APRIL 2021 # 96

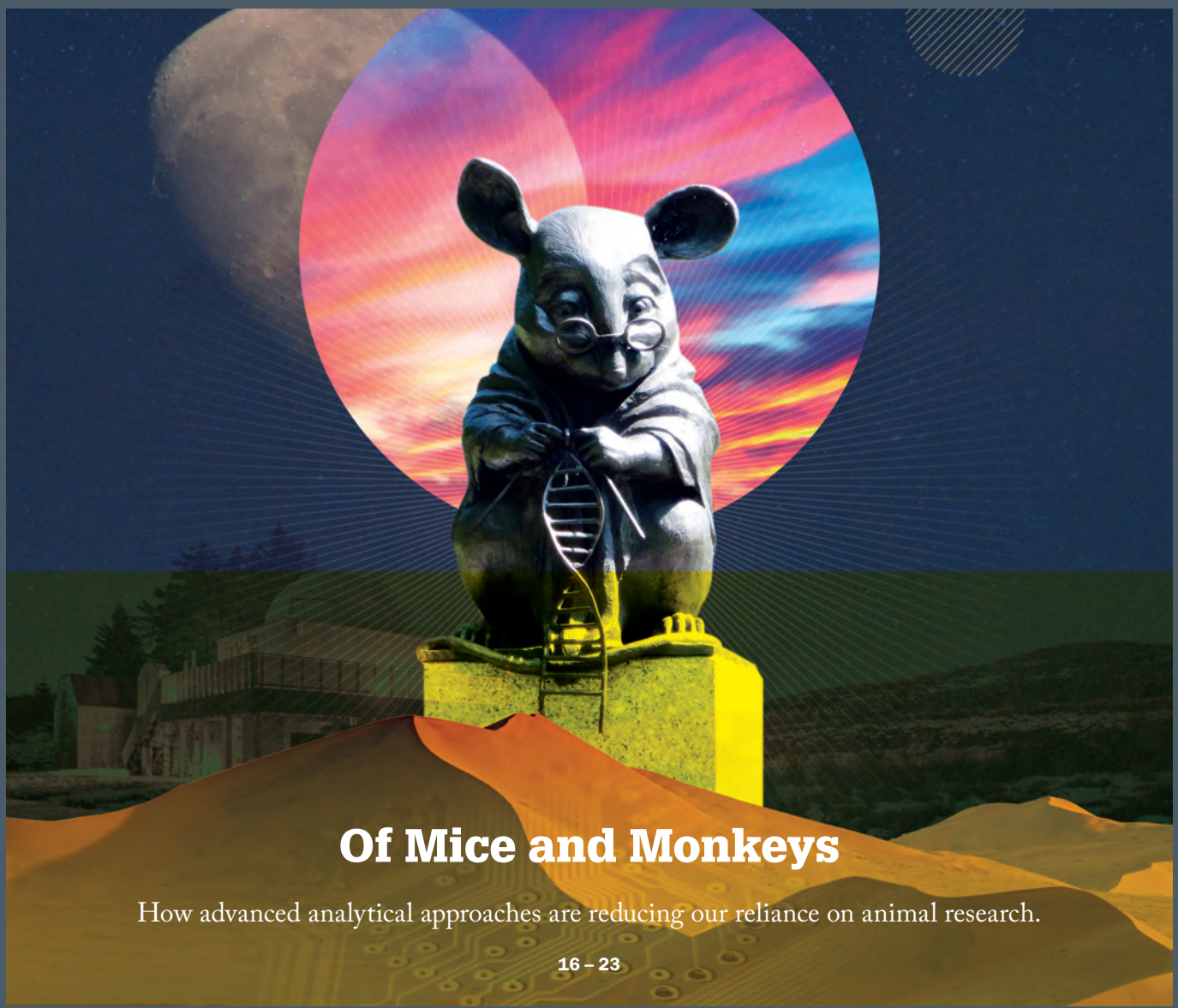
the Analytical Scientist®

Upfront
Cancer-detecting dogs and whiskey terroir
06

In My View
The language of analytical chemistry
14

Feature
Can life ever be the same without Riva?
32 – 39

Sitting Down With
Water wizard, Susan Richardson
50 – 51



Of Mice and Monkeys

How advanced analytical approaches are reducing our reliance on animal research.

16 – 23

SHIMADZU
Excellence in Science

i make the difference

The i-volution in HPLC analysis continues

The advanced i-Series of compact (U)HPLC systems has evolved to include Analytical Intelligence in the Prominence-i HPLC and Nexera-i UHPLC systems. The products combine high-speed analysis, simplified method transfer, automated sample pre-treatment, minimized environmental impact and easy maintenance with the flexibility of working remotely. They are ideally suited for applications in pharmaceutical, chemical and food industries.

Significantly improved analytical productivity
through automation and remote control, resulting in increased efficiency and a reduced risk of human error

Analytical Intelligence
integrates smart automation and utilizes advanced technology such as M2M and IOT to facilitate maintenance, simplify lab management and ensure consistently reliable results

Flexible software control
by Shimadzu LabSolutions LC/GC, LC-MS or DB/CS for full FDA 21 CFR Part 11 compliance. Software packages from other vendors are also supported

www.shimadzu.eu/i-make-the-difference

ANALYTICAL INTELLIGENCE

The Proof Is in the Pandemic

COVID-19 has shown that we can, when required, rapidly adapt and respond to a crisis. We now need to apply this same vigor to saving our planet…

April, for me, represents a key turning point in the history of our planet's two current crises (COVID-19 and climate change). On April 1, 2020, the COP26 conference was officially postponed until 2021 due to the unraveling pandemic – just one day later we saw global cases surpass one million. This month also celebrates the anniversary of another important event – Earth Day. If you're unfamiliar with the backstory, April 22 marks the day (in 1970) that 10 percent of the US population took to the streets and demanded immediate environmental action. Not only did it usher in a new era for this movement, but it was chosen as the date to sign the Paris Agreement.

I don't know about you, but I've spent many hours trapped indoors this year, contemplating the state of our planet and resolving to see a better (and greener) post-pandemic world. Thankfully, it seems we are not alone; with the countdown to COP26 fully underway, many countries are finally embracing "net zero" and making significant plans to cut their carbon emissions. It appears 2020 was the final wakeup call the world needed to realize there is no plan(et) B.

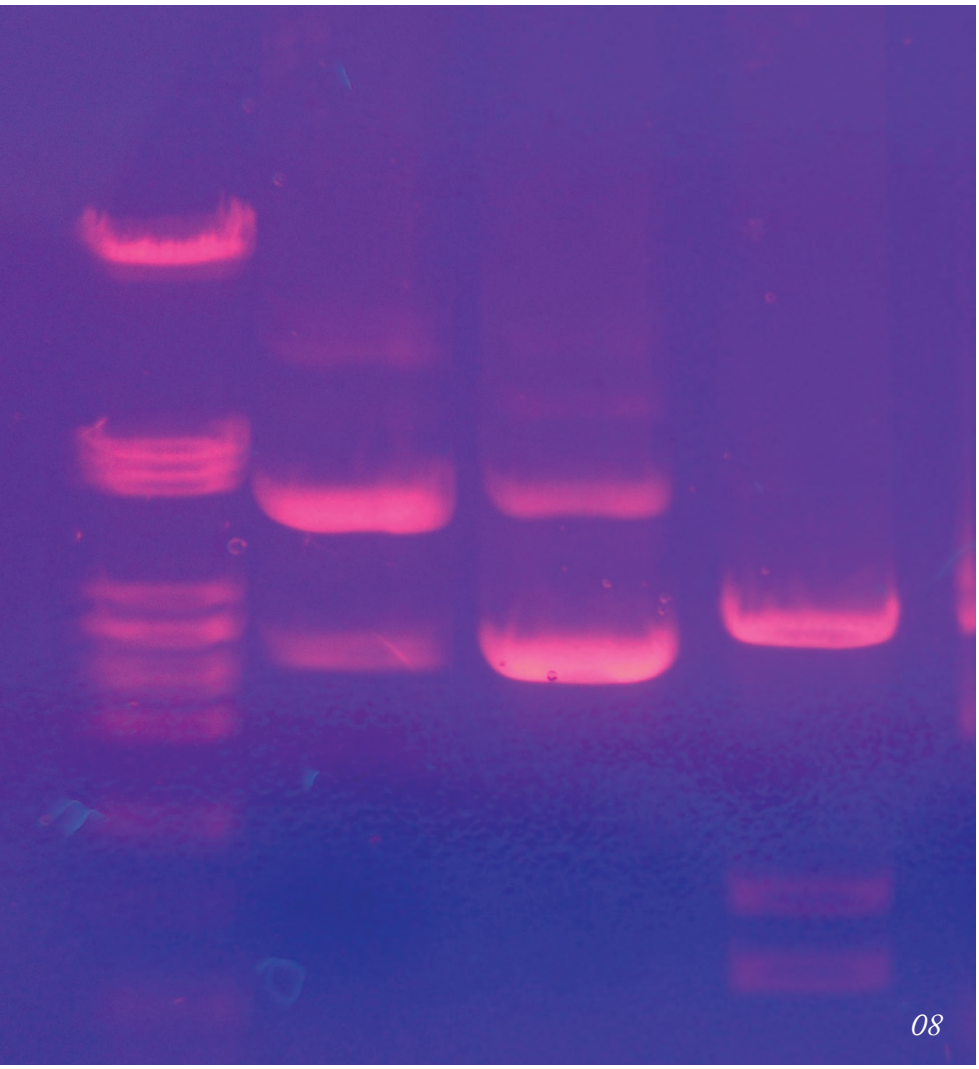
Even within our own analytical sphere, there is much to be optimistic about. Though we are all – understandably – desperate to get back to our beloved face-to-face conferences (more on this in our feature on page 32), there are certainly some positives to come from our new-found virtual world. For example, I suspect the days of hopping on a plane for a meeting that could easily be done via video call are long gone. The same connectivity also makes collaboration on global challenges easier than ever before.

There's a huge amount of work ongoing across our field to tackle a great number of environmental issues – from analysis on microplastics and microfibers, to wildfire contaminants and peatlands research. Even the polymer industry itself is now focused on providing more sustainable solutions to plastic (see page 24). But this is just a taste of the immense role analytical science can play in saving our planet – if you, or someone you know, is doing work in this area, I'd love to hear about it: lauren.robertson@texerepublishing.com.

As we emerge from our state of enforced hibernation, it's vital – for ourselves and the Earth – that we all fully wake up to real danger. If the pandemic has proven anything, it's that nature does not favor those who wait.

Lauren Robertson
Deputy Editor

Contents



03 **Editorial**
The Proof Is in the Pandemic, by Lauren Robertson

On The Cover

A monument to the sacrifices made by lab rats around the world, located in Novosibirsk in Siberia, Russia, sits at the center of a striking collage

Upfront

06 Lessons learned from cancer-detecting dogs and GC-MS spectrum art to honor Black History Month

In My View

10 The promise of single-cell analysis, with **Zachary Pitluk**

12 **Hari Narayanan** discusses typical pain points in beverage analysis - can discrete analyzers provide an answer?

14 Instrument or machine? **Victoria Samanidou** wants to address inaccurate terminology in our field

32

Features

16 **Of Mice and Monkeys**
Animal models are an unfortunate necessity in some fields - could analytical science help us to change the status quo?

24 **The Show Must Go On?**
We caught up with organizers and attendees to discuss the impact of another year without ISCC/GC×GC

32 **One Word: Plastics**
Reflecting on the current state and future of polymer research with four industry experts

Departments

40 **Solutions:** Philippe Schmitt-Kopplin and Stefan Pieczonka discuss their work unmasking the dark metabolome behind beer - and what this could mean for our understanding of civilization itself!

Sitting Down With

50 **Susan Richardson**, Arthur Sease Williams Professor of Chemistry at the University of South Carolina, Columbia, South Carolina, USA, and President, American Society for Mass Spectrometry

the Analytical Scientist

ISSUE 96 - APRIL 2021

Feel free to contact any one of us: first.lastname@texerepublishing.com

Content Team
Editor - Matthew Hallam
Lauren Robertson (Deputy Editor)
Frank van Geel (Scientific Director)

Commercial Team
Publisher - Lee Noyes
Gaurav Avasthi (Business Development Manager)
Nick Ransom (Business Development Executive Americas)

Design Team
Head of Design - Marc Bird
Hannah Ennis (Senior Designer)
Charlotte Brittain (Designer)

Digital Team
Digital Team Lead - David Roberts
Peter Bartley (Digital Producer Web/Email)
Abygail Bradley (Digital Producer Web/App)

Audience Team
Audience Growth Strategy Manager – Brice Agamemnon

CRM & Compliance
CRM & Compliance Manager - Tracey Nicholls
Hayley Atiz (CRM Assistant)

Commercial Support Team
Internal Systems Manager - Jody Fryett
Dan Marr (Campaign Reporting Analyst)

Commercial Services
Commercial Service and Social Media Manager - Matt Everett
Kevin O'Donnell (Marketing Executive)
Alice Daniels-Wright (Video Project Manager)
Jess Lines (Project Support Coordinator)
Lindsey Vickers (Sales Support Project Manager)
Jennifer Bradley (Sales Support Coordinator)

Marketing Team
Marketing Manager - Katy Pearson
Jo Baylay (Marketing Executive)

Accounts Team
Kerri Benson (Accounts Assistant)
Emily Scragg (Accounts Apprentice)

Human Resources
Human Resource Manager - Tara Higby

Management Team
Chief Executive Officer - Andy Davies
Chief Operating Officer - Tracey Peers
Senior Vice President (North America) - Fedra Pavlou
Financial Director - Phil Dale
Commercial Director - Richard Hodson
Content Director - Rich Whitworth

Change of address info@theanalyticalscientist.com
Hayley Atiz, The Analytical Scientist, Texere Publishing Limited, Booths Park 1, Chelford Road, Knutsford, Cheshire, WA16 8GS, UK

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

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

Co-author Dustin Herb stands in a field of barley

The Secrets of Liquid Sunshine

Do environmental conditions influence the more subtle flavors of whiskey?

The seasoned wine quaffers among you will already know the importance of "terroir" when it comes to the distinct flavors found in your glass. But whiskey is not wine – and here, the impact of soil, climate, and sunlight has been largely overlooked.

A team of industry and public sector researchers (presumably whiskey lovers) decided to investigate whether the environment in which barley is grown can contribute to the unique flavor components of new-make (unmatured) single malt whiskey. To do this, they used two different "analytical" methods: i) a sensory panel, consisting of six highly-trained whiskey enthusiasts who evaluated the spirit based on "holistic aroma and taste perception" and ii) gas chromatography olfactometry (GCO).

"In GCO, molecules within the spirit samples are separated via vapor point and polarity, then simultaneously identified via molecular fragment shape and abundance using MS," says Dustin Herb, co-author of the paper. "The molecules are then further characterized by another trained panel who assign an aroma and intensity."

