SEPTEMBER 2020 # 90

the Analytical Scientist®

Piracy in the Pantry

You are what you eat - but what exactly are you eating?


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Social (Distancing) Science

How can we tackle scientific misinformation online?

"If we needed masks to survive, we'd have evolved them ourselves."

"You gotta ask yourself, if the 'virus' hasn't been proven, what is the vaccine for?"

"The survival rate is 99.7 percent – why would we need treatment?"

Social media can be stressful. Above, I've included real quotes, from real people, expressing real opinions. Take a moment to digest that…

Our favorite online platforms create and perpetuate social bubbles. Inside, we feel safe – surrounding ourselves with those who hold the same beliefs and ejecting those who dare think otherwise. In the age of COVID-19, these rival bubbles are more apparent than ever.

The problem is real – and it is dangerous. Data suggest that 5,800 people have been hospitalized following their compliance with COVID-19 misinformation obtained through social media (1). Eight hundred have died. Studies have shown that certain measures, such as wearing face masks, are effective at reducing SARS-CoV-2 transmission (2) – but how do we protect ourselves when some throw their mask aside because it didn't sprout from their own face?

I've penned editorials about the need for scientist-to-public communication before, but then the aim was to maintain a bridge between research and public opinion, ensuring relevance now and in the future. This time it's about protecting people.

How can we do this? When sharing science on social media, we need to ensure the information can be universally understood and that it reaches the right audience – bursting the bubble, so to speak. Governments make attempts to break through – but trust is an issue. "Please apologize for falsifying the COVID-19 death figures and release the correct number," reads one comment on a government Facebook post.

As analytical scientists, how can you help? Could you simplify the complex without losing essential information? Could you extract understanding from confusing data? Could you present the solution to someone's puzzlement? After all, these are questions you face every day.

We must all play our part in making science more inclusive and accessible. If not, "fake news" (and fake science!) may drive the public into complacency or misunderstanding – and possibly hospital beds and funeral homes.

Matthew Hallam
Editor

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On The Cover

Perpetrators of food fraud gamble with the safety of consumers. Here, we chose to portray that gamble with a slot machine – and some fruit that aren't as they first appear.

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Sitting Down With

the Analytical Scientist

ISSUE 90 - SEPTEMBER 2020

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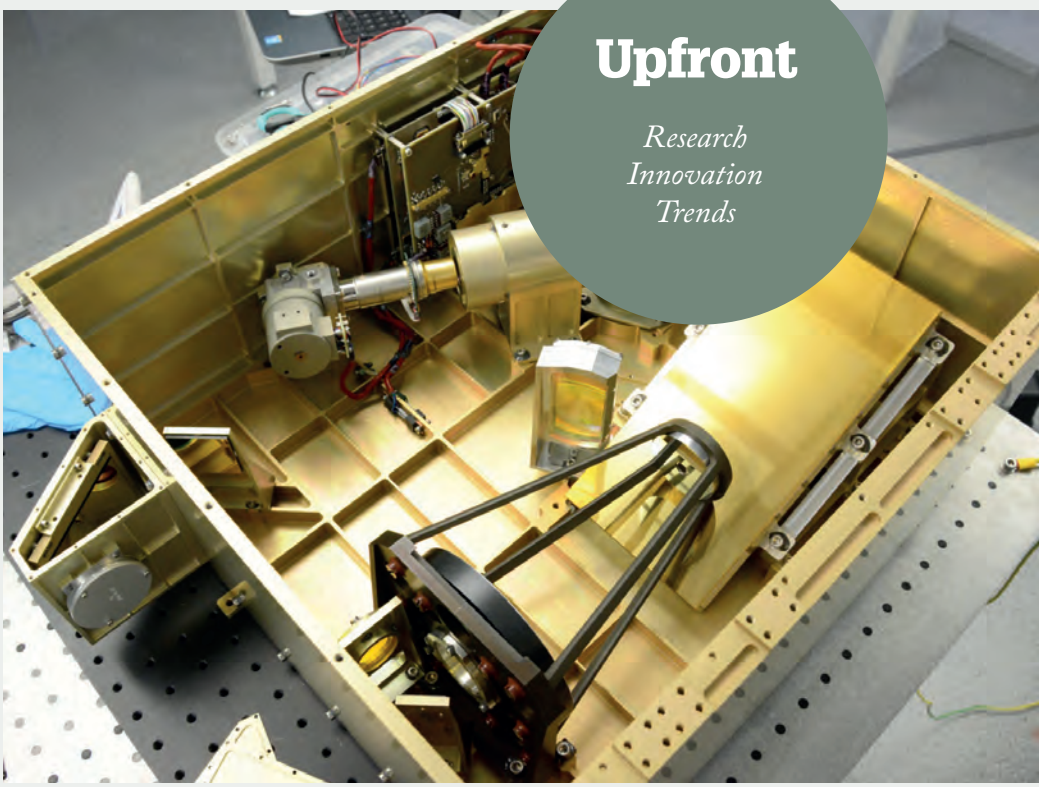
Upfront

Research
Innovation
Trends

Methane on Mars?

The ESA's ExoMars mission finds new gas signatures on the Red Planet



The Trace Gas Orbiter (TGO), part of the European Space Agency's ExoMars mission, has been studying the Red Planet's atmosphere for over two years. Specifically, it has been searching for methane – a sign of biological or geological activity – to help substantiate previous sporadic observations of the gas.

Though methane is yet to be found, new tools on the TGO have enabled the detection of unprecedented ozone and carbon dioxide signatures in the wavelength range where methane signatures would be expected (1,2).

"To our knowledge, these two spectra haven't been accounted for before, so we expect this to have some impact on other teams studying Mars," says Kevin Olsen, lead author of one of the papers. "Our results also show that ozone can be mapped in the infrared, meaning its behavior can be analyzed at lower altitudes than before to build a more detailed understanding of its role in Mars' climate."

Three spectrometers operating in complementary wavelength regions and viewing geometries were used to take the measurements: a small Fourier-transform spectrometer, a near-infrared channel, and a mid-infrared (MIR) channel. "The MIR channel is a completely new concept for atmospheric science," says Olsen. "This powerful technique is great for detecting rare gases – we can look through the atmosphere tangentially (rather than straight up or down), giving us a very long optical path through the atmosphere and increasing the likelihood that sunlight will be absorbed by a gas."

After one full Martian year (or two Earth years), ExoMars has yet to find methane. But the team hopes their findings will encourage further analysis of the available data, so that we can one day soon uncover the mysteries surrounding this elusive gas on Mars.

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TIMELINE

Chandrasekhara Venkata Raman

Exploring the man behind one of the greatest breakthroughs in spectroscopy

November 7th 1888
Born in Tiruchirappalli in Southern India

1904
Aged 16 - obtained his Bachelor's degree in Physics

1906
Aged 18 - had his first academic paper published: Unsymmetrical Diffraction-bands due to a Rectangular Aperture

TESTING, TESTING...

What's new in cannabis analysis?

- Cannabis QA The USA's National Institute of Standards (NIST) launched a quality assurance program for testing labs to help improve the accuracy of label claims on cannabis and hemp products. The program is similar to a proficiency test (without the pass/fail grade) and will involve labs testing samples of hemp oil provided by NIST (1).
- Up in Smoke Researchers used GCxGC-TOFMS to chemically characterize smoke from cannabis "blunts." They identified two compounds that have never been seen in smoke before - mellein and 2-phenyl-2-oxazoline (2).
- New FDA Guidance The US FDA released new draft guidance on clinical research. The guidance covers "sources of cannabis for clinical research, information on quality considerations and recommendations regarding calculating THC levels" and is open for comment until September 21, 2020 (3).
- CBD Label Claims Fail to Stack Up In response to a request from US lawmakers, the FDA revealed that they had tested 147 CBD-infused products and found that a substantial proportion were mislabeled – containing more or less CBD than listed or THC at prohibited levels. Plans are afoot for a larger study (4).
- Pre-Roll Panic California testing lab SC Laboratories detected worryingly high levels of the pesticide chlorpyrifos in a batch of pre-rolls and traced the problem to the rolling paper (5).

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Raman on the Brain

An enhanced spectroscopic approach could be the answer to Alzheimer's biomarker detection

Despite a large research effort in recent decades, early diagnosis of Alzheimer's disease (AD) remains challenging. AD biomarkers have proven invaluable, but we still need a sensitive and cost-effective method to detect them. Now, researchers have shown that fiber-enhanced Raman spectroscopy could help overcome the limitations of traditional spectroscopic methods and enable reliable detection of amyloid β-peptide – a major AD biomarker (1).

The approach involves integrating a hollow-core photonic crystal fiber with conventional Raman spectroscopy and coupling this to surface-enhanced Raman spectroscopy. This enabled the researchers to amplify the weak biomarker Raman signal more than 200-fold. Further research is planned, but the approach takes us one step closer to early AD diagnosis.

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1930
Became the first Asian scientist to win the Nobel Prize in Physics (and any branch of science)

1933
Became the first Indian director of the Indian Institute of Science.

November 21st 1970
Died in Bangalore, India

Mirror, Mirror Focus Small

Researchers move closer to imaging atomic-scale structures using ultraprecise mirrors and X-ray free-electron lasers

X-rays have been allowing spectroscopists to "see the invisible" for the last 100 years. During the last few decades, synchrotron radiation sources have enabled great advances in a number of disciplines – but they have their limits. To study atomic processes, X-ray lasers with a large number of photons must be focused at the width of an atom. And that's where X-ray free-electron lasers (XFELs) come in.

XFELs possess unique properties compared with conventional synchrotron X-ray sources, including unprecedented peak brilliance, nearly full spatial coherence, and an ultrashort pulse duration. But the sub-10 nm focusing of these lasers has so far proved challenging. Now, Takato Inoue and his team have reduced the beam diameter in an XFEL to 6 nanometers – making it possible to image structures closer to the atomic level than ever before.

To achieve this feat, the team had to fabricate ultraprecise focusing mirrors, and then confirm the size and shape of the resulting focused lasers. "We had to tune the mirror alignments with high accuracy," says Inoue. "Even a small misalignment in the mirrors would degrade the focused beam shape and block diffraction-limited focusing." And so a new method for characterizing XFEL beams was needed; enter speckle interferometry. "This method is based on the fact that the size of a speckle – a pattern created by the scattering of laser light – inversely changes with the broadening of a focused beam. It meant we could finally tune the alignments accurately and focus the XFEL down to the nanometer scale," says Inoue.

Next, the team wants to work on creating a more stable sub-10nm XFEL focusing system – and improve on their speckle interferometer. "If we can characterize the speckle patterns from atoms inside a thin film, we will be able to create a 1-nm focusing system in the far future."

Reference

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Search for the Unknown

A new NMR spectroscopy system could help researchers get to grips with the metabolome

Getting to know our metabolomes is tricky. We have to contend with a high diversity of molecular structures and concentrations, as well as a lack of standardized or automated methods for data collection and reporting. But a team of researchers think they can help (1).

Their multidimensional platform for identifying NMR-generated biomarkers involves eight different steps – from statistical spectroscopic tools and two-dimensional NMR analysis to separation techniques like solid-phase extraction. Although the full protocol can take up to a month, an alternative approach with fewer steps could take just two or three days to perform. This could not only speed up metabolic phenotyping studies, but also offer a cost-effective and efficient way to cover more of the metabolome.

Reference

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IMAGE OF THE MONTH

Corona in 3D

This image, taken by the Extreme Ultraviolet Imager on the ESAS Solar Orbiter, shows the upper atmosphere of the sun – the corona – in UV. The orbiter carries both remote and in situ instruments to sample properties of the sun. For example, the SPICE (Spectral Imaging of the Coronal Environment) instrument rapidly analyzes different ions in the solar wind to monitor changes in the sun's features.

Take a look at our website to see the full SPICE spectrum – and much more: https://bit.ly/2EKFzpf

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

QUOTE OF THE MONTH

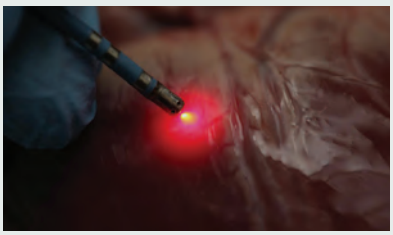
"I think what people don't necessarily realize is that Black graduate students often have to teach too. Institutions can sometimes tokenize Black students and ask them to do this extra Inclusion and Diversity work, but it's important to remember – it's okay if you don't want to do this."

Devin Swiner (@Devin_Eleven), Co-founder of #BlackinChem and PhD Candidate in Analytical Chemistry.

Mending a Broken Heart

Spectral mapping could help treat serious heart arrhythmia

The only way to treat ventricular tachycardia – a serious type of abnormal heartbeat – is by using radiofrequency ablation to prevent abnormal signal transmission from troublesome areas of the heart. But to precisely target such treatment, clinicians face the challenge of differentiating between fat and muscle tissue.



With a solution in mind, researchers have developed a catheter that incorporates near-infrared spectroscopy mapping (1). "The technique lets us distinguish various types of tissue within human hearts because fat, muscle and ablation lesions all have different scattering and absorption wavelength-dependent properties," says research team leader Christine Hendon (2).

The approach could also help researchers develop new computational models to better understand arrhythmia. But in the more immediate future, the team hopes to create an improved catheter and test their technique on large animals.

