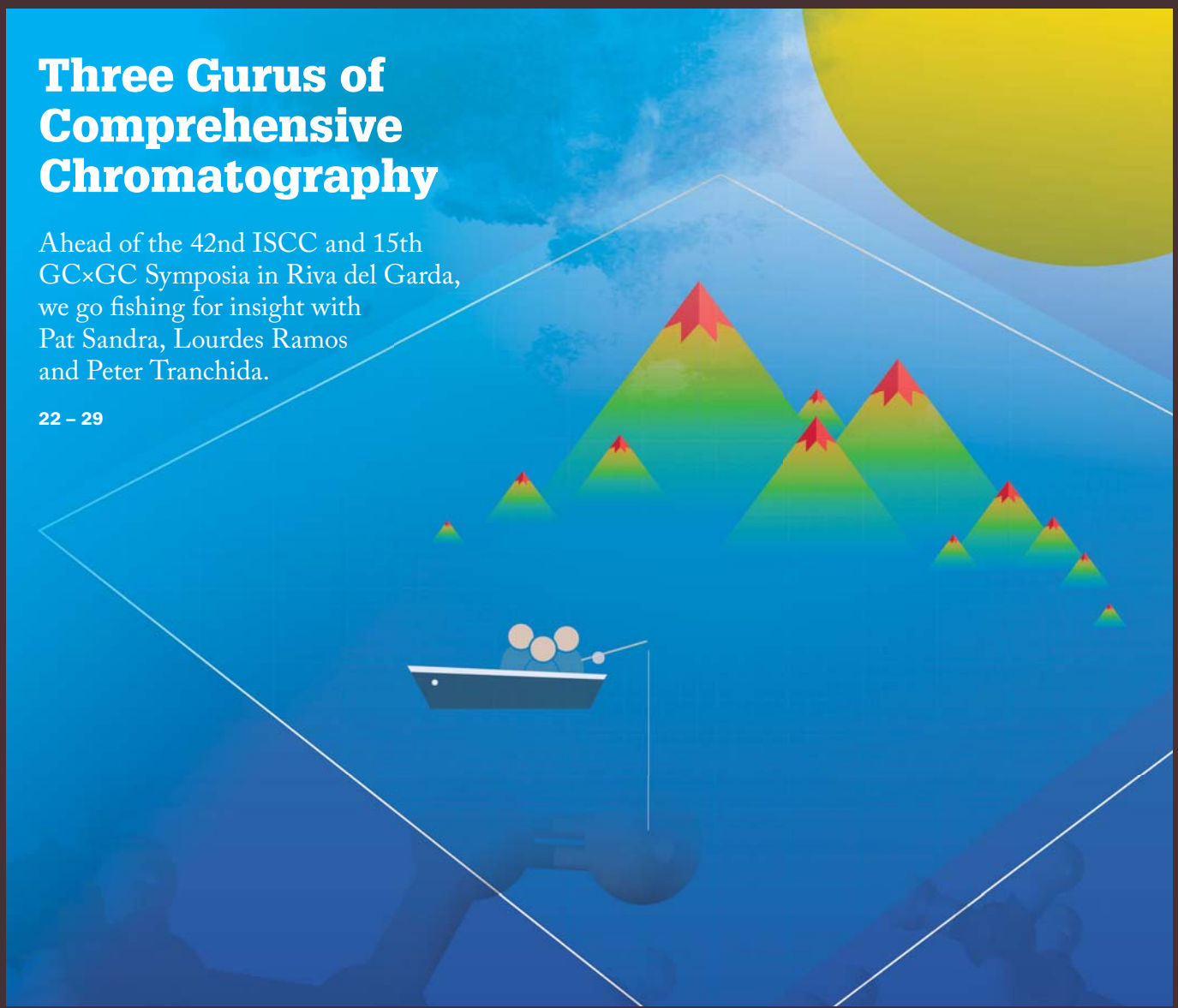
APRIL 2018 # 63

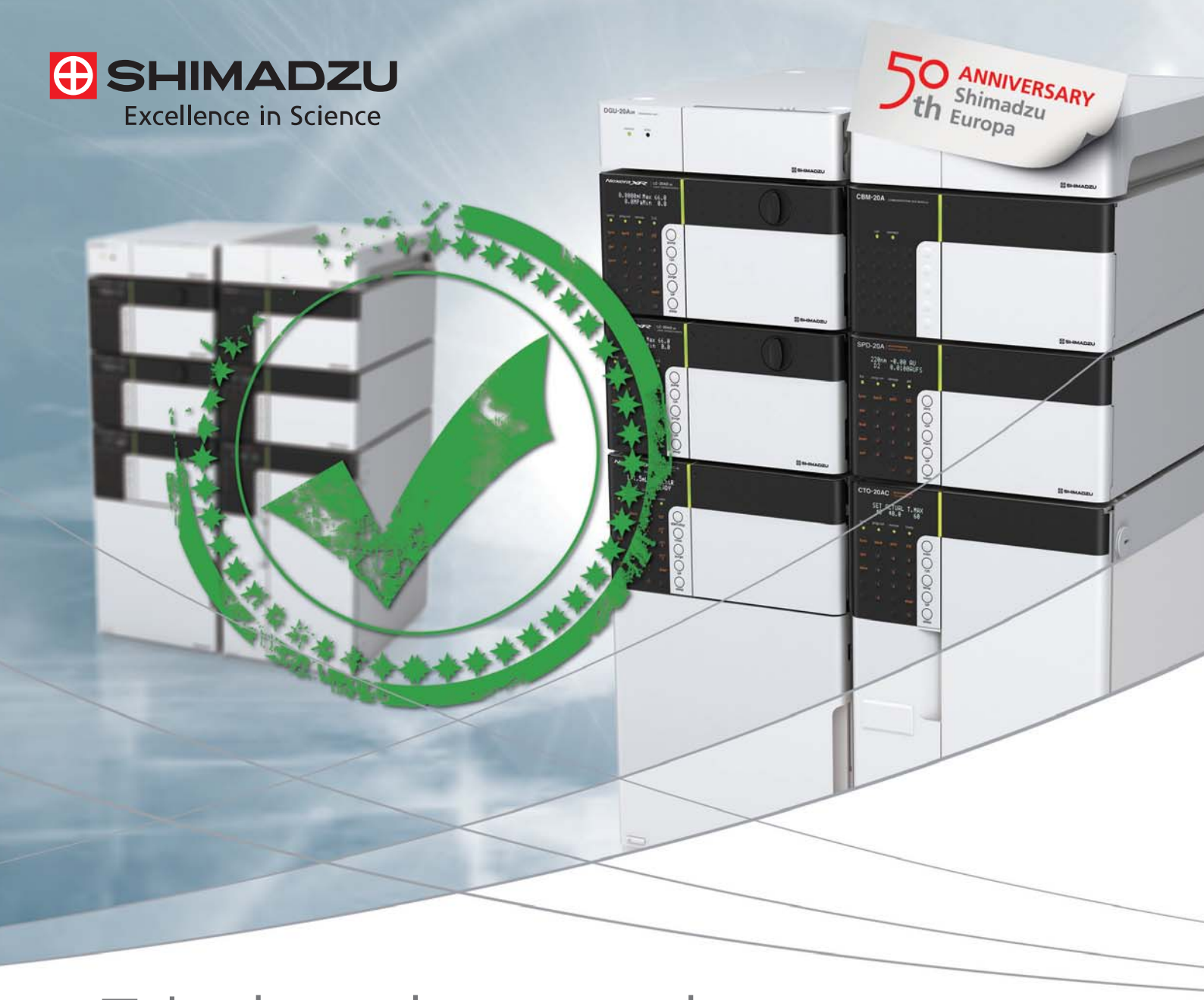
the Analytical Scientist™



Three Gurus of Comprehensive Chromatography

Ahead of the 42nd ISCC and 15th GC×GC Symposia in Riva del Garda, we go fishing for insight with Pat Sandra, Lourdes Ramos and Peter Tranchida.

SHIMADZU
Excellence in Science



Tried and trusted

Robust and reliable instrumentation for high-speed, high-resolution analysis

The Nexera XR modular UHPLC system combines the flexibility clients need with the reliability they want. Tried and trusted high performance modules provide the optimum system for analytical challenges in pharmaceutical and environmental industries as well as in biochemistry, chemistry and the food market.

On the safe side
with the 660 bar Nexera XR all-round system reliably providing accurate data, always

The flexible choice
enables configuration of customized systems to meet specific application requirements

The sensible option
offers a choice of detectors providing excellent sensitivity, baseline stability and reproducibility

www.shimadzu.eu/nexera-xr

Image of the Month

Digging Deep Into Human Prehistory

An international team of researchers combined archaeological, genetic and stable isotope data to trace four millennia of human prehistory in Iberia. Pictured here is one of the sites studied - the El Portalón cave in the Sierra de Atapuerca (northern Spain).

Credit: Eneko Iriarte, Universidad de Burgos, Spain.

Reference. C Valdiosera et al., "Four millennia of Iberian biomolecular prehistory illustrate the impact of prehistoric migrations at the far end of Eurasia", PNAS [Epub ahead of print] (2018).

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

Contents

On The Cover

Three gurus capture comprehensive chromatography insights in Riva del Garda

Upfront

the Analytical Scientist

ISSUE 63 - APRIL 2018

Change of address
info@texerepublishing.com
Hayley Atiz, The Analytical Scientist,
Texere Publishing, Haig House, Haig
Road, Knutsford, Cheshire, WA16 8DX, UK

General enquiries
www.texerepublishing.com | info@texerepublishing.com
+44 (0) 1565 745 200 | sales@texerepublishing.com

Distribution:
The Analytical Scientist (ISSN 2051-4077),
is published monthly by Texere Publishing, Haig House,
Haig Road, Knutsford, Cheshire WA16 8DX, UK
Single copy sales £15 (plus postage, cost available on request
info@texerepublishing.com)
Non-qualified annual subscription cost is £110 plus postage

MARKES international

NEW

A breakthrough in sample automation and concentration for GC–MS

Centri® – Multi-technique sample pre-concentration & injection platform, delivering enhanced analytical sensitivity and higher throughput

SPME & SPME–trap

Headspace & HS–trap

HiSorb high-capacity sorptive extraction

Thermal desorption

Since 1997 20 YEARS

Building on 20 years of leadership in trace organic chemical analysis

THE QUEEN'S AWARD FOR ENTERPRISE: 2015

For more information visit
chem.markes.com/Centri

A company of the **SCHAUENBURG** International Group

The 42nd International Symposium on Capillary Chromatography (ISCC) and the 15th GC×GC Symposium is a "hyphenated" meeting which will be held again in wonderful Riva del Garda (Italy), from May 13 - 18, 2018. Apart from the most recent advances in the fields of pressure and electrodriven microcolumn separations, and comprehensive 2D GC, This year particular emphasis will be directed to all Comprehensive Separation Technologies and MS Hyphenation and to Capillary Chromatography and 2D GC with various forms of MS from unit-mass to high resolution and from single to hybrid analyzers. Consequently, both the importance and complementary nature of chromatographic and MS processes will be given high consideration. Within the wider context of separation science, great space will be also given to the sample preparation process, in both oral and poster sessions.

The ISCC/GC×GC scientific program will be a rich one, it being characterized by:

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

Researchers in all areas relevant to the subjects of the symposia are invited to submit abstracts. As is traditional for the Riva meetings, the majority of presentations will be in a poster format and the Scientific Committee will select contributions for oral presentations.

As always, many awards will be assigned in both the ISCC and GC×GC events, recognizing excellence in both established and young scientists, in oral and poster presentations.

Exhibitors and sponsors are a fundamental part of the meeting (without them…Riva wouldn't be Riva!) and are encouraged to participate by reserving booth space, and becoming a sponsor., and to promote the ISCC and GC×GC events.

Last, but not least, the traditional "Riva" social program will be entirely maintained, with one or two events each day: cocktails, the welcome reception, the concert, the wine and cheese evening, and of course, the disco night!

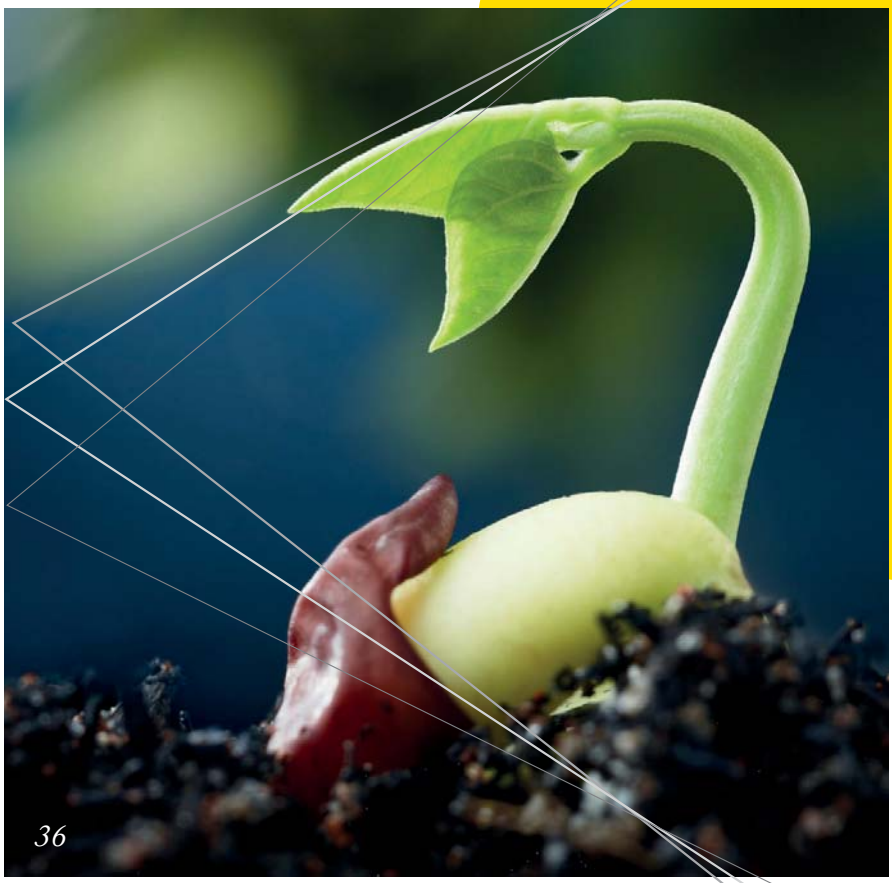
Please keep visiting our web site (www.chromaleont.it/iscc) for new information as it becomes available.

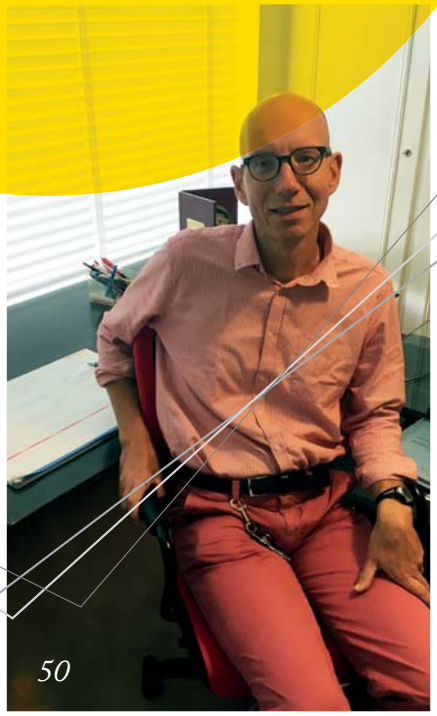
42ND INTERNATIONAL SYMPOSIUM ON CAPILLARY CHROMATOGRAPHY

AND

THE 15TH GC×GC SYMPOSIUM

Chroma leont





In My View

Features

Departments

Sitting Down With

CELEBRATING THREE YEARS OF HUMANITY IN SCIENCE

The Humanity in Science Award recognizes and rewards scientific breakthroughs that aim to have a real impact on humankind's health and wellbeing.

