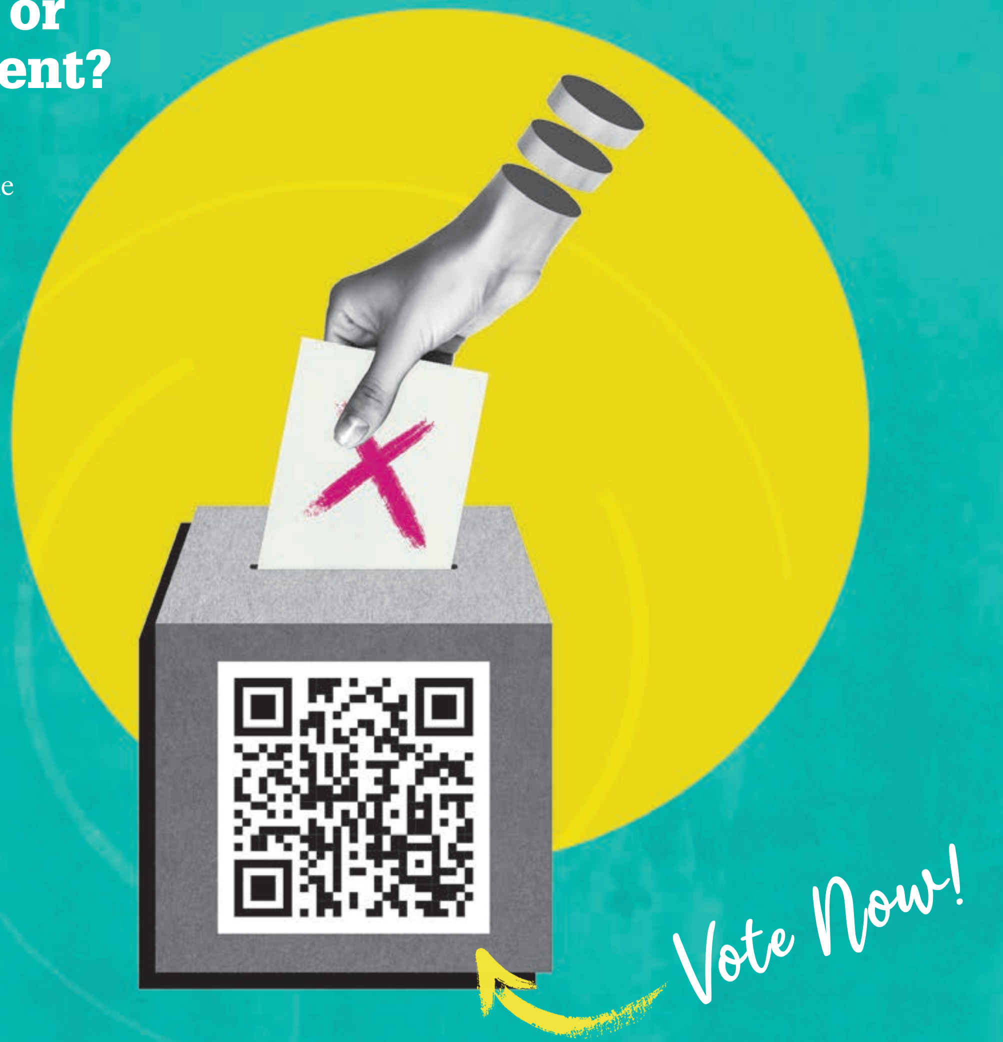
JANUARY / FEBRUARY 2024 # 115

the Analytical Scientist®

Analytical or Measurement?

Would flying under a new flag help repair the reputation of the field? Cast your ballot!

14 – 25



The Measurement Scientist?

Do we need to rebrand our field with a focus on measurement to fix analytical chemistry's perception problem?

Many moons ago, a big question loomed for the founders of this very magazine: What should it be called? The Separation Scientist had a nice alliterative ring to it – but their mission was to connect as many techniques and application areas as possible. What about The Analytical Chemist? Given the shifting scope and seemingly unstoppable advances in biological analysis, even analytical chemistry didn't quite seem to encapsulate everything – and everyone – that belongs to this field. Ultimately, The Analytical Scientist created a big enough umbrella, perhaps causing a ripple of change in how those beneath it describe themselves…

Biased as I may be, I think they made a good choice. But our decade-old debate is something of a microcosm of a more persistent, existential issue for the entire field; namely, who are we?

Last year, we asked the top 100 most influential analytical scientists of the past decade about the most pressing issues facing the field today. Education, attracting talent, and raising the profile of the field were among the most highly cited challenges. And having spoken in more depth to several leading spokespeople, the perception problem remains – with deep roots going back more than half a century.

Even the term "analytical" can be confusing. As Victoria Samanidou argues on page 20, an "analytical scientist/chemist" – developing new analytical tools and techniques – is quite different from someone doing routine, "push-button" chemical analysis. Victoria argues that this conflation has "led scientists in other fields to see all analytical scientists as mere applicationists involved in routine analysis."

So what is analytical chemistry, fundamentally? Richard Zare makes a strong case for *measurement*. "We need to redefine chemistry so that it incorporates measurement; and we need to redefine analytical chemistry so that it is understood as the science of measurement – this is what we are and what we do." So, is it time to sail under a new flag, as Gert Desmet also argued? Are you happy to be a measurement scientist?

Not everyone is so sure a rebrand is the answer. Jonathan Sweedler argues that we should all put more effort into lifting our spirits and those of our students to unintentionally raise the profile of the field; Ben Garcia wants to fight for "analytical" and believes interdisciplinary collaboration can create external advocates; and Chris Enke focuses on education – we need to stop teaching analytical chemistry as a series of unrelated techniques, he says. But where do you stand in the debate?

Analytical or measurement? Let us know!

James Strachan
Editor

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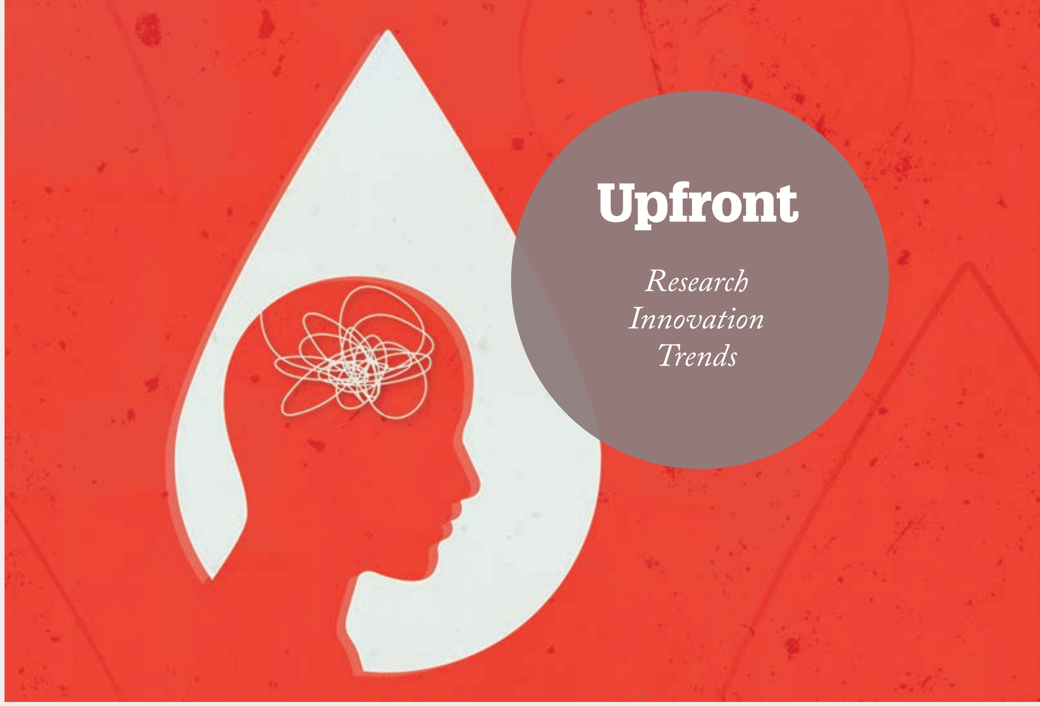


Reading Between the… Diagnoses

Metabolomic profiling reveals 17 possible diagnostic markers for mood disorders

Patients with bipolar disorder (BD) are often misdiagnosed with major depressive disorder (MDD) because of overlapping symptoms, as well as the subjective nature of psychiatric evaluation of patient self-reported information. Indeed, one third of bipolar patients remain misdiagnosed for over seven years (1).

To address the issue, a research team from the University of Cambridge, UK, analyzed dried blood spots from individuals suffering from current depressive symptoms (2).

"We initially attempted to identify biomarkers of these conditions using proteomic profiling based on mass spectrometry; unfortunately, the signal was not strong enough," says Sabine Bahn, Head of the Cambridge Centre for Neuropsychiatric Research and corresponding author. "We then turned to metabolomic profiling; we expected metabolites to be more stable in dried blood spots and provide a better signal than proteins, which they indeed did."

First, the samples were analyzed using a targeted mass spectrometry-based platform to measure the levels of 630 circulating metabolites. Next, the participants underwent a WHO validated diagnostic interview to determine whether they had BD so that correlations could be made with biomarker levels.

"We discovered a panel of 17 biomarkers that correctly detected 53 percent of patients with BD and 76 percent of patients with MDD in a group of 241 patients. These findings were then validated in a separate group of 30 patients," says Jakub Tomasik, Senior Research Associate at the Cambridge Centre for Neuropsychiatric Research and principal author of the paper.

The researchers are planning a validation study to test the performance of the biomarker panel in a new group of patients with fresh dried blood samples.

"A blood biomarker test could provide a faster and more objective way to diagnose mood disorders," says Bahn. "As such, it could substantially improve the diagnostic process, reducing the workload on physicians and helping select the right treatment early in the process."

Tomasik adds, "It would not only result in better outcomes in patients, but also contribute to more informed understanding of psychiatric disease and help reduce the stigma associated with psychiatric conditions."

References

1. *RMA Hirschfeld et al., J Clin Psychiatry, 64, 2, (2003). DOI: 10.4088/JCP.v64n0209.*
2. *J Tomasik et al., JAMA Psychiatry , (2023). DOI: 10.1001/jamapsychiatry.2023.4096.*

TIMELINE

A Race Against "Forever"

We explore the most important timepoints in PFAS chemistry and regulation

1930s

PFAS chemistry is discovered

1970s

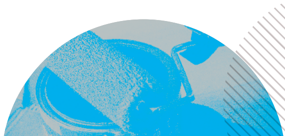
Occupational studies reveal PFAS in the blood of exposed workers

Late 1980s / early 1990s

The routine application of LC-ESI-MS/MS paves the way for the detection of PFAS

Early 2000s

PFAS testing becomes widely available and documented in environmental samples



References available online

Credit: Images for collage sourced from Unsplash.com

BUSINESS IN BRIEF

This month's latest business news; partnerships and new products designed for analytical advancements in biopharma, data management and more…

- **Shimadzu** recently introduced the AIRsight FTIR Raman microscope – the first and only microscope to combine both Raman and FTIR spectroscopy. Shimadzu says it will enable the cost-effective analysis of contaminants, microplastics, and other materials in various industries.
- **Bruker Corporation** has acquired **Tornado Spectral Systems**. With Tornado's Raman technology – including HyperFlux PRO Plus, Process Guardian, and Raman probes – Bruker is planning to advance its analytical product portfolio in biopharma.
- **Thermo Fisher Scientific** has launched its largest high-throughput array – the PangenomiX Array – for genomic analysis. The microarray combines SNP genotyping, whole genome copy number variant detection, and blood and HLA typing to enable population-scale disease and pharmacogenomic research.
- To build its portfolio, **AnalytiChem** has acquired cleanroom microbiology solutions expert **Cherwell Laboratories** – and plans to offer customizable laboratory equipment and services, including environmental and process monitoring products for the pharmaceutical manufacturing sector.
- **Waters Corporation** has launched a partnership with **Scitara**, a digital provider for laboratories. Waters is set to license Scitara's Digital Lab Exchange DLX cloud platform to communicate with its chromatography and mass spec instruments – improving data management.
- **Agilent Technologies** have announced their newest automated parallel capillary electrophoresis system – the Agilent ProteoAnalyzer system – at the 23rd Annual PepTalk Conference. Requiring minimal sample consumption, the system is designed to simplify protein analysis, reduce testing time, and lower costs.

Remembering Herbert Knauer

Herbert Knauer – inventor, chromatography pioneer, and founder of KNAUER – dies aged 92

Herbert Knauer passed away peacefully on January 18, 2024, at home surrounded by his family, according to a message from the company.

"For me, Dr. Knauer is not only our founder and an important thinker for the company who has passed away, but also an exceptionally open personality," said Carsten Losch, Managing Director of KNAUER. "He was a mentor and advisor to me, someone with whom you could discuss ideas and gain new perspectives. Dr. Knauer was always willing to pass on his enormous wealth of knowledge and experience."

Herbert – known for tinkering with new instruments in the kitchen – founded KNAUER in Berlin-Schmargendorf on October 1, 1962, with his wife Roswitha. In the early 1970s, Herbert began working on the device that KNAUER would become renowned for: a modular HPLC system. Their daughter, Alexandra, took the company reins in 2000.

All of us at The Analytical Scientist offer our sincere condolences to the Knauer family and company.

2001

Giesy and Kannan paper shows PFAS as globally distributed pollutants in wildlife

2009

PFOS and related compounds are listed under Annex B of the Stockholm Convention on POPs

2012

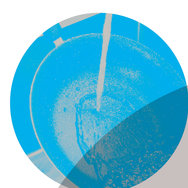
Nationwide testing for drinking water supplies is introduced by the US Environmental Protection Agency (USEPA)

2015

Long-chain PFAS (formerly called PFCs) are removed from emissions and products under the PFOA stewardship agreement

2021

The OECD PFAS database is published, containing 4,730 unique PFAS



2023

Maximum levels for PFAS in foods come into force in the EU, and ECHA publishes PFAS restriction proposal

Credit: Images for collage sourced from Pixabay.com and Rawpixel.com

Take MIE Breath Away

Meet the micro-immunoelectrode biosensor that can detect SARS-CoV-2 – in less than a minute

Could we combat COVID-19 by detecting the virus in exhaled breath? Possibly, as researchers modified a micro-immunoelectrode (MIE) biosensor to create a breath aerosol analyzer that can rapidly detect SARS-CoV-2 for direct, non-invasive screening (1).

We spoke with lead and corresponding authors from Washington University in St. Louis: Dishit Ghumra and Rajan Chakrabarty, from the Center for Aerosol Science and Engineering, John Cirrito from the Department of Neurology, and Carla Yuede from the Department of Psychiatry, to learn more about their research.

What was the inspiration behind your MIE biosensor?

Our MIE biosensor is actually adapted from an Alzheimer's disease-related technology that was originally developed in John Cirrito's lab at Washington University in St. Louis, USA. That device worked by attaching an antibody specific to amyloid-β to the surface of a carbon fiber microelectrode. Our biosensor is also an antibody-based sensor, but we attach a llama-derived nanobody specific to SARS-CoV-2 onto the surface of a screen-printed carbon electrode.

Did you successfully meet your initial goals?

We have successfully demonstrated a cost-effective point-of-care testing platform that delivers results within a minute – so, yes!

Our experiments involving sequential dilution with different SARS-CoV-2 variants, aimed at assessing the biosensor's sensitivity, revealed an impressive LoD range of 8-32 copies/mL (for Beta, Delta, Washington WA1, and Omicron BA1 variants). These findings further underscore the platform's capability to identify viral particles in as low as two exhaled breaths of patients. This non-invasive technique offers rapid and point-of-care detection without the need for specialized training. Notably, just 20 seconds of sampling yielded reliable results, contrasting with typical exhaled breath condensate (EBC)-based studies.

What impact do you think the MIE biosensor will have on healthcare professionals and patients?

Our device has the greatest potential in mass testing scenarios, particularly in settings where significant gatherings occur, such as airports, conference centers, and sports arenas. Its primary advantage lies in its ability to non-invasively and rapidly detect SARS-CoV-2 in infected individuals. The swift turnaround time holds the promise of early intervention and effective containment of disease transmission within communities.

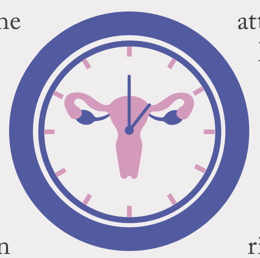
Reference

1. *DP Ghumra et al., ACS Sens, 8, 8 (2023). DOI: doi.org/10.1021/acssensors.3c00512.*

Sense and… Fertility

How an aptamer biosensor for non-invasive female hormone monitoring could open the door to personalized reproductive healthcare

Researchers at the California Institute of Technology, Pasadena, USA, have developed a skin-interfaced wearable aptamer nanobiosensor that enables automatic and non-invasive monitoring of hormones in women (1). The goal? To deliver personalized reproductive healthcare for the benefit of both patients and clinicians.