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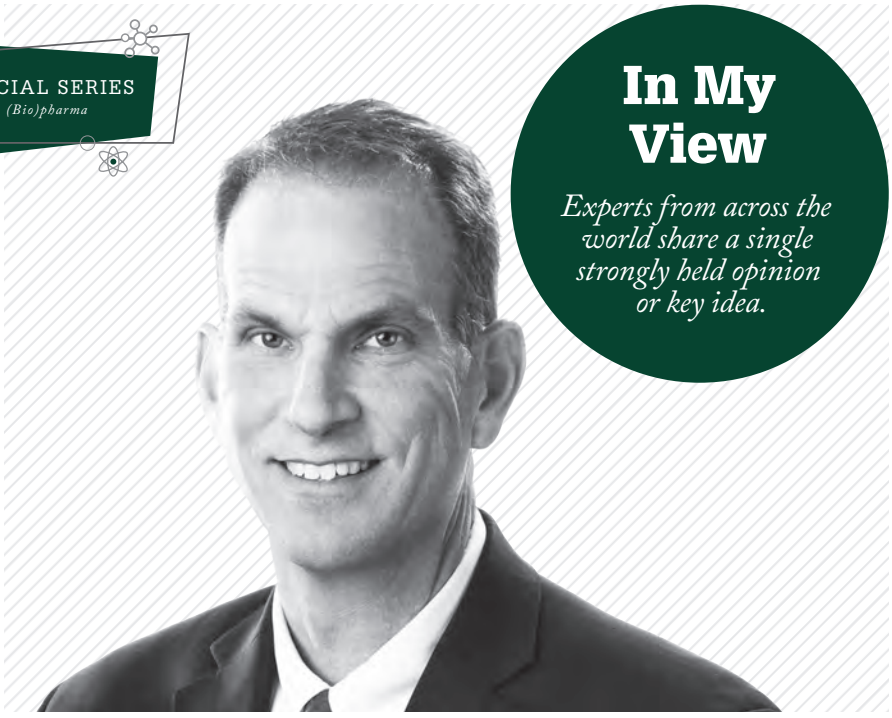
SPECIAL SERIES
(Bio)pharma

In My View

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



Nucleic Acid Therapies: New(ish) Kids on the Block

Medicines derived from genetic building blocks have the potential to transform patient care

By Brian Carothers, Vice President & GM, Nucleic Acid Solutions, Agilent Technologies, Santa Clara, CA, USA

In diseases that arise from genetic mutations, most therapies address the abnormal protein that results. But not nucleic acid therapies; these revolutionary treatments target the biological pathway behind the proteins. Consider, for example, a drug that targets the mRNA upstream of protein expression, thereby affecting protein synthesis – and disease progression.

In short, nucleic acid therapies can alter protein manufacturing throughout the body – a powerful tool for fighting disease. These relatively new treatments show promising results in both the clinic and commercial markets. Market growth is also strong, with increasing investments in research, development, and clinical programs. Coupled with the recent uptick in regulatory approvals, the future looks bright for these therapies.

These treatments are highly flexible – they not only act as gene replacements, but can also be used for immunization (with clinical trials ongoing for nucleic acid-based vaccines). What's more, their success story actually goes further back than many people may realize. The first DNA-based therapy (formivirsen, a treatment for immunocompromised patients with cytomegalovirus retinitis) was first approved in 1998. RNA therapy is a more recent development, with the first of these (patisiran, approved for polyneuropathy caused by hereditary transthyretin-mediated amyloidosis) approved in 2018. And, though patisiran is an RNA interference therapy, other types of noncoding RNA and microRNAs are also under intense investigation as disease treatments.

The synthetic manufacturing process for nucleic acid drugs is both complex and critical for success. Understanding the nucleic acid drugs' sequence, (im)purity profile, and overall material quality requires a skilled workforce wielding state-of-the-art high-performance LC and MS instruments.

Innovators in the CRISPR gene editing area are using programmed nucleic acid synthesis to produce single guide RNA (sgRNA) at chain lengths of 100 nucleotides. As a result, the diversity of structures to examine – not to mention their complexity – is rapidly increasing. This requires expanded analytical capability. Verifying the structures' sequence content and base order is particularly challenging because it involves degrading the oligonucleotide either chemically or ionically. We tend to use the ionic energy of a mass spectrometer coupled with informatics software in which the fragment data from MS/MS is compared with the theoretical oligonucleotide fragment pattern. This approach can achieve up to 100 percent quality verification for batch analysis of nucleic acid drugs.

Combining techniques like chromatography and MS is crucial for the delivery of quality product – not least in our own Nucleic Acid Solutions Division. The division is a contract development and manufacturing organization that aims to provide our clients with effective drug substance to treat patients with unmet medical needs, building on our 25 years of experience in providing microarray services for nucleic acid analysis..

The use of nucleic acids for therapy is a "fairly young" technology whose applications could stretch far beyond those currently considered – typically rare and orphan diseases. Take the case of COVID-19, for example. We could combat the virus in many different ways using nucleic acids, whether through RNA interference (RNAi) therapies that disrupt protein metabolism or as an adjuvant to support a vaccine. I am confident that, in the future, nucleic acid-based therapies will be well-established and broadly used in medicine to address population-level challenges – and I am extremely excited to be a part of this ever-expanding field.

Supporting Information for this article was provided by Blake Unterreiner, Director of Business Development and Customer Relations, and Joe Guiles, PhD Director, Product Development.

Fast and Furious HOS Analysis?

Infrared spectroscopy is a useful technique for higher order structure analysis in the biopharmaceutical industry, but conventional systems lack pace and performance. It's time for microfluidic modulation spectroscopy.

By Jeff Zonderman, Chief Commercial Officer, RedShift BioAnalytics Inc., Greater Boston, MA, USA

The bar is rising for analytical techniques in the biopharmaceutical industry. Data quality used to be the only deciding factor, but other issues are now weighing in – notably, ease of use. Usability is becoming a defining characteristic of analytical tools for biotherapeutics labs looking to do more with less against aggressive timelines. As workflows are refined to maximize information flow, high-throughput systems with automated data acquisition and processing are becoming increasingly desirable. There is a great (and growing) appetite for innovative technologies that can serve this purpose across the biopharmaceutical lifecycle.

Higher order structure (HOS) analysis is crucial in biopharmaceutical development and commercial manufacture; such measurements characterize the secondary, tertiary, and quaternary folding and spatial arrangements that define the three-dimensional shape and interactions of biotherapeutic molecules. Those with a basic grounding in biology will know that changes in HOS impact functionality – and for biopharmaceuticals that can trigger loss of stability, increased aggregation, compromised efficacy, and increased immunogenicity. In short, quantifying and monitoring HOS across biopharmaceutical development and commercial manufacture is critical to understand, identify, and maintain conditions that will reliably deliver a safe and efficacious drug.

A raft of techniques are deployed for HOS characterization, but incumbent technology for secondary structure is currently ill-matched to industry needs (and is a primary target for improvement). Current techniques include far-UV circular dichroism (CD) and Fourier-transform infrared (FTIR) spectroscopy. And both have limitations.

Automated CD instrumentation allows the sequential application of far-UV CD and near-UV CD (for the assessment of tertiary structure) on a single sample set. Such an approach sits comfortably in modern labs, though sample preparation is essential as UV CD is most suitable for relatively dilute and simple solutions. The removal of many common formulation excipients that interfere with the measurement is a common requirement (1).

Infrared spectroscopy has long been prized for its ability to measure secondary structures by probing the amide 1 band associated with stretching vibrations of the protein backbone. FTIR can measure more concentrated, clinically representative samples, and is particularly relevant for monoclonal antibodies because of its sensitivity to the β-sheet motif – a key feature of these clinically vital biologics. However, because of multiple limitations, it is reasonable to assert that FTIR is tolerated rather than loved by the industry… An inability to measure low-concentration samples without pretreatment, susceptibility to background drift, the need to separately collect buffer spectra (and the associated manual background subtraction), poor amenability to automation – all these issues hamper FTIR's use. Clearly, there is a pressing need for more suitable technologies.

Enter microfluidic modulation spectroscopy (MMS). The superior performance of MMS rests on two core technical advances: a high-power quantum cascade laser and a microfluidic transmission cell. The laser enables measurement across a broad concentration range with no sample preparation. The microfluidic cell then modulates the sample with a relevant buffer to deliver automatic background subtraction in real time. MMS systems are also highly automated, with self-monitored cleaning routines and 96 well-plate compatibility. The bottom line: acquisition of sensitive and reproducible data, with substantially less effort.

Such merits explain considerable enthusiasm for MMS from the biopharma industry and point to a bright future within the biophysical characterization toolkit. Industry leaders highlight its ability to demonstrate "high accuracy, linearity, sensitivity, and reproducibility" and "to detect very small protein structural differences, enabling a level of characterization not achievable using conventional FTIR methods" (2). Whether as a replacement for FTIR, for orthogonal measurements of secondary structure, or ultimately as a primary characterization tool for protein products, MMS shows how the right analytical tools can easily find a loving home in the biopharmaceutical industry.

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The Role of (Prote)omics in Next-Generation Drug Development

Collaboration between different omics fields will be key in supporting the next generation of medicines

By Mark Rogers, Senior Vice President, SGS Life Science, PA, USA

Everybody is different. The stark contrast in individual responses to COVID-19 has gravely highlighted this fact. And we also know responses vary when it comes to medications; what works for one person won't necessarily work for another. Next-generation medicines promise a more personalized approach to drug development. When therapeutics are customized to an individual's needs, rather than a broad population, there is a real opportunity to boost efficacy. But where does proteomics come in?

Proteomics plays a crucial role in the discovery of such drugs as it allows the variation in an individual's response to be characterized at the molecular level. In short, proteomics allows the identification of the structural differences in proteins – a major driver of variation. Subsequently, medicines can be designed to specifically target or exploit these structures.

Initial separations for proteomics were based on two-dimensional gel electrophoresis, but the field eventually moved on to separation by LC and protein identification via MS. The key difference nowadays compared with when the field started in the 70s is that we can run studies a lot quicker. Then there is "nanoproteomics." Recent advances in technology have made it possible to conduct proteomic studies on a much lower number of cells, and even perform single-cell proteomics studies. The era of nanoproteomics opens up a whole new wealth of information, including insights into rare cell populations and hard-to-obtain clinical samples.

In addition to the improvements in proteomics research, the move towards data-driven diagnoses and personalized therapies has largely been enabled by advances in other fields. Bioinformatics has seen tremendous progress, now being able to deal with the extremely large amounts of data that these studies generate – and very quickly. The other development, though not particularly specific to proteomics, is automation. We've been able to go from an almost fully manual process to one that requires almost no human interaction. For example, automation of sample preparation and data interpretation have enabled much more rapid processing at either end of the analytical method. In short, we're now able to both generate and process a lot more data than ever before.

In the next 10 years or so, I believe artificial intelligence will further help us identify target proteins and areas where there are problems. I also believe (or perhaps hope) that data filtering will improve. Around 99 percent of the massive amounts of data we collect from proteomic studies is not useful – being able to filter out that 99 percent will prove invaluable.

"In addition to the improvements in proteomics research, the move towards data-driven diagnoses and personalized therapies has largely been enabled by advances in other fields."

It's clear that to obtain a true picture of our responses to drugs, we must look in every corner of biological complexity – from the genome to the proteome and the metabolome (and perhaps beyond). The wide coverage needed is central to a challenge in the drug discovery endeavor; currently, there are many groups that work in each of these omics areas, but rarely do they come together in one place. We must break down these silos and focus on bringing different fields together. Only by working holistically can we begin to more fully understand what's going on at the cellular or molecular level in response to treatments, edging ever-closer to truly personalized medicine.

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PIRACY IN THE PANTRY

Food adulteration puts public health – and lives – at risk. We spoke to scientists from the US Food and Drug Administration's Center for Food Safety and Applied Nutrition to explore how the agency keeps citizens safe.

By Matthew Hallam

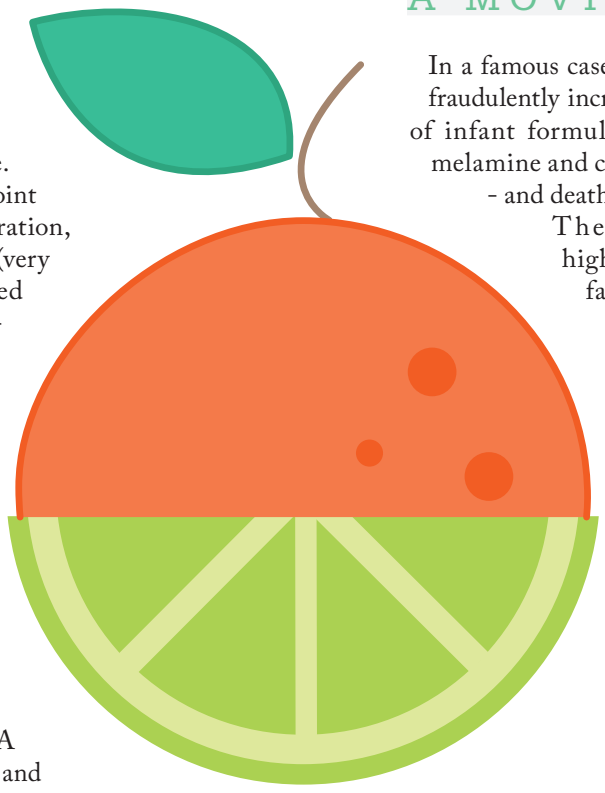
For most people, fraud is a term more often associated with forged cheques or insurance scams than the contents of their kitchen cupboards. In fact, public awareness of food fraud is almost non-existent, despite infamous incidents across the globe. Our readers in Europe, for example, will remember the horse meat lasagne scandal of 2013…

But equine pasta is just the tip of the iceberg. Today's consumers are faced with hoax honey, counterfeit coffee and bogus booze – amongst countless further imposters, each of which carries economic costs and potential risks to health. To complicate matters further, fraudsters are becoming increasingly sophisticated – in many cases, adulterated or mislabeled foods are not identifiable by appearance or taste.