HUMANITY IN SCIENCE AWARD

the Analytical Scientist

2015

Peter Seeberger & Andreas Seidel-Morgenstern, Directors at two collaborating Max Planck institutes in Germany, developed an innovative process to manufacture the most effective drugs to treat malaria from plant waste material, air and light.

2016

Waseem Asghar, Assistant Professor at Florida Atlantic University, developed flexible sensors for the rapid and cost-effective diagnosis of HIV – and other infectious diseases – in point-of-care settings.

2017

Richard Jähnke, Global Pharma Health Fund (GPHF), developed and continuously improved GPHF Minilab – a "lab in a suitcase," enabling resource poor countries to rapidly identify substandard and falsified medicines.

Nominations will open soon for the 2018/2019 Humanity in Science Award

www.humanityinscience.com

The Heat Is On

With RIVA2018 just around the corner, we're delving into the present and future of comprehensive techniques

The countdown is on for the 42nd ISCC and 15th GC×GC Symposium, taking place May 13-18 on the spectacular lakeshore of Riva del Garda, Italy. Separation scientists from around the world will exchange ideas through workshops, discussion sessions, and an exhibition displaying a wealth of instrumental innovations. Sessions will mirror the key trends within the separation science community – and this year comprehensive two-dimensional techniques will take center stage. Comprehensive chromatography is also the star of this issue of The Analytical Scientist, with a fascinating panel discussion between three gurus of the field (page 22), a technology update from a panel of top instrument vendors (page 30), and an interview with "comprehensive collaborator" Hans-Gerd Janssen (page 50).

Comprehensive two-dimensional techniques are becoming increasingly established, and are likely to experience more growth in the near future, as regulations in various fields demand deeper and more precise analysis. Commercially available GC×GC and LC×LC systems are already a huge step forward compared with the first prototypes. However, their superior performance still comes with increased complexity, and this has made the migration of 2D techniques into industrial workflows challenging.

Comparing the two multidimensional giants side by side, it is striking how much more mature GC×GC is. Indeed, we are already witnessing the evolution of the technique towards ultrafast 3D separations, as will be illustrated at RIVA by exciting presentations on partial modulation via a pulsed-flow valve (Robert Synovec) and fine tuning of soft electron ionization conditions (Peter Tranchida).

Development of LC×LC – perceived to be trickier to master – has been much slower. However, the immense potential impact of this technique has recently spurred exciting evolutions. Prominent scientists will discuss exciting new opportunities, such as integration with triple quadrupole MS to make target analyte quantification more robust (Paola Dugo), using a flat-bed stationary phase in a "spatial" mode (Peter Schoenmakers), or exploiting a single dual-mechanism polar column in the first dimension (Pavel Jandera). We are even seeing combinations like LC×LC with ion-mobility separation and Q-TOF MS (André de Villiers) – what we would call a five-dimensional separation.

The large number of participants already registered for Riva's first-ever LC×LC short course demonstrates how much enthusiasm is being generated by the ability of today's technology to create tailored multi-separation platforms. I hope the articles within will provide you a clear overview of this exciting technology – and for a more "comprehensive" discussion, I hope to see you in Riva del Garda!

Luigi Mondello
Guest 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

Keeping Plastic Fantastic

Analytical methods help save Disney cels – and could protect the art of the future

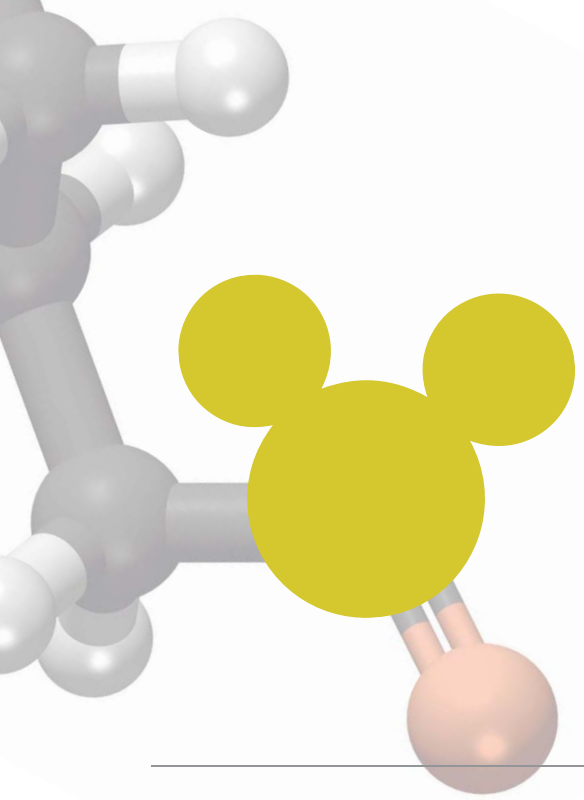
The Disney Animation Research Library is a carefully climate-controlled facility housing original celluloids of the animation giant's most beloved films. However, even in these state-of-the-art surroundings Disney's early animation cels have begun to fall prey to the ravages of time; the film has started to show signs of shrinking, cracking and discoloration. Disney called in Tom Learner, head of the Getty Conservation Institute's Science department (1) to save the day.

After analyzing cels using Fourier-transform infrared (FTIR) spectroscopy to identify the polymer base materials – cellulose diacetate and cellulose triacetate – and characterizing chemical composition using pyrolysis-GC-MS, Learner's team discovered that it was possible to re-adhere the paint by placing the cels in humidity chambers (2). For now, at least, Bambi and Pinocchio are safe.

However, prevention is almost always better than cure – and analytical science could have a part to play here too. A team from UCL (London) and University of Strathclyde (Glasgow) recently used solid-phase microextraction (SPME) ahead of GC-MS to assess potential degradation in plastic sculptures and other items, by artists including Naum Gabo and Antoine Pevsner, housed at the Tate Museum. The researchers looked for combinations of volatile organic compounds released during the decay of polymers, such as cellulose nitrate (CN), cellulose esters, polyurethane (PUR) foams and polyvinyl chloride (PVC).

The team analyzed art works by Naum Gabo [(a), (c); © Nina & Graham Williams/Tate, London 2017], and Antoine Pevsner, [(b); ©ADAGP, Paris, and DACS, London, 2017]. The arrows in (d), (e) and (f) show the artworks with the SPME fiber in place.

They discovered that in many cases, this method allowed tracking of the decay process – with classification accuracies of 50–83 percent. "Analyses of 25 CN samples shows an increase in furfural emissions […] Propanoic acid (PA) emissions increased over time for 19 samples of CP […] PUR samples



were found to emit 5-ethenyldihydro-5-methyl-2(3H)-furanone and aldehydes including pentanal, hexanal and benzaldehyde (3)". The technique could allow museums and galleries to "sniff out" the level of decay of plastic objects, and earmark those in most urgent need of conservation work.

So with Disney's cels salvaged, and a promising technique at hand for preservation of polymer-based artworks, we take our hats off to "The Rescuers"…

References

1. *The Getty Conservation Institute, "Preservation of plastics: Disney animation cells" (2017). Available at: https://bit.ly/2GdaExj. Accessed March 27, 2018.*
2. *M Giachet et al., "Characterization of chemical and physical properties of animation cels from the Walt Disney animation research library", ICOM-CC 17th Triennial Conference Preprints (2014).*
3. *K Curran et al., "Classifying degraded modern polymeric museum artefacts by their smell", Angew Chem Int Ed, [Epub ahead of print] (2018).*

Super Saliva Test

Ultrasensitive PCR powers an oral fluid assay for earlier HIV diagnosis

The advent of antiretroviral therapies to control HIV has turned a once-terminal illness into a relatively manageable disease when caught early enough. But although great strides have been made to curb the virus, 36.7 million people worldwide currently live with HIV – nearly half of whom are unsure of the status of their infection (1). Clearly, without access to adequate testing, it's difficult for both patients and the medical community to keep track. And that's why Carolyn Bertozzi and her team decided to develop a highly sensitive HIV assay for saliva (2).

At the moment, there are two main types of tests for screening HIV, each with pros and cons: blood tests are highly sensitive, but have a poor rate of compliance; oral fluid tests, on the other hand, although noninvasive, typically suffer from poor sensitivity because of the lower concentrations of anti-HIV antibodies. Bertozzi's new oral fluid assay addresses the challenge by using antibody detection by agglutination-PCR (ADAP) – making it 1,000–10,000 times more sensitive than existing tests. "ADAP is based on the concept of proximity ligation PCR, which we knew had the capability of ultrasensitive DNA detection. This ADAP was designed to bring the sensitivity of PCR to the problem of antibody detection," says Bertozzi, lead investigator and Anne T. and Robert M. Bass Professor of Chemistry at Stanford University. "The ADAP test can enable earlier detection of HIV infection in the context of population screening using oral fluid, which is easier to collect and far less risky for healthcare workers because, unlike blood, oral fluid is not infectious."

Bertozzi acknowledges that translating the research to the clinic is no small feat: "The biggest hurdles that lie ahead are larger studies with longitudinal data to judge how ADAP compares with current oral and blood-based tests." But the team sees great promise in the ADAP assays, and plans to develop analogous tests for other infectious and autoimmune diseases that produce autoantibody biomarkers.

References

1. *HIV.gov, "The global HIV/AIDS epidemic" (2017). Available at: bit.ly/2xpEQnn. Accessed February 1, 2018.*
2. *CT Tsai et al., "Antibody detection by agglutination-PCR (ADAP) enables early diagnosis of HIV infection by oral fluid analysis", Proc Natl Acad Sci USA, [Epub ahead of print] (2018). PMID: 29358368.*

Shell Shocked

Why ocean acidification could mean a literal 'sea change' for California mussels

The impact of environmental changes on our world's oceans is becoming increasingly well documented, with reports of chemical pollution, a trebling of plastic waste and dying coral reefs. With ocean acidification – a shift towards pH-neutral conditions caused by excess CO_2 in the atmosphere – mussels look to be the latest to suffer. A team of scientists from the universities of Florida, Glasgow and Chicago analyzed Mytilus californianus to assess the damage – and to discover what it could mean for these mighty mollusks.

The group hit the waters around Tatoosh Island, and compared modern muscle shells with archival records of shells from the 1970s, as well as some dating back 1,000–2,400 years. The team discovered that the calcite crystals within the shells have been uniform in size and structure for thousands of years, but those from the last 15 years show "increased disorder." Raman spectroscopy also uncovered greater variability in the quantity of calcium carbonate ($CaCO_3$), as well as elevated levels of magnesium – a sign that shell formation has been disrupted.

According to the researchers, this trend in the shell structure corresponds with an increased rate of ocean acidification. Mussels may not find themselves all at sea though, according to lead author of the paper, Sophie McColl: "Variability is the basis of natural selection, and the fact that we now see so much variability in the mussels' individual shells means there is potential for natural selection to act," she said in a press release (2). "I have too much confidence in the natural processes of ecology and evolution to think that we'll have barren oceans."

References

1. *SJ McCoy et al., "A mineralogical record of ocean change: Decadal and centennial patterns in the California mussel", Glob Change Biol, [Epub ahead of print] (2018).*
2. *Florida State University, "FSU researcher: Ocean acidification means major changes for California mussels", (2018). Available at: https://fla.st/2DZbNqb. Accessed March 27, 2018.*

From Awards to Allergens

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

Products and launches

- Inlabtech has released a new sample preparation system, the TA12 Serial Diluter.
- Leco claim that their two new instruments, the 828 and the 928 series, will "transform" carbon and nitrogen analysis to the benefit of the food and agricultural sectors.
- Astrotech has announced that the TRACER 1000, a new explosives detector, has been accepted into the Transport Security Administration's Screening Program. The detector is described as having a "virtually unlimited library."
- SCIEX's new food allergen screening method, using the QTRAP 4500 LC-MS/MS, has received official classification from AOAC International. It can detect allergenic peptides from five major classes of allergenic foods at a detection limit of 10 ppm.

Collaborations and acquisitions

- Cofactor Genomics is teaming up with the National Cancer Institute to demonstrate the utility of an immune-profiling assay – the Cofactor Paragon – in clinical settings.
- RedShift Bio has completed Phase II clinical trials of the Microfluidic Modulation Spectroscopy (MMS) platform, carried out in collaboration with several academic and industry institutions, including Waters and Technology Venture Partners.
- Science Exchange and PhenoSwitch Bioscience are collaborating to offer online access to the latter's LC-MS/MS services. "We are excited to collaborate with PhenoSwitch Bioscience to make its mass spectrometry services readily available to scientists worldwide," said Science Exchange CEO, Elizabeth Iorns.

Company and people updates

- Mérieux NutriSciences' new food chemistry laboratory is now fully functional, providing techniques such as GC, HPLC, ICP-MS, ICP-OES and atomic absorption spectrometry.
- Amy E Herr has been announced as one of the recipients of SCIEX's Microscale Separations, Innovations Medal and Award for "current and breakthrough research in the field of electro-driven separations."

For links to original press releases, visit the online version of this article at: tas.txp.to/0418/BUSINESS. Read our interview with Amy Herr at: tas.txp.to/0915/HERR.

Taking CE in Hand

More miniaturization of analytical tech with a hand-held capillary electrophoresis device

What?

A device combining capillary electrophoresis (CE) with laser-induced fluorescence detection, small enough to fit in the palm of your hand (90 x 75 x 77mm). Made from off-the-shelf components, the mini-bioanalyzer costs $500 to produce, but – say the team – still has sensitivity that is comparable with larger instruments (1).

Why?

Not only is the device likely to be easier and quicker to produce in quantity, but its portability could also lend itself to point-of-use or companion diagnostic applications. The palmtop CE has already been applied to the diagnosis of colorectal cancer, where it was able to distinguish any mutation and mutation status of the KRAS gene (1).

How?

A short glass capillary (4 cm) with a tapered end allows extraction of a single droplet from the sample. The CE separation is coupled to a laser-induced fluorescence detector, also developed by the team. The device is completed with a commercially available mini microcontroller, a battery, and an LCD screen (see image).

Who?

The project is a collaboration between scientists from the Department of Chemistry and Innovation Center for Cell Signaling Network, Zhejiang University and the Department of Cell Biology, China Medical University, China.