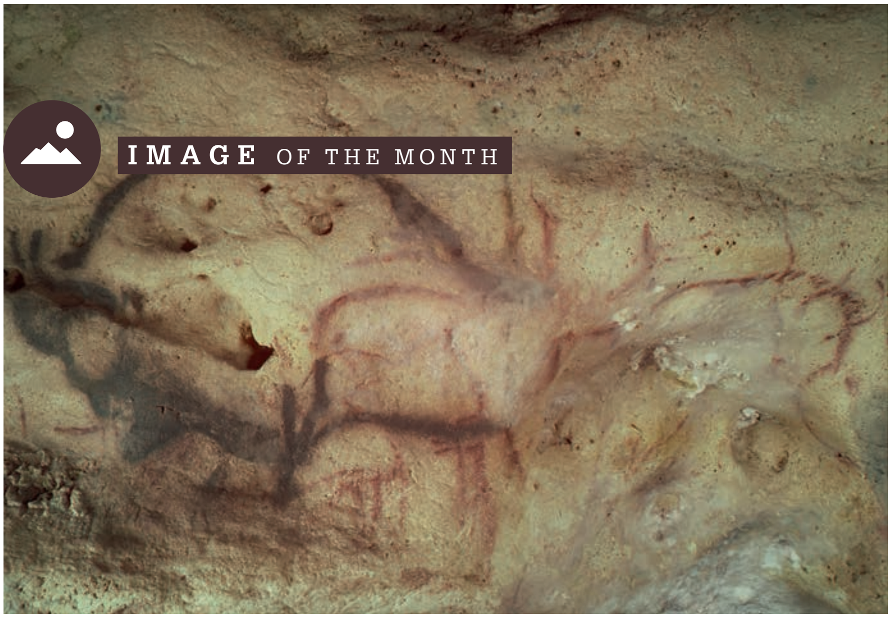
The team coupled a highly sensitive estradiol nanobiosensor with an iontophoresis module for autonomous sweat induction at rest, capillary bursting valves for precise microfluidic sweat sampling, and multiplexed temperature, pH and ionic strength sensors for real-time calibration. The authors claim the sensor offers "extraordinary sensitivity" – which they attribute to a gold nanoparticle-MXene electrode.

The team hopes their wearable sensor could be used as a standalone wearable device (similar to a smartwatch or smart ring) or be integrated with an existing wearable platform, with possible adaptation to monitor other low-level clinically relevant protein and hormone biomarkers.

Reference

1. *C. Ye et al., Nat. Nanotechnol., (2023). DOI: doi.org/10.1038/s41565-023-01513-0.*

IMAGE OF THE MONTH



A Paleolithic Enigma

The Font-de-Gaume cave is home to several Paleolithic artworks that are solely made from minerals – which can correlate to different Prehistoric groups if classified chronically. So, researchers from France combined X-ray fluorescence and non-invasive micro-Raman spectroscopy to analyze the decor of the cave – retrieving charcoal based drawings in Paleolithic artwork for the very first time. "Picasso bison" and the rest of the sample drawings are believed to have originated even before the Magdalenian era (23,000-14,000 years ago), but the team is keen on re-examining all the art panels using radiocarbon dating for more precise analysis.

Credit: Anne Maigret/C2RMF - Marc Martinez/CMN.

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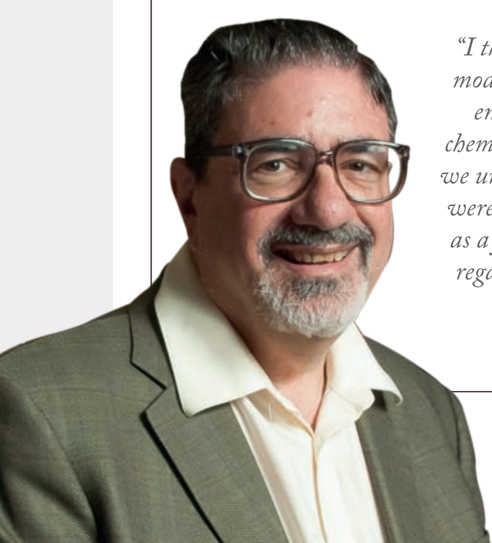
QUOTE OF THE MONTH



"I think chemistry involves three or four 'Ms': making, modeling, and measuring; and, if you include chemical engineering, you can add manufacturing. Analytical chemists, of course, do the measuring – there's very little we understand without doing measurements! And if we were to tie ourselves much more closely to measurement, as a fundamental part of the chemistry field, we would regain our standing within the chemistry community."

Richard Zare (see page 15)

The First of Us

And then there were 1,280... Genomic analysis reveals how humans almost went extinct.

A genomic inference study revealed that humankind went almost extinct, when human ancestors went through a severe population bottleneck, leaving just 1,280 breeding individuals (1).

An international research team developed FitCoal (fast infinitesimal time coalescent process) – a new tool to analyze the genomic sequences of modern human populations to calculate population size history.

Results showed a sudden, drastic reduction in populations who lived in Africa between 930,000 and 810,000 years ago.

The event, however, was not entirely catastrophic. According to corresponding author Haipeng Li, it could actually be a speciation event, "leading to the emergence of a new human species" – our more recent ancestors – and potentially have triggered numerous positive selection events for human populations to adapt accordingly.

The researchers are planning to extend their human evolution research and are also keen on pushing FitCoal into other areas, like cancer studies.

Reference

1. W Hu et al., Science, 381, 6661 (2023). DOI: 10.1126/science.abq7487.

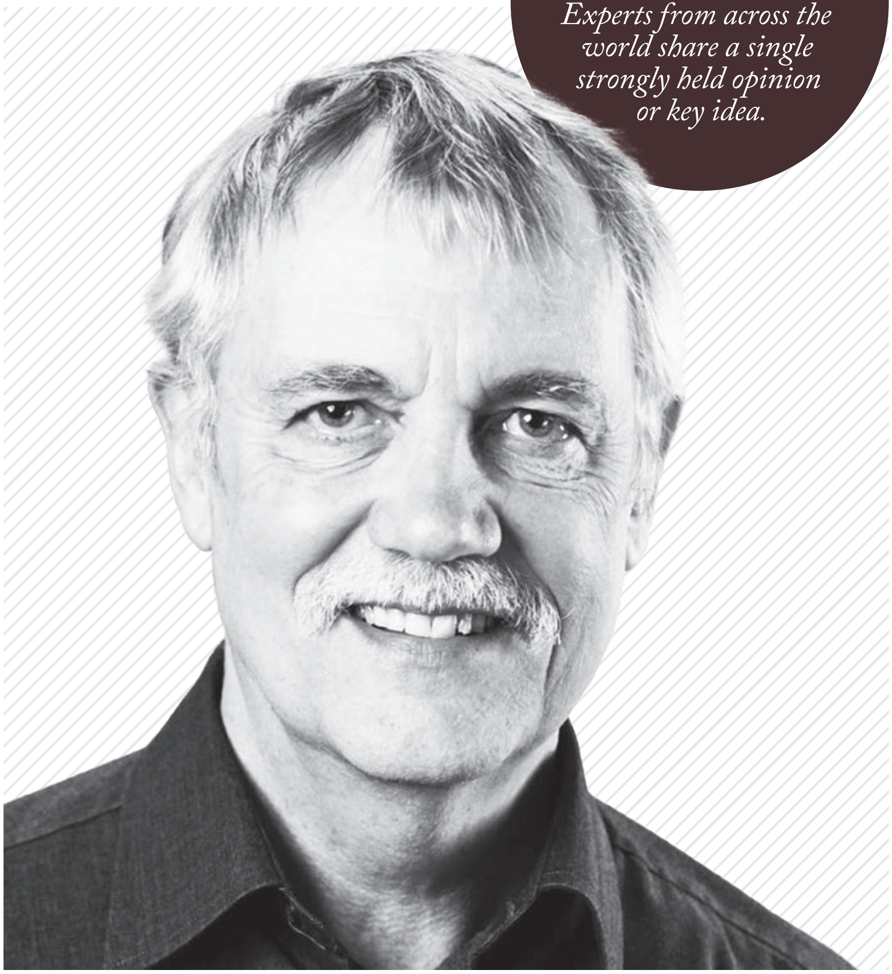
In My View

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

Three Big Challenges for Analytical Science

Confident communication, funding fundamental research, and dealing with data – how we can take analytical science to new heights

By Ruedi Aebersold, Professor of Molecular Systems Biology (em), Institute of Molecular Systems Biology, ETH Zürich, Switzerland



In recent years, the impact of analytical science in the life sciences has been particularly impressive. Advanced fluorescent imaging techniques were the basis for sequencing the genome, cryoEM single-particle analysis revealed the structure of biomolecules at atomic resolution, and mass spectrometric techniques have made great inroads towards the exploration of the many layers of information of the proteome.

Lord Kelvin once said, "When you cannot measure it, when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind." In essence, he is stating that data – which is frequently generated by analytical science and technology – is at the root of scientific investigations. This notion is reinforced if we follow advances in many fields of research including chemistry, physics, atmospheric science, and life sciences.

Why then, as the recent Power List has revealed, does analytical science not have the reputation it deserves? With Lord Kelvin's words in mind, I believe we can raise the profile of analytical science if we highlight not just the performance metrics of analytical methods, but also the contributions analytical science plays in shaping our understanding of the world we live in.

When we communicate progress in analytical science, we should increasingly focus on what results and insights can be achieved by the technique rather than, or at least in addition to the precise details of its workings. For instance, we've been working in the field of proteomics for a long time and witnessed that mass spectroscopic techniques have progressed at an incredible pace. The general life science community may find our research more captivating if we emphasized the generated data and their significance for biology and

"We must take care when delivering results to ensure each field appreciates analytical science for its true value and potential."

medicine. Rather than just focusing on the presence and quantity of any protein in a sample, we should give details on their modification, how and with whom they interact, what shape they take, and what functional role they play in the highly complex environment of a living cell. Sharing our research is important, but we must take care when delivering results to ensure each field appreciates analytical science for its true value and potential.

In addition to raising and broadening analytical science's profile, I see two other big challenges for the field. The first is a consequence of science policy and the ensuing trends in science funding, which have shifted from investigating fundamental principles towards generating rapid and tangible benefits for society. This is readily apparent in the life sciences, where large sums of research funding are allocated to translational research. Coincidentally, funding for developing new analytical methods and studying fundamental principles of living systems across a wide range of species is hard to come by. The consequence of this is starvation of the innovation engine that eventually fuels translational research.

The second challenge facing analytical science is the result of the enormous success of multiple analytical methods that are able to generate large quantities of high-quality data. In the life sciences, the quality, breadth, and volume of data we can generate from samples is astounding. We must develop computational tools to explore the full richness of the data and create new paradigms to explain results. For example, statistical associations are frequently used to detect connections within large datasets. To also detect causal relationships between associated events, we must develop new conceptual and computational approaches.

Addressing both of these two challenges – alongside changing how we communicate our findings to raise the overall profile of the field – is an essential step to ensuring the future success of analytical science.

What It Takes to Innovate

When expertise and interests align, collaboration breeds innovation

Credit: UCSD Communications

By Pieter Dorrestein, Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, and Director, Collaborative Mass Spectrometry Innovation Center, the University of California at San Diego, USA

There are multiple strategies to make the most out of an invention. One of the most important aspects of invention and discovery is getting the right information in the hands of users, testers, and labs as quickly as possible. The scientific community can be conservative in accepting change, so early assessment allows for valuable feedback – which is key for improving your work and demonstrating the usefulness of the technology. Additionally, using real-life examples showcases the practical applications and tangible benefits of your invention by demonstrating what you can achieve today that wasn't possible before. Concrete evidence and success stories help others understand the value and potential of your invention.

When introducing your work to others, it's important to use simple and accessible language. A truly innovative concept may involve new vocabulary and complex terminology – and yet, you want to ensure that people understand what you're introducing them to. Breaking down technical jargon and using relatable analogies or metaphors to convey your meaning will help your innovation reach a wider audience.

This may seem obvious, but if your project isn't completed and you don't have anything published or to show for your time, you may as well have not worked on it at all. An unusable project is worthless in the field, and you're best spending your time on more productive projects.

With this in mind, how exactly do you choose which project to prioritize? In our lab, the team takes a pragmatic approach to look at significant questions we aim to address. We share a strong curiosity of the unknown, which drives us to find answers to seemingly large and complex (or even impossible) questions.

Some of these questions include: "What is the impact of the microbiome on the chemistry of the host?" "How can we comprehensively annotate every small molecule found in humans, the ocean, animals, and plants?" "how do we democratize access to this knowledge, ensuring that scientists with limited resources can still access and leverage it in their experiments?"

These fundamental questions have far-reaching implications for various fields, including biotechnology, agriculture, medicine, and the environment. To seek these complex answers, our lab develops specific yet generalized tools to conduct key studies and learn more about diverse topics – from microbial or microbe-plant interactions, to the mechanistic understanding of how microbiota metabolism affects health conditions such as Alzheimer's disease and atherosclerosis.

To maximize success, the entire team must hold similar values and play a crucial role in decision making. When expertise and interests align, it creates an opportune moment to pursue long-standing projects and tackle bigger questions. In such cases, we leverage the expertise within the team to cover a wide range of areas. Other times, we may delay projects until the right team is assembled or more training is supplied to increase our chances of success. We also make an effort to show our belief in others, giving passionate collaborators the opportunity to take the lead on their ideas. It's also key to prioritize the team's future career and life goals – ensuring that the project will set you up for success, rather than keep you at a standstill.

By focusing on these questions, developing targeted tools, and developing a strong team, innovators can contribute to multiple scientific disciplines while addressing crucial challenges that impact human well-being and the environment.

Agrochemical Analysis at the Edge

Given the rising global demand for food, are the analytical tools, techniques and methods at our disposal up to scratch?

By Silvio Vaz Jr., Research Scientist at Brazilian Agricultural Research Corporation (Embrapa), and Professor at Graduate Program of Biofuels, Federal University of Uberlândia, Brazil

Agrochemicals are an important family of biologically active molecules used in industrial agriculture. This sector generates a diversity of analytical matrices with their own physical characteristics, which demands a range of advanced analytical techniques and methods for monitoring and quality control of processes, raw material, inputs, and products.

Due to their potential to negatively impact the environment and public health, agrochemicals must be carefully monitored and controlled. With that in mind, what is the cutting edge of agrochemical analysis – and are they up to scratch?

There are several agrochemical classes comprising herbicides, fungicides, insecticides, nematicides, and plant growth regulators (1). The kinds of molecules (or active ingredients) used in each of these classes depends on climate conditions (tropical or temperate), the crop type (corn, soybean, fruits, and so on), and the pest incidence (insects, diseases, and so on).

The end-product (or formulation) is composed of the active ingredient (generally considered the analyte) and variable quantities of additives (for example, polyglycerol ester, anionic emulsifier, non-ionic emulsifier, mineral oils, dimethylamide derived fatty acids) – the sum constitutes the analytical matrix. These additives can turn into analytes if we need to perform, for instance, chemical analysis to determine impurities (2).

Agrochemical formulations are generally produced in liquid, solid or a mixture of both physical states in the same ending-product (for example, liquid dispersions), as wettable powders, capsules, and emulsions. In some situations, independently of the physical state, derivatization may be necessary when using chromatography after the extraction step.

In other words, agrochemical matrices represent high complexity, which also often demand suitable sample preparation methods, of course.

Several advanced analytical techniques are already being used for agrochemical analysis. For example, for quantitative information, chromatographic techniques (both gas and liquid phases) are hyphenated with several detectors, including atomic emission spectrometry, optical emission spectrometry, atomic absorption spectrometry, and ultraviolet-visible absorption spectrophotometry. For qualitative information, absorption infrared spectroscopy, nuclear magnetic resonance in solid and liquid states (13C and 1H nuclei), mass spectrometry, Raman spectroscopy, thermal techniques (DSC and TGA), particle size distribution, and zeta potential are all used.

These techniques can be applied for a large variety of analytes and analytical matrices for chemical analysis of agrochemicals, depending on the application. Regulatory guidelines set limits of detection or quantification, or maximum residue limits – but issues related to costs, infrastructure, and availability of skilled labor also determine which method is used.

And that's possibly why artificial intelligence (AI) and chemometrics have emerged as important auxiliary tools in agrochemical analysis. AI can be used as a machine learning tool to extract insights from large and intractable data sets, as well as aiding in the automation of repetitive tasks (3). AI can also help make process analytical technologies (PAT) more scalable and applicable. There is room for improvement here – and I anticipate growth in the number of available advanced software and systems for laboratory automation and control.

Chemometrics does not only apply to measurements, but also to the extraction step of analytical processes because it allows users to evaluate the effect of operational parameter variation on the recovery percentage values. It is possible, for example, to compare several extraction methods and choose the most suitable one for a given group of analytes or to assess the effect of the matrix on the analyte group across methods. Furthermore, chemometrics can be combined with machine learning, as an AI tool, to monitor synthetic processes. Chemometrics for data treatment can be allied to machine learning for several spectroscopic techniques (for example, Raman spectroscopy, NMR, and XRF) to reach a better understanding of generated data (4).

"I believe this class of biologically active molecules can be well-monitored and controlled by the analytical instrumentation available today – provided those tasked with monitoring and controlling agrochemicals have complete access."

Overall, agrochemical analysis is a fascinating branch of analytical chemistry, involving a large family of analytical techniques for several matrices and methods. And it is also a growing branch of analytical chemistry – in terms of scale, scope and importance – given the rising global demand for food, which is set to grow by 35–56 percent by 2050 (5). Analytical techniques and methods can help food safety by guaranteeing the absence of harmful bacteria, viruses, parasites, or chemical substances – and promoting sustainability in agriculture and livestock.