The task of detecting fraudulent foods has thus fallen to the analytical community. Laboratories across the world are playing the role of detective, piecing together molecular clues to identify the criminals tampering with our food chains. We caught up with the USA's ultimate defenders of public safety, the Food and Drug Administration (FDA), to explore how we can protect the consumers of tomorrow.

DEATH IN THE POT

The manipulation of food and beverages is an ancient practice, evidenced by the sweetening and preservation of wine with additives such as honey, herbs, seawater and lead in both ancient Rome and Greece. And, though it's difficult to pinpoint the exact origins of food adulteration, it is known that imported spices (very valuable at the time) were mixed with various seeds and berries – and even dust – throughout the Middle Ages. King John of England passed a law in 1202 outlawing the adulteration of bread with dried pulses, and the first US food safety law (the Massachusetts Act Against Selling Unwholesome Provisions) was passed in 1785.



It was in 1820 that the analytical chemistry community began to take aim at the issue, starting with the publication of "A Treatise on Adulterations of Food, and Culinary Poisons" by German chemist Friedrich Accum. Printed with a foreboding cover featuring spiders, snakes, and skulls, and inscribed with the words "There is death in the pot" (2 Kings 4:40), the book tackled issues from coffee bulked out with dried peas to the adulteration of beer with opium.

In the preface, Accum states, "To such perfection of ingenuity has the system of counterfeiting and adulterating various commodities of life arrived in this country, that spurious articles are every where to be found in the market, made up so skilfully, as to elude the discrimination of the most experienced judges." Though Accum's habit of "naming and shaming" individual suppliers meant the book was met with a degree of controversy, his warnings about the dangers of food fraud are still very relevant today.

"Food fraud or economic adulteration is a difficult issue to quantify," says John Callahan (co-chair of the FDA's Foods Program Economic Adulteration Working Group). "In 2010, the Grocery Manufacturers Association estimated that the yearly cost of food fraud in the US is between $10 and $15 billion (1)." More recent estimates have been as high as $50 billion globally. Yet, the economic costs pale in comparison to the human costs.

A MOVING TARGET

In a famous case from the late 2000s, attempts to fraudulently increase the apparent protein content of infant formula by adding nitrogen-boosting melamine and cyanuric acid led to kidney disease - and death - among infants across China (2). The tragic melamine incident highlights some of the challenges faced by analytical chemists trying to stamp out food fraud. "It is a constantly evolving situation," explains Shaun MacMahon (the Office of Regulatory Science). "As techniques are developed to address specific fraud issues, people intent on adulteration often shift their approaches to avoid detection. The melamine situation, for example, arose because total nitrogen analysis by

"AS TECHNIQUES ARE DEVELOPED TO ADDRESS SPECIFIC FRAUD ISSUES, PEOPLE INTENT ON ADULTERATION OFTEN SHIFT THEIR APPROACHES TO AVOID DETECTION."

THE FDA VERSUS FOOD FRAUD

Most readers will be familiar with the FDA, the agency of the United States Department of Health and Human Services concerned with the protection of public health by ensuring the safety of drugs, foods and other biological products.

Food fraud has been a major focus for the agency since its inception, rooted in the work of chemist Harvey Wiley. Harvey joined the US Department of Agriculture as Chief Chemist in 1883, and spent over two decades conducting research into the effects of harmful chemicals in food. This research took the form of standard tests to assess the purity of commercially available products, and human trials to evaluate the effects of chemical preservatives; volunteers for these trials were referred to by the press as Harvey's "poison squad." His work laid the foundation for the Pure Food and Drugs Act, signed by President Theodore Roosevelt in 1906 – the FDA was founded that same year.

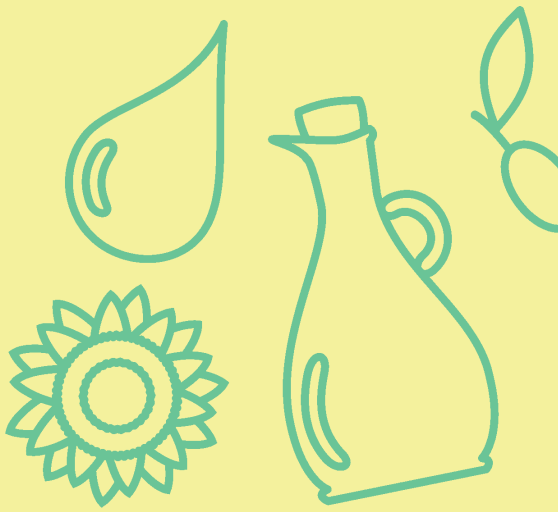
Today, the FDA is responsible for consumed food, medicine and tobacco totalling a value of over $2.6 trillion (approximately 20 cents of every dollar spent by consumers in the US). They are also responsible for the regulation of 77 percent of the entire US food supply, covering all products but meat, poultry and some egg-based offerings.

Per the Federal Food, Drug, and Cosmetic Act, poisonous and unsanitary ingredients are of the greatest concern to the FDA, but the absence, substitution or addition of constituents are also monitored. The latter sometimes fall under the umbrella of "economic adulteration," defined by the group as "fraudulent, intentional substitution or addition of a substance in a product for the purpose of increasing the apparent value of the product or reducing the cost of its production, i.e., for economic gain." The Foods Program Economic Adulteration Working Group has been formed to tackle this form of adulteration.

The FDA works with a number of collaborators to make this possible, including federal and state regulatory partners such as the United States Department of Agriculture, Customs and Border Patrol, the National Marine Fisheries Service, state regulatory agencies, and various stakeholders, such as industry trade groups. The Food Safety Modernization Act, launched by the FDA during under the Obama administration, is a key example of their work on the frontline of food defense.

CLASSIC CASES FROM THE FOOD FILES

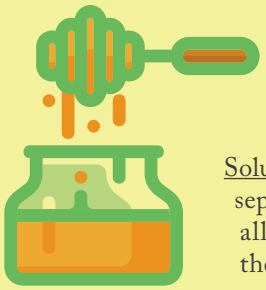
Stefan Tordenmalm, Market Manager of Processed Food at PerkinElmer, shares some of the most common types of food fraud reported by customers in food safety labs, and how analytical chemistry is helping to unmask even the most sophisticated scammers.



HERBS

Problem: herbs are a common target for adulteration. This form of fraud commonly manifests as the replacement of oregano – for example – with olive or myrtle leaves.
Solution: Fourier-transform near-infrared spectroscopy affords researchers deeper sample penetration when compared with mid- or far-infrared approaches.

HONEY



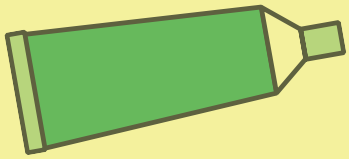
Problem: honey is highly sought after as a sweetener and – in its pure form – should not contain sucrose or maltose. But this isn't always the case…
Solution: the sugar content of a honey sample can be separated using high-performance LC with relative ease, allowing rapid identification of adulteration amongst these samples.

EXTRA-VIRGIN OLIVE OIL

Problem: olive oil is often diluted with lower-cost oils, such as sunflower or soybean oil.
Solution: studying the fatty acid profiles of olive oils using techniques like infrared spectroscopy can reveal the contents of an olive oil sample by comparing the gathered spectrum with that of a pure oil sample. Time-of-flight MS and UV-visible spectroscopy are also useful in these cases.

DYES

Problem: dyes can also be added to foods, purposefully or as the result of cross contamination. Synthetic azo and non-azo dyes are strictly regulated across Europe and the US, but sometimes make their way into spices, such as chilli powder.
Solution: these contaminants can be identified by applying ultra-high-performance LC-MS/MS or Fourier-transform infrared microscopy.

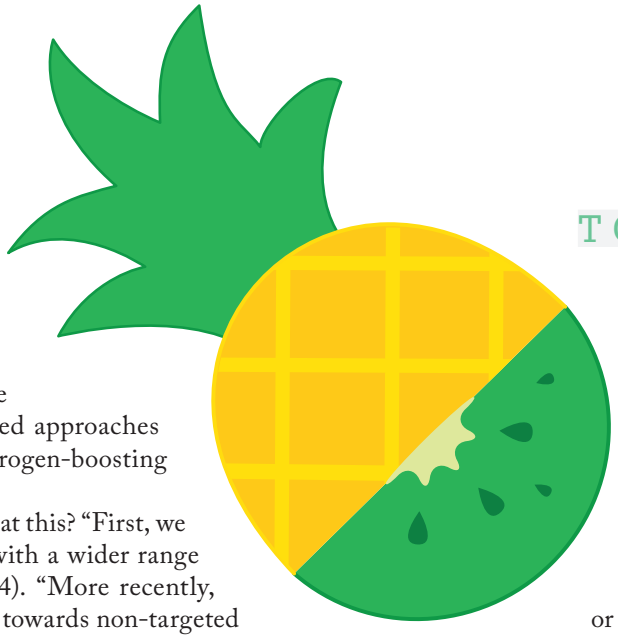


MILKS

Problem: may be diluted with less-expensive milks; a common example is the supplementing of sheep and buffalo milk with cow milk. Dilution with water has also been documented.
Solution: species-specific markers exist in each of these milks, and can be identified by applying LC linked to electrospray time-of-flight MS. Fourier-transform infrared spectroscopy is also used to detect milk adulteration.

WINES

Problem: often mislabeled in an attempt to fool consumers into paying more for wine they believe to be from a specific or more renowned region.
Solution: inductively coupled plasma MS can determine the geographical origins of the grapes by identifying levels of various trace elements in the wine, which align with the composition of soils around the world.



classical techniques was too blunt to detect nitrogen boosting. More specific techniques, in this case GC- or LC-MS, were needed. But these targeted approaches could not detect other nitrogen-boosting methods."

How did the FDA combat this? "First, we developed MS methods with a wider range of targets," Shaun says (4). "More recently, we have witnessed a shift towards non-targeted methods comprising GC or LC linked to high-resolution MS (HRMS). Such approaches streamline the identification of new adulterants."

It's a similar story for another common target of adulteration: honey. Honey tends to be comprised of nectar from C3 plants (plants that produce the three-carbon compound 3-phosphoglycerate through photosynthesis), and is characterized by a specific range of C^{13}:C^{12} ratios. Historic honey adulteration used corn syrup as an additive, but corn utilizes C4 photosynthesis, not C3, and thus produces a different range of C^{13}:C^{12} ratios. Stable carbon isotope ratio analysis (SCIRA) can differentiate these plant products with relative ease.

To evade detection, fraudsters now supplement honey with syrups from other C3 plants, such as rice. "It is much more difficult to apply SCIRA to detect this type of adulteration," says John Mangrum (the Office of Regulatory Science). "This has prompted the evaluation of techniques such as NMR and LC-HRMS to assess the true nature of honey samples."

TOOLS OF THE TRADE

GC and LC (in particular, high-performance LC) play central roles in the detection of fraudulent foods. LC is particularly useful for the identification of naturally-occurring chemical markers that characterize botanical materials and juices. And, as outlined above, the combination of LC or GC with one- or two-dimensional MS detection affords a powerful method for both targeted and untargeted analysis. In particular, advances in HRMS in the form of Orbitrap and time-of-flight instruments and electrospray ionization are making untargeted approaches an increasingly valuable weapon in the fight against fraud.

"Untargeted analyses do not require a preidentified target. Instead, HRMS enables researchers to use accurate-mass measurements to narrow down the range of potential answers to a small number of putative chemical entities," explains Ann Knolhoff (the Office of Regulatory Science). "This is having a significant impact on the development of screening approaches that could identify chemical adulterants before they become widespread." Such screening will prove key for products such as dietary supplements, which may be adulterated with pharmaceutical drugs to amplify the apparent effects of the product. With a huge variety of prescription or over-the-counter drugs used by fraudsters, untargeted analyses could save lives.

Spectroscopic approaches also play a key role – namely NMR, UV,

infrared and near-infrared. The combination of these approaches with chemometric techniques for data analysis enhances their utility. Of note, the (relatively recent) advent of cavity-ringdown spectroscopy has also reduced the cost of SCIRA, improving its accessibility for labs around the world. And, on the topic of isotopic techniques, specific isotope natural fractional NMR is making waves in the detection of suspect wines and spirits.

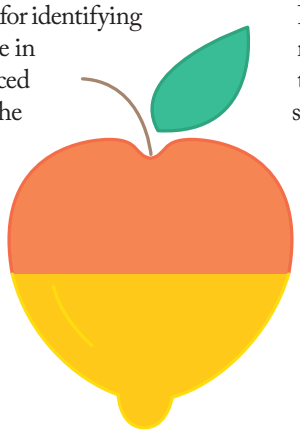
When asked about game-changing techniques in this space, Jonathan Deeds (the Office of Regulatory Science) highlighted the significant impact of DNA analysis. "Detecting fish species substitution (for example, selling farm-raised Asian catfish as wild-caught grouper) was heavily reliant on outdated protein electrophoresis, but we can now apply DNA-based techniques such as DNA barcoding for species identification," Jonathan explains. "The FDA has thus adopted this approach for identifying species substitution. We have applied this technique in investigations of octopus substitution with lower-priced and more easily obtained jumbo squid, and also the substitution of domestic blue crab with meat from lower value swimming crabs."