After much separating, sniffing and tasting, the team found that barley variety certainly plays a key role in the flavor of single malt whiskey, but so does the terroir – when and where the grain is grown and how it is managed by individual farmers. Indeed, chemometric analysis of both datasets suggested that the environment and season had more of an effect on aromatic sensory perception than variety alone.

The take home? "Using a terroir model for whisky production creates a niche among local and regional distillers to capitalize on the individual 'terroir' of their local environments – soil types, microclimates, and crop management practices," says Herb. "Furthermore, by placing a value-added label on the barley, farmers are given a profitable rotational crop to help break prevailing monocultures while increasing weed suppression, disrupting pathogen and pest cycles, improving soil health, and overall benefiting subsequent crops."

The team plan to further their research by validating their findings under commercial production scale conditions and looking at other factors that could impact whiskey flavor.

Reference

1. *M Kyraleou et al., Foods, 10, 443 (2021). DOI : 10.3390/foods10020443*

INFOGRAPHIC

The Famous Animals of Science

We look back at some of the biggest contributors to scientific research from the animal kingdom

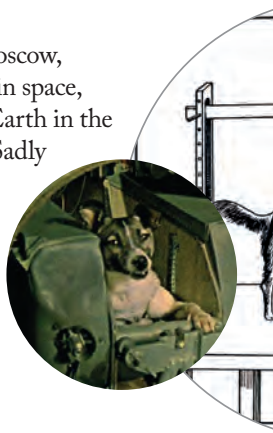
the Analytical Scientist

Dolly the Sheep

Possibly the most famous animal in science history, Dolly made waves in the media when she was born in Edinburgh in 1996. Though she wasn't the first mammal to be cloned, she was the first created using somatic cell nuclear transfer of an adult cell.

Laika

A stray from the streets of Moscow, Laika wasn't the first animal in space, but she was the first to orbit Earth in the Soviet spacecraft Sputnik 2. Sadly (and controversially) she was never expected to return – her sacrifice paved the way for human spaceflight.



BUSINESS IN BRIEF

A roundup of this month's business news, from a newly launched Orbitrap system to a cutting-edge potency test for cannabis

- Thermo Scientific has launched its new Orbitrap Exploris GC-MS, which will reduce turnaround times for analytical labs while enabling accurate quantification of trace components for both targeted and non-targeted applications in a single full-scan system. The new system is the latest addition to the Thermo Scientific Orbitrap Exploris portfolio (1).
- Thanks to the recent addition of Bruker's 1.2 GHz Avance NMR spectrometer, the Juelich Center for Structural Biology in Germany has already made great strides in the name of translational research for age-related neurodegenerative diseases. The hope is that the new system will help uncover high-level structural details about increasingly complex samples (2).
- Numares AG – an NMR diagnostics company – has announced the 510(k) submission of its AXINON IVD system to the FDA. This could potentially be the first AI-driven clinical laboratory system that uses NMR for metabolomics-based diagnostics (3).

Thermo Scientific Orbitrap Exploris GC-MS

- Waters has announced a new peptide multi-attribute method (MAM) workflow to complement their BioAccord LC-MS. The method should enable researchers to accurately assess vital product quality attributes for innovator drugs, biosimilars, and biologics (4).
- ACS Laboratory – the largest hemp and cannabis testing facility in the eastern US – has released its new "Potency 12" UHPLC test to identify the elusive Delta-8 and Delta-10 THC extracts. This makes ACS one of the few DEA-licensed labs in the US able to do so (5).

References

1. *Thermo Fisher (2021). Available at: https://bit.ly/3rAPMaj*
2. *Business Wire (2021). Available at: https://bwnews.pr/3u7lu0e*
3. *Numares (2021). Available at: https://bit.ly/39rUiS0*
4. *Business Wire (2021). Available at: https://bwnews.pr/3sC1xhY*
5. *PRNewsWire (2021). Available at: https://prn.to/3rzV6dV*

Diagnosing Oral Cancer with Raman Spectroscopy

A spectroscopic technique offers potential for noninvasive cancer screening

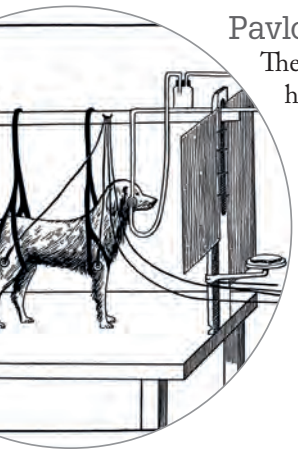
Oral squamous cell carcinoma (OSCC): common, but difficult to detect early. To address this challenge, researchers used shifted-excitation Raman difference spectroscopy (SERDS) to evaluate the molecular composition of OSCC, non-malignant lesions, and physiological mucosa – and whether they can be differentiated by Raman spectroscopy (1).

Based on physiological tissue of the oral cavity, they found that non-malignant and cancerous lesions can be distinguished with high accuracy using SERDS. The method also yielded high accuracy in identifying non-malignant lesions that required confirmation by surgical biopsy.

"Our study shows the potential of Raman spectroscopy for revealing whether a lesion is cancerous in real time," said lead author Levi Matthies . "Although it won't replace biopsies any time soon, the technique could help reduce the lapse of valuable time as well as the number of invasive procedures."

Reference

1. *1. L Matthies et al., Biomed Opt Express, 12, 836 (2021).*



Pavlov's Dogs

These famous canines helped Russian Doctor Ivan Pavlov prove that the salivary reflex of dogs could be conditioned – later known as "classical conditioning."

Schrödinger's Cat

Okay, so not a "real" cat per se, but this theoretical animal still made a significant contribution to the field of quantum mechanics.

The Common Fruit Fly

We couldn't conclude our list without giving a nod to one of the many animal models used in scientific research (more on this in our cover feature).

Sniffing Out Prostate Cancer with Artificial Neural Networks

How a machine-based cancer detection system mimics the canine nose

Though prostate cancer is the second-highest cause of cancer death in men, early biomarker detection methods – specifically, the prostate-specific antigen screening test – lack sensitivity and specificity. We need to reduce false positives and false negatives – but how? The answer may lie in our four-legged friends. Trained canines have been shown to reliably detect and diagnose cancer by smell. Granted, dogs in the lab would be a logistical nightmare and not feasible for mass testing – but that's where researchers at Massachusetts Institute of Technology (MIT) come in.

Using urine samples from patients with or without prostate cancer (confirmed by biopsy), they tested whether the cancer could be detected by trained sniffer dogs, molecular volatile organic compound (VOC) analysis by GC-MS, or microbiota profiling (1). Canine olfaction reliably distinguished between prostate cancer samples and biopsy-negative controls, whereas VOC and microbiota detected qualitative differences between the groups.

From this, the team trained an artificial neural network to mimic canine olfactory diagnosis – distinguishing between biopsy-positive and biopsy-negative samples based on the GC-MS data both alone and combined with canine olfaction data. "We knew that the sensors are already better than what the dogs can do in terms of the limit of detection, but what we haven't shown before is that we can train an artificial intelligence to mimic the dogs," said Andreas Mershin, a research scientist at MIT and author on the study (2). "And now we've shown that we can do this – we've shown that what the dog does can be replicated to a certain extent."

This multiparametric approach lays the groundwork for the development of machine-based diagnostic tools that mimic canine olfaction – and, given the dogs' keen sense of smell, it has the potential to improve diagnostic efficacy in a field where unreliable results run rampant.

References

1. *1. C Guest et al., PLoS One, 16, e0245530 (2021). DOI: 10.1371/journal.pone.0245530*
2. *2. MIT News (2021). Available at: http://bit.ly/307Yl0K.*

Gelling with MS-Based Diagnosis

New gel electrophoresis method could enable rapid analysis of protein biomarkers in clinical specimens

The use of MS-based proteomics for clinical diagnosis is steadily increasing – and COVID-19 has only accelerated its adoption for viral infections. But the traditional sample pretreatment methods required for these analyses take over 20 hours and there are still challenges around peptide recovery and reproducibility of results.

Now, researchers have developed a novel approach, termed BAC-DROP, that could help overcome some of these issues. First, the proteins are fractionated at high resolution; then, the gel itself is dissolved to release any fragments that have escaped before proceeding to MS quantification. The team have demonstrated the technique's successful incorporation into MS-based testing of clinical samples, such as hepatitis B virus. With MS-based diagnosis on the rise, this high-throughput sample preparation approach could help with translation to the clinical lab.

Reference

1. *A Takemori et al., J Proteome Res, 20, 1535 (2021). DOI: 10.1021/acs.jproteome.0c00749*

IMAGE OF THE MONTH

Portrait of a Black Female Scientist

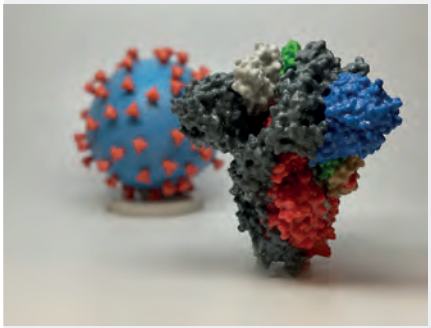
Luis Schachner produces stunning artwork using MS spectra – and this portrait of a Black researcher is no exception. "Danté Johnson, Raquel Shortt, and I were inspired to create this piece to start an important conversation about the lack of minority representation, equity, and inclusion in research" he said about it. "One of the key ideas we had was using spectra for the hair. Beautiful afros made of wonderful, thick curly hair are prominent in Black culture, so we opted to draw a striking image of a Black woman with hair made up of GC-MS traces for melanin."
Like what you see? Keep an eye out for our May feature with Luis to see more of his work and an interview with the artist himself!

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

QUOTE OF THE MONTH

"At what point does a collection of glial cells constitute a human brain? How many interacting cells do we need to label something living?"

Ian Wilson, Professor at Imperial College London, UK, discussing organ-on-a-chip technologies in our cover feature on page 21.



Spike Protein Potential

New therapeutic targets revealed on SARS-CoV-2 spike protein

Using a technique called amide hydrogen-deuterium exchange MS (HDXMS), researchers have discovered a number of potential new therapeutic targets on the SARS-CoV-2 spike protein (1).

By placing the spike protein and ACE2 receptors in heavy water (D_20), the team were able to visualize what happens when the two bind. Their discovery? This binding is necessary for furin proteases to cut the spike protein, leaving behind the S2 subunit that allows the virus to enter our cells.

"Maybe the S1/S2 cleavage that is necessary for furin cleavage can serve as a new target for inhibitory therapeutics against the virus," said Ganesh Anand, coauthor of the paper (2). "This study also may help in explaining how mutations in emerging variants might alter dynamics and allostery of ACE2 binding, potentially increasing infectiousness of the SARS-CoV-2 virus."

References

1. *PV Raghuvamsi et al., eLife, 10, e63646 (2021). DOI: 10.7554/eLife.63646.*
2. *Penn State News (2021). Available at: https://bit.ly/3lRkrih.*

In My View

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

The Vast Potential of Single-Cell Analysis

Single-cell analysis has great promise… but how can we get there?

By Zachary Pitluk, Vice President of Life Sciences and Healthcare, Paradigm4, Waltham, Massachusetts, USA

It is now four years since a group of scientists met in London to discuss how to create a human cell atlas (HCA) – a collection of maps that describes and defines the cellular basis of health and disease. Research based on this atlas has also helped researchers create more specific maps – such as the COVID-19 Cell Atlas, which could help us in the fight against SARS-CoV-2.

Cell atlases are powerful – but, to unlock insights that will enable us to help specific patients, we need reference datasets of hundreds to thousands of patients to complement population-scale genomics datasets. This vision of precision medicine is coming ever closer thanks to the technological advances – particularly in the field of data handling and analysis – and single-cell research.

Advances in single-cell genomic analysis provide the industry with greater insights from clinical trials – for example, by allowing scientists to look further into specific molecular responses to different therapies. Of the many single-cell genomic analysis methods, scRNA-seq is the most widely used. This approach involves labeling biomolecules that originate from individual cells, allowing high-throughput molecular analysis at the single-cell level. In 2013, scRNA-seq was Nature's Method of the Year. It earned the accolade a second time in 2019 due to its ability to sequence DNA and RNA in individual cells (1), allowing extrapolation of the biological differences between cells.

Massively parallel single-cell genomics assays can now profile hundreds of thousands of cells, meaning that researchers can gain more insights than ever before on certain cell characteristics and behaviors. The uptick in spatial single-cell analysis puts a further onus

"This vision of precision medicine is coming ever closer thanks to technological advances"

"With the understanding that exosomes and even naked nucleic acids can be used for intercellular communication, the need to quickly profile responses at the cellular level are even greater."

on technology development to preserve the contextual information of imaging so that researchers can augment individual cellular responses with regional and sub-regional information.

Technologies to profile DNA and proteins in single cells – as well as combinations of DNA, RNA, and proteins in the same cell – provide important additional layers of information to accelerate precision medicine. The advent of single-cell nucleus RNA sequencing (snRNA-seq) has allowed the extension of single-cell transcriptomics analyses to human diseases in which live tissue is not obtainable (2).

Computational algorithms have also emerged (and continue to evolve) to determine cell types, states, transitions, and locations – allowing single-cell analysis to extract more targeted insights from specific biomarkers. But there are 300 different cell types known in the human body, which itself compromises 37 trillion cells. And precision medicine research relies not just on the number of cells (because cells from one patient cannot be biological replicates!), but on the number of patients. It's clear that these data must be stored and processed at scale to be effective.

Single-cell analysis may help us uncover never-before-seen physiological interconnections between tissues. With the understanding that exosomes and even naked nucleic acids can be used for intercellular communication, the need to quickly profile responses at the cellular level are even greater. The ability to find gene expression fingerprints and distinct cell types that may look unrelated, but might be corresponding with each other, could transform the way we diagnose and treat disease. If the full potential of single-cell analysis is realized, we will be able to navigate the physiology of humans from the molecule up – an exciting future that now sits tantalizingly within our reach.

References

1. *Method of the Year 2019: Single-cell multimodal omics, Nat Meth, 17, 1 (2020). DOI: 10.1038/s41592-019-0703-5.*
2. *Lake B et al., "Neuronal subtypes and diversity revealed by single-nucleus RNA sequencing of the human brain," Science, 352, 1586 (2015). DOI: 10.1126/science.aaf1204.*

Beverage Analysis: Just Press Go?

To fast-track beverage analysis, laboratories should explore technology that specifically addresses the pain points of routine testing

By Hari Narayanan, Product Marketing Manager, Thermo Fisher Scientific

Behind every refreshing glass of craft beer, cider, fruit juice, or red wine, there is a team of skilled operators using complex beverage analysis workflows. To ensure customer satisfaction (and subsequent business profitability) there is a critical and constant need for high-quality and desired taste – at scale. Given its crucial role in guiding quality and taste, it's fair to say that beverage analysis lies at the heart of successful beer and wine production.