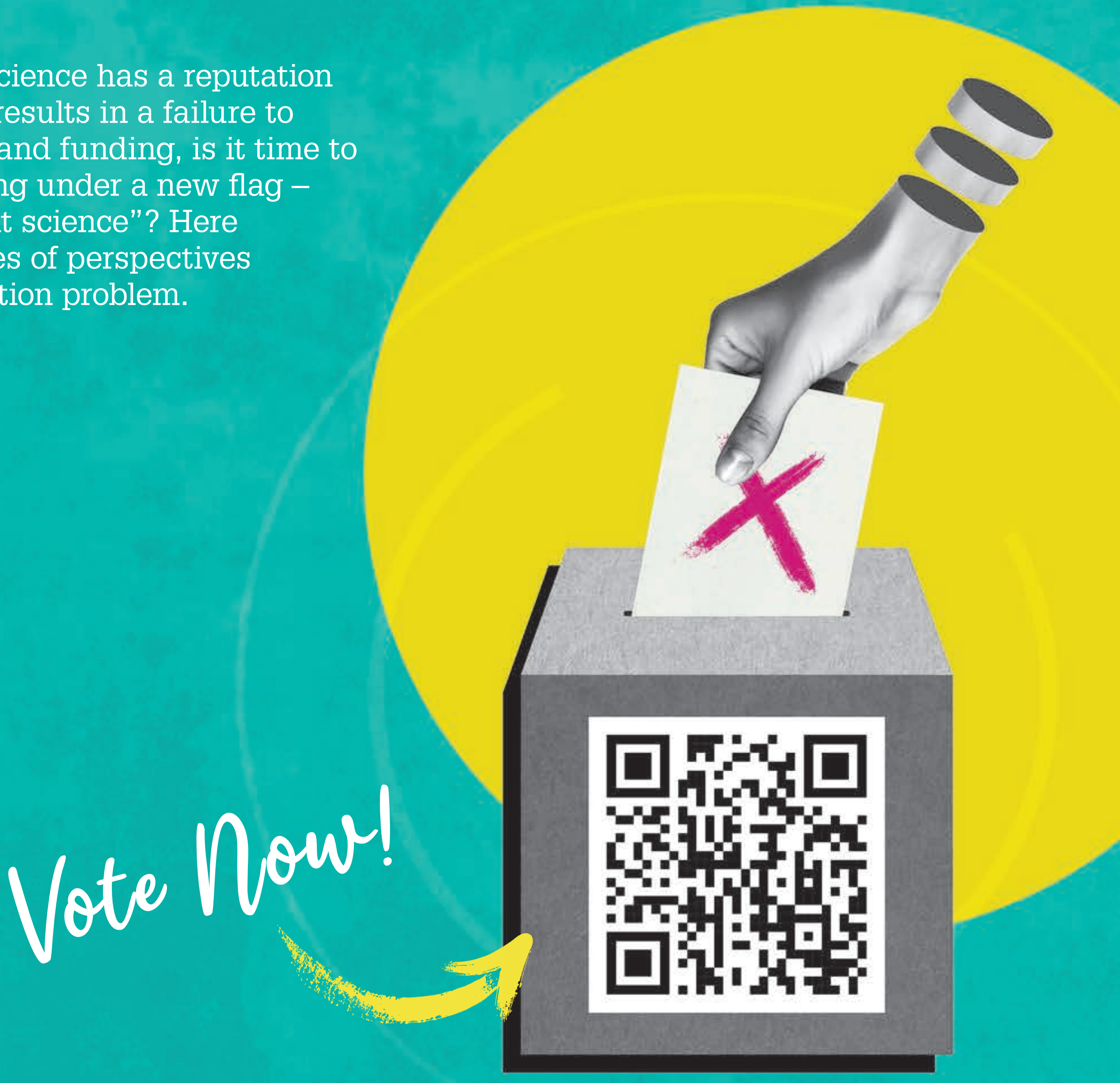
I believe this class of biologically active molecules can be well-monitored and controlled by the analytical instrumentation available today – provided those tasked with monitoring and controlling agrochemicals have complete access. Unfortunately, this isn't a given in many parts of the world. Furthermore, I strongly recommend agrochemical analysts apply the principles of green chemistry in their analytical processes to reduce waste, use safer solvents and auxiliaries, and reduce derivatives. There is room for improvement here – and, given the size of the agrochemical market, widespread adoption of eco-friendly analytical chemistry could have a major impact in the 21st century.

References

1. *S Vaz Jr, "Introduction to Sustainable Agrochemistry", Sustainable Agrochemistry, Springer: 2019. DOI: 10.1007/978-3-030-17891-8_1.*
2. *OECD, "OECD Test Guidelines for Chemicals" (2023). Available at: https://bit.ly/3LZLIxm.*
3. *K Baum et al, "From responsibility to reason-giving explainable artificial intelligence," Philosophy & Technology, 35, 12 (2022). DOI: 10.1007/s13347-022-00510-w.*
4. *R Houhou and T Bocklitz, "Trends in artificial intelligence, machine learning, and chemometrics applied to chemical data," Analytical Science Advances, 2, 128-141 (2021). DOI: 10.1002/ansa.202000162.*
5. *M van Dijk et al., "A meta-analysis of projected global food demand and population at risk of hunger for the period 2010–2050," Nature Food, 2, 494–501 (2021). DOI: 10.1038/s43016-021-00322-9.*

WHAT'S *in a* NAME?

If analytical science has a reputation problem that results in a failure to attract talent and funding, is it time to consider sailing under a new flag – "measurement science"? Here follows a series of perspectives on the perception problem.



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THE SCIENCE OF MEASUREMENT

To repair the reputation of the field, we need to redefine analytical chemistry so that is understood as the science of measurement – and a fundamental part of chemistry

By Richard Zare

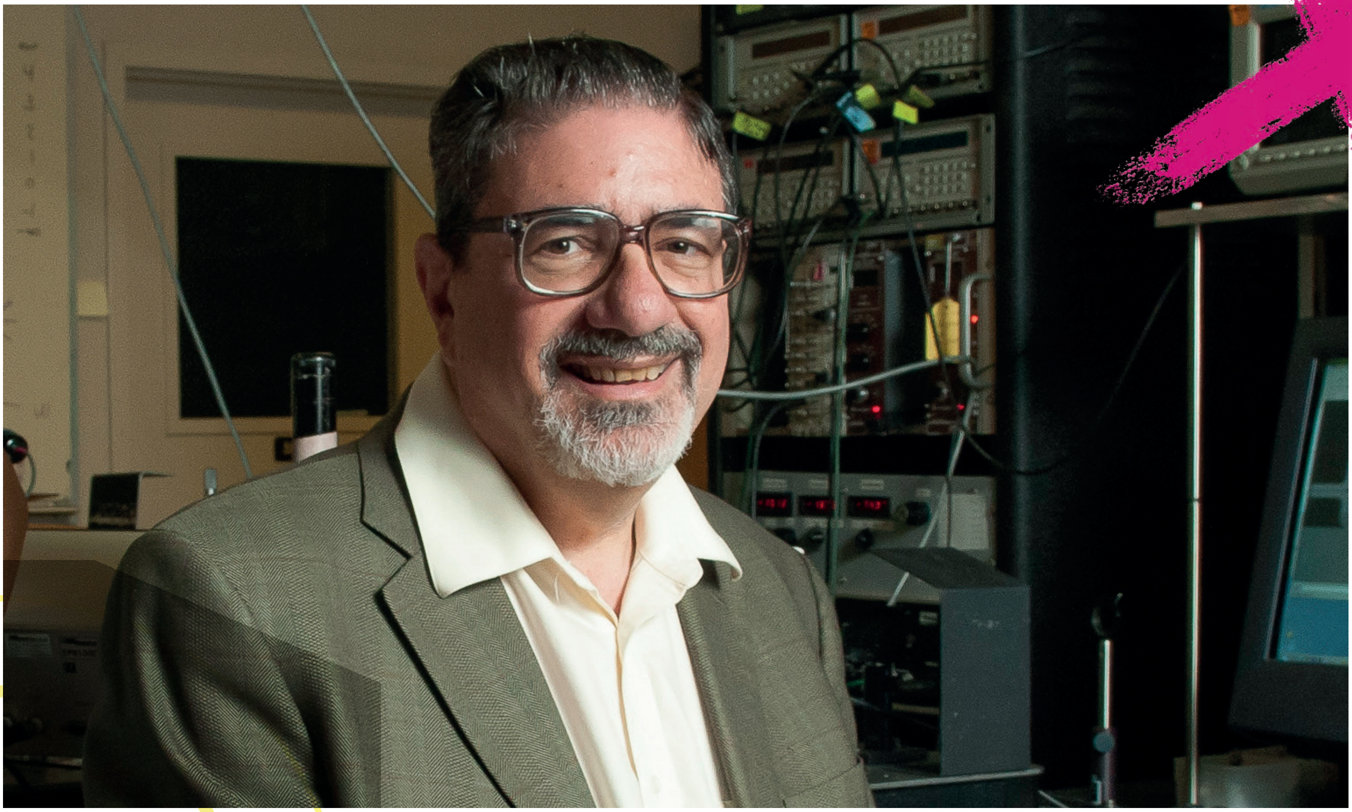
Analytical science has a reputation problem. It goes back to the 1960's when many top universities dropped analytical chemistry as a subdiscipline, with Harvard and Yale leading the way. Back then, it seemed that analytical chemists were just using existing machines to make some type of measurement – very much tied up with titration. It has not been restored, and the problem persists.

Broadly speaking, the problem is that analytical chemists tend to talk only to analytical chemists. We need to be much more inclusive. In fact, even among analytical chemists, there are subgroups arguing amongst themselves about whether mass spectrometry is better than NMR, or vice versa, for example. These are useless arguments: we know that both have advantages and disadvantages. What's missing is a big picture of chemistry as a whole.

I think chemistry involves three or four "Ms": making, modeling, and measuring; and, if you include chemical engineering, you can add manufacturing. Analytical chemists, of course, do the measuring – there's very little we understand without doing measurements! And if we were to tie ourselves much more closely to measurement, as a fundamental part of the chemistry field, we would regain our standing within the chemistry community.

Really, measurement is fundamental to everything we believe to be true in science more broadly. When we make things, we need to characterize what we're making, which always involves measurement. If we model things, the models have to be compared with what we actually observe. How do we observe? We make measurements.

We have divided ourselves up into various buckets: physical science, physical chemistry, analytical chemistry, organic or inorganic chemistry, and so on. I like the idea of chemistry. I like the idea of science even more. We're stuck with the same demarcations and boundaries given to us by history. This really limits our thinking and prevents us from innovating.



"If you develop a new way to measure something, you open up a new world. We've seen it time and time again."

In fact, many of the advances we're going to see in the future will involve combining – or dissolving – what are now considered traditional disciplines. Scientists who silo themselves aren't going to be very successful. My hope is that, as interdisciplinary breakthroughs render the traditional labels irrelevant for the modern age, measurement will become more prominent. Again, what are instrument makers doing, fundamentally? They're making instruments to measure things. And if you develop a new way to measure something, you open up a new world. We've seen it time and time again.

There have been some conferences in recent years that have focused on specific problems, rather than subdisciplines, and have invited scientists from different disciplines to come together, which is a good idea. We need more scientists working collaboratively, interacting with each other, and understanding exactly what it is we need to model and measure. Perhaps we could invite people who aren't "traditional" analytical chemists, but have a connection with measurement.

Let's take an example. Understanding the brain is going to be one of the biggest challenges for science this century. Measurement will undoubtedly play an important role here. But what do we need to measure? What are the problems that need solving? Someone like Xiaowei Zhuang, Professor at Harvard University, comes to mind. Zhuang is illuminating neurobiology with super-resolution and single-molecule imaging; and while she has a physics background, and might not call herself an analytical chemist, she's doing measurement science! Perhaps we'd have more scientists like Zhuang if science curriculums weren't so strictly divided into biology, physics, and chemistry; and a chemistry curriculum that doesn't place much emphasis on measurement.

This message needs to be received by other chemists, particularly those who are influential. We could make some real headway if leading organic and inorganic chemists helped reemphasize the importance of measurement – of analytical chemistry – in their discipline.

I know I'm swimming upstream. But I believe this is a fight worth having. If we want change, that's what we're going to have to do. We need to redefine chemistry so that it incorporates measurement; and we need to redefine analytical chemistry so that it is understood as the science of measurement – this is what we are and what we do.

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THE UNSEEN SCIENCE

With Gert Desmet

Are there negative stereotypes of analytical scientists? If so, what can we do to change this view?

One stereotype is that analytical scientists are "nitpickers." Due to the precise nature of our field, we, of course, need to ensure our measurements are accurate and act carefully when approaching projects. This "nitpicky" approach is key for getting the right results – so maybe we should embrace this view and turn it into a label of quality. Being precise is also an effective and prestigious thing. Rather than labeling ourselves as "nitpicky," we should use words like "precise," "accurate," or "categorical."

Should we change our approach with students?

Many, and especially the best, students at university are not really concerned about their future career yet. They are more curious and driven by making new discoveries. As a result, maybe we're indeed losing some of the most talented chemistry students to disciplines where there's more Nobel prizes expected. One approach we could take is in positioning analytical chemistry as a field for technology geeks. There are some beautiful instruments and decades worth of technological advancements that we should highlight to the next generation.

Have there been past attempts to improve the reputation of the field? If so, how have they fared?

Many groups have tried to evade the problem by changing the name of their group. For more than 30 years, there has been a trend in analytical chemistry departments to transform into applications focused departments. Although this worked well to attract funding and students, the field suffers major negative effects when analytical chemistry isn't advertised as a focal point. The same happened at the level of staff recruitment – retiring analytical chemistry professors are usually replaced by someone with an application science background with little analytical chemistry training. As time goes on, analytical science can be seen less and less in relevant degrees, and it's difficult to come back from these worldwide declines.

What else can we do to improve the reputation of analytical science?

Analytical chemistry should be more visible in textbooks and discussed as a vital point in scientific discovery in classrooms – both at high school level and university level. When I was in high school, I saw many students falling in love with chemistry and going down the organic chemistry route because that's the only path they believed was open to them. If we could also show students the beauty of mass spectrometry and spectroscopy at an early stage, they might see things differently.

It is important for society to understand the importance of our field and all the possibilities for future discoveries. If the Nobel Prize Committee, for example, took notice of analytical scientists in research projects, the next generation are more likely to see our field as a viable career path.

There's also so many options for careers within analytical science – from pharmaceuticals to clinical research. Showcasing the importance and broad spectrum of analytical chemistry can only benefit our cause.

We should be much louder about our accomplishments. Not only to the general public, but also to our fellow chemists and scientists. We should make it clear that everyone would benefit from improvements in analytical science. There's no reason to sell ourselves short. The world needs analytical chemistry – this was demonstrated through the COVID-19 pandemic. Thankfully, we were ready for it. But what will happen, if we aren't?

What about a rebrand?

I do think that sailing under a new flag such as "chemical measurement science" rather than "analytical science" could rid us of the image of "nitpickers" I mentioned earlier. What we do in our field is spectacular, but we're not selling it well enough – especially to the younger generation. Many of our fellow chemists consider us a service technology, but they'd be nothing without our measurements and the progress of our field. We have all the reason to be proud of our work, and I feel that a rebranding would only benefit our cause.

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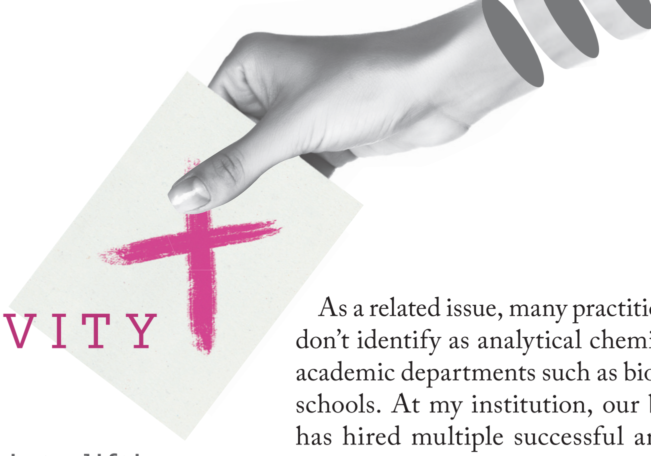

THE POSITIVITY PROBLEM

If we all put more effort into lifting our spirits and those of our students, we'd unintentionally raise the profile of analytical chemistry

By Jonathan Sweedler

My motivation for writing this article is to share my thoughts on whether the field of analytical chemistry should be renamed. For me, changing the name to something like "measurement science," as others have suggested, may have little effect. Even if you think people may more easily understand what we're fundamentally about, keeping our connection to chemistry helps to define our field. We may never get the terminology perfect, and so I propose we work on our messaging instead.