The approach is also applicable to plant-based samples. "With plants, we witnessed an initial focus on chloroplast sequencing and identification within these sequences, but movement towards genome skimming (a next-generation sequencing method that targets portions of the entire genome) is helping the community identify plant substitution much more efficiently," says Sara Handy (the Office of Regulatory Science).

A BRIGHTER FUTURE?

Looking forward, the FDA is using every weapon at its disposal in the fight on food fraud – including recalls, seizures, injunctions and import refusals when warranted. Import alerts represent a valuable tool on this front, and firms who trigger an import alert (and their products) are now subject to Detention Without Physical Examination.

Analytical advances are another key pillar of the FDA's strategy. As John says: "Food is a complex matrix, and there is seldom one method or technique that can single-handedly characterize every aspect of a sample." The solution? "Methods that integrate multiple approaches to provide full fingerprints of food will likely represent a major focus." This will likely constitute combining broad screening approaches like NMR with untargeted HRMS or inductively coupled plasma-MS to give total profiles of food products. Advances in targeted screening, DNA analysis, chromatographic separations, and MS and



NMR libraries will also be crucial.

"The development of portable devices to move methods out of labs and towards processing plants and docks would also make a huge difference, as would advances in automated sample preparation technologies," says John. Robotics approaches could facilitate greatly improved sample throughput, and portable devices could even allow consumers to assess the safety of food products in shops and markets. One thing is for sure: scientists working in this field will be kept busy.

Indeed, analytical chemists across the globe are hard at work to put consumers' minds at rest. Between new international alliances like the EU-China-Safe project and ever-growing collaborative databases to track confirmed cases of fraud, our defensive arsenal grows each day. And, with the European Commission Knowledge Centre for Food Fraud and Quality outlining such databases as critical for future success (alongside early warning systems and the creation of centers of competence), we are taking confident strides towards better food safety.

However, there is no place for complacency, with experts predicting a rise in food fraud as supply chains are disrupted by COVID-19 (5). When it comes to stamping out food fraud entirely, the words of Friedrich Accum seem as relevant today as when they were written in 1820: "The eager and insatiable thirst for gain, is proof against prohibitions and penalties; and the possible sacrifice of a fellow-creature's life, is a secondary consideration among unprincipled dealers."

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The Beer Scientist

Exploring the key analytical techniques used throughout the brewing process – and the importance of sample filtration

Presenting highlights from the Mark Eurich's webinar "Analytical testing in brewing," which is now available to view on demand at: https://bit.ly/2QbzGU0

As Plato (supposedly) said, "He was a wise man who invented beer." Though it is believed that beer was first "invented" in China over 9,000 years ago, the Western brewing process most of us are familiar with seems to trace back to Mesopotamia – between 3500 and 3100 BC. Since then, everyone from Greek philosopher Sophocles to Saint Arnold (the patron saint of hop pickers) has tooted the life-sustaining properties of this intoxicating substance. Now, there are over 22,000 active breweries worldwide, and many brewing labs rival research labs from a technological standpoint. So, let's delve into the analytical chemistry behind one of the world's favorite beverages…

Meet Mark

I'm the Raw Ingredients Quality Assurance Manager for the New Belgium Brewing Company. I started with the company in 2014, and played a key role in the buildout of a new brewery in Asheville, North Carolina. On this project, I also set up a quality assurance team and acted as its manager for five years before starting in my current role. Over the years, I've held quality and analytical roles at Coors and MillerCoors for just over 20 years, and have conducted some great research into beer flavor stability. I've also been an active member of the American Society of Brewing Chemists since 2007, and have served on the Board of Directors of the American Society of Brewing Chemists, acting as both the Publications Chair and the Technical Committee Chair.

The beer necessities

The brewing process begins with raw ingredients – water, malt, hops, yeast, carbon dioxide and spices (amongst other things). Throughout brewing, sensory (visual, taste and aroma) testing is a key part of the analysis, but many other tests are performed at the raw ingredients stage.

Let's start with water, as it makes up around 95 percent of what's in your glass. A lot of water analysis is performed at your municipal water supply – so I suggest you check your reports closely – but other tests include checking for free chlorine, pH, and microbes. There are two common yeast strains used in beer brewing – one for lagers and one for ales – so microbiological analysis is important for assessing not only yeast health, but strain type.

Carbon dioxide, which is used extensively throughout the brewing process, is mostly analyzed by suppliers using GC. Malt suppliers also perform a range of tests to ensure that the malt tastes and smells as desired. In fact, these labs probably use more fluted paper filters for sample preparation (*https://bit.ly/3jtUS4c*) than any other kind of lab. And after harvesting, hops are analyzed for moisture, acids, and oil content.

> *"It is critical that the right sample-preparation method is used for the attribute you are measuring – you don't want to inadvertently remove the compound you're measuring..."*

Obtaining the perfect sample

Many sample filtration and preparation materials and methods are used throughout the brewing process to ensure accurate analysis. These include gravity and decant filtration, centrifugation, filter paper, glass fiber filters (*https://bit.ly/2YTqLvb*), filter discs, solid-phase extraction, vacuum filtration, and diatomaceous earth. It is critical that the right sample-preparation method is used for the attribute you are measuring – you don't want to inadvertently remove the compound you're measuring, but you also want to ensure any interferences are filtered out.

Wort – the sugary part of beer – should be analyzed for a number of attributes, including clarity, density, color, bitterness, pH, fermentable

carbohydrates, metals, and proteins. It is equally important that carbon dioxide is also addressed from fermentation through to packaged product. If not, it will greatly impact the analysis being conducted. Pouring, sonication, filtration, gas purging, membrane degassing, vacuuming, microwaving, and shaking are just some of the methods used in these analyses.

Fermented beer is arguably the most difficult sample to analyze because of its complexity. It is at this step of the brewing process where the key characteristics are created. For density, alcohol and pH evaluation, filter paper or centrifugation can be used to prepare the samples. For yeast health evaluation, the sample can be diluted prior to testing. And for other microbiological testing, the sample can be plated or subjected to vacuum filtration.

The final product

To analyze mature or aged beer, yeast must first be removed by centrifugation or settling. Some breweries use other forms of yeast removal, such as cross-flow filtration. Filtration is crucial because if carbon dioxide is not properly removed, the measured pH could be artificially low due to the presence of carbonic acid. Particulate or haze should also be carefully filtered to ensure proper color evaluation.

To achieve a bright beer – beer with little or no haze that is visually stable throughout its shelf life – you need to add an extra filtration step; for example, centrifugation, diatomaceous earth, cellulose-sheet filtration, or cross-flow membrane filtration. Once the beer is packaged, sample preparation is quite simple, but any carbon dioxide must be carefully removed once again.

If you missed the webinar on this topic, you can view the on-demand video at: https://bit.ly/2QbzGU0. Cheers to that!

Ask the Expert

Do big breweries and microbreweries do different tests?

Larger breweries and smaller breweries certainly have different laboratory capabilities. The larger breweries can often use more complex instruments, but there's usually a way for a smaller facility to make the same measurements.

Do you think a more detailed metabolite profile of beer via GC or LC is needed for consistency in the future?

With the cost of these tools decreasing, I can see that being a possibility. GC is a tool that we utilize to maintain consistency in our beer products, whether it's volatiles or organic acids. With the purchase of more expensive instruments, you also need more highly skilled technicians. But still, these are currently used in some smaller facilities so I do see it happening in the future.

What analytical instruments are used to measure bitterness?

The most common is extraction. There are also more sophisticated methods, such as (U)HPLC. One technique I didn't really touch on in the presentation is segmented flow analysis, which is more complex and has a higher throughput. The other one would be your sense of taste!

The Top 10

GAME CHANGERS IN HPLC HISTORY

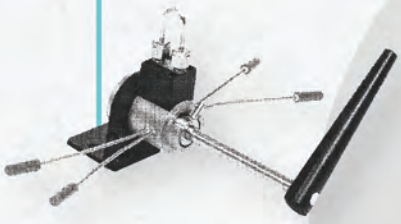
Progress in any field is expected if not inevitable; as technology advances and as new knowledge is gained, iterative improvements feed a baseline of linear evolution. But there are also often leaps forward – true innovations. Here, we look back on the first 50 years of HPLC instrumentation and select the Top 10 (okay, you got me, a tie made it a Top 11) breakthroughs that paved the way for the technique we know today.

By Ron Majors, ChromPrep, West Chester, PA, USA and John Baltrus, Co-chair, Instruments and Artifacts Committee, Science History Institute

When HPLC was "discovered" over 50 years ago, it revolutionized the field of analytical chemistry. Major developments in the technique – which seemed to occur almost yearly in the 1970s and the early 1980s – ranged from revolutionary to evolutionary. During that period, the technique quickly shifted from a large-particle, gravity-fed, large-bore glass column technique to an automated, small-particle, high-pressure, narrow-bore stainless steel column technique. In the story of HPLC development, the column and the instrument are intertwined – and both have played pivotal roles in increasing separation speed, boosting efficiency, and improving quantitation.

In this article, we attempt to identify – with the help of a panel of LC, data systems and mass spectrometry experts (see "We Couldn't Have Done It Without You") – the developments that truly "made a difference." We believe the resulting Top 10 allowed HPLC to surpass most other techniques in terms of application range and its ability to answer analytical questions. And so, without further ado...

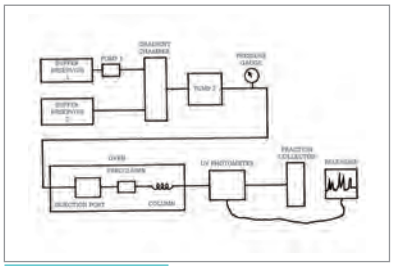

LABORATORY DATA CONTROL




THERMOSPRAY
LC-MS
VESTEC

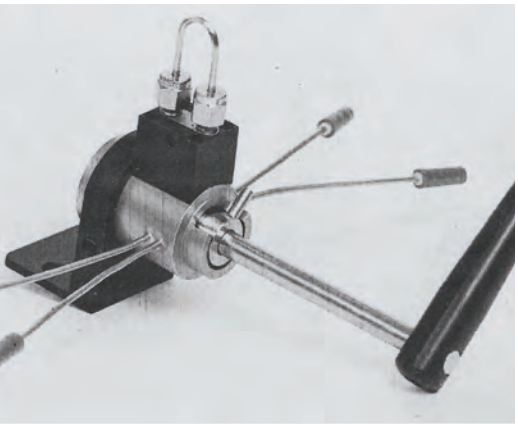
THE TOP 10

Some of the chosen products in the Top 10, though not necessarily the best sellers or performers, were the first to be introduced into the market and being first gave other instrument developers a target to beat, driving further advancements in the technology ending with today's UHPLC.



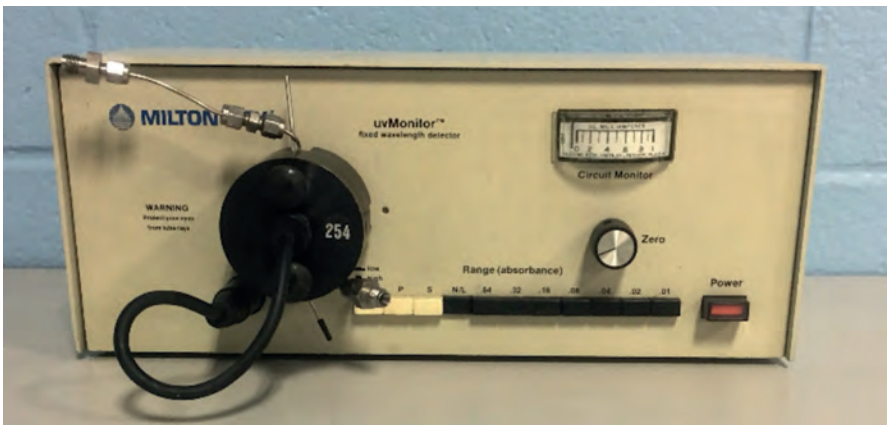
1. LCS-1000

Year: 1967
Company: Picker Nuclear
The first commercial integrated instrument to qualify as a modern LC instrument, including a UV 254nm detector, acquired by Varian Associates in 1968.



2. 6-Port Injection Valve

Year: 1968
Company: Valco
Did away with septum injector and stop-flow techniques, allowed high-pressure injections, improved retention time, reproducibility, automation and quantitation.

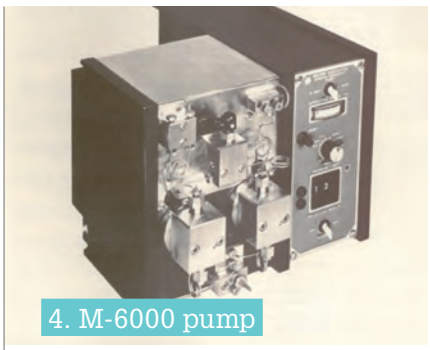


3. Modular Components

Year: 1968
Company: LDC/Milton Roy
Components like the standalone 254 UV detector, LDC RI detector and Milton Roy minipump were used quickly by modular chromatographers. The first instruments were integrated, with all internal parts in a single box. The modular market sprung up to allow researchers to get the best component (for example, pump, injector, column holder/oven, detector). LDC was the first component company to step up and supply affordable and functional modules.

4. Autolab System IV Computing Integrator

Year: 1969
Company: Autolab
The first automatic integrator for chromatography replaced cut and weigh, planimeters and recorders with built-in mechanical integration. This data system was first used in GC and adapted to LC. Features included tangent peak detection, baseline correction and normalized peak areas, and allowed the use of response factors and internal standards. Autolab acquired by SpectraPhysics in 1969.