In fact, accurate and reproducible measurements are also needed to guide production and product release as well as to ensure that alcoholic beverages are safe for consumption. But beverage analysis also faces a number of challenges that make it difficult for laboratories to work efficiently – not least the need to analyze multiple parameters at different time points under a heavy workload.

Many characteristics are routinely monitored; in wine, for example, free and bound sulfur dioxide (a regulated allergen) must be measured alongside pH, volatile acidity, total acidity, residual sugars, residual malic acid, and other wine spoiler indicators that can affect flavor and product stability.

And analysis is not a "one and done" affair. In beer production, for example, changes that affect the later characteristics can occur at any time – some of which alter shelf life. To detect such changes, beer samples must be tested at all process stages – from feed water, malting and fermentation through to the addition of flavoring agents and bottling.

"Obtaining data across numerous parameters over time requires the use of different wet chemistry methods, each of which must be calibrated and conducted by skilled operators."

Obtaining data across numerous parameters over time requires the use of different wet chemistry methods, each of which must be calibrated and conducted by skilled operators. But, given the volume of testing, it can be difficult for labs to find staff who are sufficiently proficient at titration, HPLC, spectrophotometry, and all of the other methods required for beverage analysis. And staff shortages aren't the only issue these labs face… There are time pressures, too. The use of numerous multi-step analytical approaches means the overall process is not as fast or as automated as it could be. Indeed, traditionally-used techniques are often tedious, time-consuming, and prone to manual errors. Together with the need for enzymatic reagents and standards preparation, analysts often face workflows that are difficult to execute.

In my view, routine workflows should facilitate walkaway efficiency – you should be able to simply put the samples in, add reagents, and press go… with discrete analyzers (DAs), you can. DAs make use of unique, discrete, and disposable cuvettes to gauge multiple characteristics from a single sample, drastically reducing analysis time. Tedious and time-consuming processes are replaced by automated calibration and sample dilution, thereby reducing the risk of manual error. And each sample is analyzed in a fresh cuvette, minimizing the risk of contamination and giving laboratory staff peace of mind.

But, as with any analytical technique, there are a few drawbacks to DAs that would be remiss of me to avoid. For example, the precision and accuracy of results are highly dependent on the type of photometric setup, direct read or fusion, type of cuvette (single

"For beer and wine producers, having confidence in analytical results is critical to delivering delicious, high-quality beverages for consumers to enjoy."

time disposable or reusable), and rinse cycle between measurements. To ensure accurate analysis time after time, operators must therefore be trained to complete this all-important step. This could be more challenging for microbreweries and small wineries, which can face more resource-centric challenges than their larger counterparts. What's more, some DAs are optimized for use with proprietary reagents, which can limit the possible applications using inhouse or third-party reagents, making careful instrument selection key.

For beer and wine producers, having confidence in analytical results is critical to delivering delicious, high-quality beverages for consumers to enjoy. Behind the scenes, laboratories continue to navigate an array of challenges in their quest to ensure integrity of results and support businesses in these industries. DAs offer a way to address some of the difficulties associated with current workflows, while improving reproducibility (1, 2) and reducing time invested. By implementing easy-to-use DAs and ready-to-use reagents, laboratories involved in beverage analysis can look toward a simplified, more efficient future!

References

1. *X ShuFei et al., "Determination of total sugar in wine by gallery automatic discrete analyzer," J Food Saf Food Qual, 8, 4208 (2017).*
2. *X ShuFei et al, "Determination of citric acid in wine by gallery automatic discrete analyzer," J Food Saf Food Qual, 9, 5129 (2018).*

Do all Analytical Scientists Speak the Same Language?

Instrument versus machine: the importance of accurate terminology in our field

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

A Twitter post grabbed my attention recently. Eric Dodds, associate professor and director of the Nebraska Center for Mass Spectrometry, was wondering if he was alone in being upset when hearing someone refer to an instrument as a machine.

My first reaction? At last! Someone else not only shares my opinion, but feels equally strongly. Until I saw that tweet, I thought I was the only one who had this problem – or, at least, that it was unique to my own country's academic and scientific community. It appears that is not the case!

Then I read the comments below the tweet. Experts from around the world chimed in. Some seemed to agree; others did not. One particularly funny comment even stated that when it works properly, it is an instrument, but when it doesn't, it's a machine. I understand that feeling, but I'd refrain from using it in a glossary!

As we well know, correct terminology is important in academia. Students learn from us and our words, and they should learn the right things in the right ways. That's why one of the first things I teach my third-year Instrumental Chemical Analysis students is the difference between an "instrument" and a "machine." I insist that the two cannot be used interchangeably. They aren't synonyms and I will always correct my students if they choose the wrong term.

According to IUPAC, the term "analytical instrument" refers to "a device or a combination of devices used to carry out an analytical process. The analytical process is all or part of the analytical procedure that encompasses all steps from the introduction of the sample or the test portion to the production of the result. An analytical instrument may carry out single or multiple analytical procedures. In the latter case it may be selective, i.e., designed to carry out any requested combination of procedures within the set, on each specimen (1)." The word "machine" is not recommended in this context.

So, fellow analytical scientists: please beware of your word choices! Any equipment that leads to measurements is an instrument. Machines, however, are responsible for mechanical outcomes or treatments. The inductively coupled plasma spectrometer, for example, is an analytical instrument, whereas a centrifuge could be considered a machine.

As I put these ideas to paper, it dawned on me that this is not the only occasion when two terms with very different meanings are treated as synonyms. A few common examples:

- Methods and techniques: A technique is based on chemical or physical principles, but a method describes its application to specific chemicals or fields.
- Analysis and determination: Samples are analyzed; compounds are determined.
- Robustness and ruggedness: These are often used interchangeably to signal a "good" assay. In reality, robustness refers to a procedure's capacity to measure something irrespective of small but deliberate variations in method parameters. Ruggedness is the degree of concordance between test results obtained for the same samples under various conditions – for example, in different laboratories or using different instruments (note that I did not say machines!).
- Selectivity and specificity: I can't recall the number of times I've read, "the method is highly specific…" The method either is or isn't specific. It can, however, be highly selective.

The confusion gets worse when these mistakes are found in published manuscripts.

Evidently, there are numerous terms in our field that are wrongfully treated as synonyms. We must address this issue to prevent their misguided use and to ensure consistency in peer-reviewed publications and in science as a whole.

Reference

1. *AD McNaught and A Wilkinson, Compendium of Chemical Terminology, 2nd edition. Blackwell Scientific Publications: 2019.*

OF MICE AND MONKEYS

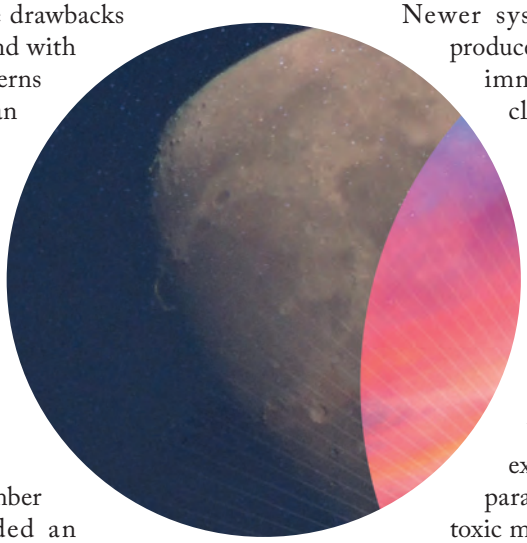
Animal models remain an unfortunate necessity in some fields of research and development, but analytical advances and new technologies are paving the way to reduce – maybe even one day eliminate – our reliance on living creatures

By Matthew Hallam

It's not "antiscience" to highlight problems with animal models. Our (sometimes) furry friends have made many sacrifices on our behalf. In fact, estimates suggest that 110 million mice and rats are killed in US labs each year. And then there are the frogs… And dogs… And monkeys… And please spare a thought for the ubiquitous zebrafish…

But the use of animals in our pursuit of (scientific) knowledge is not only a modern-day practice. In ancient Greece, the dissection of human bodies was considered taboo and anatomical exploration thus relied on live animals. It was through conducting studies of this kind that Herophilus ("the father of modern anatomy") started his own studies; the likes of Aristotle and Diocles also partook.

Today's animal studies represent a significant departure from these barbaric practices. Subject suffering is limited wherever possible - which is backed by legislation - and animals can even be housed with friends. But the drawbacks with animal models don't start and end with ethical dilemmas – there are also concerns regarding their applicability to human disease and the logistics surrounding their maintenance.



Luckily, advances in analytical science are helping us to move forward in new directions. Advances in instrumentation and methodology are allowing us to use fewer, smaller samples (and thus fewer animals!), and new models that don't rely on animals at all are emerging as alternatives.

Assuming that animal lovers outnumber the animal ambivalent, we decided an exploration of this exciting analytical frontier was long overdue.

Reduce, replace, refine

"When I started in the pharma industry some 40 years ago (not in the 19th century, as some of my students may have thought), you needed over 40 rats to gather pharmacokinetic (PK) data, and a further six rats per dose route for the drug metabolism studies," says Ian Wilson, a Visiting Professor at Imperial College, London. "This is because you needed 1 ml of plasma per time point for the LC-UV methods used in the PK studies, and this means you needed 2 ml of blood per sample. Six rats per time point were sacrificed to provide data of the required statistical quality. And that equates to an awful lot of rats."

"Today, we can do the same study in three rats or mice," he continues. "With modern analytical chemistry, we can assess PK and drug metabolism, and even conduct omics analyses using blood samples as small as fifty microliters in runs as short as five minutes." In such cases, the combination of microsampling with chromatography and high-resolution MS can dramatically reduce animal usage while increasing data quality and hitting two of the three Rs: reduce and refine. Ian's own work on gefitinib in mice, which used rapid UPLC methods followed by MS detection (1), is testament to these capabilities.

In tandem, the animal models that we use are also improving. It's widely recognized that typical model systems like rat xenografts (in which human tumors are implanted into rats, treated, and monitored) have inherent limitations, such as their inability to accurately replicate the tumor microenvironment present in human patients. Newer systems, such as humanized livers produced by infusing human hepatocytes into immunocompromised mice or optically clear zebrafish xenografts (2), may be considered more "human relevant."

From another perspective, analytical systems are also helping us identify and eliminate animal tests that are ineffective. As an example, researchers from AstraZeneca used ^{1}H NMR spectroscopy to show that cynomolgus monkeys are poor models of paracetamol toxicity by studying their urine (3). Plasma exposure was higher than in humans, but paracetamol metabolites derived from the toxic metabolite NAPQI were minimal. The conclusion: these monkeys do not metabolize the drug the same way humans do. And the outcome? Nobody should dose primates with paracetamol again!

Organoids from outer space

In proving old models redundant or unfavorable, we not only spare animals the bother of ineffective studies, but we also underscore the need for alternatives. These alternatives can come in many shapes and sizes, but in vitro systems are one of the leading choices. But, as Ian says: "There's no such thing as an in vitro rat just yet." Luckily, we have organoids to take their place!

Organoids are three-dimensional organ models derived from stem cells that are able to mimic some of the complexities of

> "Organoid models have been reported for almost every major human organ (including complex systems like the blood-brain barrier and fallopian tubes) and many of our most troubling diseases."

tissues in the human body in terms of their spatial organization and cellular distribution. They represent a welcome departure from classical cell line and animal systems, which are limited by their culture-altered biochemical processes and physiological separation from humans, respectively.

Today, organoid models have been reported for almost every major human organ (including complex systems like the blood-brain barrier and fallopian tubes) and many of our most troubling diseases. Cancer is perhaps the most successful example. Oncological research has benefited from an organoid invasion due to their ability to replicate the pathophysiological features of naturally occuring tumor processes, such as growth and metastasis.

The application of high-throughput and omics profiling technologies, as well as MALDI imaging, allows us to evaluate drug effects in these in vitro tumors. And, in the case that organoids are patient-derived, these approaches can even help us to personalize treatment and improve outcomes for patients - both in cancer and beyond. The close interaction between organoids and analytical technology thus helps us to protect humans and animals alike, while also opening doors to innovative research approaches for the future.

The Zoo in Your Lab (Part One)

A quick tour of the lab zoo – a collection of animals used for different types of testing around the world – with rapidfire reasons for their utility

Cynomolgus macaque (Macaca fascicularis)

- Offer unique insights into human biology and physiology due to evolutionary lineage
- Particularly useful for neurological and reproductive research
- Reproductive and developmental toxicology is well established

Zebrafish (Danio rerio)

- Easily kept due to low cost and small size
- Transparent eggs are fertilized and develop very quickly outside of the mother - ideal for developmental research
- Easy to manipulate genetically

African clawed frog (Xenopus laevis)

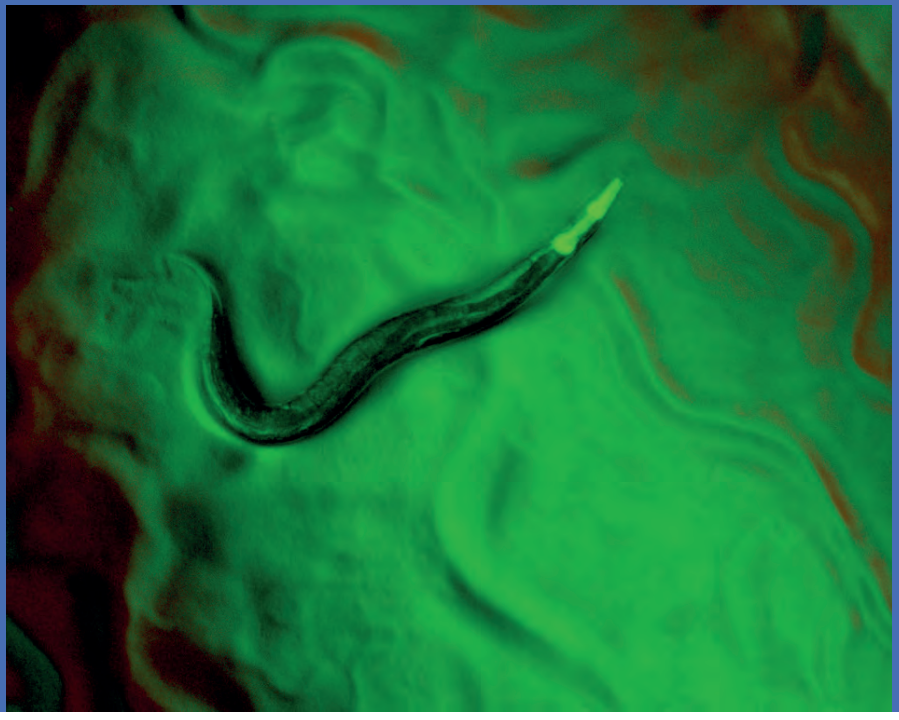
- Live up to 30 years in captivity
- Lay up to 1,000 eggs at a time - these eggs are relatively large and develop externally in salt solution, making them ideal for developmental research
- Take up little space and are easily bred and maintained
- Are the best understood amphibians

Nematode worm (Caenorhabditis elegans)

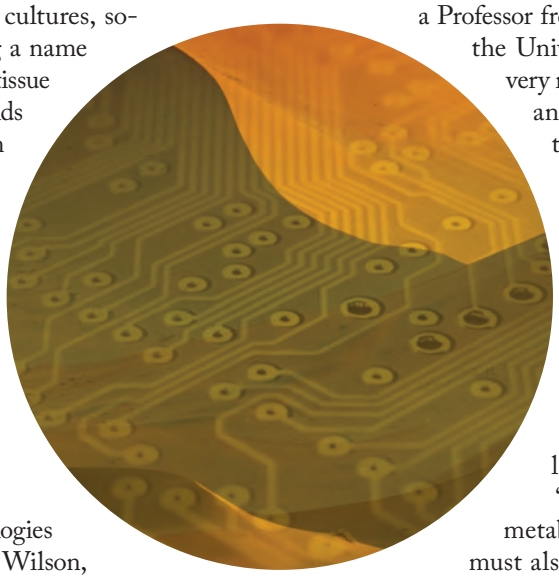
- Easily grown on plates of bacteria, and can be frozen, thawed, and revived as needed
- Has a short life cycle that lends itself to developmental studies
- Is transparent throughout its life, meaning its anatomy and individual cells can be studied with ease
- Specific development means that each cell can be traced back to the embryo stage

Dog (Canis lupis familiaris)

- Considered the most appropriate model for toxicology studies after rats
- Long history of use
- Many species are used, but beagles are the most common



On the topic of three-dimensional cultures, so-called "tissue papers" are also making a name for themselves. These systems use plant tissue material loaded onto paper-based scaffolds to mimic human tissues, allowing them to act as models for processes like cellular tissue invasion (common in cancer) (4). Tissue papers can also be implanted into animals with relative ease when the occasion calls for it as the plant-derived materials do not tend to elicit inflammatory responses!