Ever since I joined the field, there have been many comments centered on the respect (or lack thereof) we receive in analytical chemistry. These views go back to the 1950s and 1960s, when chemistry departments saw an explosion of new ideas in organic synthesis, physical chemistry, and other subfields of chemistry. These areas were perceived to be advancing quickly, whereas analytical chemistry was focused on existing measurements and thus, considered slower to move ahead. As a consequence, Berkely, Stanford, Yale, and other prestigious coastal institutions responded by not hiring analytical faculty, eventually having the field disappear from their chemistry departments. This changed in the 1970s and 1980s, as computer-controlled instrumentation greatly increased our abilities to perform measurement science, alongside significant advances in spectroscopy, separations, electrochemistry, and more. These advances have kept coming!

Yet despite these enhanced analytical measurement capabilities having increasing impact across many scientific disciplines, analytical chemistry is often viewed as a less vibrant area by some academic institutions. This view reduces our ability to recruit the best students, staff, and faculty. This incomplete understanding of the contributions of our field may be due in part to its application across disparate scientific disciplines. As one example, mass spectrometry technologies are constantly improving and being applied to an ever-greater range of fields outside chemistry. Our cross disciplinary impact convinces me that analytical chemistry is a growing, vibrant, and highly successful field, but it also makes it harder to track our impact.

As a related issue, many practitioners of analytical chemistry don't identify as analytical chemists, especially if they are in academic departments such as bioengineering and in medical schools. At my institution, our bioengineering department has hired multiple successful analytical chemists. In fact, the number of faculty who publish in analytical journals at the University of Illinois is much higher than those officially affiliated with the chemistry department. Our analytical graduates are hired for all sorts of academic and scientific positions in a broad range of fields. However, these scientists often identify with whatever field they're working in – as a bioengineer or a pharmaceutical chemist – not first and foremost as an "analytical chemist." We need to convince them it is in their best interest to do so!

It's worth noting that analytical chemists are not alone in defending their field; a lack of respect is something that scientists of all stripes suffer from. Some organic chemists complain that the organic chemists working in chemical biology don't recognize themselves as organic chemists. More interestingly, some of my colleagues outside of analytical chemistry have been envious of the large funding priorities over the last few decades that have involved measurement science. These include the national human genome, microbiome, and brain initiatives, with large components related to tool development and analytical chemistry interwoven throughout these efforts to highlight our growing impact.

All that said, perhaps we'd be even more successful, attract more talented students, and generate more interdisciplinary collaborations if more people were aware of what we do. There is more that we can do outside of top-down PR. Of course, our field does get great PR when we have researchers analyzing letters from Dracula (1) and extracting protein from a dinosaur bone and applying mass spec to discover dinosaur protein fragments (2) are closely related to chicken proteins. This is a case of analytical chemistry solving one of humanity's most long standing unanswered questions – what a dinosaur tasted like!

More seriously, there's a danger if we expose our students to too many negative opinions – we don't want negatives to be what they most remember about our field. If the overwhelming consensus and topics of our conversations are that we're not getting enough recognition and respect, what impact will that have on prospective students when choosing a field of study? We need to generate interest in analytical chemistry by sharing what we're working on with students and get them as excited as we are about our discoveries. This enthusiasm also applies to elementary, high school, and undergraduate students. Besides growing our field, analytical science education can lead students toward careers

Credit: UI News Bureau: L. Brian Stauffer photo

in pharma, bioengineering, biotechnology, environmental science, forensics, and so on. There are so many different ways for analytical chemists to thrive – we need to shout about that!

We also have to be careful that our own setbacks don't generate negative attitudes that students absorb and then redirect towards the entire field. We should acknowledge that setbacks, such as funding and publication rejections, are part of the life of a scientist. One way I've tried to combat obstacles is by bringing everything back to my students. Even after some setbacks, with feedback and reflection, they have been able to come up with amazing ideas, refine them, and, ultimately, succeed. These early career successes ensure we attract more talent to our field.

There's one student I'll never forget who came to see me a couple of weeks after they had their first first-author paper accepted – saying that they didn't think they were going to make it as an analytical chemistry grad student and should not get a PhD. They had all sorts of reasons as to why they didn't believe in themselves or analytical chemistry as a good career choice. This is the key moment to become a cheerleader – a role all mentors should take. After trying to convince them that they could do it, I finally told them: "You've got your first-author paper accepted and you're not allowed to complain for two months." They ended up leaving my office in high spirits, joking that they'd be back after two months. You know what? Their first success was enough, and they never returned to report that they were leaving our field; they now have a great career in analytical chemistry.

"Perhaps we should be looking inwards rather than spending our efforts on rebranding the entire field – especially when there are so many different opinions about how we can 'raise the profile of the field.'"

Thus, my final thought is that perhaps we should be looking inwards rather than spending our efforts on rebranding the entire field – especially when there are so many different opinions about how we can "raise the profile of the field." Perhaps if we put similar efforts into lifting our own morale and that of our students, we will raise the profile of the field to new and exciting heights.

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NO MERE APPLICATIONIST!

To raise the profile of analytical science, we need to differentiate ourselves from routine, "push-button" chemical analysts as the developers of new analytical tools and techniques

By Victoria Samanidou

Credit: Yannis Tsouflidis

Analytical chemistry was once, in the words of C.R. Fresenius, what "made chemistry a science" and "a main pier on which the whole building of science is grounded." This view was echoed by several of analytical chemistry's founding fathers, including Antoine-Laurent Lavoisier, Karl Friedrich Mohr, Izaak Maurits Kolthoff, and Justus von Liebig. Unfortunately, few outside of the analytical science world would agree today. In fact, analytical scientists are sometimes considered mere "applicationists" – a step down from core chemistry. I see many brilliant young scientists attracted to organic chemistry synthesis or biochemistry, where you'll be working on fundamental processes at a cellular and molecular level. Indeed, the professors in these fields often have higher profiles. And that's part of the reason why we struggle to attract enough great minds to analytical science – minds that could make big scientific advances. So what happened and what can we do about it?

Things changed for analytical chemistry when instruments were introduced. Of course, instrumental analysis opened new horizons and offered a plethora of opportunities for interdisciplinary research. However, as the discipline became broader, fundamental research became shallower. Despite the fact that wet analytical chemistry – both qualitative and quantitative – was considered a core science, the use of instruments changed attitudes. Samples could be analyzed by technicians without strong technical backgrounds, so people began to associate analytical chemistry with routine analysis, which led to a widespread perception of the field as second class science.

The sad thing? This wasn't actually the case – even back then. In separation science, fundamental knowledge is mandatory, otherwise a method cannot be generated or repeated. Imagine the transfer of a gradient HPLC program that separates a number of analytes to a system with different dwell volume; or imagine the science that is hidden in all sample preparation approaches. Nonetheless, a notion had spread: chemical analysis now simply involves "pressing buttons."

This, I would argue, has also disorientated analytical scientists themselves. Today, the field seems to be split into two separate disciplines: "analytical chemistry/science" and "chemical analysis." The latter is related mostly to applications, serving as a tool and providing data to other disciplines, while the former relates to fundamental core science.

Routine chemical analysis of similar samples using standard protocols usually developed by others or made mandatory by regulatory agencies is certainly a valuable service for many fields, but it is not the same thing as developing or improving techniques and tools to solve new problems, which requires deep fundamental understanding. The proliferation of chemical analysis and its association with the analytical science field as a whole has not done the reputation of the field any good.

But we also need to recognize our own part in the problem. We are guilty of failing to make this distinction between analytical chemistry and chemical analysis clear. We often consider both groups as part of the same "community," which has led scientists in other fields to see all analytical scientists as mere applicationists involved in routine analysis.

We seem to be stuck in a vicious cycle where we don't get the recognition we deserve, which leads to a lack of self-esteem, which then contributes to how others view the value of the field. We need to change this feeling to establish ourselves, once again, as highly appreciated in the community of chemists.

"The most fascinating part of analytical science has always been (at least to me) qualitative and quantitative analysis based on chemical reactions."

Interdisciplinary limits

We do often talk about the benefits of interdisciplinary collaboration – this is mandatory in analytical chemistry, by definition. Indeed, there is no reason to develop a method unless it has application to any kind of field: medicine, pharmaceutical chemistry, environmental chemistry, organic synthesis, food chemistry – you name it. But we should set the limits. The analytical chemists' task is to develop and validate the necessary method to solve the problem, check and prove the applicability with a number of real samples. Next, the recipient of the method has to apply it to their own terms and conditions. The role of the analytical scientist should be distinguishable and clear.

It is not a taboo to do chemical analyses, but analytical chemists should mainly work on the promotion of their field. Or at least they should face the truth and be aware of the level of science they are doing.

I also think we need to stick to the fundamentals in our analytical chemistry curriculums. The most fascinating part of analytical science has always been (at least to me) qualitative and quantitative analysis based on chemical reactions. A good theoretical background is a prerequisite to progress. Students must deeply understand what is happening in the tube. All experiments of precipitation, dissolution, and so on are "magic!" But, more recently, due to the fact that reagents are expensive and potentially toxic or harmful for the environment, lab practice has been all but eliminated. Students now have less contact with basic knowledge in practice.

At the same time, instruments, for students (and unfortunately for some scientists as well), are black boxes. They may know the principle of operation, they may know the software to operate the instrument and collect data – but then what? I have many times come face to face with the fact that they don't actually know what they are measuring or how to calculate the results and express the data as useful information. The more this continues, the more others will see the field as lacking depth – because that will become the case!

Students also require good training on instruments so that they have deep knowledge of what is taking place during operation. Very often a lack of good training is related to the age or condition of the instruments, which may be not in full operation mode. (The high cost of operation is evidently a drawback.) Students should also be taught how to repair the instrument.

Having said all this, we do often see students who, after finishing their master's degree or even PhD thesis in other fields – dazzled by the lights of pure scientists – come to analytical chemistry for a further degree, so they have the practical experience that is necessary for their future employment. We might have a reputation problem – sometimes struggling to attract students – but the value of the analytical science field often shines in other ways. Just look at the number of Nobel laureates from our field!

Emphasis on the fundamental

Generally speaking, all chemical unions/societies and their divisions of analytical chemistry make efforts to promote the field. But the field is its people – it's up to analytical scientists to distinguish themselves and persuade their peers. If our research deals with fundamentals, it will be published in highly esteemed journals. It will take time, but other scientists and students will get the message.

We should also focus on our own field. Interdisciplinary collaborations can continue once the necessary analytical tools have been developed and checked for applicability; we must pass the baton of routine analysis and data processing to those who need the application data for their own research demands. Again, we must differentiate ourselves.

If we emphasize our fundamental role, change gears, and get rid of our "applicationist" label, I believe we will be accepted by peers – as we once were – and also inspire young chemists to join our wonderful field.

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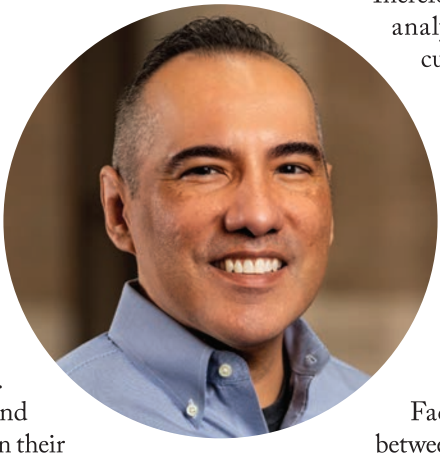
COLLABORATE TO ADVOCATE

With Ben Garcia



Does analytical science have a reputation problem?

It does and it doesn't. In industry, analytical science is quite well respected. Every major pharmaceutical company has an analytical science division with their own mass spec or NMR units, for example. The biologists, the material scientists, and others who work in industry constantly rely on their analytical colleagues – who are always in high demand.

On the academic side, things are a little different. There are historical reasons that result in analytical scientists being overlooked or viewed as simply a tool or technique we use to characterize organic molecules. Indeed, many institutions – especially in the US – don't have analytical chemistry divisions. Most chemistry departments have physical chemistry and organic chemistry divisions, and analytical chemistry is seen historically as a tool for these other chemistries. And that's reflected in how we teach undergraduates in the US. Students are often first introduced to analytical chemistry as a tool to figure out whether you have the right product following an organic chemistry reaction. The student will need to know that they should use mass spec to get the molecular weight, IR spectroscopy to see what functional groups are present on the molecule, then NMR to define all the different proton groups, and so on. So even for second year chemistry students, analytical chemistry is introduced as a series of techniques to supplement other fields.

Could the way we teach analytical science be putting some students off?

It could be contributing to a failure to attract talented and potentially analytically-inclined students, for sure. Most undergraduates don't know exactly what they want to do – nobody walks in on day one wanting to be a physical chemist or an analytical chemist (or at least most don't). We expose them to research of various types and they might hear about something in a lecture or in a lab that piques their interest. But if analytical chemistry isn't taught as an important field in its own right, if techniques in lectures or instruments in labs are introduced as supporting tools, and if there isn't an analytical chemistry department at the university, these data points paint a negative picture for a student. With so many potential career avenues available, a student might dismiss analytical science out of hand.

Therefore, we need to do a better job of introducing analytical chemistry a little earlier in the curriculum – at least in the US – to showcase what the field is really about before students have already decided they're interested in organic or physical chemistry. In fact, introducing analytical chemistry as a field in high school would be great.

Is there anything else we can do to address the reputation problem?

Facilitating interdisciplinary collaboration between analytical scientists and scientists in other fields should help to raise awareness of what analytical science can offer. There's scope for societies to do more here – which I know they're working on. I have sat in governing executive committee meetings of a few different societies and one of the things we discuss is how to infiltrate other more traditional clinical or biology conferences to show them the power of mass spectrometry. But we also want to welcome them to our meetings so that they'll see the latest developments in analytical science and potentially get inspired to work with us.

It'd be great if we could work with different organizations to put together different sessions with participants from different fields, or perhaps a technology-focused session that is focused on potential applications to a particular field. I'm hoping we can figure out ways to find strategic partners for these collaborative efforts, who might then promote our field at their universities or elsewhere.

Does analytical science need a rebrand?

I'm not so sure. Introducing something new at this point and getting a foothold to overtake analytical chemistry/science would be tough. There is a journal of measurement science. And the American Chemical Society does have some awards that are branded as measurement science awards. If everybody started using it, who knows, perhaps it would catch on. Personally, I favor fighting for analytical chemistry. It's what most people are familiar with and I think we can turn things around.

Benjamin Garcia is Raymond H. Wittcoff Distinguished Professor, Head of the Department of Biochemistry and Molecular Biophysics, Washington University School of Medicine in St. Louis, USA

MAKE ANALYTICAL CHEMISTRY COOL (AGAIN)

Here, we ask the opinions of three early-career researchers – Simona Felletti, Mimi den Uijl, and Ina Varfaj. Not coincidentally, our trio were all winners of the 2023 Separation Science Slam – a competition held at HPLC and organized by The Analytical Scientist and Knauer.

Does analytical science struggle to attract young researchers?

Felletti: Yes – somewhat. It's always been difficult to find young researchers that are interested in analytical science. But what I can say is, although we may be few, we are highly motivated!

Varfaj: I agree with Simona – those of us in the analytical community are really motivated and strongly believe in research for future needs. This passionate environment is encouraging for young scientists and should be advertised more broadly. Additionally, there needs to be a strong connection between academia and industry. It's important for early-career researchers to be able see a clear path to a career in industry as well.

What do you think is the root of the problem?

den Uijl: A lot of the issues lie within education itself. In the Dutch school system, you spend six years at high school and, after the first three, you choose which direction you want to go in. This means that it's only three years in when you start to learn the basics of chemistry – and that's where we're going wrong. We approach subjects as though you have to learn everything before doing something with it, but this gives the public the impression that chemistry is really difficult. By overcomplicating our field, we're scaring away talented scientists. This also gives the stereotype that people have to be incredibly smart to do chemistry, but if you do a PhD in any subject, you have to be very clever. So it has nothing to do with the field at all – just our presentation of it.

Felletti: Yes, the poor reputation of chemistry amongst all scientific subjects and students is scaring them from exploring the field – and it's even worse for analytical chemistry! There's also a lack of information about what analytical science researchers do. And the uncertainties around future job prospects (especially in academia) further tarnishes the view of the field. We should be dedicated to removing the initial prejudice young students have towards our field.

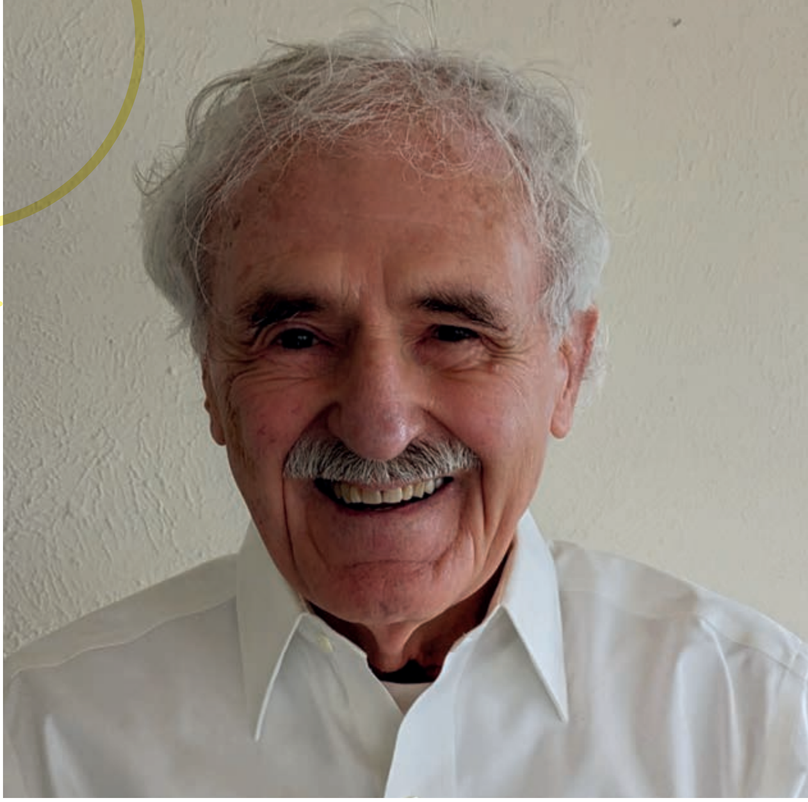
What actions can we take to overcome these challenges?