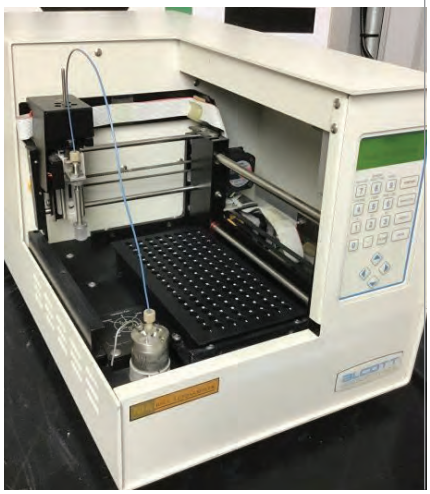


4. M-6000 pump

Year: 1972
Company: Waters Associates
First pump designed specifically for HPLC. Key features: dual reciprocating, less need for pulse damper, 6,000 psi output, and a low-volume chamber.

5. Model 708AL Autosampler

Year: 1974
Company: Micromeritics
The first automated sampling device for HPLC; improved throughput and quantitation ability. Future products improved on this unit.



6. HP 1084

Year: 1976
Company: Hewlett-Packard
Integrated HPLC system with automated sample injection, flow control, UV detector control, recording and reporting. First LC with digital processor control, with a built-in keyboard with push button control. It became the gold standard for quality and performance for many years.

9. Charged Aerosol Detector (CAD)

Year: 2005
Company: ESA Biosciences
Sometimes described as "the poor man's mass spectrometer," the CAD is a universal detector. It has much greater sensitivity than the RI detector (also a universal detector). It is still in widespread use today.

7. 8450 Diode Array Detector

Year: 1977
Company: Hewlett-Packard
The diode array detector allowed on-the-fly UV-VIS spectra during the chromatographic process, with excellent signal-to-noise performance. Productivity increased compared with stop-flow spectral scanning. Other companies soon followed with their own diode arrays.

8. Moving Belt LC-MS Interface

Year: 1976
Company: Finnigan MAT
The moving belt was introduced by McFadden, Schwartz & Bradford of Finnigan MAT. Despite some drawbacks, the moving belt provided true chromatographic interfacing, the first successful LC-MS interface on the market, and was the best of many approaches – until electrospray came along.

10. Acquity UPLC

Year: 2004
Company: Waters Associates
For the introduction of sub-two micron particles, new higher pressure instruments were required. The Waters Acquity UPLC system was the first system designed to meet the needs of the new small particle columns with a pressure output of 12,000 psi. Lower extra column effects and other embellishments were added to Acquity to meet the goals of modern UHPLC.

We Couldn't Have Done It Without You

The authors sincerely thank experts in the field of HPLC, mass spectrometry, and data systems for lending their time to help identify the real breakthrough instruments, supplying dates of product introductions, and helping to run down information that has long been "lost," especially in the commercial sector.

John Dolan (retired, LC Resources), Bob Stevenson (columnist emeritus, American Laboratory) and Dick Henry (founder, Keystone Scientific) spent countless hours digging through their files (and basements) to come up with some key contributions.

Tom Jupille (retired, LC Resources), Jane Gale (Historian at the American Society of Mass Spectrometry), Jack Henion (Emeritus Professor at Cornell University and Founder of Advion Biosciences), Dieter Hoehn (retired VP, Hewlett Packard), Geoff Cox (retired HPLC expert) and Glenn Ouchi (retired data handling expert) deserve thanks for helping to run down some critical information and provide sources of materials.

HONORABLE MENTIONS

Choosing a Top 10 was not easy. To enrich the story (and to help us sleep better at night), we also decided to highlight those technologies that strongly influenced modern HPLC technology but didn't quite make the cut.

1a. ALC-100

Year: 1967
Company: Waters Associates
The image above shows Robert Burns Woodward with his Waters ALC-100. This was a modified GPC-100 with lower dead volume. It was the first, most popular general-purpose instrument.

1b. 820

Year: 1969
Company: Dupont
Integrated with a constant pressure pump, Model 410 UV detector, oven and Dupont ZIPAX SPP columns.

2a. U6K Injector

Year: 1973
Company: Waters Associates
Developed specifically for HPLC; loop by-pass to prevent column shock, 6000 psi capability, variable injection volume.

History in the making

Within the Science History Institute, near Independence Hall in Philadelphia, you will find a permanent exhibit titled Making Modernity, which places historical analytical instrumentation in the context of the great human adventure of discovery in the chemical and molecular sciences. Other objects in the Institute's collection are documented online at the Institute's website (*www.sciencehistory.org*), while a large portion resides in storage, where it is available for use in rotating exhibits at the museum.

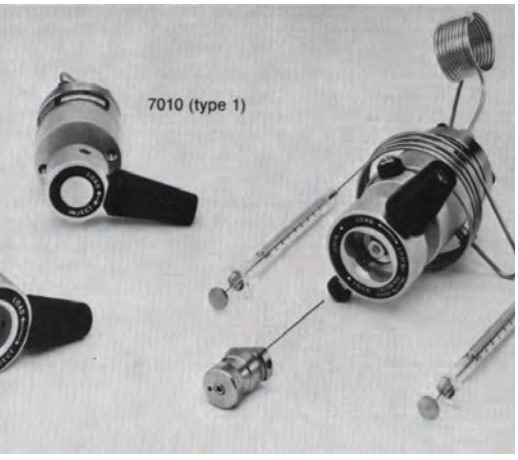
Much of the early instrumentation collected by the Institute originated from the Antiquities Museums of Pittcons 1994 and 1999. But the collection has grown over the years thanks to many donations, including a major one (133 instruments!) from Bodenseewerk Perkin-Elmer in Germany. To curate the collection, the Institute has relied on a volunteer group of active and retired chemists, who formed an Instrument and Artifacts Committee (IAC) in 2000 to provide guidance on what instruments to collect, what donations to accept, and to offer input towards the design of the permanent exhibit.

The IAC debated and then published a list of "50 Instruments That Changed the World" in 2004 and followed that with another "10 Most Wanted" list of instruments that were actively sought by the museum. Both lists were updated periodically as debate on the former continued and some, but not all, most-wanted instruments were acquired.

Today, the IAC has transitioned from creating lists to debating how best to identify and collect instrumentation that adequately documents advances across all fields of chemistry as the present becomes the past. Limited storage and display space is one challenge, but the Institute occasionally receives offers to acquire historically-significant instrumentation that is simply "too large to collect!"

In truth, the current collection is somewhat skewed towards spectroscopic instrumentation (the majority of IAC members were spectroscopy specialists in the early days, after all!). The chromatographic collection includes some early GC instruments, such as the F&M 700, P-E 154, and a Varian Aerograph 2100 among others, but we have only a limited selection of HPLC instrumentation. And that's why we are keen to collect or document instruments that have "made a difference" in the 50 years of development of the liquid-phase separation technology.

You could consider the technology featured in the "Top Ten" and "Honorable Mentions" our wish list! If you can help contact: baltrus@pittcon.org.



2b. 7125 Valve

Year: 1976
Company: Rheodyne
Allowed syringe injection into the valve center and became greatly popular. Later used as OEM by many instrument companies.

3a. CE212

Year: 1971
Company: Cecil Instruments
Standalone first variable wavelength detector with stop-flow scanning.

4a. 4100/4200 Syringe Pump

Year: 1970
Company: Varian Association
A new pumping principle and the first syringe pump for high-pressure operation and pulseless flow. Succeeded by the Model 8500. The isocratic (Model 4100) gave stable flow rate, while the gradients (Model 4200) suffered from solvent bulk compressibility, affecting flow and solvent composition reproducibility. Varian is now a part of Agilent Technologies.

4b. 110 Pump

Year: 1976
Company: Altex
First affordable standalone reciprocating pump with optimized duty cycle via variable piston speed, which lowered flow pulsations. The 110 gave a smoother flow, better baselines and improved quantitation, and set the tone for future pump development.

5a. HP 3380A Digital Integrator

Year: 1974
Company: Hewlett-Packard
Microprocessor-controlled integrator with a chart recorder and alpha numeric printer-plotter. All calculated data given on one piece of paper.

5b. PC Software

Year: 1979
Company: Nelson Analytical
Used PC as a driver for peak integration, quantitation and instrument control,. OEM to many manufacturers. After the Nelson SW, almost all instruments used a PC to control the hardware and to handle the data; standalone computing integrators died a rapid death (company acquired in 1989 by Perkin Elmer).

What about the next 50 years?

We asked our expert panel to gaze into their crystal balls and predict at least one game changer they'd expect to see in the next 50 years of HPLC

Majors: In the short-term? I'd expect to see miniaturized easy-to-change monolithic or pillar columns fully integrated into the handheld – or pocket sized – battery-powered LC system without end fittings or added dead volume. In the long-term, I think we'll see miniaturized, personal separation systems with integrated components and sensitive, selective universal detection capable of performing real-time analysis of a person's health status.

Jupille: I think we'll see a change to "instrument as an appliance," with a one-button "Analyze This!" interface. Longer term, I hope powerful AI-based systems integrated with LC hardware will make "walk-up analysis" a reality: The analytical chemistry analog of a self-driving car.

Dolan: A dedicated analyzer with integrated sample preparation. The sample could be deposited on card or finger-prick, inserted into instrument and produce complete analysis in less than a minute. It would also be great to see inexpensive continuous/periodic monitoring LC devices that predict breakdowns before they happen!

Ouchi: In the next 50 years? I think the user will be able to submit a sample to an instrument, select the analyte(s) to find in the sample and a smart instrument will automatically analyze from an inboard list.

Henry: In the short term, I believe we could see a practical version of a multidimensional LC system where current problems in quantitation are solved. In the long term, smart, automatic instruments where an unskilled user does not have to change columns, develop methods or perform quantitative analysis.

6a. LC 5000

Year: 1977
Company: Varian Associates

A completely new approach to an integrated system. The Pump was designed to accept three solvents into a single pump head with low-pressure mixing. The system had its own CRT and keyboard, detectors could attach side on, and aspects of LC except the data system - which was external - were handled by microprocessor. This system set the stage for most LCs to follow.

6b. Model 10 Ion Chromatograph

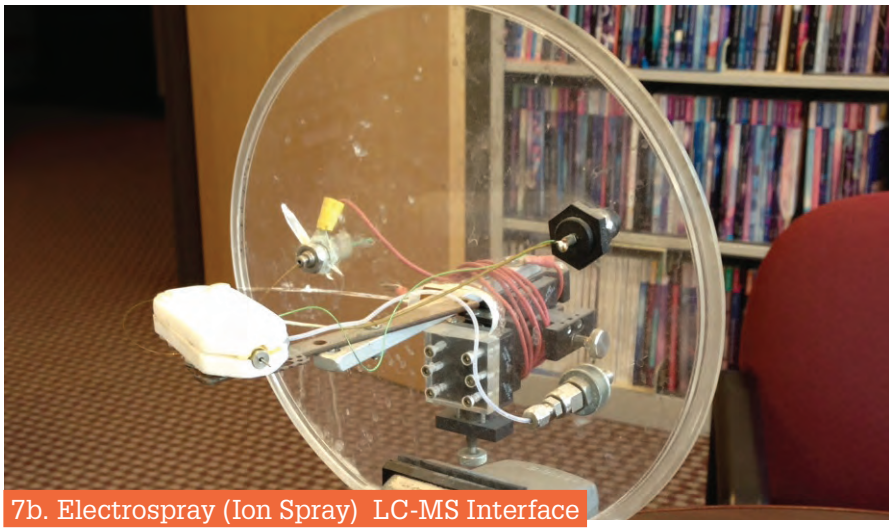
Year: 1975
Company: Dionex

Durrum instruments acquired patents from Dow Chemical and started a separate division (Dionex) to develop a product to separate ionic compounds with conductivity detection using a suppressor column to remove salts from mobile phase and reduce background conductivity. Dionex became a leader in this technology and remains #1 today (now part of Thermo Scientific).

7a. Thermospray LC-MS Interface

Year: 1987
Company: Vestec

EI-type fragmentation sometimes observed as was significant fragmentation of protonated or deprotonated molecules. Low sensitivity was achieved for non-volatile analytes across a limited range of LC conditions. This became the primary LC/MS interface until the 1990s, primarily due to the observation of EI-type fragmentation.



7b. Electrospray (Ion Spray) LC-MS Interface

Year: 1989
Company: Sciex

John Fenn (Yale University and independently) developed an electrospray ionization (ESI) source that produced intact, high-molecular-weight, multiply protonated or deprotonated ions. Fenn received the Nobel Prize in Chemistry in 1992 for this discovery. His acceptance speech was titled "When Elephants Fly." ESI sensitivity was observed to be analyte-concentration-dependent. Peaks eluting from capillary columns are significantly sharper than from wider bore columns, leading to greatly increased sensitivity with lower injection volumes. Now, with various other API techniques, this is the standard MS interface for LC. Henion et al developed (1) ion spray interface that used nebulized nitrogen to assist electrospray operation; SCIEX used the Henion patent (2) and was first to market the product.

To simply rank the Top 10 does not do justice to their impact. Head to the full version of this article on our website to read the complete story behind each of the instruments featured, including much needed context – and a history lesson to all but the most seasoned LC users!

You can also let us know whether your Top 10 matches ours – we'd love to hear your thoughts (or even grievances) and urge you to share them in the comments section on our website!