Do you want chips with that?

"The advent of organ-on-a-chip technologies show great promise," explains Steven Wilson, a Professor from the Department of Chemistry at the University of Oslo. "These systems are very representative of human functionality and they can be automated with high throughput and precision. They certainly represent a very attractive alternative to animals, but I don't think that we can completely replace them just yet."

The key tricky question that we must consider here is: can organ-on-a-chip technologies represent humans more accurately than animals? Analytical science will likely lead the way to an answer.

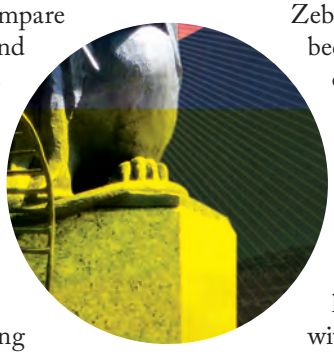
"We must explore how these systems metabolize drugs," Steven says. "And we must also map the protein makeup of these

Mouse (Mus musculus)

- Small size and large numbers of offspring
- Easy and cheap to keep
- Share many disease genes with humans
- Longstanding breeding programs mean that many different mice are available for different research purposes, such as immunodeficient and gene knockout mice

> "Can organ-on-a-chip technologies represent humans more accurately than animals? It's a tricky question, but analytical science will likely lead the way to an answer."

tiny and complex organ models if we are to compare them to the real counterparts in humans and animals. Some spectacular new breakthroughs suggest that they are very accurate indeed, as is the case with the embryo-like gastruloids. The field is exploding right now. Who knows where we will be in a couple of years!"



Of course, one core consideration in mimicking the human body is connectivity between organs; after all, when in practice does a human organ act totally alone? By connecting multiple organs on a single chip, researchers can study the interactions between the pancreas and liver in diabetes patients or the lung and brain in cancer patients. Analytical chemistry plays a central role here, too – often by the coupling of these systems to high-throughput MS systems for rapid readout.

As you might imagine, these inter-organ interactions are somewhat complicated and can differ greatly between species, so chip-based devices are a welcome addition to our research arsenal. We can even go one step further with "human-on-a-chip" technologies, which comprise many organs to replicate – to some degree – the whole human body. But if using animals for research is ethically questionable, how do we feel about using a "human-on-a-chip?"

Beyond the science

Such a question might seem odd or even silly at first. And my initial reaction to ethical considerations surrounding organs- and humans-on-chips was completely dismissive, but the field does raise unique and interesting concerns. A couple of quick questions from Ian highlight an area of potential concern: "At what point does a collection of glial cells constitute a human brain? How many interacting cells do we need to label something living?"

The next big question: if we consider these systems as living, how should we treat them? "It's an interesting question," admits Steven. "Thinking about it quickly leads us towards debates about the nature of life itself, and that provides an important opportunity for us to have interplay with the humanities. I imagine we will see more of this."

Steven suggests that we should expect to see organ-on-a-chip technologies find a routine role in drug testing and developmental biology. In this latter application, ethical concerns become even more complex. For example, it is possible to mimic embryonic development by loading a chip with a spatially controlled patterning of pluripotent stem cells (5), but does that mean that we should?

Zebrafish are used widely for developmental studies because their eggs are fertilized and develop outside of the mother's body. Observation is simple, and the fish are also cheap to house on a large scale. But how do we make the most ethical choice between experimenting with zebrafish versus embryo-like structures on chips?

From a research standpoint, it's likely that both approaches will be employed to provide the most holistic view possible. And that is very much the case with animal models now; alternatives are here, but are often used in parallel with the minimum possible number of animal studies. Though this is likely to remain the case for some time, it's exciting to imagine the doors that analytical technologies may open for us (and our animal friends) in the years to come.

References

1. *BJ Malloy et al., "Rapid determination of the pharmacokinetics and metabolic fate of gefitinib in the mouse using a combination of UPLC/MS/MS, UPLC/QToF/MS, and ion mobility (IM)-enabled UPLC/QToF/MS," Xenobiotica, 51, 434 (2021). DOI: 10.1080/00498254.2020.1859643*
2. *C Yan et al., "Visualizing engrafted human cancer and therapy responses in immunodeficient zebrafish," Cell, 177, 1903 (2019). DOI: 10.1016/j.cell.2019.04.004*
3. *H Yu et al., "Metabolism by conjugation appears to confer resistance to paracetamol (acetaminophen) hepatotoxicity in the cynomolgus monkey," Xenobiotica, 45, 270 (2014). DOI: 10.3109/00498254.2014.973000*
4. *SM Cramer et al., "Tissue papers: leveraging paper-based microfluidics for the next generation of 3D tissue models," Anal Chem, 91, 10916 (2019). DOI: 10.1021/acs.analchem.9b02102*
5. *A Manfrin et al., "Engineering signaling centers for the spatially controlled patterning of human pluripotent stem cells," 16, 640 (2019). DOI: 10.1038/s41592-019-0455-*

ONE WORD:

Plastics

We ask four industry experts to reflect on the current state of polymer research, the challenges yet to be overcome, and the trends shaping the future of the field

"All publicity is good publicity," so the saying goes – but those in the polymer industry may disagree. With sustainable development and climate change finally being given the global attention it deserves, plastics have become just one of the many perceived evils ravaging our planet. With so much negative attention focused on single-use plastics and plastic microparticles, it's easy to forget the positive contributions this industry has made to a range of industries – and our lives.

We spoke to Harry Philipsen, Elena Uliyanchenko, Jindra Purmová, and David Meunier – all polymer experts in their own right – to find out more about the analytical science behind the industry and to ask the immortalized question: is there a great future in plastics?

What's your perspective on the direction of the polymer industry at the moment?

Harry: In general, it's clear that the polymer industry is still growing – and that it will continue growing. At DSM, we are moving more and more into high-end applications – like our increased offering of high-value, specialty, high-performing polymer specialties; bio-based and circular solutions for an increased range of our portfolio – with an improved carbon footprint; and safer solutions that are free from hazardous substances. Key industry players like DSM are also focusing their activities. AKZO-Nobel chose a focus on paint and coatings, and DSM is doing that now by choosing to focus towards Nutrition, Health and sustainable living.

Elena: My impression is that the polymer industry is currently rediscovering itself. Polymers are viewed by many as the "enemy of the environment," so there is mounting pressure for the industry to change. Meanwhile, there's recently been a shift in focus within polymer applications because of their potential to help in the COVID-19 crisis. All in all, this has meant the emphasis has moved from single-use products to more durable high-end applications (for example, in the medical sector).

Jindra: Specific to our focus at Nouryon, we've now entered the growth phase and want to target four attractive end markets: agriculture, buildings and infrastructure, cleaning goods and personal care. The focus on end-markets and customers, which is reflected across the industry, requires a targeted and specific approach and of course leaves less space for exploring new techniques and fundamental analytical research. But certainly, another crucial goal is delivering innovative and sustainable solutions that answer society's needs.

What are some of the needs or demands placed on the plastics industry, and how can they be met?

Harry: It's getting increasingly competitive, of course. So there's a need to go faster and cheaper to remain competitive, but, at the same time, things are becoming increasingly complex. There is also a pressure from wider society to make everything more sustainable and eco-friendly with lower carbon footprints. For those businesses that want to stay in business, it's imperative they move in this direction – for example, by using bio-based materials or recycled feedstock.

Elena: Generally speaking, societal needs are growing and becoming more demanding – think of flexible displays, materials that can withstand long distance space travel, body parts… At the same time, as I briefly mentioned, there is mounting pressure for environmental reform within the industry. Though it is obvious that the amount of single-use products should be better controlled, it may be less obvious to the public that there is much more to polymers than plastic bags and straws. Plastics made a number of impressive feats possible: digitalization, space travel, improved quality of life for patients, solutions for sustainable housing and food production, and so on.

The plastics industry is now forced to look for "greener" alternatives, but environmentally friendly solutions are often only feasible at the expense of deteriorated properties and increased costs for us as consumers. Substantial research will be needed to create environmentally friendly plastics that are equal in properties and cost to petrochemically-derived alternatives.

Jindra: As Elena has mentioned, finding sustainable alternatives is a key demand placed on our industry at the moment. Nouryon's very motto, "Your partner in essential chemistry for a sustainable future," reflects just how key this is to the company – and analytical chemistry is crucial in this journey towards sustainability. We increasingly characterize bio-based raw materials that are often much more complex and contain other types of impurities than their synthetic equivalents. We also provide analytical methods to enable the development of sustainable production processes and are closely involved in the assessment of the environmental impact of new products in an early stage of product development.

David: In my opinion, the polymer industry must be laser-focused on delivering sustainable solutions to the many global challenges the world faces at present. My experience to date suggests that, in most instances, new sustainable materials solutions must match or exceed the performance of existing materials in the marketplace, and, because of this, delivery of these solutions will require a solid materials science understanding of structure-property relationships. As an analytical scientist who partners closely with product development experts, it is clear to me that gaining this structure-property understanding falls squarely on the shoulders of R&D laboratories, and this is not possible without the detailed structural characterization of materials provided by the analytical laboratory. As a result, I feel that R&D laboratories will be impacted by the drive for sustainable materials in a substantial, but positive manner.

Could you please provide examples of how these demands are being met?

Harry: DSM already has many nice examples of products meeting those demands. For example, polyamides with a relatively more favorable carbon footprint than the market standard, bio-based building blocks being used in a growing number of our engineering materials grades, and new food contact grades of materials with extremely low levels of leachables.

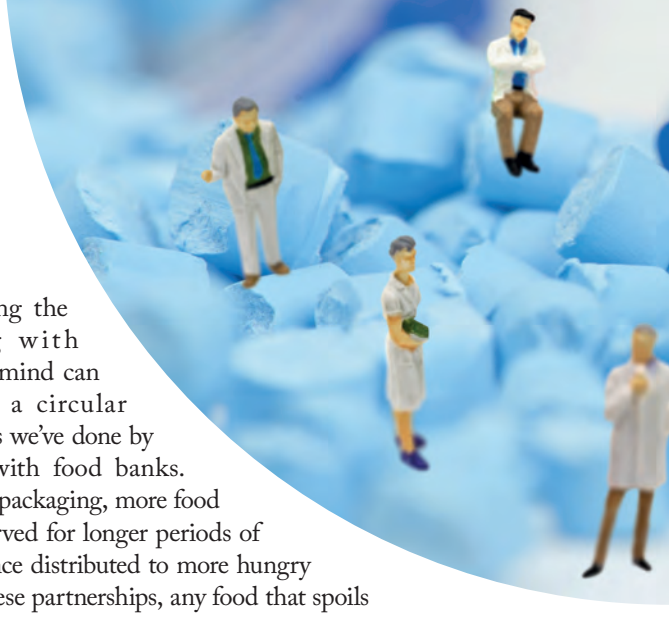
MEET THE PLASTICS FANATICS

Harry Philipsen – Harry initially obtained his PhD at the Technical University of Eindhoven (TU/e) in 1998, on the thesis "Mechanisms of Gradient Polymer Elution Chromatography and its Applications to (co)Polyesters." From 1987 to 2007 he worked at Océ Technologies, Venlo, as an analytical chemist and group leader specializing in LC and MS and as an analytical researcher exploring chemicals, mechanisms and their interactions and functioning in printer systems. In 2007, he started at DSM Resolve as business development manager, and was active in projects on breath analysis with the Maastricht University Medical Center (MUMC). He was also co-founder and chairman of United Brains Limburg (UBL), connecting SMEs to knowledge centers in the province of Limburg, the Netherlands. In 2016, as Program Manager and Project Director, he became scientifically responsible for molecular characterization (quantification and molecular structures) of synthetic polymers within DSM.

Elena Uliyanchenko – Elena has an extensive background in polymer and petrochemical characterization. Her PhD, obtained at the University of Amsterdam, focused on the application of UHPLC and two-dimensional LC to the analysis of polymers. She later went on to work as a Lead Scientist at SABIC in the Netherlands for over seven years, where she led a global team of chromatography experts working on applying analytical techniques to the analysis of thermoplastics. She recently joined Cargill where her field of interest has extended to the food industry and spectroscopy.

Jindra Purmová – Jindra holds a PhD in macromolecular chemistry and is currently team leader for separation, characterization & quantification (SCQ) at the Expert Capability Group - Measurement & Analytical Science (ECG-MAS) of Nouryon. Nouryon was formed in 2018 by splitting off the speciality chemicals division of Akzonobel, with the ambition being to transition from an ingredient supplier to solution provider. The company is not a plastics manufacturer in the traditional sense, but supplies chemicals essential for the manufacture of plastics as well as additives for improvement of mechanical and physicochemical properties. Working in the central analytical laboratory of Nouryon, located in Deventer, The Netherlands, Jindra supports the product and process development activities of all business units forming Nouryon.