Varfaj: We need to promote awareness of analytical science through career fairs, school visits, extracurricular programs, summer camps, and online resources. If professionals in the field share their experiences with students and provide accessible introductory courses, mentorship programs, and tutoring, we can build the confidence and skills of the next generation. Of course, collaboration with industry professionals to update the curriculum and incorporate real-world applications would greatly improve students' learning outcomes. A broad multidisciplinary approach that combines awareness, diversity, mentorship, and engagement would help in attracting young students to analytical science and prepare them for successful careers in this rapidly evolving field.

den Uijl: Yes, it seems that, as a field, we agreed not to share much with the public about the work that we do. This obviously makes it very difficult for us to excite the next generation of analytical scientists. If young scientists see the exciting research projects that analytical scientists partake in – and if we remove the stereotype that you have to be super smart to work in our field – we're sure to see more interest.

Felletti: The activities of scientific dissemination are pivotal here. It's crucial to show students the role of researchers and analytical scientists. Even events such as the Separation Science Slam would push this narrative and give students a perfect window into the field.

Simona Felletti is a Research Fellow at University of Ferrara, Italy; Mimi den Uijl is an Analytical Chemist at University of Amsterdam, Netherlands; and Ina Varfaj, is a PhD Research Student at University of Perugia, Italy



FIGHTING FOR SCRAPS?

Chemistry's diminished standing among the sciences has led to counterproductive departmental competition, which – alongside a fragmented approach to education – has hurt analytical chemistry. The damage has been done, but there are steps we can take to improve our reputation.

By Chris Enke

I'll begin with three reasons for analytical chemistry's diminished position on the totem pole, before offering some thoughts on what we could do to improve it.

1. The totem pole exists in all sciences, but it is particularly brutal among chemists.
2. Chemistry department divisions became hardened and competitive with each other.
3. Analytical chemistry is taught as a set of techniques rather than the science it is.

First, considering the science totem pole, physics – particularly theoretical and cosmological – is considered to be at the top. Biology and chemistry used to have a similar standing, but recently chemistry has taken a beating (see below). This loss of prestige is rough on chemists who then often take it out on each other. Brutal!

Second, this hyper-competitive spirit has long infected chemistry departments. When I first got to Michigan State, the department was collaborative. We chose which division got the next appointment based on teaching needs and gaps in research. I co-taught an analytical/physical sequence with a senior physical chemist. Then some inorganic and organic hires brought with them the zero-sum philosophy, and competition for internal resources became the name of the game.

Another unfortunate aspect of divisionism was the tendency to hire people classically positioned in that area: the organic division would not hire a protein chemist, the inorganic division rejected organometallic applicants, and so on. The result of this parochialism is that the field of chemistry lost all its exciting new areas. Only in the last two decades did it finally decide to take on biological chemistry, but it was too late to keep the core. We lost medicinal chemistry, materials chemistry, geochemistry, and molecular biology, to name a few. We will not get them back. I believe this is one reason for chemistry's loss in status. Contrast that with physics departments that embraced cosmology, cryophysics, solid state electronics, and other offshoots. Many departments have even added physical biology – jumping over chemistry, the central science, as though it didn't exist.

The third problem – a focus on technique rather than science – is something we could have done something about – and potentially still can. When I was in graduate school in the early 1960s, inorganic chemistry shared the bottom rung with analytical. Then, Harry Gray and others lifted inorganic chemistry from a collection of syntheses to the science of inorganic reactions, making them predictable. This gift of a rationale to the area lifted it up as a major contributor to material science and gave it a solid space in departments nationwide.

Analytical chemistry was taught to me as a series of unrelated techniques at the undergraduate and graduate levels. See the parallel with inorganic? The big problem: it is predominantly still taught that way. We are more accepting of expanding the purview than other divisions, taking on electrochemistry in the 1950s, chromatography in the 1960s, and mass spectrometry in the late 1970s. We might be considered more essential if we offered a unifying and predictive science of analysis.

But wait. There is a science to chemical analysis – an approach that binds and informs our methods. There is a science to how measurements (1) become meaningful numbers (2), and there is a science of how to select or develop a method (3)

> *"How about a NOVA program on the history, magic, and applications of mass spectrometry?"*

for a particular need. Scientific knowledge (4) is made up of predictive laws and their rationale. The correct application of those laws is a skill, not a science. We could focus more on the knowledge we have produced – the laws for predicting a separation method's resolution, chromatographic retention time, electrospray ionization response factor, dynamic range, and so on.

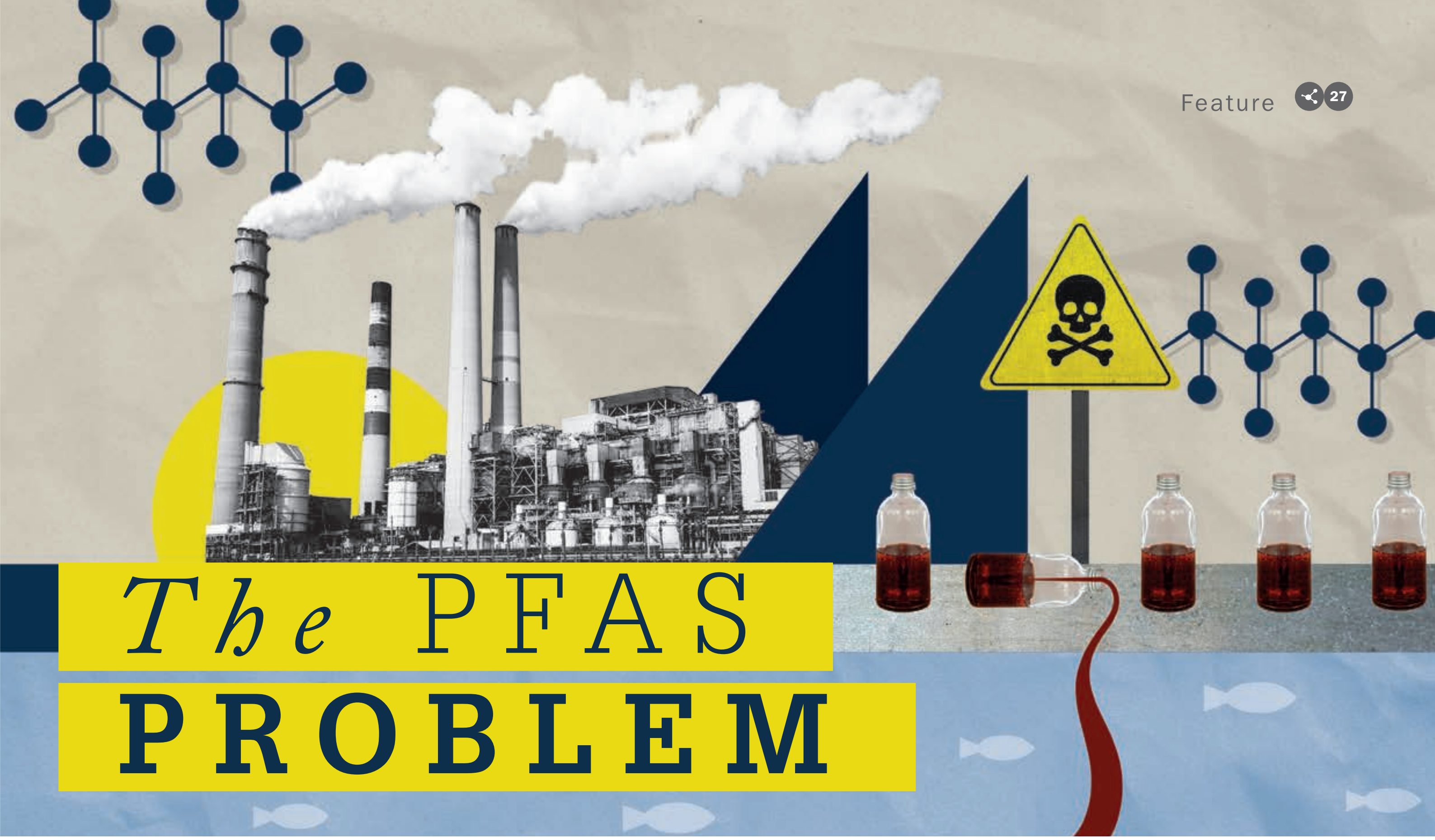
On the perception side, there are wonderful stories and fantastic accomplishments to be told. We have improved detection limits and the number of resolved mixture components by an order of magnitude every decade since 1960. We have invented and improved many tools now essential in a wide range of other areas of science and medicine. Should we remind them where they came from? And for the public, how about a NOVA program on the history, magic, and applications of mass spectrometry?

I have had a wonderful professional life in this field where there is so much room for creativity and so many wonderfully collegial people. I have not a moment of regret.

Chris Enke is Emeritus Professor, Michigan State University and University of New Mexico, USA (Chrisenke.net)

References

1. *CG Enke, "Data Domains – An Analysis of Digital and Analog Instrumentation Systems and Components," Anal Chem, 42, 1, 69A–80a (1971). DOI: 10.1021/ac60296a013.*
2. *CG Enke, "The Elements of Measurement," ACS Meas Sci Au, 2, 5, 405–413 (2022). DOI: 10.1021/acsmeasuresciau.2c00007.*
3. *CG Enke, The Art and Science of Chemical Analysis, Wiley (2000). ISBN 13: 9780471373698.*
4. *CG Enke, "The two parts of a scientific theory" (2023). Available at: https://bit.ly/3R0jMfH.*



The PFAS PROBLEM

Credit: *Images for collage sourced from Pexels.com and Unsplash.com*

As health concerns related to per- and poly-fluorinated substances (PFAS) become increasingly apparent, analytical science must rise to the challenge

When did people first become aware of PFAS? And where are they most commonly found?

Stefan van Leeuwen: PFAS – also known as "forever chemicals" – have been around for some time, but only reached scientists' radars in the late 1900s/early 2000s, when studies reported on the two major PFAS compounds (PFOS and PFOA) in the environment. The general public in Europe gained awareness more recently – since the late 2010s, when hot spots were detected and studies reported on the occurrence of PFAS in consumer products, such as food and drinking water. These reports in the media are threatening the public's sense of safety. From a food perspective, the European Commission (EC) has introduced legislative measures (limit values) for some foods – an important step in reducing PFAS exposure. However, with the potential of hundreds to thousands of other PFAS in the environment, there may be other compounds that need our attention.

Mark Strynar: PFAS have been used for decades in a multitude of commercial and consumer product applications. Their unique chemical and physical properties make them candidates for use in many applications – for example, firefighting foams, fluoropolymer production, stain resistant coatings. Though the knowledge of individual and broader class PFAS continues to grow, there is much that remains unknown about these compounds.

One such area lacking information is what is/has been produced and released into the environment. Analysis of environmental samples using high-resolution mass spectrometry and non-targeted analysis applications has been very fruitful in identifying new and emerging PFAS. For most organic environmental contaminants, the characteristics of persistence, bioaccumulation potential, and toxicity (PBT) cause concern. A select number of PFAS satisfy all three PBT concerns, while for other PFAS, PBT concerns are either partially satisfied or are completely unknown.

Due to press coverage, there is growing knowledge on this topic within the non-scientific community. However, there remains much to understand about PFAS occurrence, risk, and remediation. Learning more about which chemicals we are dealing with is the very foundation of this research. Without this knowledge, the study topics mentioned above cannot commence.

Jochen Mueller: One of the main uses of PFAS that has led to a particular contamination has been in aqueous film forming foams (AFFFs). Open release of AFFF, particularly during regular firefighting training, has led to contamination of soil, groundwater, and human exposure in Australia and across

MEET *the* EXPERTS

Credit: The University of Queensland

Jochen Mueller is Professor at the University of Queensland and Australian Laureate Fellow. He leads a research team that focuses on Exposure Science, including human biomonitoring to understand exposure trends. His research includes PFAS sources, fate, exposure, and treatment. In addition to this, Jochen established the Australian Environmental Specimen Bank.

Richard Jack is Global Market Development Manager in Food and Environmental at Phenomenex. With over 18 years of experience in chromatography and mass spectrometry for environmental, semiconductor, chemical, and pharma applications, Richard has collaborated with global regulatory agencies to develop validated methods through new applications, instrumentation, column chemistries, and software. He's currently Second Vice Chairman for the ASTM D19 subcommittee on water analysis.

Credit: Phenomenex

Mark Strynar is Senior Physical Scientist at the US EPA in Research Triangle Park, NC, USA. During his 20 years as an analytical chemist, Mark has developed analytical methods for the measurement of PFAS and other chemicals in environmental and biological samples.

Stefan van Leeuwen is Senior scientist at Wageningen Food Safety Research, Wageningen University & Research, Netherlands. First acquainted with PFAS in the early 2000s, Stefan's work has mainly focused on developing methods to analyze PFAS in food and environmental samples – investigating their presence and impact on food safety within food production systems. He initiated the first global interlaboratory study on PFAS, emphasizing the importance of quality control. Stefan currently co-chairs the PFAS Core Working Group of the European Reference Laboratory on Persistent Organic Pollutants (POPs), aiming to enhance the proficiency of food analysis in European labs.

the world. Both firefighters and the wider community have faced elevated levels of PFAS in blood, potential health effects, economic losses, and broader societal impacts.

Richard Jack: As Mark alluded to, PFAS are used everywhere, requiring a multi-faceted approach. It's also key to understand the goal of our analysis – are we simply measuring them, developing new products, trying to understand their toxicology, or looking for better ways to remove PFAS? It's important to pursue all of these goals to protect the public.

Which techniques are at the forefront of PFAS analysis?

Mueller: There are so many methods that have a role in PFAS analysis. Of course, we routinely use liquid chromatography mass spectrometry (LC-MS/MS) for the main bulk of target PFAS analysis and liquid chromatography-high resolution MS for suspect screening and discovery. IC-MS is employed for short chain compounds like TFA and GC-HRMS is used for some volatiles. DESI-MS can be very useful for "2D" visualizing PFAS in niche applications, and DART-MS is used for surface desorption work. There is also space for FTICR and NMR for identifying new PFAS. And techniques such as PIGE, µ-X-ray Fluorescence, and Fluorine K-edge µ-X-ray absorption near-edge structure (XANES) spectroscopy are also used. Every technique has its relevance.

Several sample preparation methods, such as the total oxidizable precursor (TOP) assay, have become important to PFAS analysis. LC-MS/MS and possibly increasing LC-HRMS are likely to remain essential in this area for some time – depending on the specific needs of analysis, of course.

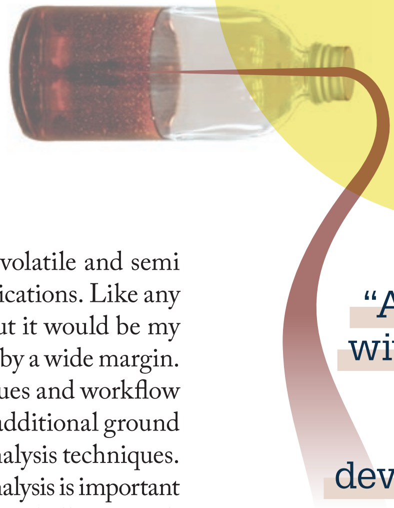
Strynar: As Jochen says, existing PFAS analytical methods that have been fully validated for performance in environmental media (for example, water, human serum, and fish tissue) are strongly dominated by LC-MS applications. There is also a fair amount of analysis that has been done for volatile and semivolatile PFAS using gas chromatography mass spectrometry (GC-MS) applications.

Both LC-MS and GC-MS have access to authentic analytical standards for method development and robust validation of each analyte in specific environmental media. Analytical methods that have been developed with these approaches perform very well for the intended purposes. However, the coverage of PFAS analysis is only for the compounds within the method and the media it was designed for.

A number of analytical techniques have sprung up to address this issue, such as non-targeted analysis (NTA), total oxidizable precursor (TOP) assay, total organic fluorine (TOF), extractable organic fluorine (EOF), adsorbable organic fluorine (AOF), and particle-induced gamma-ray emission (PIGE) spectroscopy. However, these techniques also have shortcomings and no one method answers all the questions being asked. For example, the TOP assay oxidizes precursors to terminal PFCAs with the assumption that all precursors will go to the monitored terminal PFCAs, which is not always the case; PIGE analysis shows ^{19}F content in solid samples without knowledge of the source compound and generally reduced sensitivity; and while NTA shows new and emerging PFAS, it is only those analytes amenable to the chosen extraction techniques (for example, solid phase extraction) and analysis techniques (for example, negative mode MS) employed that are detected.