We have taken these photos from our archives of press releases. Copyright owners can contact Frank van Geel (Frank.vangeel@texerepublishing.com).

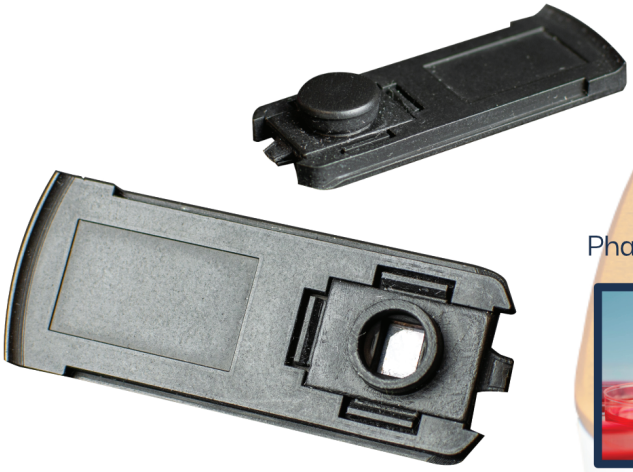
References

1. *AP Bruins, TR Covey and JD Henion, "Ion spray interface for combined liquid chromatography/atmospheric pressure ionization mass spectrometry", Anal Chem 59, 2642 (1987).*
2. *JD Henion, TR Covey and AP Bruins, Ion Spray Apparatus and Method, United States Patent No. 4861998 (1989).*

THE ARROW

Silicon ATR Consumable Slide

Analysis of Packaging adhesives



The Arrow applications

Pharmaceutical Petrochemical Life Science Glues

Did you know that your crisps packets, drink pouches or even dog food packaging are made of many polymer layers stuck together by glue to optimise mechanical and barrier properties? Conventional Lamination Adhesives used in multi-layered flexible packaging are commonly a product of solvent-based or solvent free two-pot systems that undergo the following reaction:

Polyol (-OH) + Isocyanate (-N=C=O)➡Polyurethane lamination adhesive (-NHCOO-)

The packaging industry often use FTIR to screen test the decay rate of isocyanate (NCO) in a freshly applied adhesive because unreacted aromatic NCO molecules can migrate through laminated packaging into food to react with water molecules, generating carcinogenic primary aromatic amines that are harmful to humans and pets alike! By measuring the reduction of NCO absorbance peak height over time at ~2270-2250 cm-1, this decay serves as an indicator for adhesive curing speed and food packaging safety. The spectra below were taken over time from the same solvent free adhesive on a single Arrow slide:

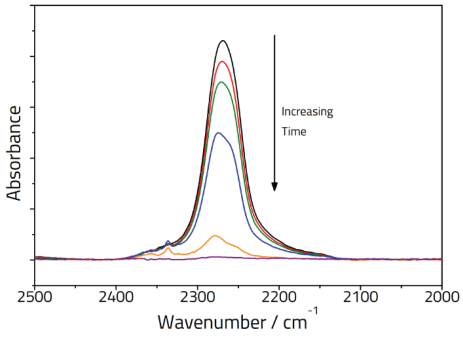


Fig1. Decay of NCO in absorbance mode over time in a two-pot packaging adhesive at standard mix ratio

Multiple Arrow Slides can also be used to compare the curing speed of different adhesives at the same time. Adhesive curing speed has many variables like OH to NCO mix ratio, curing temperature, relative humidity, the crosslink-ability of starting components and the reactivity of the aromatic NCO component amongst other factors. Sometimes the curing process can take days or even weeks, so to have just one conventional crystal ATR puck occupied for prolonged periods might not be coolest idea! High volume batch sampling using Arrow consumable ATR Slides can really save you time and speed up your work to make your organisation more competitive! Furthermore, once the polyurethane product is formed on your crystal, it could be difficult to remove and you might run the risk of damaging a relatively more expensive crystal puck; after all glue is designed to stick! So, the next time you test a sticky adhesive, varnish, paint, ink, or coating, why not give the Arrow a go?

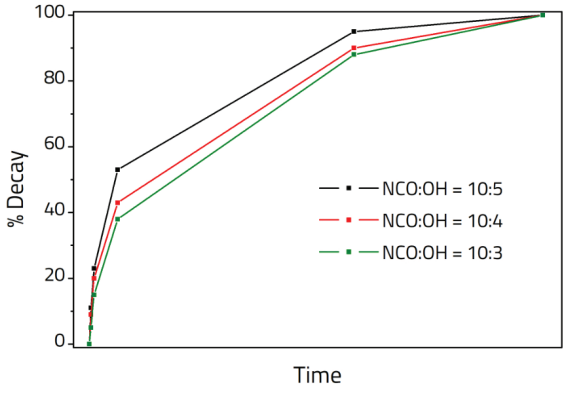


Fig2. Curing speed of adhesives at different mix ratios

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THE *Spectroscopy* SUPERBOWL

SCIX UNITES ANALYTICAL WIZARDS FROM AROUND THE GLOBE – BUT WHAT MAKES THE EVENT SO MEANINGFUL FOR ATTENDEES? AND WILL THE EVENT MAINTAIN ITS COLLEGIATE FEEL IN THIS YEAR'S VIRTUAL INCARNATION?

SciX, like many conferences, is trading its conference venue for chatrooms and virtual whiteboards in 2020. We caught up with five key members of the team – Mary Kate Donais, Linda Kidder Yarlott, Karen Esmonde White, Ian Lewis, and Becky Dittmar – to consider what SciX means to the analytical chemistry and spectroscopy community. Get ready to explore the past, (virtual) present, and (currently uncertain) future of this key event in the analytical calendar.

TELL US A BIT ABOUT SCIX…

Karen-Esmonde White: The Federation of Analytical Chemistry and Spectroscopy Societies (FACSS) has been bringing together its member societies for an annual conference called SciX since 1974. The conference attracts approximately 1,000 scientists from around the world and is respected for its exceptional spectroscopy program, featuring over 35 sessions in fundamental research and industrial applications for molecular and atomic spectroscopy. Growth of the applied science program and expansion into the separation sciences in particular have allowed the conference to expand since it became SciX in 2012. As an example, I'm very pleased to have witnessed the biomedical, data sciences, process analysis, and pharmaceutical offerings more than double in the past 10 years!

We are also pleased that member societies make SciX the home of their annual meeting, including the Coblentz Society, the Society for Applied Spectroscopy, and the North American Society for Laser-Induced Breakdown Spectroscopy. And, in 2018, the AES Electrophoresis Society made SciX their annual meeting home, too. This new addition complements our strong spectroscopy program and brings cutting-edge research in separation sciences to SciX.

Becky Dittmar: I think Karen covered most things! But I'll add that the aim of FACSS is to bring scientific organizations together for scientific exchange, and the aim of SciX conference is to provide a venue to allow that to happen on a personal level. An important element of SciX is that the program is put together by scientists with a variety of backgrounds and interests. Applied science is provided with just as prominent a position in the program as fundamental research, and scientists – whether in

OUR QUARTERBACKS





Mary Kate Donais

"My analytical chemistry career has seen me work across federal government, industrial, and academic settings. Now, as a professor at the Department of Chemistry of Saint Anselm College in Manchester, New Hampshire (a small, liberal arts college), I aim to broaden students' understandings of spectroscopy and wider (analytical) chemistry while exploring the application of these approaches to studying art and archaeological goods. I appreciate all the people I have the privilege to work with in my role as SciX Program Chair for 2020."

Linda Kidder Yarlott

"My professional passion is to match customer needs with analytical tools; as the Life Science Business Development Manager for Horiba, this is exactly what I do. SciX is the perfect venue to explore this intersection, and my decades-long affiliation with the conference has paved the way to a fulfilling career. I was first asked to organize a Raman session for FACSS as a postdoc. A word of warning: be careful what you agree to, as that one small role expanded over the years, leading to my involvement in the governance of several Federation Societies (SAS and Coblentz) and organizing the Molecular Spectroscopy program for seven years. In 2020, I'm proud to act as the General Chair of SciX, working alongside a great committee to deliver quality content to our attendees around the world."

Karen Esmonde-White

"I am the current Marketing Chair of FACSS and SciX, which means that I am part of the FACSS executive committee and a co-chair of the biomedicine section of the SciX meeting. My career at SciX began in 2010, when I organized a new session in drop deposition. I've been organizing sessions in the biomedical, Raman, and "Contemporary issues in analytical science" sections ever since! I've also taken on more responsibilities. I served as chair of the biomedical section since 2014, but took a break from the in 2018 to serve as the program chair. Outside of FACSS and SciX, I am a product manager at Kaiser Optical Systems, Inc., lead a Girl Scout Brownie troop, yearn to thru-hike the Pacific Crest Trail, and grow preternaturally delicious vegetables."

Ian Lewis

"I am the current FACSS Treasurer (on the FACSS executive committee), and I also act as a co-chair of the Raman section of the SciX meeting. My first organizational involvement with FACSS was as a session chair in 1994, and I also served as the conference program chair in 2007 and Governing Board Chair in 2012 and 2013. Outside FACSS, I am the Director of Marketing at Kaiser Optical Systems – an Endress+Hauser company. My role with Kaiser focuses on translating and delivering the potential of Raman spectroscopy into industry settings."

Becky Dittmar

"After being awarded a FACSS student award while in grad school, I soon became an active participant in SAS, the Coblentz Society, and FACSS/SciX, holding numerous voting-level positions in each organization. I joined 3M after graduate school as a spectroscopist in the corporate analytical lab, and after 10 years of lab work, I broadened out into management, Six Sigma, product development, and manufacturing quality over my 27-year career. I believe that a good analytical lab can make a huge impact on quality; a combination of good people, good equipment and – often – good luck is key to succeeding in this field."

leading roles in academia, government laboratories, or industrial positions – are all featured and heard.

CAN YOU TELL US MORE ABOUT THE SCIX REBRAND?

Ian Lewis: I'll take this one! FACSS, like many analytical chemistry and spectroscopy meetings, found itself shrinking in terms of attendees, exhibitors, and total number of presentations in the early 2000s. Understanding this, FACSS held a set of strategic retreats that culminated in rebranding the annual North American meeting as the SciX conference. This led to seven new member organizations joining FACSS. Three of these organizations are based outside North America, helping to increase the visibility of SciX internationally and expanding the international diversity of attendees. Though the location of the SciX meeting does affect the attendance, attendance, exhibitor numbers and presentations are consistently above the numbers we saw back in 2006.

WHAT ARE THE HOT TOPICS IN SPECTROSCOPY RIGHT NOW?

Ian Lewis: There are four areas showing significant growth in Raman right now: (1) use of surface-enhanced Raman spectroscopy (SERS); (2) nanoRaman and imaging; (3) biomedical applications; and (4) process implementations for monitoring and control. The first two are driven largely by university research, while the latter are more driven by industry.

Linda Kidder Yarlott: Simplified systems that allow non-experts to get actionable data. AI may constitute one aspect of this, but it encompasses much more than that in terms of industrial application and the interface designs needed to facilitate its use. If instrument designers can provide actionable information while minimizing mistakes in acquiring and interpreting data, then we could open the door to fresh opportunities in less-developed markets, or even for mass-consumer markets (like the FitBit, for example).

Karen Esmonde-White: I have a background in pharmaceuticals, process analysis, and clinical translation. And I'd say these past 10 years have brought many new uses of analytical chemistry in the fields of medicines, biological tissues/fluids, agriculture, and advanced materials. Ten years ago, I never would have guessed that I would be carting a Raman instrument into a dental office for clinical research! In these fields, it's rewarding to see spectroscopy being recognized

as a valuable technology. The fun, and the challenge, for us in the field is to harness that level of chemical knowledge in a meaningful way for non-specialists, so that they can continue to help us bring the technology to new places.

Mary Kate Donais: Portable instrumentation! These instruments are facilitating research that was not previously possible. The object of interest no longer needs to be moved to a lab or destructively sampled. The instrument can instead be transported directly to the object of study. In the field of cultural heritage research, portable instruments are making a real difference, and more and more applications are emerging for portable X-ray fluorescence, Raman, laser-induced breakdown spectroscopy, and various other techniques!

Becky Dittmar: As I've moved further away from direct science, I don't have much to add here, but improved testing for food safety and the understanding of viruses (topical) are areas that require a broader scope. Another current concern is the effect of social media and politics on science. How can (or should) scientists help drive a more rational approach? We typically work behind the scenes, but we need to be visible and valuable enough to provide legitimate direction and engage kids in STEM – all while doing our day job.

THE CONFERENCE IS ONLINE FOR 2020 – WHAT ARE YOUR MAIN GOALS?