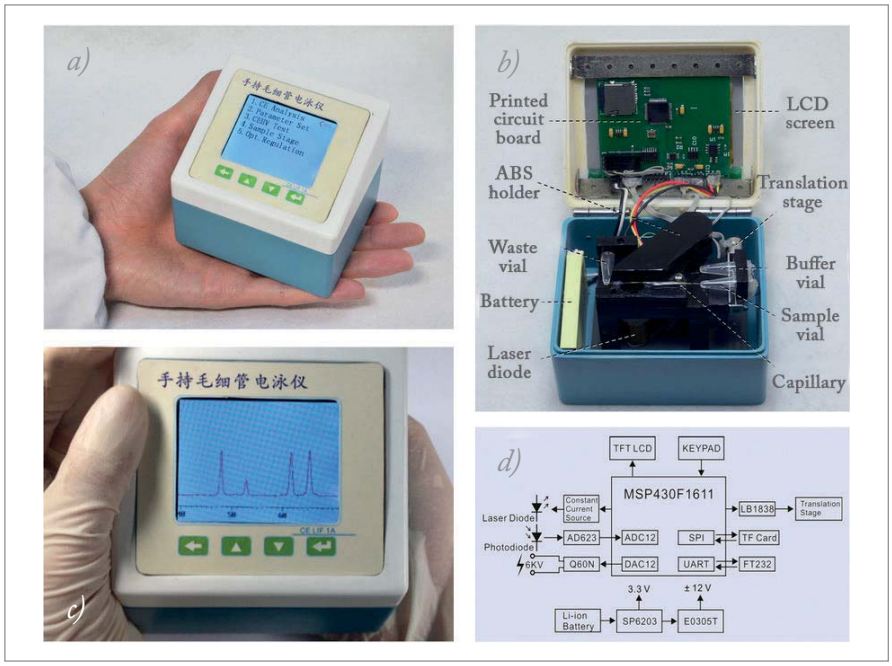
What next?

The team are certainly planning on commercializing the current device, but are already using similar low cost components in an attempt to miniaturize other devices; for example, for immune and biochemical assays.

Reference

1. *Jian-Zhang Pan et al., "A low-cost palmtop high-speed capillary electrophoresis bioanalyzer with laser-induced fluorescence detection", Sci Rep, 8, 1791 (2018).*

Figure 1. Fully-integrated palmtop CE bioanalyzer. (a) Overall appearance. (b) Uncovered appearance. (c) Electropherogram of separation of amino acids. (d) Electronic module of the bioanalyzer. Reproduced from (1).



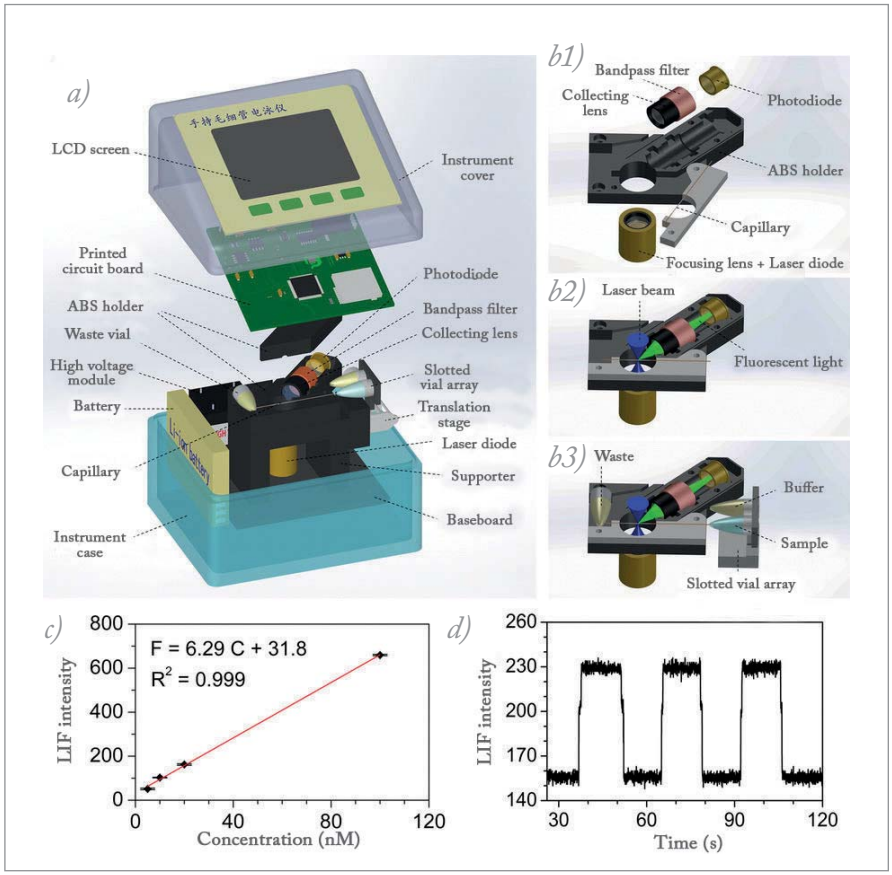


Figure 2. (a) Instrument structure; (b1–b3) LIF module: (b1) Optical components, capillary and holder; (b2) Assembled LIF module; (b3) Assembled LIF module integrated with a capillary and slotted vial array. (c) Linear relationship of fluorescence intensity to concentration in the test of LoD for sodium fluorescein. (d) Typical recording of LIF intensity signals of 5 nM sodium fluorescein in the test of LoD. Reproduced from (1).

Stop the Press: NIR Alert

Could near-infrared chemical imaging offer improved 'real-time' monitoring of tablet manufacture?

The pharmaceutical industry is in continuous need of improved process analytical technology (PAT) for monitoring, analysis, understanding, and control. We spoke to Himmat Dalvi, (Associate Professor, Department of Chemical Engineering and Biotechnology Engineering, and Pfizer Industrial Research Chair at the Université de Sherbrooke, Canada) about a new analytical tool – near-infrared chemical imaging (NIR CI) – that promises to help in the manufacture of more uniform tablets.

What inspired your research?

Pharmaceutical dosage form manufacturing is undergoing a paradigm shift, from quality by testing to quality by design. The new approach demands more product and process understanding, process monitoring, analysis and control than simply manufacturing a product using predetermined fixed process parameters and "passing" or "failing" based on quality specifications. Our main purpose in this research (1) was to evaluate the feasibility of a new process analytical tool, NIR CI (which can provide spectral and spatial information), against existing technology, NIRS (which provides spectral information only), for feed frame monitoring.

Why is it important to monitor powder potency inside a feed frame?

The feed frame drives powder blends into tablet moulds. It operates within a high-speed industrial tablet press, and offers the last opportunity to examine the powder blend before tablet compression. However, it also applies considerable strain onto the moving powder blends, which can lead to undesirable quality phenomena, such as powder segregation. To protect the final product's quality, we need to discover occurrences like this in real time, so that intervention is possible. It also reduces the need for end product testing.

What are the limitations of NIRS?

NIRS has not yet developed into a fully robust and understood PAT tool for feed frame monitoring, as parameters, such as spectral baseline variations and the variable location of NIR probes on the feed frame, lead to variable concentration predictions from lab to production or batch to batch.

How did NIR CI compare?

NIR CI not only performs on a par to NIRS for concentration monitoring, but also shows potential in probing local concentration variations, thanks to the larger sample area it makes available to us.

What difference could your research make?

Our research proves the feasibility of NIR CI for testing moving powder samples with accuracy on a par with NIRS, while also allowing analysis of an increased sample area – thus opening doors for turning NIR CI into robust PAT tool for feed frame monitoring. It provides a visual presentation of the process, which could be very useful for process operators in spotting any adverse quality phenomena, such as segregation, in real time. It could also be used for similar operations involving powder samples in motion.

Reference

1. *Himmat Dalvi et al., "Concentration monitoring with near infrared chemical imaging in a tableting press", J Spectral Imaging, 7, a5 (2018).*

Innovative solutions for LC/GC/MS systems

NEW - NEW

New IonLC Desk

IMPROVES SAFETY & ERGONOMICS

EASILY MOVABLE

KEYBOARD & MONITOR ARM

ADJUSTABLE HEIGHT

Contact us | www.ionbench.com | contact@ionbench.com

And also... Dedicated noise reduction enclosures from MS NOISE

MS NOISE

A wide range of
noise reduction enclosures
for *vacuum pumps, water chillers, ultrasonic baths, nitrogen generators, ...*

Contact us | www.msnoise.com | contact@msnoise.com

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

Translational Proteomics: Solving the Reproducibility Riddle

Data analysis in proteomics is not fit for purpose – here's how we can get on track.

By David Chiang, Chairman, Sage-N Research, Inc., City, State, USA.

Proteomics, with its unlimited potential for biomedicine, has so far fallen short. I believe the reason is simple: sophisticated big data is being processed by simplistic bioinformatics with underpowered computers. Novices are dazzled by thousands of proteins characterized at the push of a button. But experts find that it is mostly common proteins that are correctly identified, much of the quantitation is suspect, and – critically – it is hard to tell whether an identification is correct. How can we improve the utility of proteomics for identifying important low-abundance proteins? The trick is to borrow data analysis from numerical data mining in physics, not abstract statistics.

Let's say we run a pneumonia sample to identify pathogens from proteins with a mass spectrometer. We process a gigabyte file with 50K raw spectra with a fast PC program that identifies and quantifies peptides and proteins from 20 percent of the spectra at 1 percent error. When analysis is so easy, who needs hypotheses or data understanding? We just need "better" software – defined as faster and cheaper and reporting more proteins. Of course, this assumes 1 percent error is enough, a self-estimated error is always robust, and quantity means quality – all of which are obviously incorrect.

As an analogy, imagine a novel space telescope with revolutionary accuracy, which eases data analysis; no cosmologist would acquire ad hoc imaging data and then shop for prototype software that identifies the most stars for publication, sight unseen. This unscientific approach would find thousands of bright stars but give irreproducible discoveries of faint ones. Content-rich physical data are heterogeneous, with varying signal-to-noise. Deep data require exponentially more computing to mathematically scrub.

Experts can best interpret tricky data. But it's impossible to uncover one-in-a-million breakthrough data points from particle colliders, telescopes, and now mass spectrometers without computers. Such data require semi-interactive divide-and-conquer – using servers to run overnight "what if" scripts to isolate interesting data pockets for interactive analysis.

For clinical research, 1 percent error is hopelessly imprecise. In infection research, where 99 percent of detected proteins are human, 1 percent false discovery rate (FDR) could mean no pathogen information. For every 10K peptides identified, 100 are incorrectly assigned to corrupt quantitation of 100 proteins.

Clinical research requires 100 percent accuracy for a few low-abundance proteins, not 99 percent including thousands of irrelevant abundant ones. It requires a precision paradigm centered on raw data, not probability models.

In conventional proteomics, data interpretation is outsourced to calculations few understand. Researchers

"In my view, the narrative that omics means hypothesis–free science is fundamentally flawed."

choose a subjective search engine, rely on subjective probabilities to judge peptide IDs, depend on Bayesian inference to aggregate peptide IDs to identify a protein, and evaluate results quality with a single error estimate.

A precise and rigorous abstraction requires three changes. First, simplify protein inference by representing each protein with its longest identified peptide (ideally long enough to be protein-unique). Second, peptide ID filtering should use only physical mass data, not model-based parameters, such as search scores. Finally, the search engine must be demoted from a central role to merely an "educated guesser" of peptide ID hypotheses to be mass-filtered.

For example, in infection research, we develop a hypothesis, acquire data, and then interpret data. The experimental goal is to identify and characterize at least one critical peptide from its noisy spectrum. Importantly, this analysis can be manually validated by an expert.

We may hypothesize a certain pathogen, design a data-independent acquisition (DIA) experiment to maximize the odds of finding certain protein-identifying peptides, then do perhaps a dozen runs to try to capture literally one-in-a-million spectra relevant to our hypothesis. Deep research is inherently a numbers game; new technologies just help increase the odds.

In my view, the narrative that omics means hypothesis-free science is fundamentally flawed. The role of computers and artificial intelligence is to assist – not to replace – scientists who formulate hypotheses and interpret data.

More Alive Than Dead?

Why deadlines – though rarely welcome – are essential for good time management and self-motivation.

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

When checking my emails every day, I get many messages warning me about deadlines; deadlines for an abstract, for the final manuscript, for revisions, for submitting a chapter or even a book, or to register for a conference. I'm sure many of you share this deadline drama! Deadlines may be set for the principal investigator to submit a project proposal, an analytical chemist to evaluate the results of sample analysis, a reviewer to submit their report on a manuscript, a student to submit a project, a postgrad student to submit their thesis...

Usually, the dates are closer than we'd like! And how many times have each of us been frustrated by not being able to meet tight deadlines? Whether working in academia, industry or publishing, there will always be a deadline (or four) to deal with – and we will frequently find ourselves rushing to be on time.

How people respond to that depends on the individual and their way of coping with stress. Some react positively to such a pressure, becoming more productive, whereas others shut down (1). The approach may also depend on the final reward – or penalty – for meeting the deadline (or not).

But are they a necessary evil? In my opinion, deadlines serve not only as a motivator but as a powerful time management tool. If you want to be more productive, a deadline helps to focus your attention. One often needs impressive self-discipline to accomplish something without a defined timeframe. Based on my experience of teamwork, without a defined end point every person will work at his or her own pace, and rarely with highly promising results.

Some people actively demand a deadline before they even consider working on a project. Some years ago,

"In my opinion, deadlines serve not only as a motivator but as a powerful time management tool."

"Let's be honest – meeting deadlines makes us feel that we've overcome a challenge."

a colleague of mine was invited to contribute a review article for a special issue I was guest editing. They pleaded with me to give a short deadline, so that they would be obliged to work hard on the preparation of the manuscript!

Let's be honest – meeting deadlines makes us feel that we've overcome a challenge. Usually, when I am back from either a short or long break, I face many deadlines waiting to be met. At one time, I would have been anxious about managing it. Now, after years of experience, I am not discouraged – the initial feeling of panic has been replaced by the knowledge that the deadlines will motivate me, help me plan my schedule and make time management easier.

Deadline is a word whose etymology contradicts current use. After all, deadlines can make us more productive, creative, inspired… And so, rather than "killing" us, we need to use them to keep us going and to reinvigorate our motivation.

When thinking of deadlines, I'm often reminded of carbon – which under high pressure turns to diamond. (The process also needs high temperature, but, as any scientist in Mediterranean region will tell you, that's where the analogy falls down – it's even tougher to meet deadlines during a heat wave.) So next time you get one of those deadlines in your email inbox, embrace it - and follow the advice of the ancient Greek poet Hesiod in his didactic poem, The Works and Days: "Do not put your work off till tomorrow and the day after; for a sluggish worker does not fill his barn."

Reference

1. *Io9, "Why do we work better under pressure?" (2014), Available at: http://bit.ly/2C4xw3P. Last accessed: February 19, 2018.*

QC = Quality Cannabis

When it comes to quality control, do cannabis growers and suppliers need to take a leaf out of the pharma industry's book?

By Andrew James, Marketing Director, Ellutia, Ely, UK.

In many regions, cannabis is now considered by the public as a medicine, perhaps not so different from aspirin or ibuprofen. However, when you judge medical cannabis by the standards of the pharmaceutical industry, it's easy to see that it falls short in terms of rigorous safety and potency testing. The grand challenge for global cannabis producers and processors is to ensure the same standard of reliable, safe and consistent products as pharmaceutical (and indeed food and beverage) manufacturers.

Despite many countries and states having passed regulations that allow medicinal and/or recreational cannabis use, regulation across regions for content, composition, adulterants, potency or levels of toxic residues are lacking standardization. Strong regulations are being introduced in some regions (California, for example, see tcs.txp.to/0318/pesticides), but the responsibility for testing generally lies at the feet of a small number of approved independent testing laboratories.