Even with the shortcomings mentioned above, I believe that NTA methods are crucial in the determination of novel PFAS. Whether NTA is used individually or in support of other analytical techniques, it has a strong role to play in discovery and analysis. Though there isn't one comprehensive approach, NTA methods have the perfect blend of sensitivity and specificity to be applied on a regular basis and meet most PFAS study demands.

What remains lacking is a universal NTA method or ability to quantitate newly discovered PFAS – though progress is being made on both fronts. Additionally, GC-MS NTA applications are far behind the LC-MS applications currently in use. Though we consider many PFAS to be ionic (anionic or zwitterionic) and



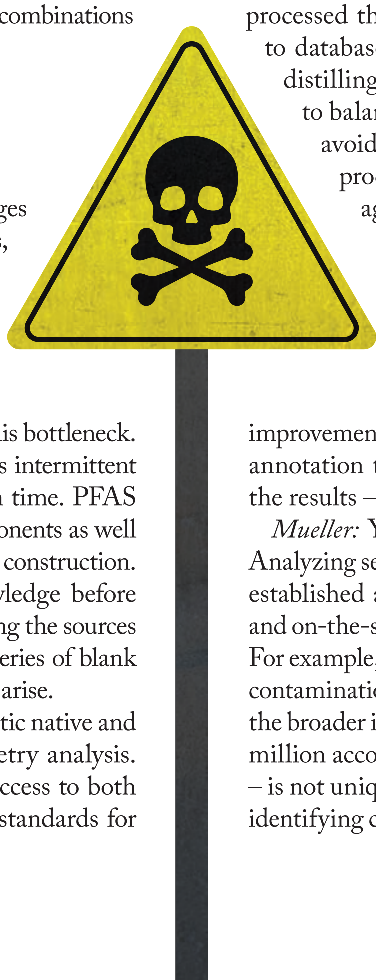
respond well to LC-MS, there are a host of volatile and semi volatile PFAS amenable only to GC-MS applications. Like any other method, NTA has its pros and cons, but it would be my preferred choice for PFAS analytical sampling by a wide margin. With the addition of other analytical techniques and workflow applications, I anticipate that NTA will gain additional ground – so long as they are supported by additional analysis techniques.

van Leeuwen: I'd add that sensitive targeted analysis is important for dietary exposure assessment, but this can cause challenges with a high variety of matrices (such as fat, protein, and carbohydrate-rich samples) reaching lower (sub)ppt levels. To get an idea of the potentially hundreds or thousands of PFAS we have yet to detect and their relevance for our exposure, we also work with high resolution mass spectrometry (HRMS) identification and chemical and biological screening assays. These complementary approaches allow us to identify a response in a sample extract or identify compound, indicating a potential effect on the immune system or other effects. Chemical screening and HRMS identification can provide answers on the total amount and identity of individual PFAS present in a sample. In my opinion, a combination of these approaches can provide us with understanding of the levels, identities, and possible effects of PFAS in our food. There is no single analytical solution or one-stop-shop. The aim of research in this area dictates which analytical approach – or combinations thereof – to take.

What are the bottlenecks in PFAS analysis?

Strynar: PFAS analysis presents several challenges – the first being contamination of sample blanks, regardless of the chosen method employed. The ubiquity of PFAS in analytical equipment, solvents, and lab consumables require relentless QA/QC investigation. Using system blanks, solvent blanks, process blanks, and field blanks we can control and overcome this bottleneck. However, we shouldn't consider this "solved," as intermittent PFAS contamination can crop up at any given time. PFAS contamination will reflect analyst-chosen components as well as what vendors have chosen in lab equipment construction. As with all analytical work, the more knowledge before approaching analysis the better. By understanding the sources of the blank contamination based on a robust series of blank samples, it becomes easier to solve issues as they arise.

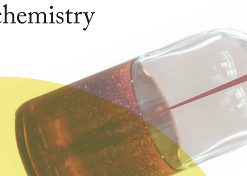
The second challenge I see is access to authentic native and isotope labeled standards for mass spectrometry analysis. Isotope dilution targeted techniques require access to both high purity stable isotope labeled and native standards for developing methods. NTA doesn't require access to isotope labeled standards, but it does require native standards for unequivocal compound identification. And though there is a high degree of confidence in HRMS analysis of unknowns via NTA, the highest degree of confidence cannot be achieved without confirmation through an authentic standard. Of course, traditional toxicology studies and some new approach methodologies (NAMs) require the same standards at even higher amounts.



Finally, the last analytical challenge I see specifically related to NTA is data reduction. Vast quantities of data must be processed through peak picking and alignment, matched to databases, and undergo background subtracting and distilling into a concise report of findings. It is crucial to balance these tasks and complete a thorough job to avoid missing anything important in the analysis process. Most analysts who conduct NTA would agree that most of the time and effort is spent doing this. Writing code to aid in processing, the conversion and uploading of data files, and long-term data storage only add to this challenge. Most analysts have found their own solutions, but I expect they would agree that there is always room for improvement. Additionally, there is no substitute for manual annotation to ensure the highest degree of confidence in the results – which is the only solution in some instances.

Mueller: Yes, there are plenty of challenges to tackle. Analyzing selected PFAS with long human half-lives is well-established and widely accessible, but developing cheaper and on-the-spot methods could identify unknown problems. For example, a cost-effective in-field method would allow for contamination tests on food and water. However, addressing the broader issue of the vast number of PFAS – around eight million according to Schymanski's keynote at Dioxin2023 – is not unique to PFAS and reflects a broader challenge in identifying chemical hazards. The environmental chemistry

"Analyzing selected PFAS with long human half-lives is well-established and widely accessible, but developing cheaper and on-the-spot methods could identify unknown problems."



TAKING *a* STAND AGAINST **PFAS**

We need to learn from past pollutant scares and test for PFAS before production and market release – following a "benign by design" approach

By Jacob de Boer

Having worked for almost fifty years on persistent organic pollutants, I have seen a lot of processes reoccurring. Many halogenated compounds have caused concern for human and environmental health. First produced without initial testing, analytical scientists detected them some years later in food and the environment. Once toxicologists assessed the effects and discussed them with authorities and industry, we started to see severe worldwide restrictions. I have also seen that the sensitivity of our instruments has improved by a factor of at least a million. This impressive achievement means we now have an early warning system: we can now detect compounds at a level before they are doing harm.

Today, the focus has shifted to PFAS. Due to its strong immunotoxic effects, we need to push our detection systems to their limits – but it can be done. We have wonderful mass spectrometers and advanced chromatographic systems that enable us to tackle the PFAS problem, while new approaches and instruments are in development. Labeled standards have become available, but the complexity of PFAS mixtures requires morestandards (native and labeled) to be made.

My hope is that commercial analytical standards producers, such as instrument companies, will reduce the prices of these standards because otherwise research may stop simply for cost reasons. In addition, the production of certified reference materials should be encouraged worldwide because they are essential to maintaining good QA/QC with properly validated methods. It is important that the European Joint Research Centre and the National Institute of Standards and Technology in the US will continue their efforts here.

Of course, it would be much better if we didn't have to focus our analytical work on detecting new persistent chemicals in the environment and our food, but so long as we continue to produce them – that's our job. However, chemicals should be tested before production and market release – following a "benign by design" approach. Learning from past cases like DDT, polychlorinated biphenyls, and now PFAS, it is clear that these scares will return if we do not introduce such pre-production tests. In the short term, it is essential that we accept the European proposal to ban PFAS – as a group of chemicals – to prevent further global contamination.

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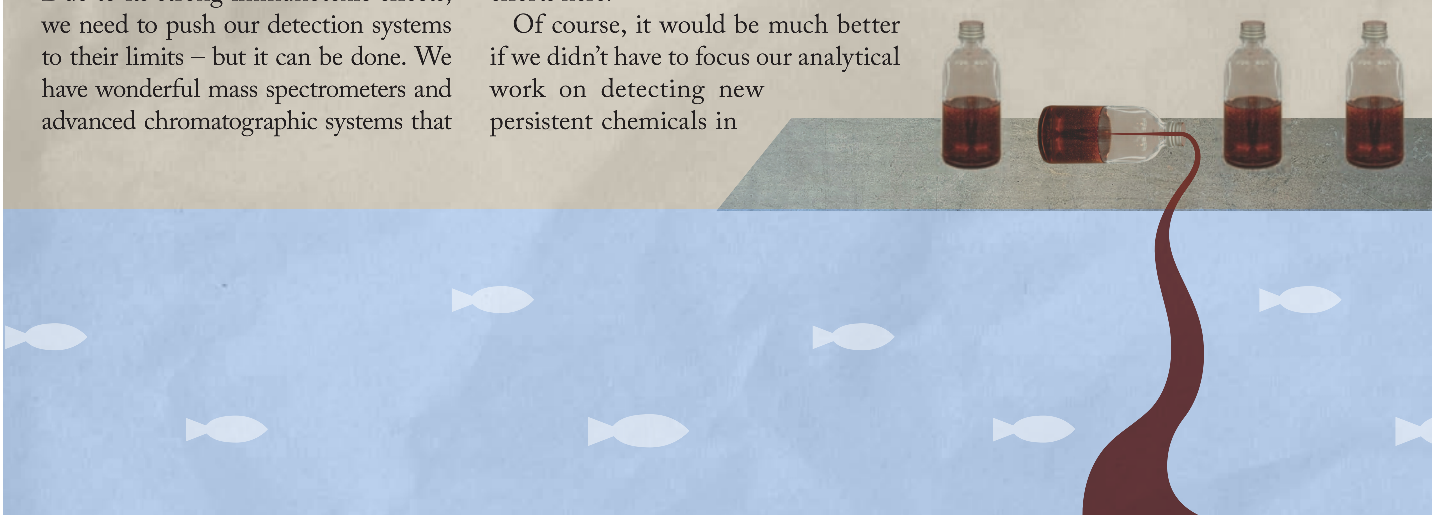


"There's no single targeted method that can cover all PFAS at the moment from short and long chain to neutrals and volatiles."

field suffers greatly from observation bias – concentrating on what tools can easily detect and overlooking the wider chemical universe due to limitations in exploration ability.

van Leeuwen: Robust and accurate targeted, quantitative methods are essential for compliance testing of food and consumer products. These targeted approaches will also be crucial if measures to reduce PFAS exposure are effective. I expect these targeted methods to turn into multi-analyte methods, accommodating 40 or more PFAS for which chemical reference standards are available. The challenges here are reaching the (sub)ppt levels needed for exposure assessment. This requires controlling and reducing blanks due to the omnipresence of PFAS in laboratory materials, equipment, and environment. In cases such as PFOA, we may not be able to reach below ppt levels due to these blanks, which could negatively affect our ability to see dietary exposure for this compound. In addition, the diversity of matrices is challenging, as is the wide array of phys-chem properties of different PFAS. There's no single targeted method that can cover all PFAS at the moment from short and long chain to neutrals and volatiles.

HRMS is a powerful tool for identifying unknowns and is increasingly applied by research groups – both GC and LC based. These techniques result in large datasets with long evaluation times, and stronger tools for additional support. The unequivocal identification of PFAS resulting from HRMS relies on comparison with an authentic chemical reference standard. Unfortunately, the availability of standards does not keep up with the speed of HRMS identification or the diversity of new PFAS invented by chemical industries. This calls for a re-consideration of what we want from compound identification in relation to risk assessment and governance given a plethora of peaks in a chromatogram. This is a generic question, not only for PFAS, but also for other fields where HRMS is applied for identification of chemicals, transformation products, and natural toxins.

Chemical screening assays are instrumental to understanding the "total PFAS" in a sample, but the outcome is method-defined – affecting interlaboratory comparability and interpretation of results. Nevertheless, chemical screening assays are required to gain understanding of organo-fluorine compounds that may be within a sample.

How could we go about solving the PFAS problem?

van Leeuwen: I believe there have been errors with past governance of chemicals in order for current PFAS exposure through food to get so high. And that's why I'm happy to see the European initiative for proposed restriction to reduce PFAS emissions as a class of compounds; I hope this inspires other parts of the world to follow suit. This restriction will also lead to innovation towards safe and sustainable PFAS alternatives that can be applied in products and processes. However, given the legacy and current application of PFAS, alongside the diversity of compounds and environmental media, we will need to increase our range of analytical approaches to solve societal questions.

Strynar: Agreed. Solving the PFAS use and occurrence issue must start with analysis. Detection, quantitation, toxicology screening, epidemiology, and remediation all are reliant on some analysis as the genesis. Regulatory response and decisions are dependent on this analytical data, and, as such, it must be of the highest quality.

Jack: I also agree. Ensuring accurate analysis is the first step to mitigating environmental contamination and its effect on the environment and human health. As scientists, we can also use the bridge between several groups involved with PFAS by becoming advocates for change. Connecting with toxicologists, clinicians, food manufacturers, and packaging companies can push the drive for the development of alternative products and movement away from PFAS.

Speaking more broadly, banning the use of PFAS to remove the problem before it develops any further. Next, establish reasonable regulations for drinking water. Most people in developed countries get their drinking water from one location, making it easier to test and treat in this area as a starting point. On a similar note, we should establish regulations for wastewater discharges – especially for manufacturer sites – to protect wildlife and drinking water sources.

It's also important for PFAS to be regulated in foods. Banning it completely from food contact material, such as plastic wrappers and paper, will be complicated, but we can start with high-volume foods and those affecting children – such as infant formula. Finally, as Jochen mentioned, PFAS cause serious issues for firefighters in AFFFs, so we should be working on developing replacements.

Mueller: Mark and Richard are right – we must lean into our strengths. An interesting paper published in 2022 (1) suggests that chemical production is a major risk to our planet because of our inability to assess and monitor chemicals and their consequences. I think this sums up our issue. If we cannot progress with carbon dioxide – a chemical we understand quite well – then our chances of getting anywhere with PFAS are incredibly slim. I find it interesting that we concentrate heavily on PFAS, creating worldwide agreements for specific chemical groups, when the real issues lie elsewhere. For example, our tools are limited to comprehend all aspects of chemical risks, and the chemical industry is very profit-driven.

To really solve this problem, we should pause chemical production until we establish more comprehensive tools to assess and monitor their consequences. Ironically, we may need to create more chemicals to achieve this. There's a slim hope that we'll discover potential issues before reaching a point of no return. Another small hope lies in the efforts towards a circular economy, but similar to addressing carbon dioxide, progress is far too slow.

What is the role of the analytical scientist in the broader PFAS problem?

Mueller: I don't see myself as an analytical scientist – analytical chemistry is just a means to answer questions, and I don't believe this role is larger or smaller than others that work on this issue. We all have a social responsibility to be mindful of worldwide issues like PFAS. I will say that analytical scientists should look beyond analytical chemistry and understand the representatives of samples that are analyzed.

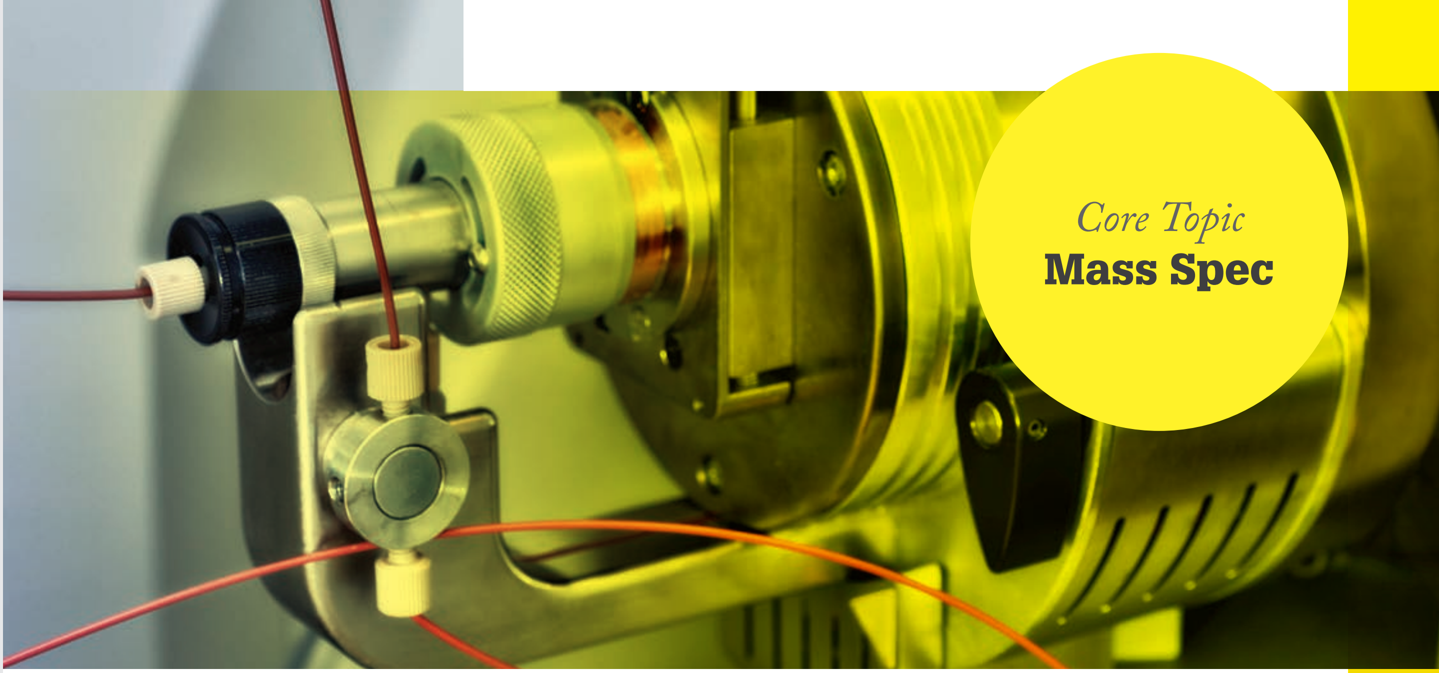
Jack: Analytical scientists help by providing accurate information from analysis, validating expertise, and confirming and verifying the compound in a variety of matrices – allowing informed decisions to be made. The analysis itself is rather easy, but the sample preparation is where challenges lie. The matrix can interfere with the analysis or damage the instrumentation. Accuracy and reproducibility is crucial for clean-up decisions, identifying violations, keeping clean-up costs to a minimum, and understanding toxic concentrations.