David Meunier – David is currently a Fellow in Dow's Core R&D Analytical Science group. He joined Dow after receiving a BS in Chemistry from North Central College, Naperville, Illinois and a PhD in Analytical Chemistry from the University of Illinois at Urbana-Champaign. David is a global technology leader in the area of macromolecular characterization with expertise in SEC, molecular topology fractionation, liquid adsorption chromatography, two dimensional LC, multi-angle light scattering, differential viscometry and spectroscopic detection methods. His interests lie in advancement of these capabilities for elucidation of structural heterogeneity in synthetic polymers through resolution of co-existing distributions in molar mass, long chain branching, chemical composition, grafting and functionality, and establishing process-structure-property relationships.



Elena: Many companies are looking to renewable sources for the manufacturing building blocks for polymers. This approach produces the same polymer structures as the oil-based route, so the polymer properties are not jeopardized. However, this does not address the major issue: the poor recyclability of plastics. The industry needs fresh out-of-the-box solutions; for example, fundamentally new (maybe hybrid) materials, more durable polymers to create less waste, novel recycling approaches, new feedstocks that can be transferred into polymers....

Some promising efforts in terms of environmentally friendly plastics include PEF biobased plastic developed by Avantium as an alternative for PET (common in plastic bottles) and the generation of feedstocks for polymer production from mixed plastics waste introduced by SABIC. I believe that the latter example is a great step towards "greener" polymers and sustainability because it addresses simultaneously two huge environmental concerns: plastic waste that can't be recycled and limited natural oil resources.

Jindra: Using efficient production processes, producing low waste streams that contain no toxic compounds, using renewable raw materials, or offering biodegradable products – these cannot be optional in the modern world. Some examples of the latter in Nouryon's portfolio are modified biopolymers that are used to improve viscosity and other rheological properties in the construction or paint sector. Their high content of biodegradable constituents also decreases the environmental impact when used in mining. Modified biopolymers can also have widespread use in food or pharma products where they add desired properties but do not alter the flavor, nutritional value, or performance of the active ingredient.

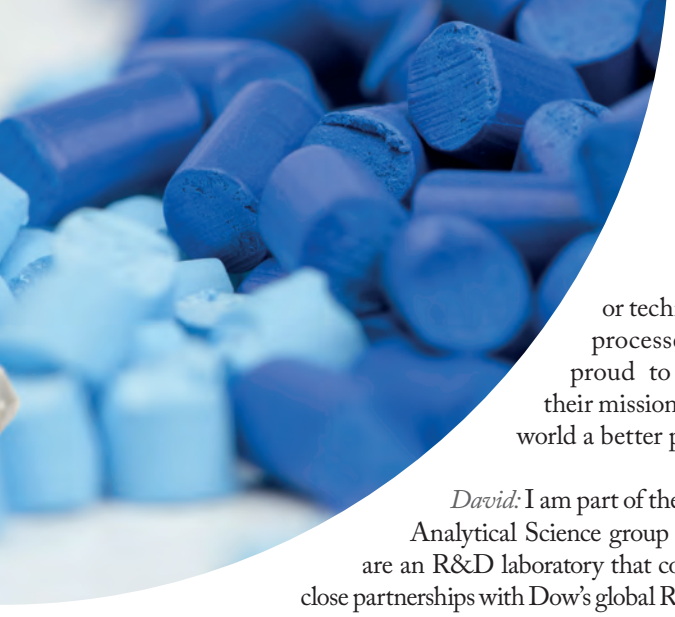
David: There are numerous factors driving our industry towards sustainable and safer materials. Global challenges like food, climate, energy, waste and fresh water, are significant drivers for change. If I consider one example – food – it is well known that proper packaging can greatly reduce food waste. However, it is somewhat less known that designing the packaging with recycling in mind can help create a circular economy – as we've done by partnering with food banks. With proper packaging, more food can be preserved for longer periods of time and hence distributed to more hungry people. In these partnerships, any food that spoils before it can be distributed is composted, and the compost is provided to farmers in bags made from the recycled food packaging. Additionally, there are numerous opportunities to design new materials to enable the use of recycled materials that simultaneously improve the performance of existing materials and reduce the energy intensity of the manufacturing process. To provide one example, Dow recently launched a new silicone-polyethylene hybrid material (AMPLIFY™Si Silicone Enhanced Polymer System) that improves performance in plastics composites and helps divert plastic waste from landfills. Additionally, the product improves processability, thus easing energy costs and lowering the carbon footprint of the manufacturing process.

> *"Analytical science is key at pretty much every step because you always need to be able to understand how the materials are functioning at a fundamental level.*

What is the current role of your R&D lab?

Harry: We are now called the Applied Science Center, and we provide the scientific basis for product and application development. So, if for example you are working with fuel tanks and need to determine the permeability of fuels through polymer-based layers, we can investigate the material characteristics and provide answers to those questions. But we get involved in all sorts of projects, for example, optimizing plant efficiency or exploring how bio-based materials will impact the properties of a product. Analytical science is key at pretty much every step because you always need to be able to understand how the materials are functioning at a fundamental level. We may employ techniques such as X-ray scattering or solid state NMR to study the morphology and mobility of various phases in a material or perhaps use hyphenated separations to understand the fine chemical microstructures.

Jindra: The central analytical laboratory of Nouryon, where I work, supports the R&D product and process development activities of all our business units. Relatively recently, we have made our knowledge available to the wider community through the ECCD – Expert Capability Center Deventer. We use our broad knowledge of chemical products and processes, experience in complex matrices, and state-of-the-art analytical equipment to help predominantly (but not exclusively) Dutch start-ups and SMEs. We help them develop new and improved products



or technologies and processes, and are proud to be part of their mission to make the world a better place.

David: I am part of the Core R&D Analytical Science group at Dow. We are an R&D laboratory that collaborates in close partnerships with Dow's global R&D, TS&D (technical service and development) and Manufacturing, and Engineering groups to help deliver sustainable solutions and processes to meet customer needs and help address critical world challenges. We are a comprehensive analytical department with in-house state-of-the-art capabilities in spectroscopy, separations, microscopy, rheology, and surface analysis. And we partner with government laboratories and universities for access to certain high-end capabilities, such as advanced photon sources. Our lab collaborates with all businesses and functions to solve problems, improve existing products, and develop the next generation of products with sustainability as a key driver. Additionally, we partner closely with our manufacturing plants to optimize our processes for more efficient operation, while helping to enable next generation process technologies for emissions free manufacturing operations.

What are the main current challenges in the development and/or analysis of polymers?

Harry: One of the key challenges is balancing the complexity of the materials or the "questions" we are being asked to investigate with the need for rapid and cheap analysis. Often, we come up against a case where certain hyphenated techniques might be able to provide a lot of detail on the material composition of a product, but the need to optimize on a case-by-case basis means we simply don't have the time to use it. I realize people are working on making these techniques more accessible and easy to use for industrial labs – these efforts are important and closely followed by us.

Another technical challenge is that, although we can get a lot of information on e.g. chemical microstructures of a material, we then need to couple that to final properties to see what effect any changes in microstructure might have. To do this, you ideally want to separate materials according to their chemical composition and then perform mechanical tests. The challenge is that separation provides you with milligrams of material for testing, whereas we typically require grams for mechanical testing.

There is also an issue around needing true quantification and qualification of components at very low levels to meet stricter and stricter regulations – this is particularly pertinent for anything being used in the body, the environment, or in food. When it comes to qualification, we often rely on MS, but then accurate quantification is a challenge. As an example, we are working on strategies towards making universal detectors like ELSD and CAD in LC also much less dependent on the nature of samples and the used solvents.

Elena: If we're going to see a new generation of plastics and new approaches for plastic recycling, we need an in-depth knowledge of material composition. And that places great value on analytical techniques – MS and high-resolution NMR, for example – that can provide detailed knowledge on polymer structure. Because of polymer complexity at the molecular level, application of MS or NMR often requires an upstream (multi-step) separation. Development of a suitable separation method and hyphenation to other techniques is a labor- and time-consuming task. The challenge in polymer analysis is not only to find the right analytical approach, but to understand and correctly interpret the results. In many cases, this requires experts to develop a method and to process the data. It is not sufficient to purchase expensive and sophisticated instruments and place them in the lab if analytical scientists cannot make full use of the equipment and software capabilities. Unfortunately, with advances in analytical instrumentation, getting the right personnel has become a bottleneck. And I can only see the problem getting worse; polymer chemistry does not seem to be a very attractive field for the younger generation.

Jindra: One of the challenges we are facing at Nouryon is a great variety of products or processes that require analytical support and a limited amount of time to solve the problems. The challenge of limited time is often tackled by laboratory automation, miniaturization, or the application of ready-to-use kits. On the other hand, such an environment is less favorable for exploring and implementing new methods and/or techniques. And that's why a well-balanced collaboration with academia is of vital importance.

Polymers, especially natural or hybrid copolymers, form extremely complex mixtures. Unraveling these distributions, expressing the results in a comprehensible manner, and finally linking them to physico-chemical or mechanical properties is, in my opinion, the largest challenge in polymer characterization. Therefore (big) data processing methods must be developed alongside the separation techniques.

David: From my vantage point, I see increasing demand on our laboratory resources for compliance with government regulations like REACH and POP, and although the work is of critical importance for our industry, these demands compete with our ability to enable development of newer, safer, and more sustainable materials. There are also the technical challenges associated with making "virgin-like" materials out of recycled plastic. These technical challenges must be solved in a cost-

effective and low carbon footprint manner so that recycling can become a viable option for eliminating plastic waste.

What role should the R&D lab have in new product development, and how does that work in practice?

Harry: I think it is becoming increasingly clear just how important it is for analysis to be fully integrated into product development – which in itself is being driven more and more by what we call the "voice of the customers." This is why we reorganized last year to create the Applied Science Center, where analytical scientists together with other (senior or principal) scientists are fully integrated into product – and application – development projects. We lay the scientific foundation for product development, but we might also be involved in helping teams set up a proper analytical strategy. It's extremely important that analysis is not isolated in an industrial lab; the insights we can provide are crucial to product development, but it's always easier to demonstrate this added value when you are fully integrated in the product development process.

Elena: In any product development project, analytical scientists should have a seat at the table with product developers, material scientists, and other professionals. I believe an "analytical mindset" is very helpful to establish relationships between polymer structure and properties. Working on multiple materials and projects, analytical scientists can often share learnings and experiences across an organization that can help provide valuable insights during the development process. Unfortunately, this does not happen that often in practice; analytical scientists are often only approached when questions or problems arise during product development.

Jindra: Analytical specialists should be involved in the early stage of product – or, more importantly, process – development. For example, well placed and designed sampling points or implementation of in situ monitoring techniques are crucial for reliable output. Choice of the right analytical technique and/or appropriate sample preparation from the beginning of the project can prevent delays and scope changes at a later stage. Also, biodegradability and environmental fate assessment of the new product or ingredient in the early product development stage saves a lot of time and effort in the later registration process.

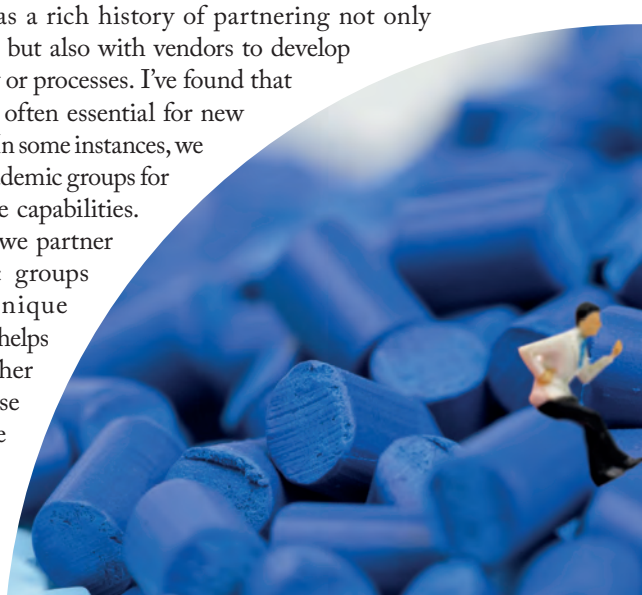
How does – or should – academia play a role in product development?

Harry: That's actually a very interesting question and has much to do with the changing perspective in industry. We often collaborate with academia, and we can get a lot of great information from such collaborations. In particular, academia is one of the only viable routes for solving fundamental challenges in our industry, such as the coupling of certain techniques. However, with the pressure to become more and more application orientated and to get speedier with our development, it becomes a challenge to involve academia. The whole trajectory of a project with academia could take six years – and that's simply too long for a lot of industry projects. Academia can certainly play a role, but we need to look at how best these partnerships can work; for example, focusing on faster and shorter term projects.

Elena: I think there's great potential for academia to create fundamentally new polymer solutions. The strength of academia is in addressing fundamental challenges and making major advances in science: developing new detection techniques, new separation media, new instrumentation and bringing it to the level where it can be applied in industry. It is very important that industry and academia maintain close connections – firstly, so that industry can take those ideas developed in universities to consumers, and secondly, to ensure academia has a clear view on the challenges that industry (and society) faces so that they can be addressed as a high priority.

Jindra: As I mentioned earlier, well-balanced collaboration with academia is of vital importance for ECCD. We participate in private-public collaborations with several universities and knowledge institutes. Academia should be, and often are (in the form of spin-off companies), the driving force behind product development. Universities and research institutes should be given the time and funds for fundamental research and to explore the feasibility of newly discovered principles for real-life applications. Depending on technology readiness level, collaborative projects with industrial partners or instrument suppliers can often accelerate the use of new technologies by industry.

David: Dow has a rich history of partnering not only with academia, but also with vendors to develop new technology or processes. I've found that collaboration is often essential for new breakthroughs. In some instances, we partner with academic groups for access to unique capabilities. In other cases, we partner with academic groups to evaluate unique technology that helps us decide whether to make in-house investments. We



"There's already so much we can do with polymer analysis, so I don't particularly see there being many new fundamental technique developments in the short term – but there are still some challenges that need to be addressed."

also partner with academia to solve grand challenges. These types of projects are typically longer term (3–5 years), but significantly higher risk. Finally, and importantly, academia is responsible for producing the next generation of industrial researchers. The global challenges our world faces will not be solved overnight. It is imperative that the next generations of researchers are well-versed in these issues. And those seeking careers in industry should arrive ready to face and solve these problems.

What do you foresee in the future of polymer analysis?

Harry: There's already so much we can do with polymer analysis, so I don't particularly see there being many new fundamental technique developments in the short term – but there are still some challenges that need to be addressed. I'd like to see more techniques, such as two-dimensional chromatography, being fully translated to routine analysis in industrial labs. Also, the coupling of techniques like differential scanning calorimetry or X-ray diffraction would be a great development to see in the future. It would mean overcoming the significant challenge I mentioned previously with regards to the different amounts of sample needed – but I don't think this is impossible.