For consumers, the lack of regulatory standardization means that it can be difficult to make informed purchase decisions. If no product carries an approval, consumers tend to assume that all products are of equal quality and will focus their purchasing decision primarily around price. In such a situation, it's all too easy for unscrupulous or careless vendors to sell cannabis and cannabis-

"When you judge medical cannabis by the standards of the pharmaceutical industry, it's easy to see that it falls short in terms of rigorous safety and potency testing."

"There should be much more in-house testing going on throughout the supply chain to identify and eliminate problems earlier."

derived products with potentially harmful contaminants, such as mycotoxins or pesticide residues. From an analytical chemistry viewpoint, this is more than a little alarming.

But what is the answer? Although testing at independent laboratories is a crucial final step before sale (I am certainly not advocating self-certification!), I believe there should be much more in-house testing going on throughout the supply chain to identify and eliminate problems earlier.

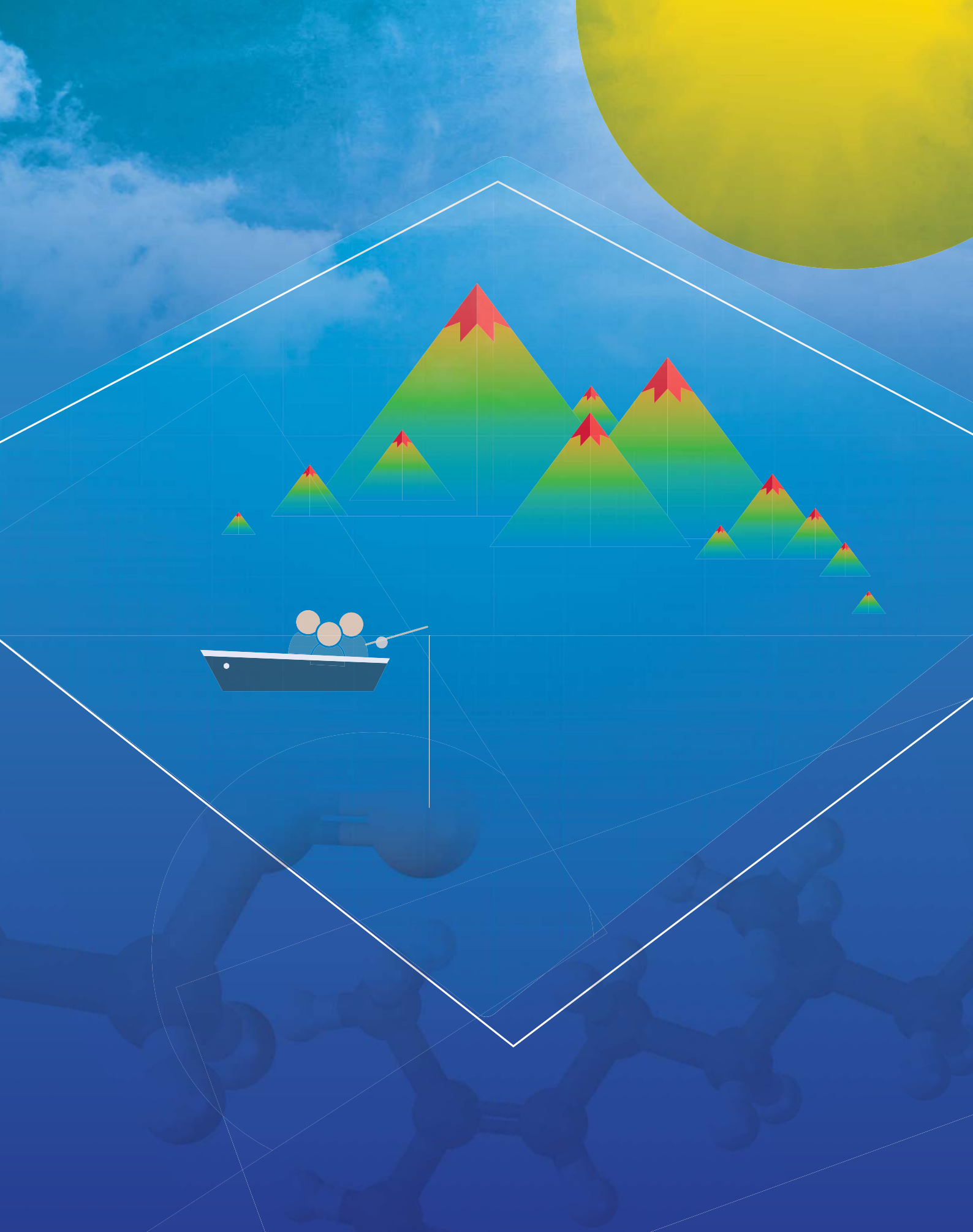
Bringing testing in-house is often dismissed because of a belief that it will be too expensive and complicated, but both the costs and complexity are overestimated, in my view. Analytical instrumentation that was previously thought to require laboratory experience and a deep understanding of analytical chemistry is now being used in cannabis testing after relatively little training. Today, a focus on cost-effective and user-friendly instruments is increasing the application base into areas with less experience – including the cannabis industry. Simplified and robust gas chromatography (GC) systems, for example, are becoming more widely employed in potency testing, terpenes profiling, pesticide screening and residual solvents analysis, all of which can significantly benefit the cannabis industry. And many vendors are developing solutions specfically for the growing cannabis market. Increased communication and training from vendors and instrument manufacturers is needed to help those in the cannabis industry navigate their way around the complexity of the analytical instrumentation available.

It is clear to me that the cannabis industry requires major change before it can truly flourish. Just like the pharma industry, the cannabis industry (and consumers) can only benefit from carrying out regular QC checks. Indeed, analytical science must be universally applied to verify the quality of products and guide their appropriate use (for example, high CBD/low THC strains for medical use).

And so, I support standardizing testing methods and greater regulation; however, it's important that testing doesn't become so costly that smaller companies cannot compete. The solution lies in low-cost, simple-to-use analytical instrumentation, applied early and throughout the supply chain. With better information, companies can make more informed business decisions, to help them expand and become more competitive. Meanwhile, increasing quality and reliability will build consumer confidence and aid market growth.

Three Gurus of Comprehensive Chromatography

With the 42nd ISCC and 15th GC×GC Symposia soon rolling into Riva Del Garda, we grill three superlative separation scientists on the progress – and pitfalls – of comprehensive chromatographic techniques.



What techniques fall under the umbrella of "comprehensive chromatography"?

Pat Sandra: For me (by definition) comprehensive chromatography requires two-dimensional (chromatographic!) separation with on-line, full continuous development in both dimensions. Off-line fraction collection after the first dimension and analysis on a second column is, in my definition, not comprehensive, and neither are heart-cutting (for example, GC-GC) and multiple heart-cutting (for example, mLC-LC) methods.

All individual chromatographic modes combined on-line in two dimensions can be considered comprehensive. Combining phases is only possible with LC and SFC as they are both in the fluid state.

Lourdes Ramos: For years, the main (and almost exclusive) comprehensive chromatography techniques (CCTs) in use by researchers have been GC×GC and LC×LC, although the latter has been slower to develop. Several research groups have now started to explore the feasibility of alternative couplings, in particular SFC×SFC and CE×CE. Investigations are at an early stage but the promising results reported to date and the potential advantages for particular application fields (for example, SFC×SFC in oil and petrochemical research) will encourage further evaluation of these new CCTs.

Peter Tranchida: Good answers – I will only add that there have also been a few LC×GC experiments reported over the years. However, heart-cutting LC-GC appears to have a much more solid basis, and a wider past, present and (probably) future use. Apart from GC×GC and LC×LC, it is hard to make predictions on the future of other comprehensive 2D chromatography methodologies, as they are currently used in only a few research groups.

How established are the two main technologies (GC×GC and LC×LC)?

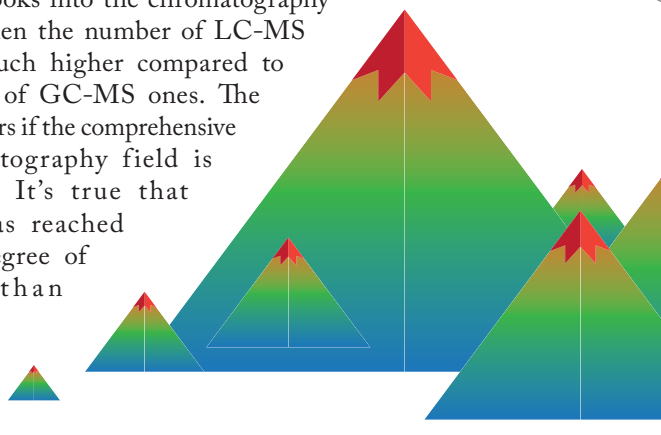
LR: Today, GC×GC is a well-accepted analytical technique for the characterization of complex samples, particularly in the petrochemical, food and environmental fields. GC×GC can be considered a mature technique – that said, technological advances continue, mainly associated with the hyphenation of the technique with advanced detectors offering extra identification capabilities. By contrast, LC×LC has yet to reach maturity, despite the important progress made in recent years. Although suitable instrumentation has become commercially available, a number of technical issues limit its practical application, including problems with mobile-phase compatibility, proper focusing of the transferred fractions and detection capabilities.

PS: I would argue that both GC×GC and LC×LC are mature enough to be implemented in R&D and (to a lesser extent) in QA/QC, with hardware and software commercially available and performing well. The nature of the mobile phase means that peak capacities in GC×GC are higher than in LC×LC. On the other hand, LC×LC is more powerful, as more modes can be combined (higher orthogonality) and hyphenation with high-resolution mass spectrometers is more successful (and straightforward) because of the higher peak widths in the second dimension compared to GC×GC.

However, for the most part, CCTs have not yet fully moved from R&D to QA/QC labs. The exception is in the petroleum industry, where group type separations are extremely important. I have visited petrochemical sites where GC×GC is connected on-line to distillation/cracker towers.

> "Both GC×GC and LC×LC are mature enough to be implemented in R&D and (to a lesser extent) in QA/QC."

PT: If one looks into the chromatography literature, then the number of LC-MS papers is much higher compared to the number of GC-MS ones. The opposite occurs if the comprehensive 2D chromatography field is considered. It's true that GC×GC has reached a greater degree of maturity than LC×LC; I



The Gurus

Pat Sandra

Pat Sandra is Emeritus Professor of Organic Chemistry at Ghent University, and Founder and President of the Research Institute for Chromatography (RIC), Kortrijk, Belgium. "Through the activities of RIC, I got in touch with the real analytical needs of the industry and found we could help in providing solutions that are economically relevant. Moreover, it allowed me to keep my best PhD students around me, which resulted in high scientific output in a non-academic environment," he says.

Lourdes Ramos

Lourdes Ramos is a research scientist at the Department of Instrumental Analysis and Environmental Chemistry, in the Institute of Organic Chemistry (CSIC, Madrid, Spain). Her research activities include the development of new miniaturized sample preparation methods for the fast determination of organic microcontaminants in environmental and food samples, as well as the evaluation of new chromatographic techniques – especially GC×GC-based approaches – for unraveling the composition of complex mixtures.

Peter Tranchida

Peter Tranchida is an Associate Professor at the University of Messina, Italy. A food chemist, he has a great passion for separation science. Peter is a proponent and practitioner of multidimensional chromatography – and often adds a third, mass spectrometric, dimension. He believes these powerful methods can provide new insights into old samples, and help unravel the composition of complex food samples. "After each analysis," Peter says, "I feel like a child opening up a Christmas present."

just hope that stability does not lead to stagnation. Comprehensive 2D-LC may be less mature, but it is undergoing a lot of exciting evolution.

What is the key benefit of comprehensive chromatography?

LR: Comprehensive techniques solve problems that are difficult or impossible using the corresponding monodimensional (1D) chromatographic technique. Their improved separation power has many benefits, from increased sample throughput (by simplification of the sample preparation step or simultaneous screening of several groups of compounds co-eluting in 1D techniques), to the accurate characterization of complex mixtures, or the discovery of emerging issues (such as previously unknown pollutants).

PT: CCTs generate a planar separation space. Due to the use of two different selectivities, there is a higher chance of analyte separation, and the room for peak accommodation (peak capacity) is greatly increased.

PS: Because of the increased peak capacity, comprehensive techniques are having an impact on (mainly untargeted) analysis of complex samples; for example, petroleum samples by GC×GC, or post-translational modifications in (bio)pharmaceuticals by LC×LC. In future, we can expect to see comprehensive separations being used to streamline workflows; for example, in QA/QC labs LC×LC-UV is simpler than LC-MS for impurity screening.

> "The greatest impact has been in untargeted applications, where comprehensive chromatography has revealed hitherto unsuspected complexity."

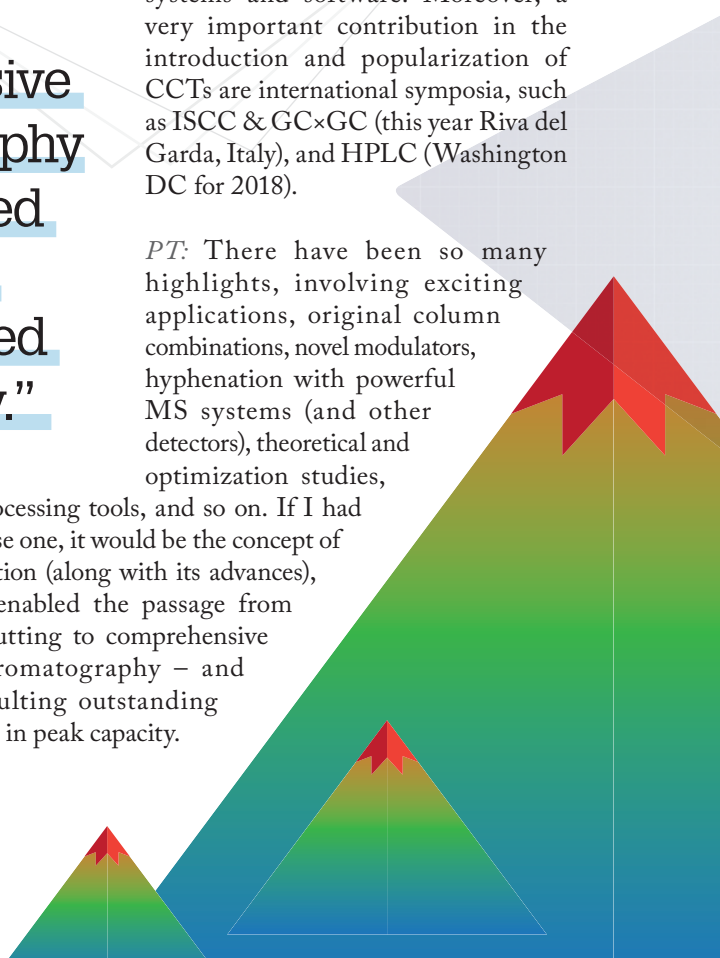
What are the big milestones so far in the development of CCTs?

LR: Two key aspects contributed to acceptance of GC×GC. First, modulators allowing the quantitative and accurate transfer of the eluent from the first dimension into the second one as a narrow and focused fraction. Second, software allowing the processing and management of the large volume of data generated by the technique.

Concerning LC×LC, the relatively recent commercialization of several instruments is moving this technique from highly specialized laboratories into more general use.

PS: For me, the standout factors in their development have been the enthusiasm of proponents in the early years and the recent introduction of commercial systems and software. Moreover, a very important contribution in the introduction and popularization of CCTs are international symposia, such as ISCC & GC×GC (this year Riva del Garda, Italy), and HPLC (Washington DC for 2018).

