

It looks to bring the analytical community together from all over the world. Some groups are large and capable of producing their own national meetings, but they might only cover a subset of the analytical sciences and spectroscopy community. We have worked very hard to build an environment that combines networking, good technical talks and a well-attended exhibition. We are also trying to make it more student friendly; any student who works at the registration desk receives free registration – and many have taken this as an opportunity to get to know people. It's network and community building – critical to solving complex problems – in my opinion.

What's the secret to a successful conference?

Keeping up to date. If you don't have topical conversation points and new input, you're stagnating – and people won't come because there is no value. It's also important to make sure there is a variety of speakers and perspectives – a good research group will continue to produce high quality research for a number of years, so you've got to make sure students and post-docs get an opportunity to speak as they are the future of new groups.

And finally… The beard.

It's a bit "Lord of the Rings" at the moment as I am the program chair for the ICAVS conference in New Zealand in 2019. The first time I had a long beard, it become an incentive for my wife to finish her PhD; she doesn't particularly like it and so I agreed it would be all gone when she finished. She completed it in 2003 and I made good on that commitment. But it had become a bit of a trademark –and I never said I wouldn't grow it back…

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