Elena: New molecules and new properties require techniques that can take an in-depth look at polymer structure and composition. Multidimensional separations coupled to MS, NMR or IR are already developed; however, they are complex and expensive (especially considering both instrumentation and the need for trained staff), so only the largest industrial companies or academic labs can afford them. And yet, many out-of-the-box developments happen in SMEs – companies that often don't have access to high-end instrumentation or the expertise to further expand their ideas. Simplification of polymer analysis and data interpretation – and increased accessibility – is very important.

I also foresee developments in the correlation of macroscopic properties with chemical composition, artificial intelligence and machine learning, and the prediction of polymer properties based on chemical structure to produce new materials with a specific set of properties.

Jindra: Even though polymers have been around for a long time and the research field is rather mature and structured, increasingly complex bio-based and renewable materials will need new methods to study their structure. As Elena mentioned, I'm not sure advanced multidimensional separations coupled to detectors such as NMR, IR or pyrolysis-GC-MS will become simple enough to leave the academic and/or large industry laboratories in the foreseeable future. However, miniaturization and accessibility of data processing aids might help with the more widespread use of these techniques.

Additionally, polymers in the field of biology, biomedicine, and nanomedicine will need methods for monitoring their location and performance in vivo. Miniaturizing and non-invasiveness are the key requirements in these applications. I can also see a future where analytical method development moves towards portable, easy-to-operate devices for fast material identification in the context of the circular economy. I think spectroscopic techniques that are already widely used in this form for analysis of small molecules will play an important role here.

David: The ability to control molecular architecture has been – and will continue to be – essential for meeting most sustainability targets, and this requires the right measurement science capability. As molecular architecture comprises many overlapping dimensions of structural heterogeneity, it is clear that fast, multidimensional, information-rich techniques will be needed. In concert with the development of these advanced techniques, it also seems clear that advances in data science approaches, such as artificial intelligence, machine learning, and advanced artificial neural networks, will be required for rapid data interpretation and decision making. I expect these areas to be fertile ground for development in both industrial and academic laboratories.

The Show Must Go On?

NO RIVA. NO FORT WORTH. HOW DO ORGANIZERS – AND ATTENDEES – FEEL ABOUT THE LOSS OF ISCC/GC×GC?

What makes the ISCC/GC×GC meetings so special?

Giorgia Purcaro: Riva and Fort Worth are the conferences with a capital "C" in the field of separation science. No other conferences have the same ability to gather together such high-level scientists in the area, from across academia, private companies, and institutions. Moreover, historically it has been the place where the most important advancements in the field of separation science have been disclosed and shared. It has always been a place of inspiration, and these meetings have seen the birth of many new ideas. The cozy and peaceful atmosphere allows you to completely disconnect from your daily routine and focus on separation science for a week!

Philip Marriott: As anyone who has decades of diligent ISCC/GC×GC participation will know, this conference was – and remains – synonymous with all the "breaking news" and technical innovations in capillary GC. This premier meeting on capillary separation technology has quickly become a must-attend for leading scientists and instrument manufacturers in the field. You can benefit from dedicated technology sessions, you can hear the latest research and technical innovations through lectures and posters, and you learn about emerging researchers and their research in keynote lectures. And it all happens in a most relaxing, pleasing, visually stunning, and gustatorily satisfying environment – especially when held in Italy.

Luigi Mondello: Riva, in particular, is a unique event – a conference where tradition meets innovation. You can begin to get a sense of the magic by listening to the way people speak about it. It is "the Riva event" first, and the ISCC and GC×GC conference second. In Riva del Garda, amongst such beautiful surroundings, we create a special atmosphere where people feel like getting together for a whole week to talk about science and life. It is the right place for companies to present their products, for young scientists to meet experts, and for delegates to promote international collaborations, exchange ideas and find new opportunities. And everything is accompanied by fine Italian food in a friendly and informal atmosphere!

Kevin Schug: Let me answer this from the stand-point of raising money from sponsors and vendors for the recent Fort Worth meeting – the lifeblood of the conference. I have never considered ISCC and GC×GC to be one of those meetings where vendors leave with a huge wad of new leads in hand. And that is often a difficult measuring stick for some companies to set aside. However, here you have gathered, year-after-year, the great thought leaders in separation science. And, they are right there – accessible and available for interaction, with no place to run and hide. I think the size of the conference (around 350 attendees in 2019) is perfect for some real meaningful and personal interactions.

Tadeusz Gorecki: For the longest time, this has been the most important conference for me. I attended it for the first time in 1991, and have done everything I could not to miss it since. After I moved to Canada, I also started attending the North American branch of the conference.

Riva has always been special. The unique combination of the perfect location, the great scientific minds converging there and the fantastic social program was truly unbeatable. The only issue was that it was exhausting – there were just too many exciting things happening at once; by the end of day four, I would dream about getting some rest! The North American ISCC has always been a somewhat more muted affair, especially when it was changing its home every two years. Still, it gave me the opportunity to meet a different group of participants with fresh ideas.

Hans-Gerd Janssen: I've always found the Riva and Fort Worth meetings to be inspiration points. You see the ideas of others, and although these might not be directly applicable to your situation, new lines of thought can arise from these interactions. Inspiration also comes from the challenging discussions with fellow scientists in the lecture rooms, viewing the posters, in the corridors, and at the social events. The meetings also show you which groups to monitor in literature for the next year.

What about the importance of this conference to students?

Giorgia: As a student, Riva was the place where I found my inspiration and passion for chromatography. I also began to feel part of the family. I think the Riva/Fort Worth meeting has a fundamental role in motivating young scientists by showing them the potential of what they can achieve and what limits they can surpass.

Philip: I have brought a good number of – very thankful – research students to Riva, and to its US counterpart. Perhaps my enthusiasm for Riva is contagious, but they all invariably exhibit an air of great anticipation and excitement – it becomes all-consuming discussion in the office. One student prepared a long list of all the "famous" scientists she wanted to talk to – meeting them all, she was overwhelmed by their approachability and their generosity with time and advice. For most, this was their first conference, and the sheer "density" of the program made for an exhausting experience. But come Friday, we've always found the extra energy to tackle the chapel hike!

Luigi: This conference always offers great opportunities for students. Every year, many fellowships give young scientists the chance to attend the conference at zero cost. In addition, reduced registration fees have always attracted young scientists from every part of the world. For them, Riva is a big amusement park, where they can take an active part in the event.

A word from the organizers

Luigi Mondello and Kevin Schug offer their perspective on canceling the Riva/Fort Worth conferences – and the lessons learned

What's the real impact of having to cancel the meetings?

Luigi: The Riva conference requires more than a year of preparations for organizers, vendors, and delegates to make all the necessary arrangements – such as hotel and travel arrangements, scientific and social programs, exhibitions, and vendors sessions. The pandemic in Europe started in Northern Italy, with the first "red zone" very close to Riva. At that time (early March 2020) almost everything was ready for Riva2020. We took a few days to discuss and find the right solution – should we move Riva to later in 2020, postpone one year, cancel the event? It was not easy at that time, because the course of the pandemic was unpredictable. Finally, on April 1, 2020 we announced the cancellation. Today, one year later, I am sure that it was the right decision both for the safety of all the participants, and for the serenity of the organizers, despite the fact it cost us a lot in terms of work (pre- and post-cancellation) and money.

Kevin Schug: As the chairperson and organizer of the 2021 meeting in Fort Worth, now cancelled, the past year has been an emotional roller coaster. Of course, we first lamented the cancellation of the 2020 meeting in Riva. Our thoughts continue to go out to our Italian friends for their losses, both personal and otherwise, as a result of this pandemic. It's now a year since that cancellation was announced, and we felt it would be likely that the US meeting in 2021 could bring a reunion of the international separations community. We had plans to expand the conference scope. Our local organizing committee had brainstormed some new opportunities to entice new attendees. We even had some sponsors chomping at the bit to get back to an in-person event. Alas, as 2020 came to an end, it became quickly apparent that convening an international meeting, even in late spring 2021, would not be possible. Unfortunately, we now have even more uncertainty, as there are currently no future plans for reconvening ISCC and GC×GC… However, I believe that will rapidly change as we move out of the fog of this pandemic.

What are the lessons learned from this experience?

Luigi: For all of us, the pandemic was unexpected and certainly changed our lives. Organizing the Riva conference has been a big challenge every time – I've been doing it since 2012. Every time it has been even more complex to attract money and people, due to the increasing number of events competing with Riva all around the world. I truly believe canceling Riva2020 was the correct decision. Riva is Riva and cannot be adapted into a series of webinars or an online event.

Kevin: Thinking on this from the organizer's side, I will be blunt: having a member of our scientific community take on significant personal liability for the financial success of a conference is not a model that will work going forward, in my opinion. I do not plan to put my name on another such contract, especially given the legal consultations we had to endure to invoke a force majeure cancellation for the 2021 meeting. I would suggest that a society of some kind needs to be formed to oversee the annual organization of the conference and to serve as the financial back-stop for the meeting. The model very successfully propagated by the American Society for Mass Spectrometry would be one to emulate, in my opinion.

Kevin: For students and other early-career scientists and professors, there is a real opportunity to connect with, rub elbows with, and even have a drink or share a meal with renowned international leaders in separation science.

Tadeusz: I often had the feeling that my students benefited from ISCC conferences even more than me. They all loved them and were extremely excited about everything that was happening. The chance to see and listen to the great scientists they knew only from papers was invaluable for them. They also got a chance to hone their skills as presenters in front of a demanding but always friendly audience. Finally, they loved the exhibition and the interactions with instrument companies. Being able to see and touch the latest and greatest toys was the cherry on the cake.

What's the importance of social interaction/ networking at these events?

Giorgia: Social interaction is the most important aspect of a conference for brainstorming and inspiration. This is where you can have true peer-discussion and advancement, not only between academia but also with instrument companies. The face-to-face discussions in front of an instrument with real data are an important moment of exchange and enrichment for both sides.

Moreover, Riva and are full of social events that constantly stimulate networking in a relaxing and friendly environment. Despite the number of attendees, participation always reminds me of a family reunion… And each time, we return home with some new friends to contact for the next project and some new ideas to try as soon as possible in the lab! These feelings are irreplaceable.

Philip: Many of the scientific problems that we tackle these days require collaborative efforts between laboratories. In-person conferences offer a setting where these interlaboratory exchanges can be initiated during a coffee break, an impromptu dinner, or a conversation during a sponsored social event. Some delegates find that even the shuttle journeys – Milan-to-Riva and sometimes the bus from Verona – become an opportunity to renew acquaintances, meet new fellow travelers, engage in discussions, and perhaps do a spot of mentoring.

Hans-Gerd: Social events for me are about building and maintaining personal relations. You don't necessarily exchange information, but you build relationships with others. Later, when back in the lab, it is then much easier to contact these people and ask them for a favor. And the likelihood they will help you is much higher if you had a nice evening with them!

What – in your view – would be the impact of the ISCC/GC×GC conferences ceasing to exist?

Giorgia: I don't want even to think about a future without the Riva and Fort Worth Conferences. As I mentioned, I think it is the only place where all the experts in separation science are gathered together and where you can see the potential of techniques despite the specific application. The Riva aand Forth Worth conferences are the places where you imagine the unimaginable, where you see the instruments pushed beyond their limits, where you learn at each lecture, where you get to know the authors that have inspired and driven your work so far.

Philip: Importantly for me, Riva was the place I first hit upon the idea of cryogenic modulation – in a lecture by Hans-Gerd Janssen on the topic of large volume injection in GC. I can't imagine the thought processes that led to the idea, but I am a firm believer that if you attend conferences with the right attitude, an open mind that's willing to think laterally, and soak up the energy, then this might transform the next years of your research. It would be a shame to see this opportunity gone.

Luigi: ISCC and GC×GC have a long history of successful events, year after year. This is because there is no other conference series that includes all the same elements – it's completely unique. Therefore, I sincerely hope the pandemic has only temporarily stopped such a great event, and that it will be planned again, in full safety, by people that truly loved it – the "Riva conference lovers."

Tadeusz: It would be tragic if the ISCC/GC×GC conference ceased to exist. The conference is truly unique, and I really cannot see any viable alternatives. No virtual meetings or webinars will ever be able to recreate the unique atmosphere and energy of the conference. There is no replacement for heated discussions with fellow scientists over a glass of wine. Hopefully, other meetings will step in to fill the void, in the unlikely case that we aren't able to meet again in Riva/ Fort Worth. One possible example could be HTC: it takes place in an attractive historical location (Ghent) and gathers many of the same scientists. Belgium is famous for its beers and chocolate, so there is potential. Unfortunately, Ghent in winter is definitely not as welcoming as Riva del Garda in late spring…

Hans-Gerd: Surviving a year without a conference is possible. I had to do that before when my company introduced travel bans for financial reasons. But if you are no longer exposed to the high level discussions at a conference, at some point you will be trapped in your own limited creativity. Literature complements discussions, but does not replace them.

A word from the instrument manufacturers

Ralf Loescher (LECO) and Björn Thoralf Erxleben (Shimadzu) give us their perspective on the impact of conference cancellations

What is the importance of these conferences to you?

Ralf: The ISCC/GC×GC symposia are seen as something to look forward to by so many scientists from across the world. Traditionally, it could be said that this was a community, and there has been a closely knit association of specialists from both academia and industry sharing a common aim to develop new and deploy best practices to further capabilities, which translate to real life measurements benefits. These events have allowed a group of revered experts to take the stage alongside many aspiring scientists – and for new ideas to be shared and refined in a forum of experience, insight, and innovation. It is definitely true that the mix of the eagerly anticipated social agenda alongside high-class scientific content has equally been a catalyst for momentum in analytical research and development as well as instrument sales and product development.

Björn: At these events, attendees get direct contact and communication with scientists about their direction, wishes, and recommendation for future development. They also provide sales leads and firsthand information about trends in the market. Finally, they are a good forum to listen to a bigger group of researchers.

What do you miss by not attending these conferences?

Björn: ISCC has, for years, been a place for both scientific sessions and social interactions. It was always a good opportunity to meet all the people working in this field – to talk to the opinion leaders in comprehensive chromatography and show new developments suited for such applications. Posters and oral presentations gave an idea of the latest work and potential of different techniques.

Ralf: The COVID-19 crisis has been hard in general for so many, but speaking purely with regards to this community, who do so much look forward to participating, it's worth remembering that there's a reason why; the feelings and atmosphere experienced is special. Not just because of the joy of coming together but because of what it leads to. There's nothing better than real, in-person interactions and exchanging ideas, which always lead to inspiration and learning that drives science and can contribute to making the world a better place.

From your perspective, can virtual events replace in-person ones?