PT: There have been so many highlights, involving exciting applications, original column combinations, novel modulators, hyphenation with powerful MS systems (and other detectors), theoretical and optimization studies, data processing tools, and so on. If I had to choose one, it would be the concept of modulation (along with its advances), which enabled the passage from heart-cutting to comprehensive 2D chromatography – and the resulting outstanding increase in peak capacity.



Where are CCTs most valuable?

PT: The greatest impact has been in untargeted applications, where CCTs have revealed hitherto unsuspected complexity. For targeted applications, on the other hand, the specificity of mass spectrometry plays a fundamental role.

LR: The unique separation possibilities of GC×GC have made it particularly desirable for petrochemical, food and fragrance applications. However, GC×GC is now increasingly used for forensic, environmental and health application studies, because its enhanced resolution capability allows non-orientated (and retrospective) studies.

PS: I'll go a step further and say that CCTs are of value in all research areas where detailed profiling and fingerprinting is of utmost importance or where 1D separations do not provide sufficient resolving power – in other words, analysis of complex samples. However, they are not yet fully accepted in QA/QC labs for several reasons:

- QA/QC labs (and the regulatory organizations controlling these labs) are conservative
- For many applications, it is too expensive to change standard operating procedures (SOPs)
- In many cases, no SOPs are available with these techniques
- QA/QC labs are mostly doing targeted analyses
- Quantitation is still difficult, requiring complicated software

How does the impact of LC×LC compare with GC×GC?

"In the long term, I believe that LC×LC will prove more impactful and widely applicable than GC×GC."

PS: In the long term, I believe that LC×LC will prove more impactful and widely applicable than GC×GC for three reasons. First, there are many more involatile compounds than volatiles. Second, a larger number of orthogonal modes of LC can be combined, compared with GC. Third, LC is much less efficient than GC, so the benefit of additional dimensions is greater.

So why hasn't LC×LC taken off? There are two main reasons: i) a large number of LC methods are developed under regulated conditions so are time-consuming to change, and ii) commercially available instrumentation was lacking until recently. Moreover, LC users have proven to be much more conservative than GC users.

However, applications for LC×LC are emerging, including foodomics, stability studies of small-molecule pharmaceuticals, post-translational modifications in biotherapeutics, omics, and heavy petroleum products.

LR: LC×LC allows the analysis of both volatile and non-volatile compounds, which in principle could mean that it has broader applications once it reaches maturity. Nevertheless, the improved resolution provided by GC×GC and the limitations of LC detectors makes me think that the two techniques will remain complementary for a long time to come.

PT: LC×LC was introduced around the same time as GC×GC, over 25 years ago. However, the number of published papers in LC×LC is much lower than in GC×GC. There are certainly more variables to be optimized in LC×LC, and more difficulties in the coupling of two LC dimensions. Furthermore, the first-dimension/second-dimension flow ratio is often low, leading to problems with dilution and MS hyphenation.

What have been the pitfalls in GC×GC development? Any lessons learned for LC×LC?

LR: Looking back through the literature, CCTs have been used for the resolution of an extremely limited number of analytes. And though this may be acceptable as a proof-of-concept, it is difficult to justify in subsequent application studies. Likewise, researchers must determine whether the goal of their study justifies the use of the powerful CCT configurations sometimes seen.

PS: I agree with Lourdes that GC×GC is too often used in studies where fewer dimensions would have sufficed. For targeted analysis GC-MS/MS remains the standard, and even in untargeted applications GC-GC and mGC-GC may have sufficient resolving power. GC×GC has other limitations too – high-speed (low resolution) MS systems are still mandatory for optimal performance, data handling is complicated, and too few quantitative studies are published. We need to develop more validated SOPs for QA/QC, and emphasize producing quantitative data with relative standard deviations (RSDs), rather than a nice contour plot for a report/publication.

PT: An important lesson is that we must give mass spectrometry its due. We are apt to focus too much on the spectacular appearance of 2D chromatograms, and sometimes forget about the great amount of information present in mass spectra – and the capability of MS to distinguish between co-eluting compounds.

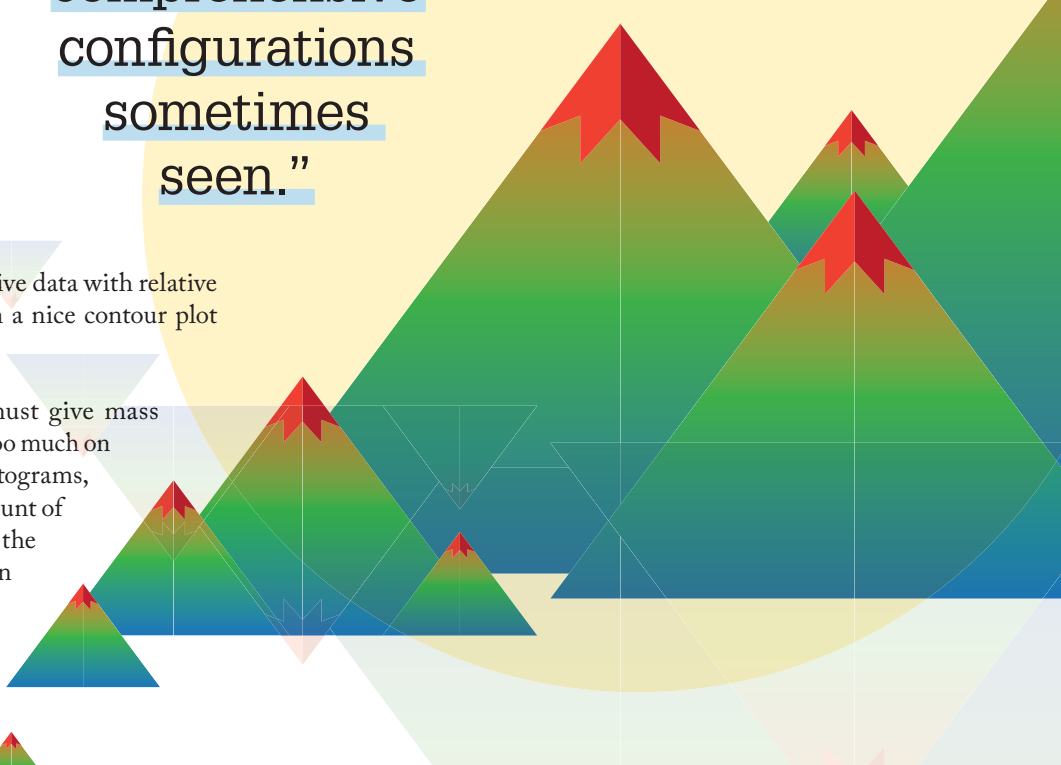
> "Researchers must determine whether the goal of their study justifies the use of the powerful comprehensive configurations sometimes seen."

PS: I agree with Peter – developments in mass spectrometry in recent years have been immense. Ultimately, we must focus on what technique gives us the information we need.

What is the promise of these techniques in the future?

LR: In my field of environmental analysis, GC×GC was, until recently, almost exclusively used for identification and quantification of preselected compounds in mixtures too complex to analyze by conventional GC. Now, interest is slowly turning to non-targeted strategies for retrospective analysis and identification of emerging contaminants. The ability to assess the total burden of organic pollutants in a single analysis, including contaminants not previously described, is an opportunity to better protect ecosystems and the people who rely on them.

PT: As we've discussed, the greatest impact will be in untargeted applications – both in scientific papers and meetings, "the capability of such technologies to resolve 100s if not 1000s of compounds",



has been often emphasized – and so I can envisage great opportunities in proteomics, lipidomics and metabolomics, with the goal of improving health. Health can also be related to food, and there have been several interesting investigations focused on the elucidation of bioactive food constituents.

What are the barriers to wider use of CCTs?

PS: First, there is an education problem – knowledge and know-how in chromatography is decreasing among scientists, while the complexity of CCT instrumentation is increasing.

For selected applications CCTs are far superior (qualitatively and quantitatively) compared with data obtained with 1D, but too often that isn't demonstrated clearly in the literature – the analytical goal of studies must be well defined and documented. I hope future research will concentrate on untargeted analysis, and illustrate the benefits over 1D with real practical problems. For example, in petrochemical characterization no 1D method can compete with GC×GC in giving group type characterization (in preliminary experiments identified by mass spectrometry) and quantification via FID detection.

However, as mentioned above, GC×GC should not be in competition with high-end mass spectrometers – the power of a GC (1D and 2D heart-cutting) combined with QTOF-MS or Orbitrap is immense. When developing methods, "figures of merit" should be compared between 2D and 1D, to avoid unnecessary complexity.

LC×LC still has a number of technical challenges that limit its use – widespread adoption won't happen until the problem of a high flow in the second dimension and low flow in the first dimension is solved.

> "Widespread adoption won't happen until the problem of a high flow in the second dimension and low flow in the first dimension is solved."

PT: I would like to see more compact, less expensive (to purchase and to operate), and easier-to-use instrumentation. The sheer bulk of the instrumentation is an obstacle to widespread adoption – a conventional GC oven occupies about the same space as a triple quadrupole MS system! I would also like to see flexible instrumentation with the capability to switch between one-dimensional, heart-cutting and comprehensive 2D operational modes.

LR: In recent years, GC×GC has been increasingly combined with more powerful detectors, in particular high-resolution mass spectrometers. Ion mobility spectrometry adds a useful extra dimension to the separation-plus-detection process for particularly complex determinations. Another priority is modulators: reducing consumables in cryogenic modulators, improving the performance of those based on valve systems or (better still) developing a universal modulator.

TECHNOLOGY PANEL: COMPREHENSIVE CHROMATOGRAPHY

Experts from four major instrument manufacturers tell us what's new in comprehensive separations – and give their predictions for what the future has in store.

A BRIGHT FUTURE

By Tom van de Goor, Sr R&D Manager, Agilent Technologies, Waldbronn, Germany.

Agilent Technologies has seen comprehensive two-dimensional techniques become increasingly established, as customers realize that the higher separation power can save them time in their overall workflow. GC×GC systems have long been on the market. Commercial LC×LC systems appeared only a few years ago but are already being used widely in academia and industry. For complex samples, such as petrochemicals, biopharmaceuticals, and natural products, or in omics-types studies, we even see combinations like LC×LC used with ion-mobility separation and Q-TOF MS (LC×LC-IMS-Q-TOF) – we could call this a five-dimensional separation.

GC inherently has more separation power than LC; but LC is probably applicable to many more compounds than GC, and so the potential impact of LC×LC systems is much higher. We have seen a strong rise in the use of other 2D-LC techniques, such as multiple-heartcutting (mLC-LC) or high-resolution sampling (HRS-LC×LC), in the pharmaceutical and chemical industries, most often in the development stage of new drugs or chemicals. Here, moderately complex samples with 10 to 100 components are being analyzed by LC×LC to save time and get results faster compared with multiple 1D LC methods. Another area of impact is within the strongly growing biopharmaceutical space, where highly complex samples need greater separation power.

A challenge for comprehensive chromatography techniques (CCTs) has been information overload. Completely separating and identifying every component in a mixture sounds desirable, but most analysts have a few vital questions; it is challenging when the answers are hidden in overly complex data sets. For example, the combination of GC×GC and high-resolution accurate-mass (HRAM) MS has proven a powerful comprehensive technique for differentiating complex samples and discovering unknown components; as a result, data are often complex. Software can be very helpful in automating differential analysis (identifying the differences/similarities in sample sets), and identifying the chemical characteristics of the differing components, but it may not produce a comprehensive chemical explanation. Better software is perhaps the key to expanding the role of GC and 2D-LC MS-hyphenation in general routine analysis.

Commercially available GC×GC and LC×LC systems are already a huge step forward compared to the "homebrew" systems from some years ago. However, there are still opportunities to achieve further integration with MS, especially in terms of data analysis. In the QA/QC area, compliance of all software packages for data acquisition and data analysis would be required. Moreover, we could imagine dedicated analysis kits consisting of columns and methods for specific applications. Size reduction could become important, too, along with software tools to assist the user in the method setup. Finally, even though the overall, ongoing costs might be lower in the complete workflow, finding the initial capital remains a key barrier in the adoption of commercially available GC×GC and LC×LC systems.

> "The most obvious opportunities are within research and academia as regulatory testing constraints act as a barrier to the adoption of new technology in general."

That said, there is no shortage of interest in CCTs, with conference sessions on multidimensional chromatography often standing room only. The most obvious opportunities are within research and academia as regulatory testing constraints act as a barrier to the adoption of new technology in general.

In my view, there is no technical reason why CCTs cannot be embedded into today's workflows. In general, the analytical world is rather conservative and we rarely see new technologies "taking off" immediately. However, we are confident that CCTs – and especially LC×LC – will continue to grow and become an established technique in analytical labs around the world and in multiple applications.

BALANCING ACT

By Claude R Mallet, Senior Scientist, Work Flow Integration, Separation Technologies, Waters, Milford, Massachusetts, USA.

High sensitivity and fast separation are the top features requested from users for new instrumentation. Those features are highly desirable, but often users will need to spend more time on other key steps, inevitably creating bottleneck effects in the analytical workflow.

Multidimensional chromatography solutions clearly offer superior performance for many applications involving analysis of complex matrices. However, this increased performance comes with increased complexity. The addition of fluidics, pumps and circuitry has fed the perception that it is difficult to master CCTs, particularly LC×LC, which has slowed down adoption.

Comprehensive LC×LC is primarily used to slice a single high-resolution separation of a complex sample into discrete volumes followed by a re-injection onto a second resolving dimension. The resulting separations are then re-assembled using 3D contour plot software. In this configuration, the overall resolution is governed by timed-base multiplexing using slow elution parameters in the first resolving dimension and fast gradient conditions on the second dimension. The feed rate between both dimensions and refocusing issues are the prime operating parameters.

In a recent collaborative publication, a loop/trap using a built-in dilution stream with a pulse elution of increasing eluotropic strength on the first dimension resolved three main issues with comprehensive LC×LC – under-sampling, refocusing, and time constraints (1). With a time decoupling effect, both separating dimensions are now totally independent of each other – and that opens opportunities for novel separation strategies for complex matrices.

With today's technology, it is possible to create tailored multi-separation platforms. For example, many fields are locked into strict operating parameters and a vast majority of methods that use standard HPLC with UV detection as a starting point for low cost operation. Most users can relate to the low performance of validated LC-UV methods when dealing with unknown entities; however, the idea of switching to UPLC-MS and going through re-validation is daunting. With a selective heartcutting approach, a validated method can be directly coupled to a UPLC-MS method via a loop/trap interface. In this type of setup, an unknown signal from a validated HPLC/UV separation is simply diverted to an enrichment trap for desalting, refocusing and solvent exchange. The captured entities are back flushed onto a UPLC-MS separation, thus providing instant MS data with either low or high resolution capability.

More sensitive detection leads to more complex systems, and a need for intuitive, easy-to-use control software. Today, most software is constructed to control a small number of components for simple separation and detection – perhaps a single pump, autosampler and detector or a single platform. In future, multi-component software control will offer more options, including automation and multiplexing capability, leading to fully integrated workflows that include sample preparation, separation and detection. Upgrading to XYZ robotic handlers with single or dual arms will use time-dependent features to create a seamless and fully integrated workflow.