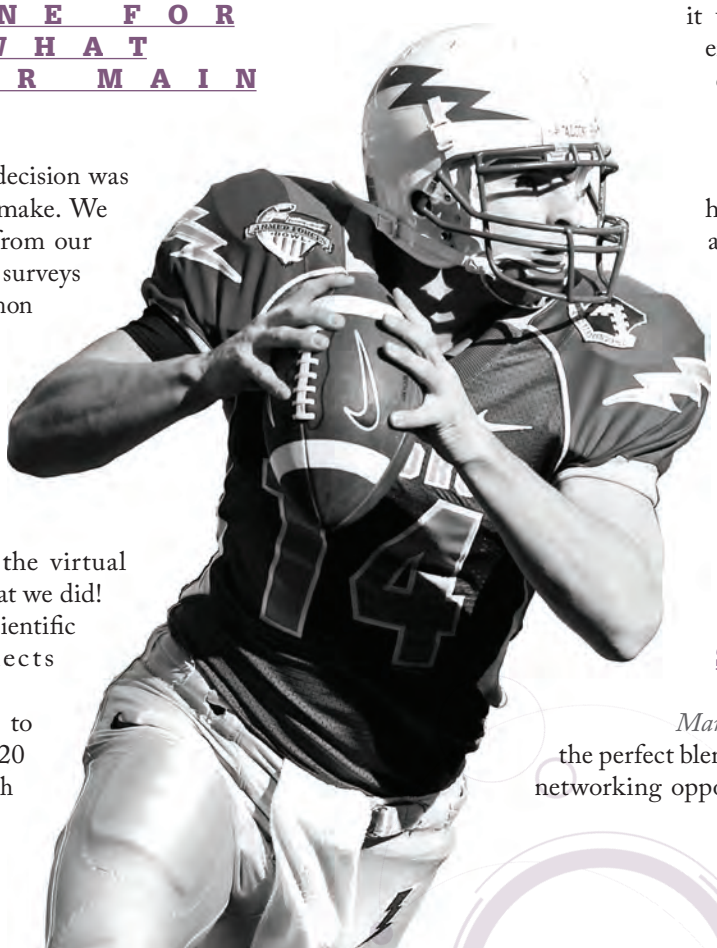
Linda Kidder Yarlott: This decision was extraordinarily difficult to make. We were guided by feedback from our attendees, as we sent several surveys out to gauge interest. A common thread in the responses was the importance of maintaining contact with the SciX community. We also heard loud and clear that the content needed to be tailored to the virtual environment – so that's what we did! Our program plan (both scientific and networking) reflects this goal.

Ian Lewis: The decision to offer a virtual format in 2020 is based on the desire to reach scientists who might never be able to attend an international meeting, or who can only rarely attend. These scientists have, historically, been unable to benefit from the talks at SciX or the networking opportunities. The virtual format offers these possibilities to all who register!

Coronavirus is another obvious factor in the decision, and the ensuing lockdown has given people an opportunity to re-evaluate projects; current, future, and shelved. Working, for the most part, with industry, I believe industry-based researchers have been less affected than university research teams. One trend I'm seeing is that people are searching further for concise virtual training and information exchange opportunities.

Karen Esmonde-White: As Ian says, the goal for the virtual meeting is to bring SciX to those who couldn't normally attend – and to help attendees fully experience the breadth and depth of the scientific program. I enjoy attending new sessions at SciX to learn about different fields, and I know that other attendees do also! The "complaint" I often hear at SciX is that there are so many good talks and it's impossible to attend every talk. With a virtual program, including recorded talks available after the virtual meeting, attendees can now live without fear of missing anything important.

Becky Dittmar: Going virtual this fall is obviously necessary in the pandemic environment – but it will be a huge challenge to enable the networking that is so critical to our success at physical meetings. Setting up "forced networking" remote meetings (brown bag lunches, remote happy hours, and such like) around topics of general (faster testing for viruses) and more specific (career opportunity discussions for students) interests might help in the virtual adjustment. This year's program will be particularly tailored with these considerations in mind.



WHAT MAKES SCIX SO SPECIAL?

Mary Kate Donais: For me, SciX is the perfect blend of quality science and strong networking opportunities. Every year affords

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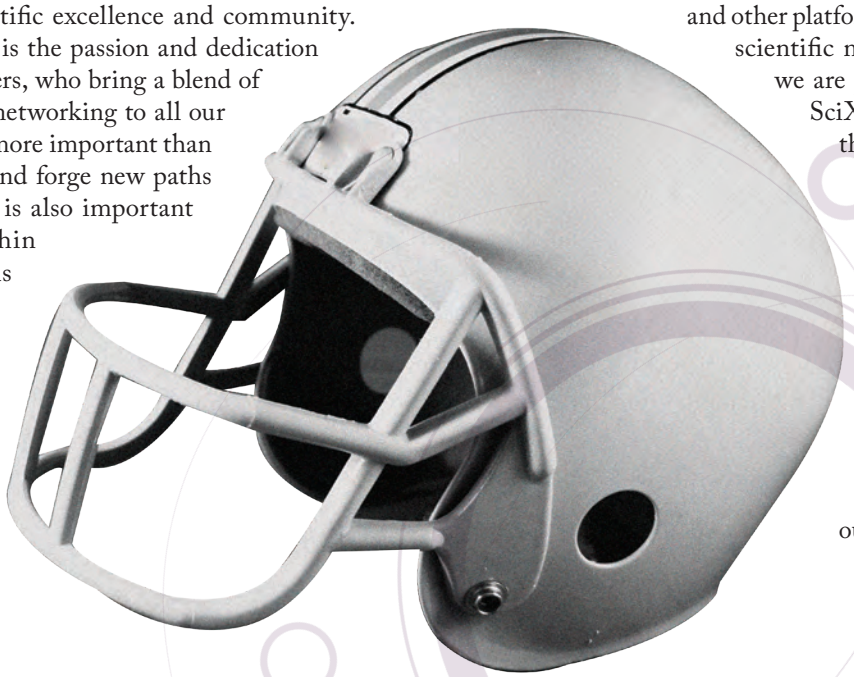
the opportunity to learn a great deal, meet new people, and catch up with friends in the field. The conference also brings together a number of key professional organization for me – SAS, RSC, ACS, Society for Archaeological Sciences – so I can meet up with society leaders to discuss recent activities and member opportunities.

My early years attending SciX truly shaped my career. Attending SciX gave me and (later) my students an opportunity to present research, while also helping to strengthen my involvement with the Society for Applied Spectroscopy. Those roles led me to roles on the SciX leadership team. And, throughout, my circle of colleagues and friends has grown, leading to new professional opportunities and collaborations.

Becky Dittmar: International SciX venues are a great growth opportunity in locations that don't already have an analytical chemistry support structure or conference. They enable scientists who are unable to travel (students and industrial scientists, for example) to get exposed to the network and technical advancements in a casual environment. Again, the focus is on the ability to network – everyone in attendance is your peer.

With the growth of supporting organizations, SciX can also help you learn about areas outside your expertise. A successful scientist cannot focus on one "method" and expect to grow and succeed. I moved away from spectroscopy some time ago, but I'm able to maintain a connection to my spectroscopy network and (when time allowed) learn about advancements that could be relevant in my industrial career by volunteering at the conference.

Karen Esmonde-White: SciX is a great meeting because of its emphasis on scientific excellence and community. What is unique to SciX is the passion and dedication of the volunteer organizers, who bring a blend of world-class science and networking to all our attendees. In 2020, it is more important than ever to exchange ideas and forge new paths to address challenges. It is also important to feel grounded within the community. On this topic, one of the primary goals of SciX is to tie everything together for attendees, from the latest research and technology to making new connections and strengthening old friendships.



And, as a final note, I think one of the things that makes SciX so special is the fact it is volunteer-driven and community-focused. I think that many people respond positively to being part of a community where they feel welcome and where they know they can have a positive impact. As a result, SciX continues to grow, evolve, and thrive! The next generation of scientists bring new ideas to the program, new volunteers bring passion and new technologies to build community, vendors showcase their latest technologies, and our attendees are active in helping to shape the long-term vision of the federation and the conference.

Linda Kidder Yarlott: I agree with all of the above! Also, SciX has a great strategy to bring in thought leaders and industry luminaries. Innovation awards, plenaries and keynotes that highlight impactful and innovative science (and a tremendous expansion of the exhibits) all interact to keep the level of scientific engagement at a very high level. SciX is where I come to engage with the thought leaders in analytical instrumentation. The emphasis on networking and collegiality means that I can approach the luminaries and ask questions. This was the case when I was starting out, and is still true today.

AND WHAT ABOUT THE FUTURE OF SCIX?

Mary Kate Donais: We are recognizing more and more the need to communicate with our worldwide audience through multiple channels. Not only do we strive to produce quality in-person conferences, but we also use social media and other platforms to bring together scientific minds. For example, we are providing some pre-SciX webinars this year; these will help spread the word regarding SciX 2020 while delivering quality scientific content in a fresh format. As for the future, I can only imagine that we will make increasing use of such tools to expand our reach even further!

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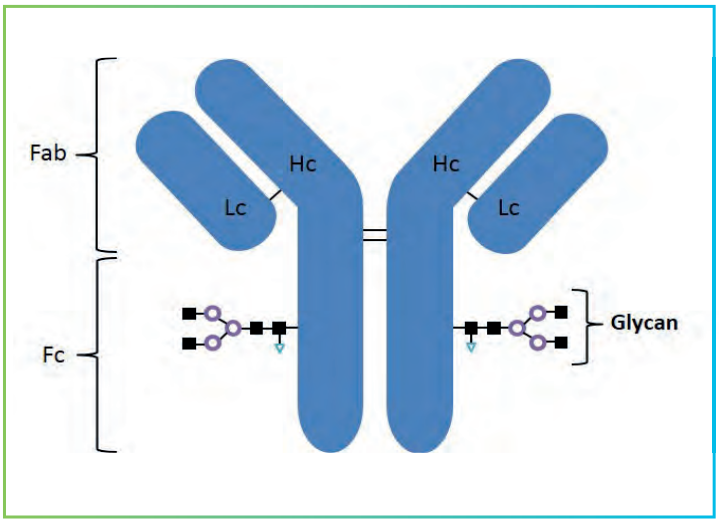
mAbs are heavily glycosylated proteins, which means they have oligosaccharide species (glycans) attached at specific locations on the molecule. All mAbs contain at least two glycosylation sites (usually on the heavy chain), as depicted in figure 1, with the presence of glycans affecting the safety and efficacy of the drug. For this reason, the glycosylation pattern must be thoroughly characterised during mAb production to ensure the target drug has been correctly synthesised. In fact, glycosylation is a post-translational modification which is considered a Critical Quality Attribute and therefore should be monitored according to the ICH Q6B guidelines.

FIGURE 1: Schematic showing glycosylation regions of a monoclonal antibody
Fc = Crystallisable fragment, Fab = Antigen-binding fragment, Hc = Heavy chain, Lc = Light chain



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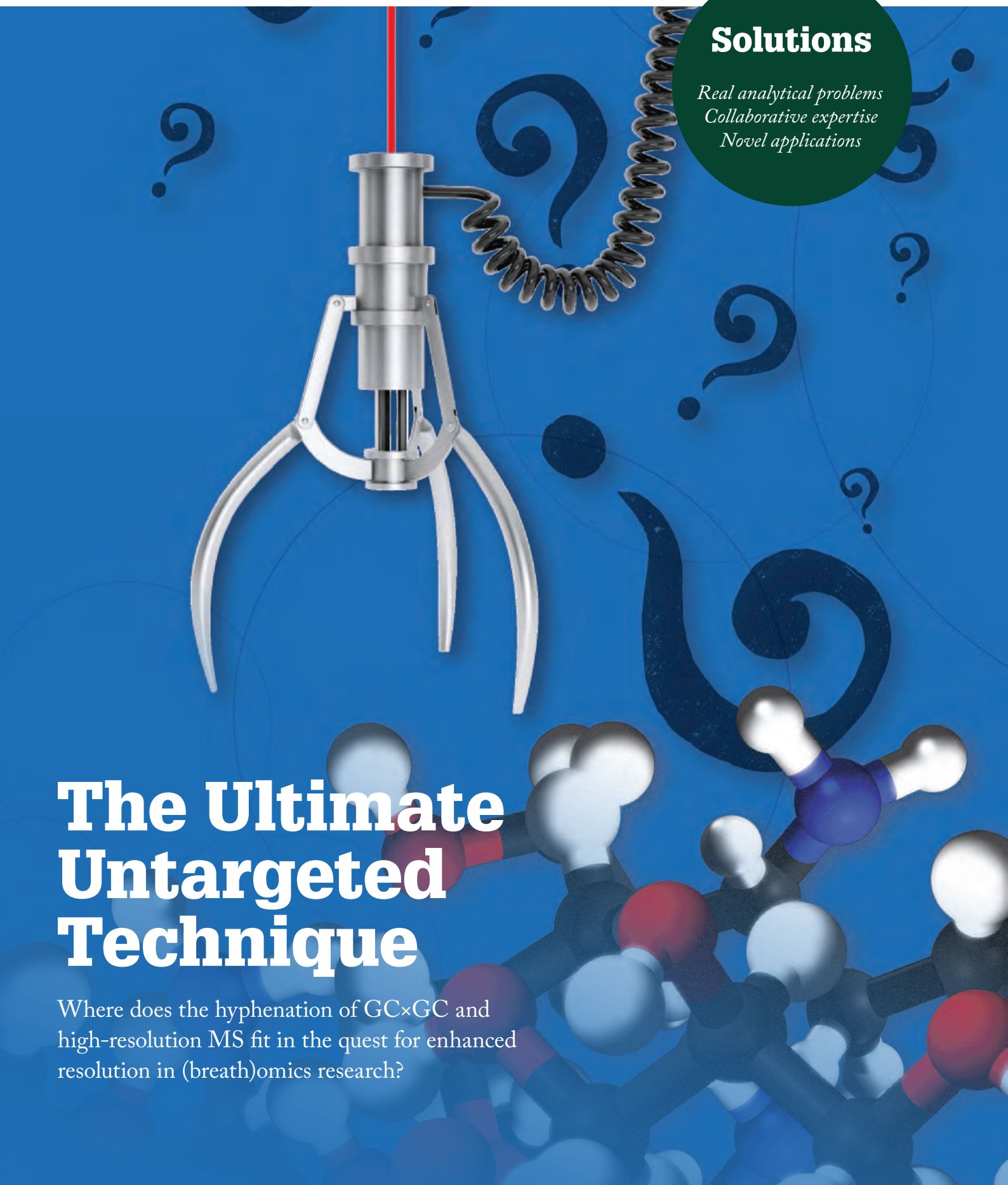


The Ultimate Untargeted Technique

Where does the hyphenation of GC×GC and high-resolution MS fit in the quest for enhanced resolution in (breath)omics research?