Björn: For an instrument vendor, web conferences and webinars offer less (or nearly no) place to get in dialogue with scientists and present instrumentation and new developments. You also miss the feedback you get from meetings at the booth. On a more positive note, recorded sessions can be watched afterwards with no issue around parallel sessions or missed presentations due to meetings.

Social interaction, open exchange of thoughts, and relationships with scientists are all important because any input about new ideas, trends and "wishes," as well as science-driven "small talk," decreases the distance between researchers and industry. It is somewhat difficult to quantify the impact, but future development at the industry level needs such social interaction as a source of new ideas. Where else is there a chance to meet opinion leaders that mainly work with competitors?

What are your thoughts on the future of such events?

Björn: I think conferences will take place again in person after this situation passes, but whether the size and spending will be the same is questionable. Online conferences have established and improved during last year, so I'm sure there is a place for them in future. It might be that we will see a kind of hybrid event in future: a classic conference with online capabilities. It's difficult to say how much this may impact the total number of participants, but it will. For online conferences, there should be a discussion of how we can better include industry instead of just being a sponsor.

Ralf: In future, we will definitely do things differently, but the blend of possibilities in terms of how we interact could be more powerful based on how we've adapted during the COVID-19 crisis.

At LECO, the use of online meetings, which have now become routine, has also led to a strengthening of the interactions and collaborations between our internal employees globally and also with our partners and customers. We see that real benefits can be achieved in future by mixing the online activities with those vital personal meetings. It can only improve communication!

By blending the interaction of those able to travel and attend in person, together with many more enthusiasts in other locations remotely at the same time, the community will certainly grow and get stronger.

What are your thoughts on virtual conferences as an alternative?

Giorgia: I acknowledge that, in the beginning, virtual meetings seemed a good alternative – but they have become so easy to organize and increased in frequency so much that it has become impossible to follow them properly. They also don't have the same efficiency – they are limited, there is always another meeting waiting for you, there is always another task that it is occupying your mind. Being in a conference, far from your office, you can leave everything else behind and take the time to fully focus.

However, virtual events have opened up some nice new opportunities. Attending is obviously simpler – which is a big plus for students and smaller research groups with a limited budget, and means these events can reach a wider audience. Short workshops or webinars of a couple of presentations have also gained popularity and are a very effective way to guarantee dissemination of information.

Luigi: For all the reasons that have already been mentioned, I do not believe the Riva conference can be replicated as a virtual meeting. We have to wait until we are able to plan an in-person event that will celebrate science in the same way. I truly hope this opportunity will come soon. Of course, we have been very lucky to have online platforms that give us the possibility to have meetings and conferences that continue our research activities.

Kevin: I attend conferences as much for the social interaction and "catching up" as I do for the scientific content. I do not think that experience can be well replicated in a virtual environment. I believe that much of the success I have had working with different companies has come from interactions forged and strengthened through personal interactions at conferences like ISCC and GC×GC. Even now, as I work to develop new relationships with new partners, the virtual medium proves to be more difficult. Perhaps there is so much happening in the virtual space, some communications get lost in the noise.

Hans-Gerd: Webinars are a very good alternative for information exchange, and it is easier to skip a lecture that you find less interesting. What is missing from virtual events is the interaction with the speaker, the ability to ask questions, to give suggestions. Actually, I think the fact that you can easily move away from a not-so-interesting lecture is detrimental for creativity. In a lecture room, you start to think about your situation with certain aspects of the lecture in the back of your mind. Unintentionally – and without noticing it – the lecture will inspire you. There is nothing else to do in the room other than think!

Also, posters for me are a very important aspect of a scientific meeting. In a typical Riva meeting you can maybe attend 40 lectures, but you can easily see 500 or more posters. And posters are intended to stimulate discussion. For me, the weakest point of virtual meetings is the difficulty of seeing posters. I have seen several options for virtual poster presentations. Alas, none of them really worked. The best is the three-minute poster presentation backed up by a digital copy of the poster, but it's still impossible to sit through 500 posters of 3 minutes each.

What do you foresee for the future of such events?

Giorgia: Although I think the physical conferences are irreplaceable, I think we will see an increase in the organization of virtual events. Most probably, these will be hybrid situations

where a few sessions are made virtual to reach a broader audience or to guarantee the participation of authors with travel constraints. Still, nothing will be able to fully replace a physical presence at conferences.

Philip: GC×GC has a vibrant, enthusiastic and committed community who will demand – in the nicest possible way – that the meeting continues to serve the needs of the users who surely are still fascinated by the power, beauty and utility of the method. We hope that the best days of GC×GC are still to come!

But who knows in what form this will be. We cannot accept a no-conference future. But maybe face-to-face conferences will become a part of a new mix of online offerings, including other avenues of information transfer. A "hybrid" model allowing online attendees to participate in some manner in a face-to-face meeting may be a way of meeting the desire of an in-person meeting for some, with the lower costs and maybe convenience of the virtual environment. Making this attractive but not destroying the budget of a conference (for example, if too many opt for virtual) will require some careful planning. Moving forward, there might be a need to have discussions between industry and academic institutions to develop a new model of conferences that provides benefits to companies and researchers – and their institutions.

Luigi: ISCC is a well-established event, with more than 40 successful editions. The Symposium began in Hindelang, Germany, in 1975, chaired by Rudolf E Kaiser, and was moved to Riva del Garda in 1983, under the chair of Pat Sandra. Pat greatly contributed to the growth and success of this symposium, increasing its popularity and international character, and introducing non-EU editions (Japan and USA) from 1986. Since 2006, ISCC has been merged with GC×GC, due to the increasing popularity of comprehensive GC and the common interests of many ISCC attendees. Due to the high level of the scientific program, the importance of the topics, and the way the conference is organized – I can imagine that the conference will soon return to an in-person event on the shore of Riva del Garda again.

Kevin: I see ISCC and GC×GC as the premier conference for GC, in general, and for multidimensional separations. Of course, there is so much more, but I feel that these areas are not as adequately emphasized at other meetings. It would be a shame for the conference series to falter, especially as the popularity of multidimensional separations is on the rise. But, the crystal ball is still too hazy. I expect we will have more clarity as we get to the end of 2021, and I expect that ISCC and GC×GC will return in-person, in some form, sometime, and somewhere.

Tadeusz: I might be old school, but I cannot imagine science without real conferences. Virtual meetings have their merits, especially for people who cannot travel for one reason or another, but they are no replacement for face-to-face meetings. Social interactions over Zoom are not the same as real-life interactions, as we have all painfully learned during the pandemic. I am pretty sure that there will be some virtual component to future conferences to gain a broader audience, but I am convinced that real conferences will make a quick comeback as soon as the COVID situation improves sufficiently.

Hans-Gerd: The field of capillary chromatography is too important not to have meetings any more. There are still many issues to solve in the field, and doing that will require the combination of creative minds, which is most readily obtained via in-person meetings. For me, it is back to the old system, but with parallel virtual broadcasting to combine the best of both worlds, reduce the environmental impact of travel, save time, and expand the target audience. This is the time for new ideas, building on the good aspects of the past, improving the shortcomings, and using new technologies.

Solutions

Real analytical problems
Collaborative expertise
Novel applications

The Dark Metabolome in Your Glass

Unmasking the metabolome of beer to protect the quality of pints and empower archeological sample analysis

By Philippe Kopplin and Stefan Pieczonka

Beer is one of the oldest known beverages – and it remains a firm favorite today. In fact, beer development – and the processes involved – have paved the way for many facets of modern science. An example: fermentation for brewing led to the discovery of microorganismal metabolic regulation through the cultivation of single yeast cells.

Nowadays, food, its safety, and nutritional value are crucial factors regarding our health and well-being. And that's why we study so-called "dark metabolites." These are components of food and beverages that are as-of-yet unidentified. In the case of beer, these metabolites persist in spite of the empirical knowledge accumulated through brewing research over the years.

Our mission is to describe the richness of beer compositions – including these hidden metabolites. This knowledge could also enhance our understanding of archeological beer samples and the people who drank them. We'll toast to that!

To the metabolome - and beyond!

Metabolite profiling of food provides extensive and valuable data regarding food safety and quality. Advanced analytical strategies can decipher complex biological and chemical systems and fathom their interaction with each other and our bodies. But, in addition to already well known molecules, a flood of uncharacterized compounds from food and beverages (the dark metabolome!) influence our metabolism and our health. Our work simply stimulates an awareness of that which remains unknown.

Beer just happened to be the perfect matrix for applying our approach. This is in part because of its rich molecular diversity; there is a wide range of raw materials present in beer, as well as additional thousands of compounds produced through processes such as malting, boiling, and fermentation.

We set out to characterize this highly complex system on a compositional level by extracting metabolic profiles, which in turn drive certain attributes of the drink the world loves so much. The aim: to produce a fundamental base of knowledge about the beer metabolome and its origin beyond common databases. Using such a database, old beer and beer-like beverages (archeochemistry) as well as modern industrialized beer (quality control and inspection) can be put into context.

"Beer development – and the processes involved – have paved the way for many facets of modern science."

A visualized approach

We needed a holistic approach to decipher the diversity, plurality, and complexity of beer samples. But extraction methods and chromatographic pretreatment can limit what can be made analytically visible in terms of polarity and physicochemical properties. Another approach was needed...

A flow-injection analysis (FIA) approach used in clinical metabolomics and for further food samples was our weapon of choice. By diluting beer and then directly and continuously injecting it into the MS system, we can analyze beer with minimal changes to its chemical composition. With FIA, characterizing much of beer's molecular diversity becomes a tangible task; however, it's not all "sunshine and roses." Such approaches require the highest possible mass resolution to avoid overlapping signals and to differentiate all possible elemental compositions.

The most advanced mass spectrometers in terms of mass resolution and mass accuracy are high magnetic field Fourier transform ion cyclotron resonance (FTICR) instruments. Thus, FIA-FTICR-MS approaches have the power to resolve not hundreds, but tens of thousands of features that might otherwise remain hidden in a very short window of time. The magic happens with a measuring time of 10 minutes and as little as half a drop of beer.

Because of its unmatched mass accuracy, which amounts to 0.1 ppm, it was possible to assign a sum formula and concrete elemental compositions to each mass signal. Or, in layman's terms, the MS method can assign a compositional name to previously uncharacterized molecules!

But the approach isn't without its drawbacks... FIA-FTICR-MS lacks information about isomers and concrete molecular structures, which requires a second analytical technique. Another weapon was needed! After raiding our analytical armory for a second time, we decided to characterize the most important molecules on a structural level using UPLC-ToF-MS – and some trusty van Krevelen diagrams!

A pint of van Krevelen, please!

The van Krevelen diagram makes sense of the compositional information that a molecular composition provides. By plotting the ratio of hydrogen to carbon atoms of a molecular formula against the O/C ratio, we can identify regions in the diagram that reflect the compositional nature of respective molecules and associated biochemical origins.

The tentative classification of metabolite compositions of beer into substance classes lies in their biosynthetic pathway. In gluconeogenesis (glucose production by metabolic processes), the addition of water to the pyruvate gives the carbohydrates very saturated and oxygen-rich compositions, which are located in the upper right region of the diagram.

In contrast, the basic building block of fatty acid synthesis, acetyl-CoA, is obtained via an oxidative decarboxylation of the pyruvate. Another dehydration step during chain expansion leads to less oxygenated lipid species. These can be found on the top left of the van Krevelen. Polyphenols are significantly more unsaturated and have lower H/C ratios.

A pint of beer can be mapped according to the corresponding sugar phosphate, nucleotide, and phospholipid spheres. Due to the divergent biosynthetic pathways of the amino acids and the associated different residues, a peptide region is difficult to narrow down. Small organic acids usually have a very high O/C ratio that can exceed the value of one.

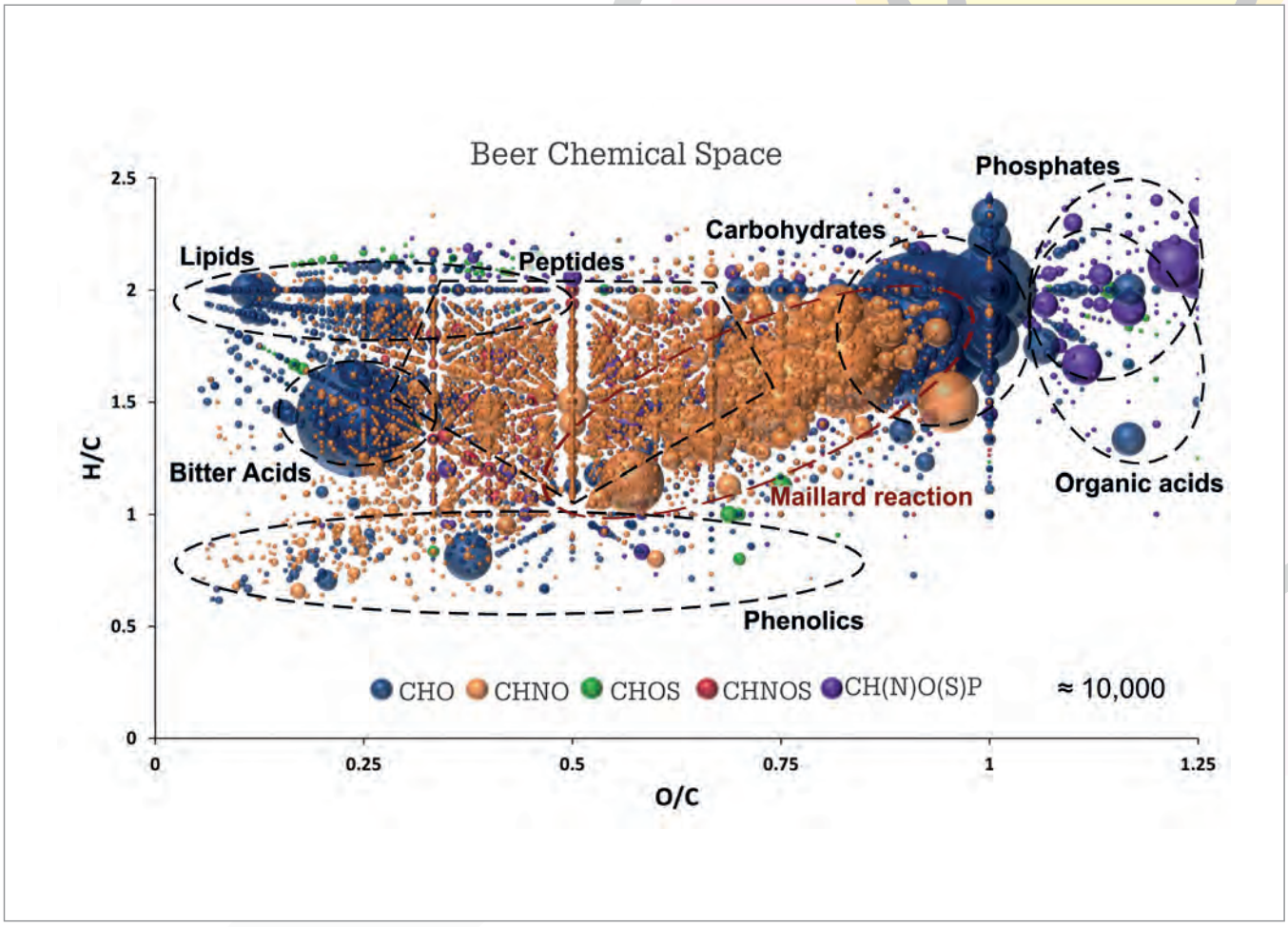
Due to their special biosynthesis, the hop-specific "bitter acid" compounds in beer have both the phenolic base structure and the compositional characteristics of terpenes, which the prenyl side chains are based on. Accordingly, these "terpeno-phenolics" show a very characteristic positioning in the van Krevelen. Hence, it is possible to visualize the entire holistic variety and complexity of the beer metabolome in one diagram! But it is necessary and extremely important to say that these classifications are by no means fixed boundaries; they merely represent well-founded reference points!