Reference

1. *SS Jakobsen et al., "Increasing flexibility in two-dimensional liquid chromatography by pulsed elution of the first dimension: a proof of concept", Anal Chem, 89, 8723–8730 (2017).*

TIME TO THINK 2D

By Marco Koenen, Managing Director, JSB Group and ZOEX EU, Eindhoven, the Netherlands.

As a partner of GC×GC pioneer ZOEX, JSB has a broad view of the market and applications of GC×GC technology. What are we seeing? GC×GC is increasingly moving into standard QC, which tells us that the technology is maturing. In addition, there's a shift from thermal modulation towards flow and reversed-flow modulation, making the technique accessible at a lower-budget. On the other hand, we have also seen high-end GC×GC QTOF applications growing in number, mainly in environmental or food research.

In contrast, LC×LC is relatively new and requires a reasonable degree of application-specific and method development experience. The early adopters are all looking at this technology but I have not seen it trickle down to general QC applications.

Comprehensive technologies give the researcher or analyst a head start, and today's technology is easier to use than ever. Software allowing "blinking" is a great help in evaluating images, group typing is becoming a standard option, and automatic reporting has become much easier. More and more contract laboratories active in the petrochemical industry and environmental analysis are looking at GC×GC as a viable technology for their day-to-day work, and we expect to see other industries follow suit.

In the near future, we expect to see greater use of comprehensive 2D separations in proteomics, allowing researchers to more completely map the physiology of a tissue. Food safety is another area where we expect to see growth, as regulations demand deeper and more precise analyses.

JSB is dedicated to supporting GC×GC as a technology, and we are investing heavily in hardware and software development. Personally, I am a strong believer in the technology, having seen many examples of customers solving huge problems by using comprehensive techniques. I believe that 2D is the future, and that many industries should be "thinking 2D".

COMPREHENSIVE COLLABORATIONS

By Björn-Thoralf Erxleben, Senior Manager, Shimadzu Europa GmbH, Duisburg, Germany.

The growth in comprehensive chromatography technologies, such as LC×LC, GC×GC, and even LC×GC, is exciting. Though heartcutting multidimensional systems are typically easier to operate, the full advantage of orthogonal multi-dimensional chromatography is only addressed by comprehensive chromatography.

Shimadzu has been manufacturing GC×GC systems for many years, and it's been great to see the number of systems in use growing. But we recognize that the complexity of the systems and applications require expert operators, as well as solid data processing and interpretation.

The advantages of LC×LC systems are clear, but the number of systems currently up and running is still somewhat small, thanks to the tricky combination of a very slow and a very fast separation, plus dilution of the sample resulting in very low concentration in the second dimension. Miscibility issues between first and second dimension and the necessary use of MS detection also limit the solvent selection. A combination of these factors means that so far we mainly see these systems used in R&D and operated by experts.

Looking back over the past decade, advances in MS detection played a fundamental role in the development of comprehensive chromatography methods. Improved sensitivity compared with standard detectors and the chance to perform structural elucidation with fast MS systems have made a big difference.

"We believe that technology optimization is best achieved when instrument suppliers work hand-in-hand with key researchers at universities and institutes."

We've come a long way since the first 2D chromatography systems, but I look back with fondness to seeing those first applications running in a customer lab. Although the instrumentation was basic, the potential of these techniques was obvious very early on, and those initial systems were the starting point for improvements in hardware and software that are still ongoing. Our key technology challenges these days are

development of flow modulators for GC×GC and optimizing the transfer valve in LC×LC, as well as software optimization for method development.

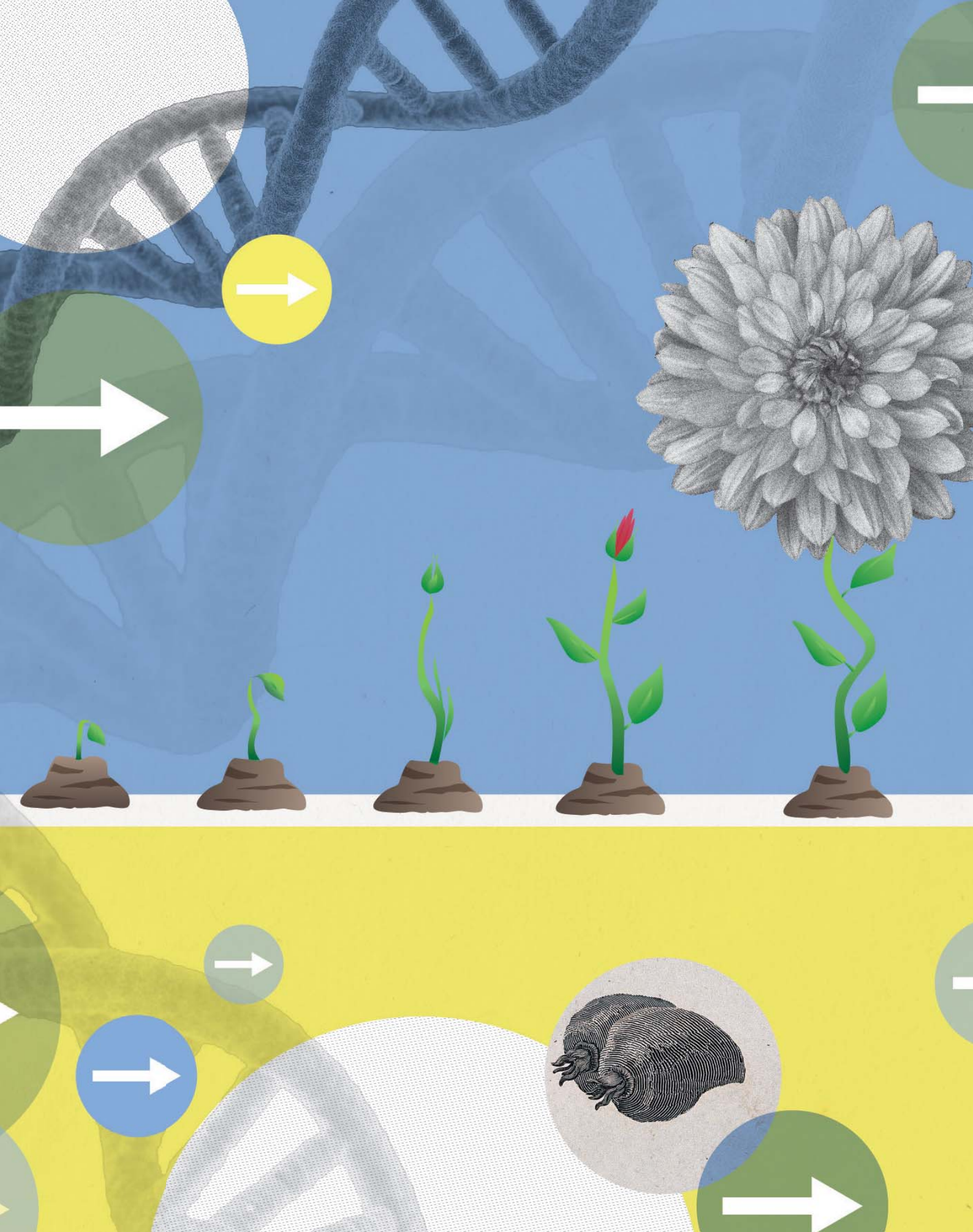
The challenge is to make even complex aspects, such as processing software and peak integration from the separation contour map, accessible for non-expert users. Better integration of special features for comprehensive chromatography in "standard" chromatography software is one aspect – it is important that the user interface allows a simple switch between standard features (library searches, integration and quantitation) and special features (3D mapping, image comparison, and so on).

Looking beyond GC×GC and LC×LC, coupling of two different techniques (for example LC×GC) still has many challenges, with the analytical requirements and limitations of both techniques to be considered. Although the advantages of a LC sample prep step before GC separation are obvious, only a few such systems have been built so far. Recent and future development has also been focused on SFC and LC separations, with SFC×LC generating interest because of the potential for analysis of complex samples and for full automation of both separation and extraction. Especially on the LC/SFC side, we expect more ready-to-use application systems for routine tasks. Whether those systems are comprehensive LC×LC systems or heartcutting multidimensional LC(SFC) systems will depend on the specific application and ease of use for operators.

We believe that technology optimization is best achieved when instrument suppliers work hand-in-hand with key researchers at universities and institutes. Shimadzu has long-term collaborations ongoing with Luigi Mondello and Paola Dugo at the University of Messina, who together have been a driving force for developments in terms of comprehensive LC×LC and GC×GC. Working with academic groups is at once a challenge, motivation and incentive for our development and application teams.

SUPPORTING GROWTH: FROM SEED TO STEM

Whether tapping into the relentless curiosity of the under 10s, furthering the understanding of high school pupils or equipping grad students for the most promising future, meet three scientists working to inspire the next generation of analytical chemists.



REACHING OUT

Susan Olesik, Dow Professor and Chair at The Ohio State University, USA, explains why time and effort spent inspiring young minds is an investment in the secure future of science, technology, engineering and mathematics (STEM) fields.

Tell us about your school outreach initiative…

In 1999, I started an outreach program called "Wonders of Our World" in elementary schools. Now in its nineteenth year, the goal of the program is to improve science education in elementary schools. We bring scientists and students from the university into schools to carry out scientific experiments with the kids. So far, we have reached over 10,000 children and 1,000 teachers. We "adopt" schools for a period of three years, and over that time students involved in the program achieve a 30 percent increase in their standardized test scores in science and math. Those scores stay high even after we leave – so we know we've had a long-term impact. We have also seen a number of volunteers decide to go into science education as a result of the experience, so it's had benefits all round.

There is a lot of research indicating that middle school is the point at which women and underrepresented minorities decide against science as a career. So we have added a middle school outreach program and a high school mentoring program.

Why did you start the initiative?

It was an interesting confluence. When I was teaching general undergraduate chemistry, I found myself talking to a student who didn't know how to balance an algebraic equation – middle school math. That same month, I visited my daughter's elementary school classroom as a helper, and found that although the students were taught basic math, they struggled to apply it. I realized that the school needed to fortify their science and math, and that's where this program got started. A year later, I took the program into inner-city Columbus, where it's had a major impact. People from inner city schools across the country visit us and go on to model some of our programs in their areas.

Why are such programs important?

In the USA, we don't have enough science and engineering majors to support our growing STEM sector, and I think that's true in most countries. Showing students that science is an exciting career is not only important when it comes to filling currently vacant STEM roles – but also, ultimately, in fortifying our economy. Another issue, especially in inner-city USA, is that many underrepresented minorities don't consider college as an option – let alone a career in STEM.

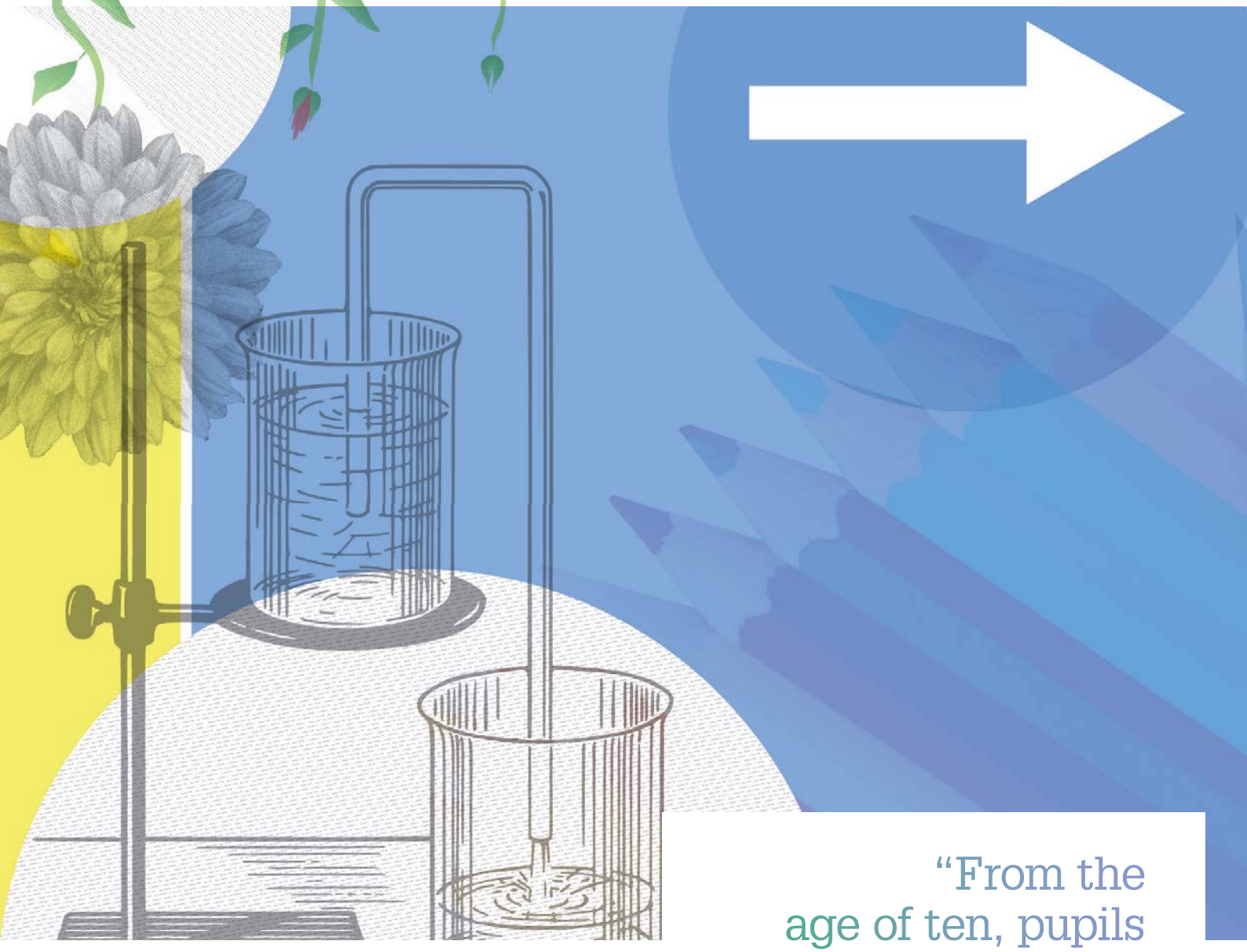
It must also be very rewarding…

It's incredible to see how excited the kids are when they see our vans pull up at their school – they are so enthusiastic about the science they're doing. Elementary school kids are some of the best scientists I have ever seen. When I talk to them after the experiments, I often marvel at the wonderful questions they ask, and wonder why my college students aren't as inquisitive as these young kids! We are now starting to see some of the minority students who we worked with in Columbus city schools volunteering in our program at OSU, and helping the next generation move into college – that's very rewarding to see.

> "Showing students that science is an exciting career is important when it comes to filling currently vacant STEM roles – and in fortifying our economy."

What advice would you give to analytical scientists who want to be better mentors?

If the field of analytical chemistry is to blossom, I think we need to support each other. I worry that the field is not as strong as it needs to be, and I would like other analytical chemists to consider mentoring junior faculty and recruiting more students into this vibrant field.



"From the age of ten, pupils start thinking that science is not for them."

MAKING EVERY ENCOUNTER COUNT

Helping people to engage with chemistry is key to boosting public perception of its importance.

With Dayna Mason, Education Coordinator at the Royal Society of Chemistry, UK.

Science outreach is increasingly important. The number of people applying to chemistry degrees in the UK is falling, and recent report discovered that – even from the age of ten – pupils start thinking that science is not for them (1). It's not that they don't enjoy studying it, but they don't see science as a career path.