Pierre-Hugues Stefanuto, Delphine Zanella and Jean-François Focant, Organic and Biological Analytical Chemistry Laboratory, MOLSYS Research Unit, Liège University, Belgium

The rise of omics has been a hot topic in our group for the past few years – in part because our own expertise aligns somewhat with the needs of these fields. Metabolomics is then particularly challenging for the separation science community, demanding the application of high-end iterations of various techniques, including LC, GC, MS, and NMR. In fact, when it comes to metabolomics, most analytical tools have a "seat at the technique table" – after all, multimodality is the only way to make sense of such high sample complexity.

Multidimensional chromatography holds one of those seats, and often comes up in conversations on how separation power should be best enhanced. Such discussions essentially center on a single question: would it ultimately be better to have analytical separation based exclusively on an ultra-high-resolution mass spectrometer or through a combination of high-resolution techniques with orthogonal dimensions (chromatographic and mass spectrometric)?

There is likely no definitive answer to this question, but we hope our works demonstrate the use of comprehensive two-dimensional GC (GC×GC) coupled with high-resolution MS (HRMS) as one compelling option. By combining these techniques – and thus exploiting several levels of orthogonality – we have been able to improve both the versatility and the robustness of the unknown compound identification process – particularly in the young field of breathomics, which we'll talk more about later.

Pieces of the puzzle

On the chromatographic side, linear retention indices provide a first identification metric for unknown compound that can be compared with true-standard values and commercial libraries (for example, NIST, Wiley). It is also useful to estimate the carbon number of unknown compounds; in the context of GC×GC, the structured elution pattern provides information regarding the carbon number – and it also indicates the polarity and even the chemical class of the eluting unknowns.

Next comes the ionization method – the physico-chemical transformation link between chromatographic

"GC×GC–HRTOFMS has become increasingly available for routine analysis over the last decade."

separation and MS analyses. In the context of GC, electron ionization (EI) offers a key advantage over LC-based approaches, which suffer from time-consuming peak annotation (1, 2). In fact, EI provides a highly reproducible fragmentation pattern regardless of the analytical conditions or instrument (3), which allows us to compare fragmentograms with reference libraries to provide MS-based identification. At the end of the process, MS analyzers add the final touch of the identification step with an efficiency that is directly proportional to their mass resolution and accuracy – two metrics that are constantly increasing for all types of MS analyzers (and independent from the chromatographic separation side).

GC×GC-HRTOFMS has become increasingly available for routine analysis over the last decade. This trend began when it was used to completely characterize single samples (4), but as data processing methodology for low-resolution data evolved and was applied to HR data, GC×GC-HRTOFMS soon became useful for studying larger samples (5). Nevertheless, untargeted metabolomics is a complex playground; sample preparation and optimization, QC elaboration, data processing, and so on, all still represent real challenges. Building on this early work, GC×GC-HRTOFMS has now been extensively challenged by metabolomics with various levels of success (6). In our group, we have been investigating different applications.

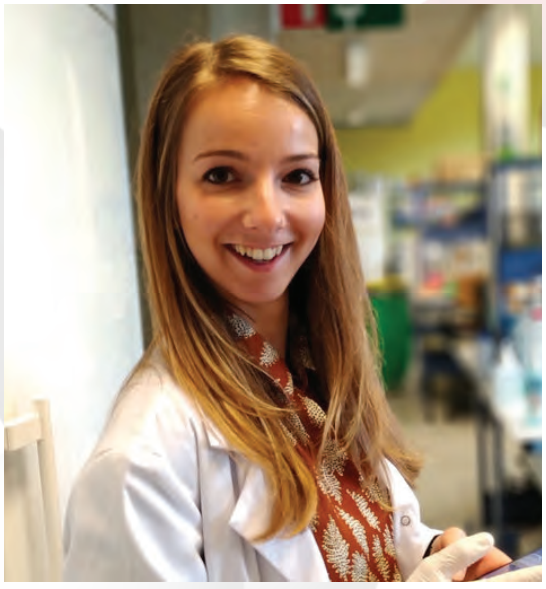
"Our lab has worked on various untargeted volatilomics applications – from food to plants – but the medical field has been our main target over the last five years or so."

Looking to serum

To develop and validate a reliable analytical method, we have focused on the analysis of derivatized serum samples. This matrix has been investigated thoroughly using standard GC; this work, conducted by pioneers like the Fiehn Lab, provides a strong basis on which future research can be built.

Our first step was the optimization and validation of analytical conditions using a NIST standard reference material for human plasma (1950) (7, 8). We demonstrated the applicability of our method through a proof-of-concept study that identified 33 serum metabolites specific to Crohn's disease. Orthogonal identification capacities allowed us to annotate half of these with Metabolomics Standards Initiative level two confidence. Now we're taking advantage of a sensitive, high-speed MS analyzer to conduct this research with minimal sample volume and preparation, providing an exciting focus for the coming years.

Our larger aim is to develop a multiomics screening platform for this universal matrix. Though small molecules can be characterized by GC(×GC), complementary



information that completes our knowledge of these samples will come from LC(×LC)-MS and MS-only screening. Thus, combined approaches are needed to lift the veil of relevant metabolic pathways.

Research is in the air

Another area for GC×GC-HRTOFMS application is volatilomics, which describes the metabolomics-type screening of volatile organic compounds in complex matrices. The best way to characterize small volatile molecules in normal conditions is to transfer them directly into the analytical instrument, avoiding extensive sample preparation. In this field, however, the constant development of trapping devices (solid phase microextraction fibers, thermal desorption tubes, and so on) allows for the robust sampling of volatile molecules. Yet, the validation of routine analytical strategies for volatilomics remains challenging. This is mostly because of a lack of reference materials and difficulties performing interlaboratory testing.

Our lab has worked on various untargeted volatilomics applications

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"Breath research is a growing and challenging field for analytical scientists. From reliable sampling to robust processing, all involved steps need to be carefully controlled."

– from food to plants – but the medical field has been our main target over the last five years or so. During that time, we have worked on the development of a complete analytical workflow for exhaled breath characterization (9, 10).

Breath research is a growing and challenging field for analytical scientists. From reliable sampling to robust processing, all involved steps need to be carefully controlled. The strategies employed must also be adapted to context-dependent needs. GC×GC-HRTOFMS has been our "go to" instrument for this type of research. For on-site support and diagnosis, direct MS methods (for example, selected-ion flow-tube MS and proton transfer reaction-MS) seem to be the fastest and most-adapted tools.

Based on a number of studies on lung cancer detection and inflammation phenotyping, we've conducted the first large-scale study on breath, combining targeted and untargeted screening (11). In vitro models then allowed us to determine the cellular origins of these volatile molecules (12). Combining information from volatile molecules identified by such methods and larger molecules in the liquid phase is necessary to complete multiomics visualizations – underscoring the power of complementarity between techniques.

With the increasing use of GC×GC-HRTOFMS in untargeted metabolomics, the future looks exciting (6, 13). Still, multiple challenges should be tackled to make GC×GC-HRTOFMS a truly recognized contributor to large-scale untargeted screening. The biggest challenges remain at the level of the study design and data processing workflow – it is paramount that the robustness and accuracy of every individual measurement is consistent throughout the entire batch. This will only be achieved with a better definition of QC procedures (especially for volatile samples), a better understanding of chemometric tools, and the development of integrated software solutions to manage the different steps from injection to processing output. But none of these challenges are unique to the technique; therefore, strong collaboration between different fields of analysis will be required to successfully overcome them.

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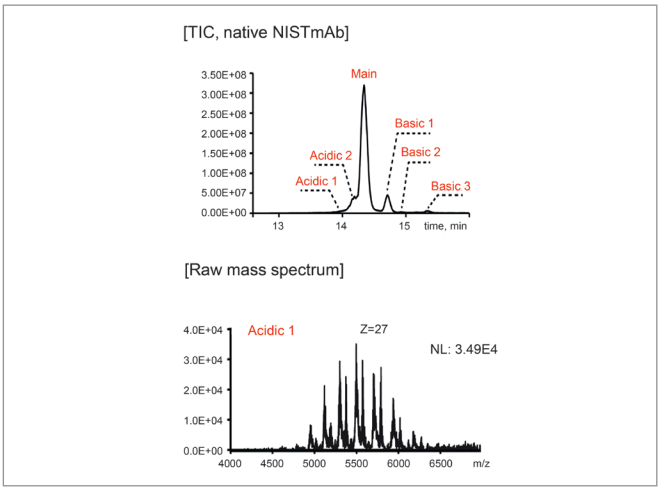
Native Online SCX-MS Analysis of Monoclonal Antibodies

Cation exchange chromatography (CEX) is a non-denaturing technique used for separation and isolation of protein charge variants before characterization via MS. This is usually a two-step process, where the specific charge variant peak of interest has to be isolated prior to characterization via mass spectrometry because in CEX mostly non-volatile buffers are used, which are not compatible with MS. The coupling of MS to CEX would save time and exclude possible artefacts of the long isolation process.

In this application note, high resolution SCX was coupled directly to an ultrasensitive online native MS. A combined pH and salt gradient based on a MS compatible buffer system was utilized. YMC's BioPro IEX SF, a non-porous strong cation exchange column, was used for the characterization of the NIST mAb (and five in-house mAbs with different pI). The mobile phase composition and gradient were optimized to achieve an efficient separation of charge variants.



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A Keen Collaborator

Sitting Down With… Chris Palmer, Professor of Chemistry and Biochemistry, University of Montana, USA

How did you get into science?

I was motivated by my father's example. He was an industrial food scientist who went on to become a professor at both MIT and Virginia Tech. I also loved chemistry, probably because of the quantitative relationships integral to the field. I much preferred that to the list-memorizing you might do in other fields. So I set out to study chemistry, first with a Bachelor's degree at Juniata College and then a PhD at the University of Arizona, and later with a series of postdocs in Virginia, the Netherlands (at the Unilever Research Laboratory), and Japan (at the Himeji Institute of Technology). The opportunity to collaborate was another big factor in my choice to pursue science – I find the networking aspect of my role incredibly exciting.

Can you tell us a bit more about this collaboration?

Science has a great capacity for uniting people from incredibly diverse backgrounds. Although we may speak different languages, the common language of science brings us together. In this way, our field breaks a lot of barriers. This was certainly my experience when studying overseas, anyway.

I've also collaborated a lot in my own professorship, working in Belgium, Brazil, and Australia (where I took a sabbatical at the Australian Centre for Research in Separation Science at the University of Tasmania). It's an eye-opening experience to work in truly international laboratories like that. In Australia, for example, I worked alongside scientists from Egypt, Iran, Israel and various countries across Europe. It's an amazing aspect of our career and one that I encourage my students to take full advantage of. I think it's particularly important for Americans to travel and collaborate in this way because we tend to have a very US-centric view of the world.

What were you researching at those labs?

At Unilever, I learned a lot about the application of analytical techniques in industry – particularly capillary electrophoresis, which I was working on at the time. Electrokinetic chromatography was my focus in both Japan and Australia, and in Brazil I worked on solid-phase extraction (SPE) technology. Specifically, I was studying the application of ionic amphiphilic polymers – which I had previously developed for applications in electrokinetic chromatography – to generate high-affinity and selective sorbents for SPE. We demonstrated some highly effective extractions of polycyclic aromatic hydrocarbons from aqueous samples, as well as fungicides and a mycotoxins from wines.

What are you up to at the University of Montana these days?

One example is our research on particulate matter pollution in communities in Montana and Alaska. We collected PM2.5 (particulate matter with diameter <2.5 μm) then developed and applied chromatographic methods to determine its chemical composition, which in turn allowed us to apportion the pollution to various sources. We concluded that around 75 to 80 percent of the PM2.5 was coming from residential wood stoves during winter months. This is a common source of pollution in many places around the world – particularly in mountainous communities. We've also used nanodiscs and capillary electrophoresis to study the chemical interactions between small molecules or proteins and membrane surfaces. Understanding these interactions, and the transport of small molecules across membranes, is important for pharmaceutical development and understanding bioaccumulation of environmental pollutants. The conformation and activity of various proteins is also affected by their membrane interactions; a great example is the initiation of cell apoptosis by cytochrome c-lipid binding in mitochondrial membranes.

"Science has a great capacity for uniting people from incredibly diverse backgrounds."

One of the best things about the university is its collaborative culture. We are a relatively small university, so collaborations are crucial for us to conduct cutting-edge research. I often need to use another laboratory's instruments and I'm always welcome to do so. I also have a small research group – typically up to five students at a time – but we're able to carry out exciting research because we constantly work with other groups across the campus.

How are you involved in SciX?

I am the Governing Board Chair for 2020 and 2021. I was invited to my first SciX meeting some 25 years ago to give a talk as an early-career scientist. What I really appreciated back then was the supportive and welcoming environment – after all, they had invited me to speak to and interact with leading minds in the field. That spurred my increasing involvement with the conference, and I've held a number of leadership roles in the governing board over the past decade. What's changed in those 25 years? We have a lot more separation science-based content than we used to (this was traditionally very spectroscopy-based), and it's become increasingly international, which can only be a good thing in my mind!

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