A complicated concoction

Our FIA-FTICR-MS approach was able to resolve thousands of yet unknown metabolites in the beer matrix and assign them to possible structural families in the van Krevelen diagram. The definite compositions then enabled us to integrate these molecules into a network via distinct mass differences. These conversions of sum formulae mirror chemical and biochemical reactions and give us information about the processes happening during brewing (and even inside the raw materials used) on a molecular level.

On this basis and through statistical data mining (OPLS-DA), we extracted deep metabolic information reflecting the types of beer analyzed (lager, craft, wheat, abbey). The holistic picture obtained through FIA-FTICR-MS indicated that the hop components in particular differ between these classes. As craft beers are dry hopped (adding hop umbels after the fermentation), these hop components are more oxidized and more phenolic compounds can be extracted.

Far less hops are used when brewing wheat beer, which consequently



A van Krevelen diagram that shows the distribution of 10,000 compounds from the beer metabolome by their H/C and O/C ratios. The diagram maps the compositional space of beer and enables specific patterns to be recognized.

demonstrates reduced richness of these compounds. On the contrary, the metabolic signature of wheat beer is characterized by the additional grain used; wheat secondary metabolites (phytoanticipines) define the unique metabolic profile of wheat beers. And we were also able to describe a previously unknown derivative of those plant defense molecules, which shows the capability of our approach to investigate hidden metabolites.

Numerous empirical studies suggest that the molecular composition of a beer is very diverse. In brewing literature, rough estimates of the exact number of molecules it contains circulate continuously. We have shown that these estimates are clear underestimations – even without isomeric compounds and molecules inaccessible with ESI and sensitivity limitation.

At last, the typical molecular composition of this unique beverage has been revealed.

This base of knowledge may be used to monitor, control, and guide brewing processes to ensure authenticity, and also to investigate unknown samples (such as historical beers) on a molecular level. By showing the potential of extracting certain molecular patterns from this diversity, our work adds value to modern food safety and quality control. Integrating our foodomic approaches into nutrition and health studies could, for example, help correlate a defined molecular pattern with specific outcomes or observations.

The beer of yesteryear

The history of beer accompanies that of our culture and civilization – by no means a run-of-the-mill story of

antiquity and tradition. It all started thousands of years ago, when mankind set out to produce durable beverages from domestic cereals. Since then, the tale has evolved alongside jurisprudence (such as the Bavarian Purity Law, which was introduced more than 500 years ago), technology (refrigeration by Linde is a great example), and science (including the discovery of fermentation by Pasteur and single yeast cell isolation by Hansen, as well as today's cell and gene editing and single-cell metabolomics).

Our study thus provides not only a way to understand beer in previously impossible depth, but also a way to retrace the evolution of brewing means – and even of civilization itself. Different methods of brewing inevitably leave imprints on the metabolic profile of the final (delicious) product. And, for very old but well-preserved samples, it will be possible to trace the methods of brewing used, as well as some of the raw materials and additional processes used.

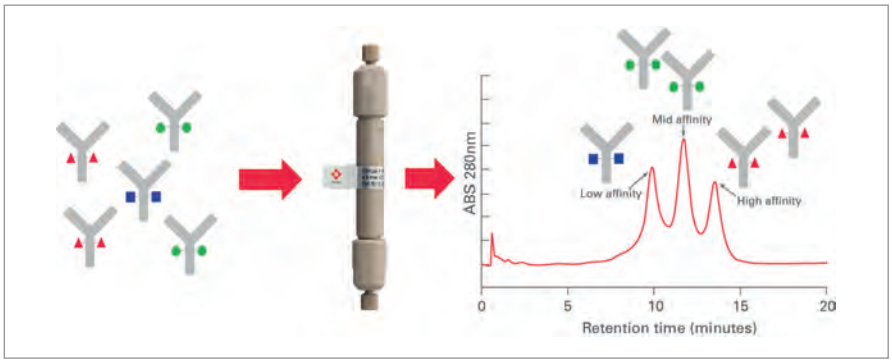
It may come as no surprise that information of cultural importance can also be extracted from archeological samples with our method. Which type of beer was brewed in a specific region at a specific time? Was it already possible to continuously brew with bottom-fermenting yeast (refrigeration)? Are there any clear indications for or against complying with the purity regulations? How was the grain malted (as is reflected in its darkness and dark metabolome)? Answers to all of these questions can be found within.

Admittedly, samples of beer or beer-like finds from earlier human history are rarely so well preserved that one can work with a liquid that has remained behind. In these cases, the residue crust must be examined, and its molecular pattern compared with the beer we know today. We are not limited to individual potential marker molecules, which often are ambiguous. We can offer whole metabolite profiles from hops, used cereals, yeast and fermentation or Maillard processes that offer an extensive base of knowledge about the beer's metabolome.

As for the future, we see this study as a starting point. We hope to open and answer many more questions about the brewing industry – and our society – as time progresses. So let's raise a glass to the future – cheers!

We would like to acknowledge Marianna Lucio and Michael Rychlik for their valuable contributions to this work and Martin Zarnkow and Patrick McGovern for their stimulating discussions in the last decade on beer and civilizations – we couldn't do it without them!

How Fc receptor affinity chromatography correlates with antibody glycosylation and ADCC



Therapeutic antibodies not only specifically bind molecules, but also activate immune responses through interaction of their Fc part with Fc receptors on immune cells. The FcγIIIa receptor is particularly important as it leads to the death of pathogenic cells. The process is referred to as antibody dependent cellular cytotoxicity (ADCC) and increases with along with affinity to the receptor. This in turn depends on Fc glycosylation.

Tosoh Biosciences' TSKgel® FcR-IIIA chromatography columns employ the FcγIIIa receptor as a ligand and thus separate antibodies according their affinity to the receptor. They analyzed the FcR affinity profile in a Rituximab sample in only 30 minutes. Fractions with high, mid and low affinity antibodies were then subjected to a cell-based ADCC assay and glycan analysis.

Learn how ADCC activity and glycan pattern correlate with FcR affinity bit.ly/FcR-Affinity

Avantor® chromatography solutions for the analysis of nitrosamines

Nitrosamines have become an increasingly prominent concern as they are highly potent genotoxic impurities which may inadvertently be formed during the manufacture and processing of various consumer goods. The recent detection of nitrosamines in, and recall of, some pharmaceutical products has further increased concern over the presence of these compounds. Additionally, environmental contamination through the release of nitrosamines, along with their formation during treatment processes (e.g., water treatment), are also areas of concern. Nitrosamines are a class of organic compound containing a nitroso group bonded to an amine (Figure 1) and are typically formed by reaction of a nitrosating agent, such as nitrite, with various amines. Due to many nitrosamines being classified as probable human carcinogens, it is essential to establish and quantify their presence in a broad range of products and sample matrices. This technical note details several chromatographic solutions that can be applied to the determination of nitrosamines.

Download full app note at https://bit.ly/3njNPNV

Spotlight on... Technology

Superior, Repeatable, Traceable Pipetting with the Andrew+ Pipetting Robot

Andrew+ offers fully automated pipetting executed using OneLab software, as well as more complex manipulations, using a wide range of Domino Accessories and Andrew Alliance electronic pipettes.

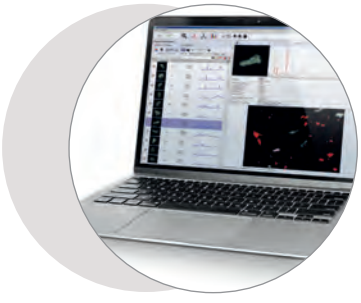
OneLab now makes compliance to requirements easy, as required by both FDA 21 CFR Part 11 and EU Annex 11, enabling regulated labs to take care of documentation requirements, without compromising its market leading versatility and ease of use.

Register now for a Demo of Andrew+ and OneLab! https://www.andrewalliance.com/deminars

Future-proof and safe cold storage needed?

The Eppendorf CryoCube® F570 ULT freezer: Low energy consumption of 7,4 KWh/ day (-80 °C) is combined with powerful pull-down within 210 min and fast recovery back to -80 °C after door opening. Your solution for daily usage – keep valuable samples safe at constant conditions, supported by green cooling liquids.

Learn more: www.eppendorf.com/freezers



ParticleScout Enhanced for 2021 – Raman-based particle analysis tool

WITec's ParticleScout now offers even greater speed, precision and user-friendliness. New features include acquisition time optimization, smart zoom, multiple sample area targeting, illumination options, smart separation of adjacent particles, wedge sectioning of round homogeneous samples and report formatting templates for data presentation.

www.witec.de/particlescout/

Turn Your GCxGC-TOFMS Data into Chemistry with LECO ChromaTOF® Tile

Revolutionize the analysis of GCxGC data with LECO's new ChromaTOF® Tile. By using tile-based Fisher ratios, statistically significant differences between sets of GCxGC data files rise to the top. Days and weeks of data sorting can be reduced to just minutes, so you can spend less time finding the differences and more time finding out what they mean.

https://eu.leco.com/product/chromatof-tile

An Affinity for Water

Sitting Down With… Susan Richardson, Arthur Sease Williams Professor of Chemistry at the University of South Carolina, USA and President, American Society for Mass Spectrometry

Tell us a bit about your current role…

I'm currently a professor of chemistry at the University of South Carolina, where my research mostly focuses on the use of GC, LC, and MS to analyze drinking water disinfection byproducts (DBPs). I am also the President of ASMS for 2020–2022. I absolutely love it here at the university; it's a great environment to work in. I love interacting with all my graduate students – and the undergraduates who want to work in my lab – because the energy they bring to the lab is infectious. I genuinely feel like we're a family. I couldn't ask for a more fulfilling job than having the opportunity to train the next generation as part of my legacy.

And before that you were at the Environmental Protection Agency (EPA)?

Yes, before I came to the University of South Carolina in 2014, I was at the EPA's National Exposure Research lab in Athens, Georgia, for almost 25 years. I had a great career there and did a lot of fantastic research, but it got to a point where I realized it was time to move on – and I've not looked back since!

You mentioned your work focuses on DBPs – can you tell us a bit more about these contaminants?

DBPs are not the classical pollutants that one might think about, like those emitted by industry into rivers. Instead, these are actually formed during drinking water treatment itself. The conundrum here is that, for over 100 years now, we have been treating our water with disinfectants (like chlorine) to make it microbially safe. The unintended consequence is that we've created DBPs that, in turn, are detrimental to our health. My goal is to find out more about these harmful DBPs, discover ways to get them out of the water and to keep them from forming in the first place, and ultimately make drinking water safer for all.

How did you get involved in this area of research?

For context, it was only in the 1970s that anyone started looking at these byproducts from our water disinfection processes. In 1989, I got my PhD in physical-organic chemistry and ended up as a postdoc at EPA because of my experience using high resolution magnetic sector MS. After about two years, I was approached by two scientists who wanted to collaborate on a project around DBPs. Although I didn't know much about drinking water disinfection contaminants, they knew I had experience in identifying unknown compounds. I immediately recognized it as a really important issue that not many people knew about and saw it as an opportunity to use my expertise to help solve a real-world environmental health problem.

You triggered somewhat of a resurgence in DBP research – could you tell us more about that?

There was a lot of nice research published on DBPs in the 1980s, but it then sort of dropped off the radar. I think this is mostly because the Safe Drinking Water Act regulations were established in 1979, so people were lulled into a false sense of security – they thought that, because the EPA was regulating some of the first DBPs found to be toxic, everything was under control. Meanwhile, we were finding all these other DBPs that weren't being regulated at all and were potentially more toxic than the regulated ones. Eventually, I secured US$1.2 million in funding from the EPA and I drew a committee of people together to look more closely at the more than 500 DBPs that were discovered by 1997. We narrowed this down to our top 50 (most likely to cause cancer), and I ran a nationwide study to gather new quantitative data on these compounds. So that's really how this resurgence was triggered – and there are now many other researchers measuring these DBPs.

What's your focus for the next five or 10 years?

I've been working closely with toxicologists for many years, including a big study funded by the National Science Foundation. In this study, we want to find out the driving factors – or, as we call them, "forcing factors" – behind the toxicity of drinking water. On the basis of this, we've recommended that the EPA should be regulating two key classes of compounds: haloacetonitriles and iodoacetic acids. Of course, the EPA moves quite slowly, so I don't know whether this will happen in the next five or so years – but it's something I'd really love to see.

Could you tell us a little about your role as President of ASMS?

I started my two-year term last July. My favorite conference – and favorite society – has always been ASMS. I've been attending since around 1990, and it's amazing to see how much it has grown over the years. As VP for Programs, my role was helping to organize the annual ASMS Conference, choosing the topics and who will chair each session, and so on. As President, I lead our board meetings and appoint people to different committees – like the awards or nominations committees. It's a big job, but I love it – this society has always been close to my heart.

It must have been difficult this last year with the pandemic?

Certainly! We held our virtual "ASMS Reboot" last year, which was a big success, but we are desperate to have the meeting in person this year. We usually meet in June, but this year we've decided to postpone until October 31 to try and ensure we can go ahead with face-to-face plans. We suspect we'll have reduced numbers, but I think, by this point, everyone is feeling cooped up and just wants to get back out there and network with some great scientific minds again!

avantor™

Find out more at **vwr.com/chromatography**

Automated UHPLC method development solutions with novel stationary phases

Solve HPLC method development challenges systematically and efficiently – using Avantor® ACE method development kits – providing chromatographers with more choices for alternative selectivity, without compromising stability or robustness. Combined with ChromswordAuto 5 Hitachi Edition and VWR Hitachi ChomasterUltra Rs, maximise productivity in your method development processes.

VISIT OUR VWR CHROMATOGRAPHY SOLUTIONS WEBSITE

- Product pages, application areas and product links
- Knowledge Centre: Videos, white papers, technical papers
- Application library: Search for thousands of applications

vwr.com/chromatography
vwr.com/ace

02/2021-BB-KS
ZPROVWRI24887-EN