Perhaps even worse, a RSC report (http://RSC.li/PAC) discovered that, in the UK at least, the public barely engage with chemistry at all. This void leaves chemistry vulnerable to stereotypes and misunderstanding. People generally recognise the value of chemistry but they don't have tangible examples of

"By having open conversations with people about what they do, chemists can make it more accessible."

chemistry in action and they don't feel informed or confident about the subject. Additionally, most people associate chemists with pharmacists and are not aware of the wide range of industries that chemists work in. But there's a lot we can do together to change this.

Encouragingly, the "Science for All" work performed by the UK's Department of Business Innovation and Skills (BIS) shows that people do want to know more about chemistry now than they used to, but that they feel less informed than in the past. By having open conversations with people about what they do, chemists can make it more accessible.

Teaching teachers

Four days a week, I work for the Royal Society of Chemistry (RSC) as one of the Education Coordinators (ECs) in Wales. The fifth day, I specifically work for the School of Chemistry at Cardiff University in outreach and engagement.

In my RSC role, I help teachers teach chemistry more effectively and support engagement with chemical sciences across the whole region. Working with teachers gets more "bang for your buck" since each teacher can reach hundreds of children. In my university role, we work with teachers and with students; Cardiff University delivered "Spectroscopy in a Suitcase" workshops until last year (a scheme previously covered in this very magazine [tas.txp.to/1116/suitcase]). I also supervise some final year Bachelor of Chemistry students running workshops in schools. Much of the work I do at the university is about helping undergrads and postgrads gain the skills to do outreach; for example, to deliver workshops or to run activities at public events.

When I have my RSC hat on, I help teachers find free resources (like those on our website), and demonstrate activities; for example, I recently ran a "DIY Chemistry in the Classroom"

workshop which made use of things you could buy from the supermarket. We dyed a cotton sheet yellow using turmeric, and turned it red by painting on it with bicarb – a nice way of looking at acids and alkalis. We also did some of the experiments from the RSC website; for example, investigating the absorption of water in disposable versus cloth nappies.

Beyond these workshops, our website – Learn Chemistry (www.rsc.org/Learn-Chemistry) – is a one-stop shop for chemistry teaching resources. The RSC also has a grant scheme called the Outreach Fund, which can offer up to £10,000 for outreach projects for schools or the public.

My personal driver? Helping people! Whether it's a school audience, teachers, RSC members, or the general public – I like being there to help them to understand something, or to see something in a different light. I really enjoy watching other people being thrilled by science. Another big motivator is giving people the confidence to do outreach – and ensuring that their activities are clear, engaging and inspiring. When it goes well, they come back buzzing!

Keeping it real

The RSC has put together a Communication Toolkit covering seven key principles; the first one is that every encounter counts. It's important for chemists to get involved, and we have 50,000 members who could make a massive difference.

You don't necessarily have to work in schools, but you can help overthrow stereotypes about chemists and chemistry. Start small, with the conversations you have in everyday life – tell people what excites you about your work. Why is it important? Keep it simple. Last year we handed out glo-sticks during Cardiff's Pride Cymru event and talked to people about the chemistry of the glo-stick. Even short interactions like these can get people thinking about the chemistry all around us.

Reference

1. *King's College London, "Aspires 2" (2017). Available at: bit.ly/2oP7JTR. [Last accessed April 3 2018]*

"Each track addresses an area of importance, where a lot of progress is being made in the contemporary analytical chemistry world."

CHARTING A COURSE

The EACH Erasmus Mundus Master's program coordinated by the University of Tartu is just one example of an innovative, future-facing analytical chemistry graduate course designed to prepare students for a fulfilling STEM career. Here we speak to the program's Director, Ivo Leito, to find out how collaboration with partner universities benefits students, and – crucially – also helps meet the needs of society.

With Ivo Leito, Professor of Analytical Chemistry, University of Tartu, Estonia.

The Excellence in Analytical Chemistry (EACH) program has a long history. Originally, our analytical chemistry group here at the University of Tartu created a study program called Applied Measurement Science, which embraced both

analytical chemistry and chemical measurements, as well as physical measurements and calibrations, and metrology. Later, we sought out partners with complementary competencies in other European countries to create an Erasmus Mundus Joint Master's Degree – a prestigious international study program. The four partners – Tartu, The University of Uppsala, The University of Claude Bernard Lyon 1 and Åbo Akademi – each bring something unique to the table.

On track

At Tartu, we cover general analytical chemistry and the metrological and socioeconomic aspects of analytical science. This is covered in the first "bridging" year, when we make sure all the students have a good understanding of the fundamentals of analytical chemistry. Each student takes a socioeconomic module, which offers the chance to learn the language of their second-year university, plus courses covering measurement and the law, economics and the environment, which put analytical activities in a societal context. There are also courses that give them a grounding in data handling and statistics, as well as optional courses, a practical placement and electives.

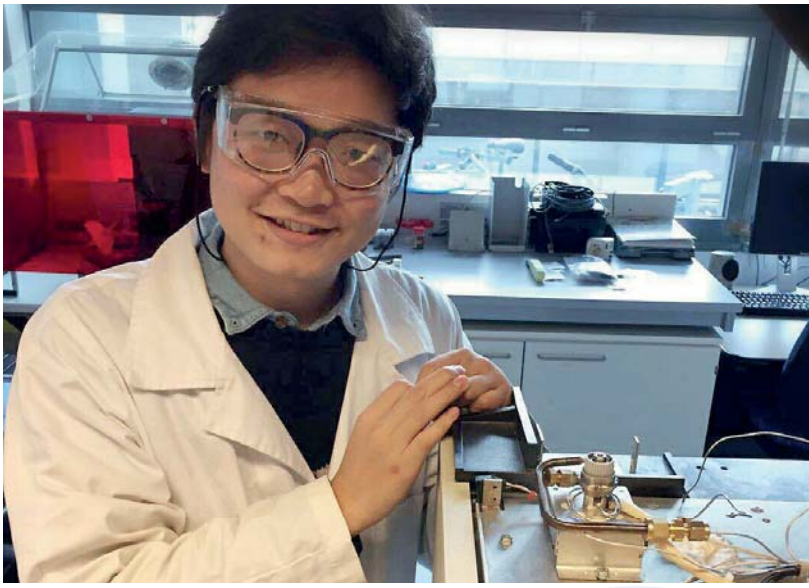
Year Two is a specialization year, which can take place in one of the three remaining universities, and this is where the very specific strengths and key competencies of those universities come into play: Uppsala is very strong in organic and biomedical analytical chemistry; Åbo Akademi in modern analytical devices and miniaturization; and Lyon in process control and analytical chemistry applications within industry. Each track addresses an area of importance, where a lot of progress is being made in the contemporary analytical chemistry world.

We have many applicants but, sadly, only a limited number of EU-funded scholarships. There are students from all over the world. The regions with the largest numbers of students are Southeast Asia and the Balkan region.

Two-way street

We are proud of the quality of the analytical education we provide. We reassess regularly, to make sure the course reflects the needs of the analytical chemistry field and equips the students for the future. We constantly collect and analyze student feedback, and make changes in response. Right now, we are in the process of buying a dedicated LC-MS instrument, purely for the student lab, which will allow us to reshape the introductory lab course.

Every semester (usually every two or three weeks), we have at least one small guest lecture course by visiting scholars. It's an open call – anyone on the planet can submit an application to participate in EACH as a visiting scholar and present a



short course. We have had a real variety of guests, including speakers from industry and academia, and from all around the world. It's a great way to broaden our students' horizons.

The practical placement at the end of the first year is mandatory. Such placements/internships are very beneficial for the students; it's good for them to gain experience in the world of work as early as possible. But finding placement possibilities is one of the most challenging parts of the program for me as the director. Companies can be reluctant to take part – often because staff don't have time to supervise, but also, because the students as a rule are not fluent in the local language. But there is a lot to be gained from the internships from a company's point of view – for example, trainees can undertake non-standard developments and investigations, problem-solving, and so on, for which the staff don't have time.

A 'golden era'?

Analytical chemistry is becoming more and more important, and has an increasingly strong position at universities. In Europe, there is more demand for analytical chemists than higher education can supply, and we are keen to expand our program. We are working towards providing more lab experience, and a greater variety of industry placements. At the second-year universities, there is ongoing debate on the development of interesting research topics for Master's theses. Already, important scientific results have come out of those projects (1–3).

The American Chemical Society recently did a survey on the top ten trends driving science/contemporary research (4) – and they concluded that we are living in a 'golden era' of measurement science. We believe that to be true, and we are committed to providing an education that will help students to excel in their future careers.

References

2. *H Liu et al., "Is vacuum ultraviolet detector a concentration of a mass dependent detector?" Journal Chrom A, 1530, 171–175 (2017).*
3. *R Neupane et al., "Effect of mobile phase composition on the analysis of aggregates of antibody drug candidates (ADCs) using size exclusion chromatography", Anal. Methods, 10 938–941 (2018).*
4. *ACS Axial, "Discover the top ten trends in science" (2017). Available at: https://bit.ly/2q1q4P1. [Accessed April 3, 2018].*

the Analytical Scientist™

Register now at

www.theanalyticalscientist.com/register

It is quick and easy and completely FREE

As a fully registered user you will benefit from:

- Unlimited access to ALL articles
- Full access to digital and archived copies of every issue of The Analytical Scientist
- Print (and PDF) copies delivered direct to you
- Email news alerts
- Networking opportunities
- Detailed Application Notes and Product Profiles

There are many good reasons to register to The Analytical Scientist. Here are just a few:

- From environmental testing to the -omics, pharma to food, The Analytical Scientist focuses on the people, technology and innovations shaping measurement science.
- We cover analytical science by telling stories – delving into the hopes, fears, motivations and aspirations of the key figures in the field.
- Analytical science is no longer a series of individual techniques, but a group of integrated and complementary methods – we encourage cross-pollination of ideas through an accessible, solutions-based approach.

Celebrating measurement science and building a community for analytical scientists everywhere

Register now at **www.theanalyticalscientist.com/register**

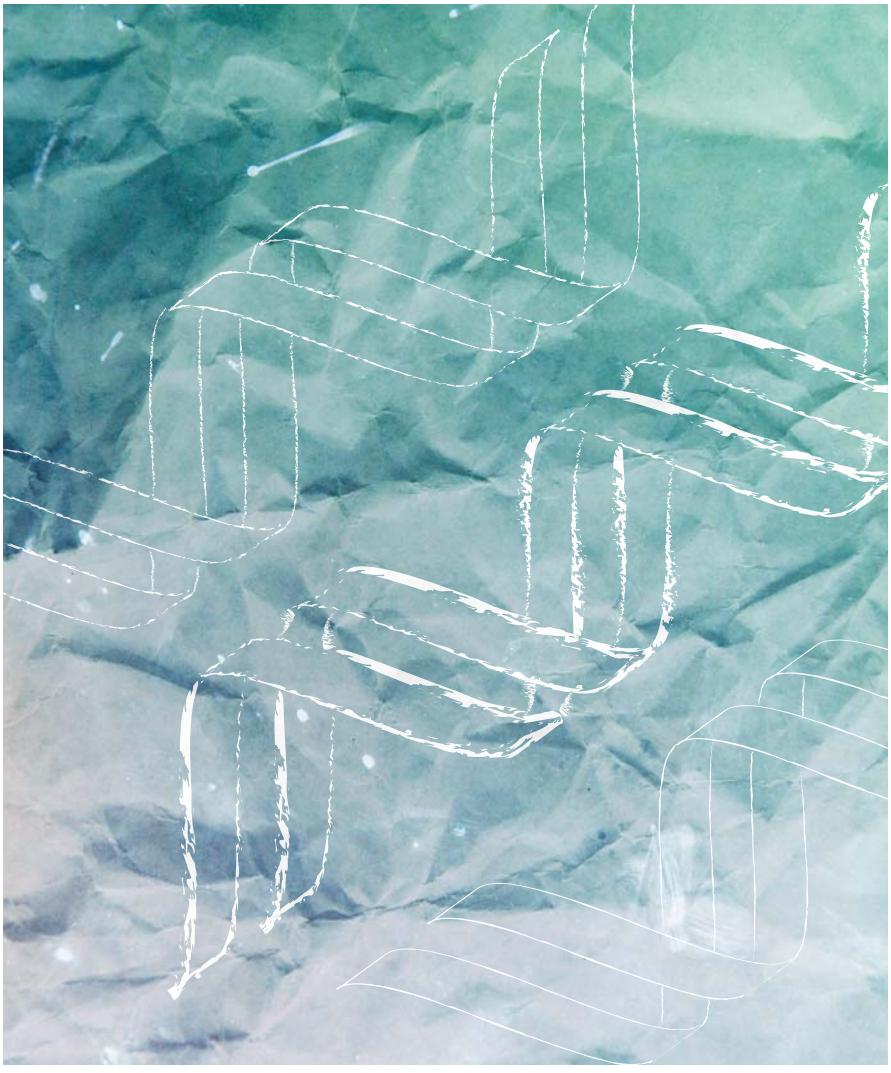
Solutions

Real analytical problems
Collaborative expertise
Novel applications

A Sketch For Success

A new rapid DNA re-identification technique can make cell line authentication and other processes faster, easier and cheaper.

By Sophie Zaaijer



The problem

You've just published a paper in a highly ranked cancer research journal. It's a project that has taken years of your life and hundreds of thousands of dollars in funding. It has been challenging, exhausting, and exciting – and it's just the first step on the road to a much broader answer; maybe even a cure.

But there's a problem. Another laboratory, attempting to reproduce your results, hasn't been able to. Why? Extensive testing points the finger at the cell line you used in your experiments – a cell line you use in almost all of your work. Suddenly, you're faced with questions: Is that cell line really what you think it is, genetically? Can you trust it? And if not, are your results still meaningful?

Background

Cell line authentication is a vital part of medical research – and yet, because of the time and effort required by current methods, it's often postponed or overlooked. This, and many other problems across research and clinical boundaries, could be solved by the application of a rapid DNA re-identification method. That's why my colleagues and I developed MinION sketching (1) – a new way of using existing

"It was the idea of a portable DNA sequencer that really triggered our imagination."

technology to make DNA identification fast, cheap and manageable.

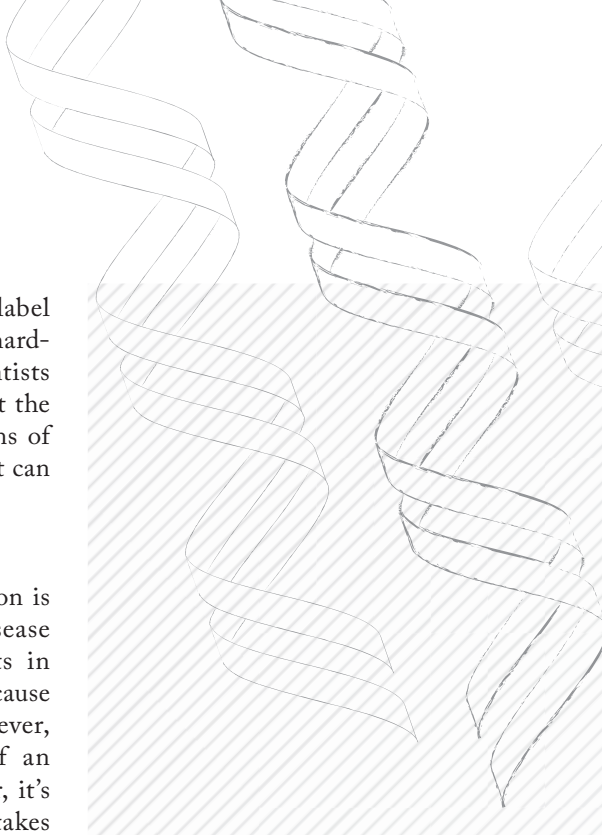
It was the idea of a portable DNA sequencer that really triggered our imagination. The ability to take a DNA sequencer anywhere to analyze nature outside the walls of a specialized laboratory is a true game changer. Imagine being able to re-identify individuals at crime scenes almost in real time – using this knowledge to prevent a perpetrator from striking again. DNA fingerprinting currently takes days, between sample transport, queuing, preparation, and running the DNA sequencing devices and interpretation software. A portable DNA sequencer would solve this problem, we thought, allowing us to re-identify DNA samples on-site.