Strynar: Analytical scientists play a critical role in the PFAS issue. We need to continue applying existing analytical methods to generate sound defensible data for occurrence, risk, and remediation efforts. To continue our understanding of the changing PFAS landscape, we also need to conduct exploratory investigations using NTA, organo-fluorine, TOP, and PIGE methods. As method developers and PFAS scientists, we owe it to consumers to do both and do them well. At the EPA, our mission is to protect human health and the environment. Real and concrete regulatory decisions are made based on analytical data, and I believe it's our responsibility to help alleviate past PFAS contamination while looking to the future for new issues that may arise.

van Leeuwen: I agree with Richard and Mark. As analytical scientists, it is important for us to shed light on identities and quantities of new and legacy PFAS, the fate of PFAS in the environment, occurance in consumer products, and efficiency of remediation technologies. In all parts of society, analytical scientists play a key role – and the PFAS problem is no different. However, collaboration with other scientists is always needed to provide the best results in research initiatives.

Reference

1. L Persson et al., Environ. Sci. Technol. 56, 3 (2022). DOI: 10.1021/acs.est.1c04158.



Credit: Shutterstock

Reverse metabolomics progress. Emily Gentry – in collaboration with Erin Baker, Pieter Dorrestein and others – started working on her "reverse metabolomics" project in 2018. The idea is to acquire MS/MS spectra data from newly synthesized compounds, which are then searched for in public metabolomics data to uncover phenotypic associations. Over the past five years, Emily and colleagues found 145 new candidate bile acids in animals and humans – and a new biomarker and therapeutic target for inflammatory bowel disease.

History goes through… the stomach. Studying the diets of ancient civilizations can reveal more than just culinary habits – bridging everything from lifestyle to religion, via environmental and social changes over the centuries. And that's why researchers from China combined turned to gas chromatography-mass spectrometry to gather multiomic data from pottery artifacts found in the Xiawan site of Taihu Lake, China. The team used mass spec lipidomic analysis as a pre-screening method prior to proteomic analysis and identified a variety of fish and ruminant proteins from the organic residues – suggesting the Xiawan ancestors were involved in fishing, millet agriculture, and possibly the domestication of pigs.

Mission possible. Approximately 241 million people are infected with the malaria-causing *Plasmodium* parasites every year – mainly in sub-Saharan and Asian countries. Daniel Bressborn and colleagues developed a fully automated extraction system equipped with LC-MS/MS to improve administration of piperaquine – one of the most common antimalarial treatments – in remote areas with limited access to equipment and electricity. The method was adapted for quantification of the drug in dried blood spots to also enable sampling in young children, toddlers, and infants who may not be able to provide large blood volumes.

Hair care catastrophe. Hair products contain various ingredients, including VOCs. Some of these compounds, such as cyclic volatile methyl siloxanes (cVMS), may be harmful when inhaled. In an attempt to learn more about cVMS, a team of researchers measured VOC concentrations with proton-transfer-reaction time-of-flight mass spectrometry – discovering that combined heat and hair styling products rapidly changes the in-door air chemical composition. Further studies are required to test the long-term health impacts of exposure to cVMS.

References available online

IN OTHER NEWS

Researchers use desorption electrospray ionization mass spectrometry imaging to visualize the signal intensity of drugs in different brain regions following the intranasal administration of two drug delivery systems.

Native mass spec and mass photometry advance traditional venom characterization analysis – successfully profiling the venom of forest cobras, paving the way for -omics based investigations of snake venoms for antidote treatments.

PFAS were detected for the first time in unhatched eggs of the endangered turtle species Caretta caretta, following analysis with high resolution MS; the authors stress the need to monitor PFAS contamination in accordance to time trends.

Physicists demonstrate for the first time the use of superconducting nanowires as detectors for protein beams in quadrupole mass spectrometry.

Three Dimensional Defense

Patrick Fedick walks us through life as a US Navy analytical chemist – and explains why he's combining 3D printing with mass spectrometry

What role does analytical science play in national defense?

Analytical chemistry is crucial to national defense. Some of the common and routine roles include quality assurance and lot acceptance tests for chemicals that will be used for propellant formulations or standard analytical chemical confirmation for our brilliant synthetic chemists. There are also a number of threat detection systems that are crucial to national defense and protecting our warfighters, such as threat detection systems to combat chemical, explosive, biological, radiological, and nuclear incidents.

Some of the more interesting areas that I have had the pleasure of working on since starting at NAWCWD include running chemical analysis on weapon systems pulled from the fleet to ensure lifecycle specifications, surface analysis of microelectronics to ensure genuine parts for our various systems, and sampling at ranges to ensure the tests did not release any toxic materials into the environment. There are also the always fun conversations: "Pat, we found this [insert physical state here] [in an old bunker, on the range, in a vehicle]. Can you tell us what it is so that we can proceed with […]?" Analytical chemistry is key to so many areas and is a reason NAWCWD constantly invests in our people and instrumentation to make sure we have world-class facilities.

What are the unique advantages – or challenges – working at NAWCWD?

As noted above, NAWCWD has a lot of varied analytical science work and it is a great place to do analytical chemistry. One challenge as a DoD laboratory is that we have to strike a fine balance with information that we can publish in the open literature and what is kept proprietary. This at times can make postdoc recruitment challenging; however – shameless plug – I have five postdoc billets open currently!

Another challenge is the location of NAWCWD, which is relatively remote due to the testing that occurs here. Most people who succeed here have an appreciation for the outdoors/hiking/dirt biking, and so on because we are close to amazing trails, mountains, and ski resorts. The final challenge: though there is great academic freedom, most research is focused on the global Navy or DoD mission. Most times when we stumble across an interesting idea that may not align with our mission, we try to collaborate with academics to make sure we are still making these scientific advances while still keeping our day-to-day focus on the NAWCWD mission.

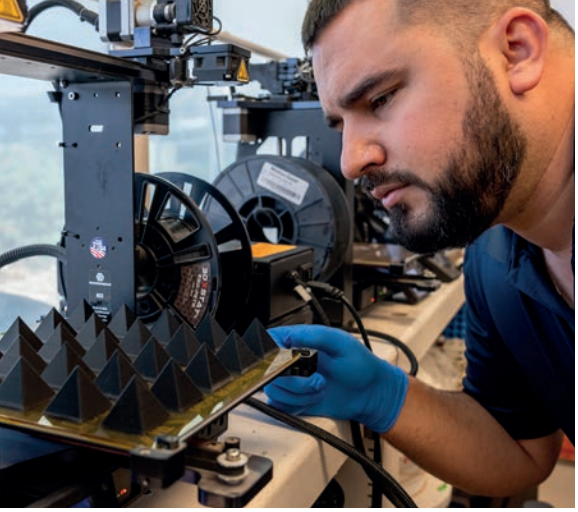
Those minor challenges are completely overshadowed by the major advantages. The first major advantage of working at NAWCWD is definitely the instrumentation. We often say, "We are instrument rich and people poor." When I started four and half years ago at NAWCWD, the mass spectrometry laboratory had three mass spectrometers. Today, we have replaced them all with newer systems and we now have 21 mass spectrometers and are still growing. We have almost all capabilities that any mass spectrometrist could want and my analytical colleagues that run other centers would say the same about their instrumental specialties. Similarly, the rapid prototyping and high throughput robotics laboratories have been set up in the last few years with significant investment. A second advantage is for the analytical chemists who do not necessarily want to lead a group or write research proposals, there are a number of positions at NAWCWD for analysis. Another advantage is the access we have to some interesting research topics that usually aren't done in academia due to safety concerns, such as novel explosives research. It is because of the analytical support facilities at NAWCWD that we are able to perform research in these wonderfully obscure areas.

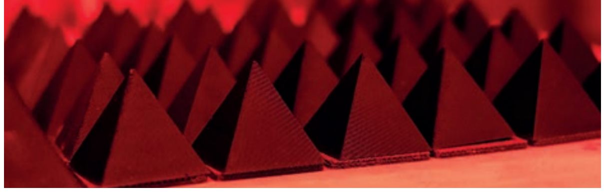
Finally, we have world class scientists that we get to interact with daily. On my first day at NAWCWD I was introduced to Dan Harris – the author of Quantitative Chemical Analysis. His office was three rooms down from mine!

Tell me about your research into 3D-printed cone spray ionization-mass spec…

We developed 3D-printed cone spray ionization – mass spectrometry (3D-PSCI-MS) as a rapid, reproducible, and low cost analysis method for bulk solids and trace analytes within bulk matrices. Printed with conductive plastic, the cones for 3D-PCSI have a ~100–200 µm hole at the tip. Solid material is scooped/placed within the cone, extraction and spray solvent is added on top, and then high voltage is applied. An electrospray-like Taylor cone is formed at the tip of the cone, where the analyte of interest is ionized but the bulk matrix, such as dirt, is trapped within the cone.

The idea for this ion source was drawn from my experience at Purdue University with Graham Cooks. At the time, we were doing forensic analysis





Credit: NAWCWD

with paper doped with nanoparticles that acted as a single sampling substrate for paper surface enhanced Raman spectroscopy and then paper spray ionization (PSI) mass spectrometry. This method worked well for trace drug analysis but there was a need for a method for bulk drugs. Around the same time, Purum Kim and Sangwon Cha at Hankuk University of Foreign Studies in Yongin, Korea, published their ionization source paper cone spray ionization (PCSI). PCSI seemed to be the answer to this problem for bulk analysis.

One of my last projects at Purdue University was a chemical education experiment that taught undergraduate senior analytical chemistry students these dual techniques, either pSERS and PSI-MS for trace drug analysis or PCSI-MS and traditional Raman spectroscopy for bulk drug analysis. During the experiment, the students had a lot of trouble folding the cones into an optimal geometry for proper spray. Even when the teaching assistants folded the cones for the students, they still had trouble

MEET THE EXPERT

I am a Research Chemist in the Analytical Branch of the Chemistry Division at the US Naval Air Warfare Center Weapons Division (NAWCWD) in China Lake, California. I run my own research group as well as a number of centers including our Mass Spectrometry Center, our High Throughput Robotic Screening Center for Advanced Energetic Materials, and our Division's Rapid Prototyping Center. These centers provide customers with novel solutions to Naval problems, primarily in the propellant, explosives, fuels, and pyrotechnic area, as well as supporting a variety of missile programs.

My research group focuses on three major areas that are intertwined; energetics, environmental analysis, and mass spectrometry. Our explosive portfolio explores several ways of performing synthesis through microdroplets and thin films, exploring new reactor designs to improve these synthetic methods and scale them to larger reactors, incorporating robotics into automated synthesis and formulation, and finally adding process analytical technologies (PAT) into synthetic steps. Our environmental portfolio is split between thermal destruction analysis of both emerging contaminants, such as per- and polyfluoroalkyl substances (PFAS), and pyrotechnics, in-situ PAT for remediation monitoring, new photochemical remediation methods, and finally in-field detection.

The portion of our laboratory focused on in-field detection leads to the core of this article. We have developed a new ionization source called 3D-printed cone spray ionization (3D-PCSI), which we couple to field portable mass spectrometers for in-field environmental and threat detection work.

positioning them due to differences in sizes – and some of the students even bent the tip on the cone.

By this time, I already knew I was going to be working at NAWCWD, and I was now questioning if there was a better way of doing a cone spray based technique that would be more rugged and reproducibly shaped. Around the same time, I had been aiding Adam Hollerbach on his project involving a 3D-printed ion mobility spectrometer. Adam taught me a lot about 3D-printing and working with him I thought a conductive plastic cone may be the way to go!

The result – 3D-PCSI-MS – is rugged, reproducible, and made with commercially available polymers.

What challenges did you face during the development of 3D-PCSI-MS?

Since this is an external ionization source, the major concern is chemical compatibility. The carbon nanotube doped PETG filament that we routinely use is really robust for most ambient ionization solvents. We knew this from past ion mobility work and a simple literature search; however, it was a major issue brought up by reviewers when publishing our first manuscript on the technique. We were rejected from the first two journals – the major concern was the plastic compatibility with the solids and the solvents. It was frustrating because these chemical compatibilities are out in the open literature and were not a major concern at all – in my humble opinion! Luckily, the reviewers at Chemosphere saw the value and published the first manuscript. As a matter of fact, for the third manuscript on 3D-PCSI, we actually ran chemical compatibility tests for most of the conductive plastics just to have a peer-reviewed reference to point to. We are currently working on more exotic plastics and high-temperature polymers and are examining chemical compatibilities and benefits of some of these "super polymers."

"3D-PCSI-MS is extremely rapid and can be used for environmental field mapping, such as PFAS contamination, which is currently a major concern for the DoD, or for rapid threat detection."

The second challenge for the initial development was funding for the device. The project started from NAWCWD internal Ignites funds, which are "shark tank style" seed funds. Most of the microfunds went to purchasing the printer, filaments, chemicals and other supplies. There was only a small amount of research and development funding for this original project. Luckily, this led to excellent collaborations to maximize the effort on the limited funds with other scientists, including Christopher Mulligan at ISU, Elizabeth Dhummakupt and Daniel Carmany at Army DEVCOM CBC, Ryan Bain at ATF, and finally our wonderful Naval Research Enterprise Internship Program (NREIP) summer interns. I would also be remiss if I did not call to the attention the tremendous effort of two post-doctoral scholars, Hilary Brown who was the driving force for the testing and development of the cones, and later Brian Molnar who supported many of these projects.

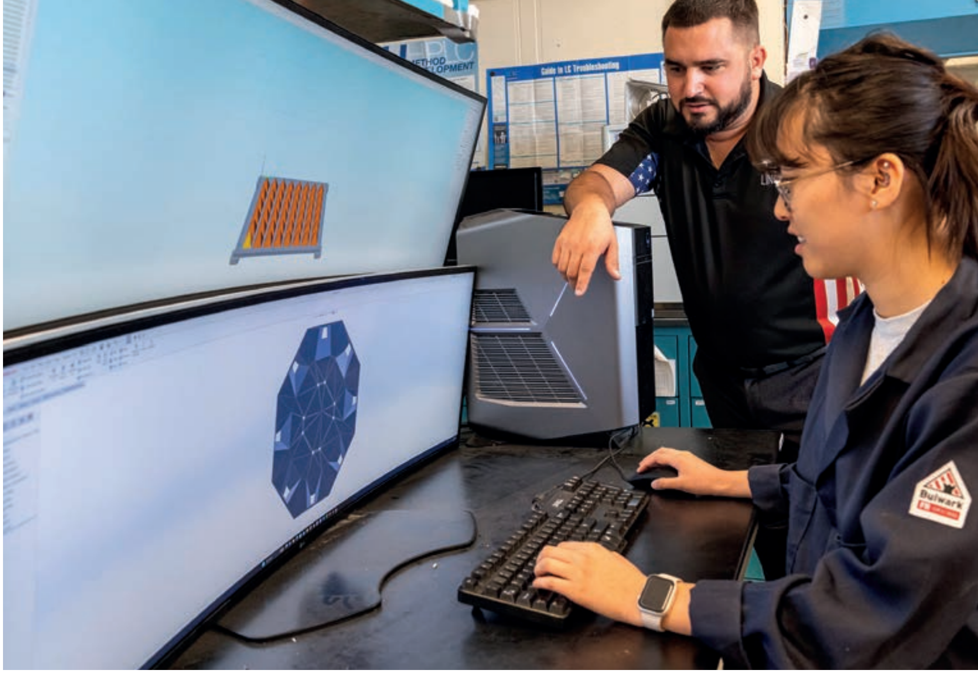
Now that we have successfully demonstrated 3D-PCSI-MS for a number of case studies and taken the technology from basic research to a demonstration and evaluation technology, we have projects funded by Navy Environmental Sustainability Development to Integration (NESDI) and Army Engineer Research and Development Center (ERDC) programs, which helps with this technology development.

We are now trying to commercialize this technology, which brings a new area of challenges that have been fun to start to tackle.

What specific DoD applications do you envisage for 3D-PCSI-MS?

We have demonstrated 3D-PCSI-MS coupled to field portable mass spectrometers for the analysis of PFAS, explosives, chemical warfare agent simulants, live V-agents, and drugs of abuse.