While working on developing robust methods to employ portable DNA sequencers in the field, we realized that the method we had devised (see "MinION Sketching") could also make a difference to a long-standing problem: periodic cell line authentication in research labs. Cell lines derived from patients are crucial for the research of specific diseases. In the lab, such cells are carefully studied to understand the molecular mechanisms behind the illness. Although each cell line behaves a little differently on a molecular level, they often look very similar under the microscope. As a result, accidental contamination, mislabeling or label swapping is an unfortunate and hard-to-track inevitability; for scientists who may spend years figuring out the underlying molecular mechanisms of a particular diseased cell line, that can lead to disaster.

The solution

The lack of cell line authentication is a long-standing problem in disease research and, because it results in irreproducible research, a major cause of wasted research money. However, the problem is not because of an absence of available tools; rather, it's because of the time and effort it takes to use those tools. Our method enables rapid, on-site identification via DNA fingerprinting, an approach borrowed from the forensic sciences as an excellent method to help authenticate the origins of cell lines. The methods currently offered by third parties or done in-house are long and tedious; our method, in contrast, allows rapid checking by DNA fingerprinting as part of the standard laboratory toolkit. And that could reduce scientists' resistance to regular testing. Not only will this be a step toward making research with cell lines more efficient, but it will also eventually bring us closer to cures for a multitude of diseases.

When we started our project, the MinION portable DNA sequencer had a high reading error rate. For approximately every 10 nucleotides it read, one was wrong. The difference between individuals is about one in every 1,000 nucleotides – so a 10 percent error rate was unacceptable! We needed to find a way to bridge the gap and still be able to use some of the MinION data. To that end, we developed a weighing method in which we determine the probability that a given nucleotide reading is an error and then consider the probability that we might see it in



MinION Sketching

The method, which requires a MinION portable DNA sequencer and custom software, involves two steps.

1. We sequence random strings of DNA from a given cell line or sample. From these random strings, we select individual single nucleotide polymorphisms (SNPs) that vary from person to person and can thus be used as identifiers.
2. We run a Bayesian algorithm that compares these SNPs with the database of genetic profiles on file. For cell line authentication, that might be a database containing the genotypes of every cell line used in the laboratory; for person re-identification, it might be one that contains the sequences of individuals in the relevant population. As the software cross-checks each variant, it updates the probability of a match until it narrows the options to a single reference profile.

the general population. Of course, the less commonly observed a nucleotide is in the population, the more informative it will be in attempting to trace a sample back to a single individual.

The MinION reads DNA in real time, so each informative nucleotide that comes off the DNA sequencer is another piece of evidence. The evidence sequentially updates the posterior probability of a match to one reference file in the database. If the MinION sketch does not match any entry in the database, all posterior probabilities will stay low and the method won't yield a match – but if the probability of a match is high, the method will flag that file in the database for review. We have tested extensively for false positives and optimized our method so that we don't run into such problems. The re-identification opportunity is only as good as the database, of course – as with all forensic methods – but if the database doesn't contain a corresponding reference file, there will be no match.

Beyond the solution

The technique has a number of applications, both within and beyond the walls of the laboratory.

Basic research

Cell line authentication isn't the only use for MinION sketching. Because it doesn't selectively amplify specific stretches of DNA like other methods, it allows for the identification of pathogens infecting those lines. For instance, Mycoplasma contamination often affects laboratory cell lines and can be challenging to detect.

Forensic science

Our method can be used as a tool for rapid re-identification of individuals after mass disasters. After such events, family members are understandably keen to locate their loved ones. They can contribute by sharing their SNP reference files with the forensic team to facilitate matching and re-identification analyses. The samples can rapidly be checked on-site, even in remote areas, letting families be reunited with their missing members – an amazing advancement. 2017 was the 20-year anniversary of GATTACA – a movie that predicts a future in which identities

"The best part? In many of these examples, it's not a "blue-sky future" projection – it's already here."

are verified not by cards or photographs, but by DNA fingerprint matching. With MinION sketching, such a future may not be far off. Will we soon give up our passports in favor of our DNA?

In the clinic

DNA fingerprinting is an easy way to track clinical samples. It can allow the identification of infectious pathogens, too, as well as any antimicrobial resistance markers that might affect treatment decisions (2). I also foresee its application in organ transplantation verification; immediately before surgery, the patient and the donor organ can rapidly be authenticated as a last check for a correct donor-recipient match.

There are many opportunities to use our method in other fields. For instance, we have investigated its use in dog and cow re-identification. This enables high-resolution tracking of individual species. Instead of a microchip system, owners can be reunited with their lost dogs via a quick DNA test. Cows can potentially be traced from farm to table. If we can do that, what about tracking high-value horses? Cats? Animals at risk of poaching (2)? The list is endless!

The best part? In many of these examples, it's not a "blue-sky future" projection – it's already here. People can begin using MinION sketching right now! For cell line authentication, for instance, the first task is to compile a good reference database of all cell lines present in the laboratory. Then, it's just a matter of a few easy steps:

1. Set up of our Person ID pipeline on a computer (see "MinION Sketching"). This requires some command-line knowledge.
2. In the wet lab, extract DNA from each cell line.
3. Perform a MinION library preparation of the DNA.
4. Sequence the DNA and generate a MinION sketch.
5. Run the Person ID pipeline and analyze the matching results against your compiled database.

MinION sketching is a "new kid on the block" for a vast number of applications. My colleagues and I are still working to develop it, of course, but it's already available for use – and it's a simpler, cheaper alternative to many of the current options. It's my hope that, as both the technology and the availability of reference genomic data advance, researchers and laboratory medicine professionals will be able to work with confidence, knowing that their cell line – and their science – is trustworthy.

Sophie Zaaijer is CEO and co-founder of PlayDNA, and Runway Startup Postdoc at the Jacobs Technion-Cornell Institute, Cornell Tec, New York, USA.

References

1. *S Zaaijer et al., "Rapid re-identification of human samples using portable DNA sequencing", Elife, e27798 (2017). PMID: 29182147.*
2. *A Irwin, "How forensic science can stop slaughter of endangered wildlife" (2016). Available at: http://bit.ly/2cV7115. Accessed 18 January, 2018.*

The Comprehensive Collaborator

Sitting Down With... Hans-Gerd Janssen, Science Leader Analytical Chemistry, Unilever Research Vlaardingen, and Professor of Biomacromolecular Separations, van't Hoff Institute for Molecular Sciences, University of Amsterdam, the Netherlands.

How did you get into analytical chemistry?
I've always been practically minded – I wanted to build things, even as a child. I initially wanted to study mechanical engineering at university but a few trial lectures left me uninspired so I switched to chemical engineering. I pictured myself in a hard hat, building huge chemical plants, but I found that the engineering side of things was frustratingly inexact, full of estimates and guesswork – chemistry was more satisfying. And with analytical chemistry I could fulfill my childhood desire to build things and solve practical problems.

Do you have an overarching goal?
Some samples contain more information than we can currently extract, while others offer up a huge amount of data but we are unable to interpret it. My goal is to build systems that allow us to generate more data, and develop methods that allow us to extract more information from the data. Comprehensive chromatography and hyphenated methods are the main avenues I'm using to achieve that.

What qualities make a good analytical scientist?
First and foremost, you must enjoy working with others. I enjoy solving the analytical problems faced by scientists working in different environments, whether in the laboratory, in hospitals, or out in the field. It's a mutually beneficial relationship – they provide the impetus and the testing ground, and I provide the technical know-how. Good collaborators make sure that your work is recognized, but analytical scientists are seldom front and center, so you have to be happy working in the background.

You wear two hats – one in industry and another in academia. How do you find time?
I believe that both of my employers benefit from splitting my time. Problems that I cannot easily solve at Unilever often become longer-term projects at the University, so the two roles are complementary. Though there is a lot of overlap in subjects and topics, I am strict in splitting my time: Monday to Thursday at Unilever, and Friday at the university.

Do you find time for any interests outside of work?
As well as spending time with my family, I enjoy gardening and home improvements – building things in my shed. And, like most Dutch Catholics, I enjoy good beer and a celebration too!

Are you a practicing Catholic?
Somewhat. I often think that the natural world is so wonderful that there must have been a higher force involved. Just think of the human body – thousands upon thousands of researchers have spent lifetimes trying to unravel its mysteries and yet we still only grasp a small part of the complexity within ourselves. I agree with what Milton Lee said about science and religion both being, in a sense, a search for truth (1).

How different are the cultures of academia and industry?
Very different! In industry, the goal is to solve a problem – the focus is on reliability and delivering on time. In academia, you have much more freedom, and only one goal – to publish. Academia is better at fundamental research and coming up with new ideas, while industry is risk-averse. The gap is most obvious when it comes to transferring new technology from the university to industry. Academics tend to consider a new tool or technique "ready" once they publish it. But these early versions are rarely reliable or efficient enough for use in industry.

How can we bridge the divide?
I don't think we should try to make academia more like industry, or vice versa – or we would risk losing what makes them each so valuable. Instead, I think we need something "in between" to commercialize technology developed in academia. I'm not sure what that should look like, but it might involve small instrument companies or university spin-outs.

What has been your proudest career moment?
Being appointed professor at the University of Amsterdam was a proud moment, and made even better because so many of my colleagues at Unilever got in touch to congratulate me. It was great to hear how much my work is appreciated.

Any low points?
I once worked on a project for two years before realizing that what we hoped to achieve was simply not feasible. I concluded that my desire to make the project work had blinded me to the reality of the situation.

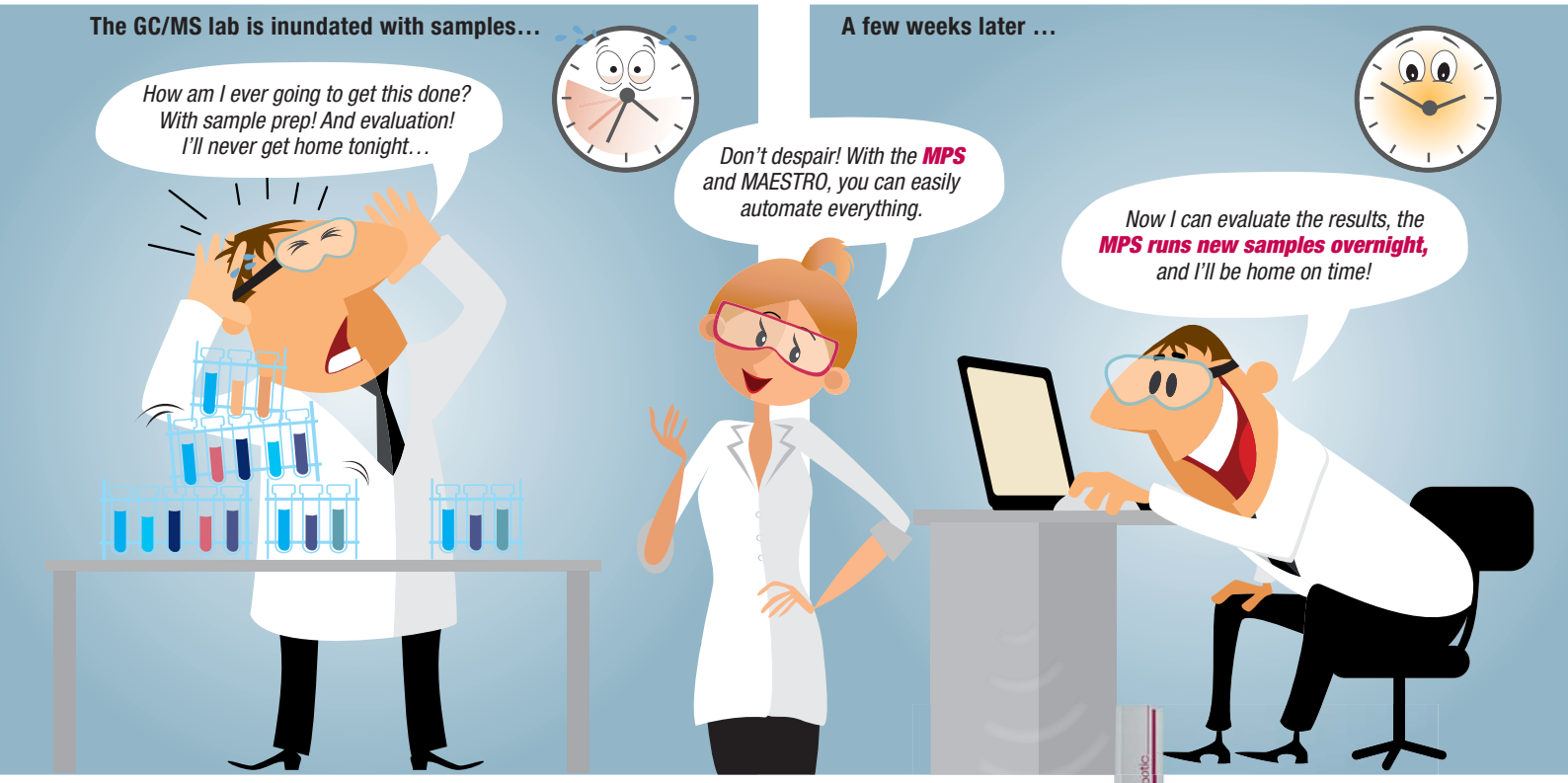
What advice would you give to your younger self?
Have faith in yourself and celebrate your successes. But, equally, don't assume that because you have solved difficult problems before, you can solve every problem. When designing experiments, do not try to confirm your hypothesis – instead, set out to design an experiment that will kill your idea.

What are the biggest challenges facing analytical science right now?
We are very good at finding out what molecules are present in a sample, but that isn't always enough. We need to become much better at localizing compounds and exploring their behavior – the consequences of them being where they are. For example, a molecule bound to a protein may behave very differently to a free molecule. Exciting new techniques, such as imaging mass spectrometry, have a role to play here. But the goal also leads us to another challenge: very localized sampling, down to a cubic micron.

Reference

1. *tas.txp.to/0217/Lee*

Run, Run, Run!



The MultiPurpose Sampler **MPS** automates your sample preparation and introduction for **GC/MS** & **LC/MS** in the easiest possible way.

In the integrated MAESTRO Software, just enter your sample preparation method by mouse-click, step by step.

The daily analysis sequence is set up in no time and automatically checked and verified, making sure that your work gets done on time.

What can we do for you?

Agilent Technologies
Premier Solution Partner

GERSTEL

GERSTEL 50

www.gerstel.com