The major benefit of 3D-PCSI-MS? If the solid fits within the cone, we can extract the analyte of interest and spray it into the mass spectrometer. In a manuscript that is currently under review, we demonstrate this with soils, tree bark, newspaper, rubber from a boot, jeans material, cloth, grass, flowers, bottle caps, and leather from a wallet that were all contaminated with chemical warfare agent simulants. 3D-PCSI-MS is extremely rapid and can be used for environmental field mapping, such as PFAS contamination, which is currently a major concern for the DoD, or for rapid threat detection. Some of the work that will soon be coming out of our laboratory will also add to the capabilities of 3D-PCSI – so be on the lookout in 2024!



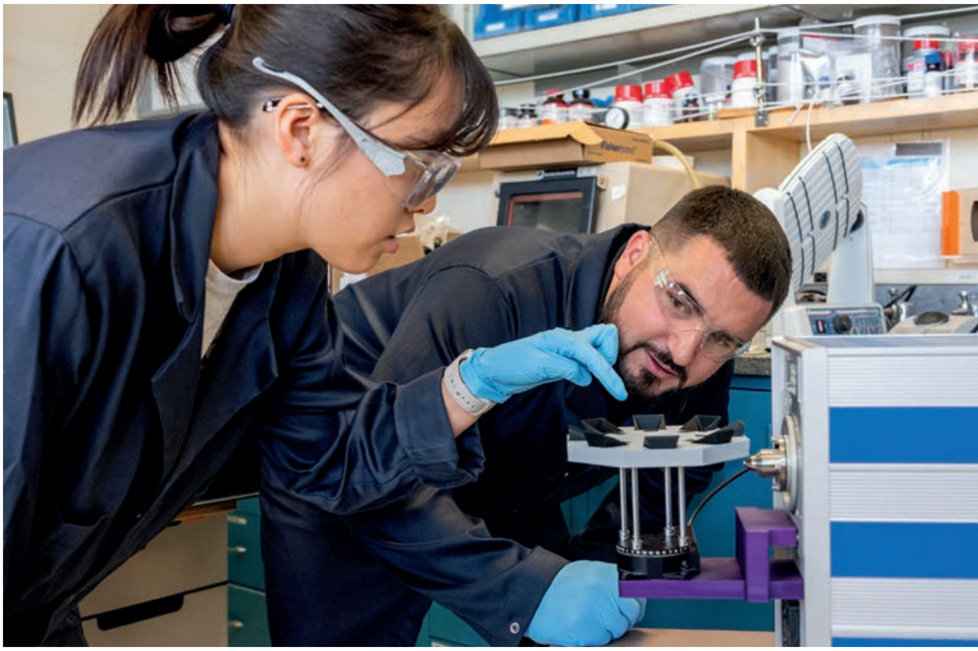
Do you expect to see more groups attempting to 3D print mass spec components?

We actually frequently use 3D-printing in new microdroplet/thin film reactor development. We also support other groups by making fast prints for projects so they can visualize their part before they send it off to get it precision machined.

I have been amazed at my summer NREIP interns, specifically TJ Pinedo and Caleb Potter, and how extremely proficient in 3D printing they are – most started as hobbyist printers. I can vocalize an idea and I will have 10 prototype designs on my desk by the end of the week. I think 3D-printing and CAD design will soon be a required course in college science degrees because of its potential across all scientific fields.

The major benefits of 3D-printing are the capability to rapidly prototype custom parts on demand for a low cost. The low cost of 3D-printers has also made the technique more appealing across the academic landscape. At American Society for Mass Spectrometry (ASMS) 2023, there was even a display in the main convention center covering all the 3D-printed parts and devices that participants had developed over the last year! That's how you know it is being picked up globally.

One of the final advantages that comes to mind is the reproducibility of 3D-printing. Many manuscripts are adding the CAD files to the Supporting Information so other groups can use their setups. I have always admired Robert Winkler's 3D-printed low-temperature plasma probe manuscript, and all of the detail he provided for others to use. Gone are the days when you needed a ring stand, clamp, and a copper clip to do ambient ionization, with most of the error coming from hand positioning the ionization source. Most groups I visit or collaborate with have some 3D-printed part to make analysis easier. We even 3D-print the pressure pin overrides for more recent mass spectrometers that companies have added to prevent individuals from using non-commercial sources…



Credit: NAWCWD

Any plans to continue this work?

Yes! We have four manuscripts with 3D-PCSI in for review currently and two manuscripts going through the Navy release process for novel reactors that incorporate 3D-printing. We have been expanding our printing capabilities and have been collaborating across NAWCWD more frequently to aid in other projects. Our lab has expanded from the traditional benchtop FDM and SLA printers into high temp FDM polymers and are seeking to transition into metal printing as well!

Credit: Shutterstock

Core Topic

Chromatography

Back to the roots. Traditional Chinese medicine goes back at least 2,000 years and is famous for its use of natural ingredients, such as ginseng root and *Valeriana jatamansi*. The latter has attracted the interest of Haochang Chen and colleagues, given the difficulties researchers have had analyzing the plant with conventional tools, such as high-performance liquid chromatography (HPLC). The team pioneered an online extraction system using two chromatographic separation methods – conventional HPLC and supercritical fluid chromatography (SFC) – characterizing over 117 different compounds, of which 33 were reported for the first time.

Nothing goes to waste. To minimize the waste produced by crude oil refining, one of its main by-products – petroleum coke – can be repurposed as a fuel and as carbon anodes for steel making. However, only material that is low in sulfur can be used – and analysis is costly. A low-cost and simple sulfur determination method that combines ion chromatography and pyrohydrolysis was developed by a research team at the Federal University of Santa Catarina, Brazil. The method was optimized using a Box-Behnken approach, ultimately demonstrating satisfactory accuracy and achieving a detection limit as low as 0.8 mg kg^{-1}.

Wine and… AI. Researchers from the University of Geneva, Switzerland, combined machine learning with gas chromatography to characterize the age and origin of Bordeaux 12 red wine samples. The team recovered the estates with 100 percent accuracy and vintages with up to 50 percent accuracy. “Interestingly, we observed that the entire chromatogram is informative with respect to geographic location and age, thus suggesting that the chemical identity of a wine is not defined by just a few molecules but is distributed over a large chemical spectrum,” said the authors.

Accelerating drug discovery. Krzesimir Ciura from the Medical University of Gdańsk, Poland, investigated the molecular interactions between xenobiotics and phospholipids – an interactivity crucial for effective drug design and development. Using immobilized artificial membrane chromatography (IAM) – a promising alternative to standard lipophilicity analysis, Ciura proposed an interpretation model based on quantitative structure-retention relationships (QSRR). From a data set of 508, the model was validated and according to the author the results confirm “great predictive abilities.”

References available online

IN OTHER NEWS

Researchers present a new approach to gain additional insights in polymer characterization using size-exclusion chromatography with triple detection – and offer an open access tool.

Scientists reveal changes in human sweat metabolome through gas chromatography coupled with high-resolution mass spectrometry – enhancing the diagnosis of sleep apnea.

Researchers combine nile red staining, flow cytometry, and pyrolysis gas chromatography-mass spectrometry to identify small microplastics, providing a more complete picture to help improve real-world applicability of risk assessments.

Chromatographic analysis of hydrocarbons in bone and cave samples in Richards Spur, Oklahoma, indicates that the source originated in the Devonian age – 21 million years older than previous samples and the oldest identified 3D fossilized skin thus far.

Small but Perfectly Formed

Are ultra-short chromatography columns fit for pharma?

By Davy Guillarme

In our laboratory, we've been trying to assess the feasibility of using ultra-short columns (2–20 mm) – much shorter than the standard 100–250 mm – for the analysis of therapeutic proteins for some years. And I had the opportunity to present our results at HPLC 2023 in Düsseldorf, Germany.

Ultra-short columns have a number of advantages; namely, shorter analysis and equilibration times, reduced cost in production, and significantly reduced pressure drop. The approach is not new – it was first trialed in the 1980s – but the quality of columns and chromatographic systems back then hindered the technology's full potential. Additionally, the biopharmaceutical market was in its infancy, whereas today it's booming – further reason for the scientific community to take interest in this approach.

But how exactly can these macromolecules be successfully analyzed by such a short column? To understand this process, we must first note that proteins have a very specific retention mechanism in liquid chromatography: on/off or bind/elute. By increasing the composition of the mobile phase by just a few percent, the state of the protein changes – it no longer interacts with the stationary phase and traverses the column at the same speed as the mobile phase, which is not retained. This means that only the first few millimeters of the column are used for discriminating proteins – the rest of the column is useless!

For example, when analyzing intact monoclonal antibodies (mAbs) of 150 kDa, our laboratory achieved a resolution in a 5 mm column that was identical to the resolution observed in a 150 mm column, when using similar gradient time. When decreasing the gradient time to less than 1 minute, the performance achieved on the shortest column was far superior to the one obtained on the longest column. The same behavior was also observed when analyzing large fragments (sub-units) of mAbs – with a size of 25-50 kDa.

All that said, there is one major limitation associated with the use of ultra-short columns. We realized that, as the column volume is reduced, the contribution of the chromatographic system to the peak broadening/extra-column effects becomes significant. Therefore, it is imperative to use chromatographic systems that are perfectly optimized in terms of volume so that significant performance loss can be avoided.

Obviously, this issue could be overcome if the providers of chromatographic instruments completely redesigned their HPLC instruments to reduce all the tubing located between the injector and detector. In particular, the tubing that connects the column outlet and the detector inlet is one of the most important sources of band broadening when working under gradient conditions. A short column in a miniaturized oven located directly at the detector entrance would be highly valuable to minimize extra-column effects…

This ultra-short column strategy has mainly been evaluated in reversed phase liquid chromatography (RPLC) mode, but the same on/off retention mechanism is also observed in ion exchange chromatography (IEX), hydrophobic interaction chromatography (HIC), and hydrophilic interaction chromatography (HILIC). We have already proved that separations of therapeutic mAbs can be achieved in less than one 1 minute in IEX with columns of only 10 mm; however, due to the non-porous nature of the IEX material, the column volume was limited and band broadening was non-negligible under IEX conditions. Peaks appear to be broader in IEX than RPLC; indeed, the full potential of short IEX columns cannot be reached. In the case of HILIC, the problem comes from the sample diluent – proteins are formulated in aqueous media, while HILIC works much better when the sample is diluted in acetonitrile. Therefore, with a short HILIC column, we must inject very low volume to maintain sharp peaks, leading to severe loss in sensitivity.

I believe the ultra-short-column approach has already shown it has the potential to be applied across a wide range of macromolecule applications in the pharma industry – from oligonucleotides to viruses. And continued research in this area will help us better understand the behavior and potential of ultra-short columns from a mechanistic point of view. I'm excited to see what the future holds!

Davy Guillarme is Senior lecturer and Research Associate (MER), The University of Geneva, Switzerland and Associate Editor, Journal of Chromatography B

Mastering the Craft of Chromatography

Innovation in separation science continues apace, but a lack of skilled personnel with an understanding of the fundamentals will hold the field back

By David McCalley

Though chromatography has come a long way since I started my career, there are various difficulties that hinder the development of the subject. As the field stands at the beginning of 2024, the biggest challenge seems to be a lack of personnel who really understand the principles behind the techniques. Many can be classified as "application scientists" who follow set methods and are more interested in the results than studying the techniques themselves. I think the effects of serious skill shortages in the fundamentals of the subject have been avoided so far because a vigorous handful of academics and industrialists have been able to keep the research and development flag flying. But it's clear that the number of skilled personnel decreases year by year as they retire and are not replaced. Some are made redundant by outsourcing in industry. Outsourcing may have short term financial benefits to an organization, but once important skills are lost, a downward spiral can take effect.

In the UK where I am based, some recruitment from continental Europe or further afield has partially plugged the skills gap, but unfortunately other countries seem to have similar problems with the availability of people who are accomplished in the fundamentals. Research and development, even on a modest scale, are vital to the health of a subject area – not only to push forward the boundaries, but also in broadening experience by research-informed teaching and learning.

Despite challenging times, there are various exciting trends emerging in the field. Take the development of pillar array columns by Gert Desmet and colleagues in Brussels; higher column efficiency can be obtained with a regular structure of pillar arrays, which avoids many of the problems associated with preparation, packing, and performance of conventional columns. This is interesting stuff – there's plenty more to be discovered and challenges to solve; for example, problems occur when increasing the diameter of these new columns to match those commonly found in particulate columns.

Multidimensional chromatography – and its promise of increasingly higher resolution of complex samples – offers another vigorous area of research. But again, further development and successful implementation of this technology will depend on the availability – or training – of highly skilled personnel. It is possible that candidates for research training in chromatography with qualifications in disciplines other than pure chemistry may provide a larger recruitment pool. Many such personnel with a background in pharma, clinical, environmental, or forensic science already work with chromatography applications, but could be encouraged to take up more fundamental studies.

"We have not solved all the problems in chromatography, even though it is a 'mature' technique."

Perhaps if we – as a collective – exude sufficient infectious enthusiasm, we can use these methods to attract new talent. I hope so. We have not solved all the problems in chromatography, even though it is a "mature" technique – nor have we met all the needs of society. But therein lies the beauty of analytical science: exciting discoveries and much-needed progress are there for the next generation of chromatographers to make. Especially those who are ready, willing and able to embrace the fundamentals of the subject!

David McCalley is Professor in Bioanalytical Science at University of the West of England, Bristol, UK

A REFLECTION ON THE LAST 70 YEARS OF ADVANCING PHOTONICS

In 1953, Hamamatsu TV Co., Ltd. embarked on a visionary journey, dreaming of linking optical technology with industry — a dream that laid the foundation for what is now Hamamatsu Photonics K.K. Over the past seven decades, our commitment to advancing photonics technology has been unwavering, shaping our identity as a beacon in the field.

From our humble beginnings in Hamamatsu, Japan, we've dedicated ourselves to the exploration of "light" in all its facets. This dedication led us to consistently advance light technology, focusing on high-performance sensors and light sources with attributes such as sensitivity, speed, brightness, and long life. However, our philosophy extends beyond product-centric goals, emphasizing high-value-added and unique solutions tailored to specific customer needs.

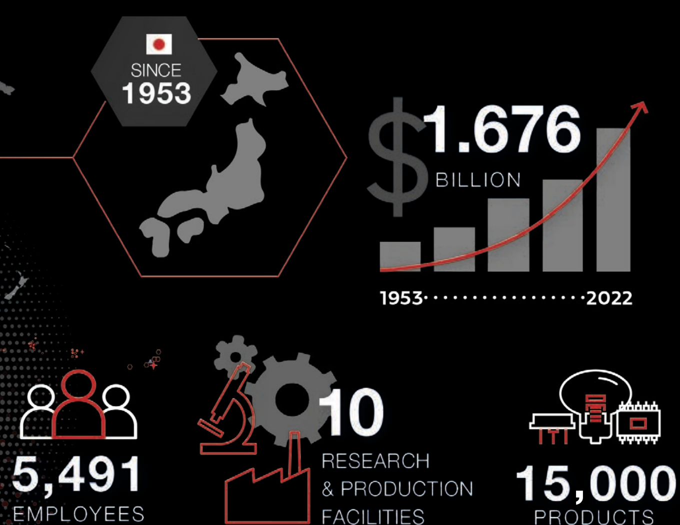
At the core of our success lies three pillars: people, knowledge, and technology. We believe that our advancements contribute not only to our customers but also to societal betterment and scientific progress. Each employee takes pride in knowing that our technologies shape a better society — a driving force that propels us forward.

Throughout our history, we've tackled and embraced numerous challenges as opportunities for change and learning. Our commitment to pursuing the unknown and unexplored areas propels us to create new markets, harnessing the power of photonics technologies for a better society and planet.

Over the years, what started as a modest venture has blossomed into a global force. Present in more than 100 countries, with 5,491* passionate employees driving innovation, we now offer an extensive portfolio of 15,000 products. This expansive growth mirrors our commitment to meeting the diverse needs of a global clientele and underscores our position as a leading player in the industry. Our annual revenue of 1.6 billion* dollars is a testament to the trust placed in us by our valued customers worldwide.

As we celebrate our 70th anniversary, Hamamatsu Photonics reflects on its luminous journey and envisions a future where light technology continues to illuminate the path to progress and innovation. With a steadfast commitment to our founding principles, we look forward to shaping a brighter, more sustainable future for all.

**Figures from Sept 2022*



HAMAMATSU PHOTONICS Europe GmbH,
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Any questions, please contact: marcom@hamamatsu.eu

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Core Topic

Spectroscopy

Refined gold. The two most common screening methods for liver cancer diagnosis, imaging tests and serological marker detection, are limited in terms of their sensitivity; whereas puncture biopsies, while accurate, are very painful. Surface-enhanced Raman spectroscopy (SERS) has extremely low detection limits and ultrahigh sensitivity, but selecting an appropriate substrate has limited its application in disease diagnosis. In a recent study, researchers from Kunming, China, used Ag@SiO_2 nanoparticles as the SERS-enhanced substrate – which have high absorption and conversion efficiencies while also being biocompatible (which regular gold isn't). The result? A classification accuracy of 97.98 percent, sensitivity of 97.14 percent, and specificity of 98.44 percent.

What lies beneath. We've all seen plastic litter washing up on beaches or floating atop rivers, but how much plastic lies at the bottom of lakes? Well, we don't really know. "I think that's a real issue, because when we think about how plastics may be moving in freshwater systems, there's a good chance that they'll end up in a lake," said Monica Arienzo, a lead author of a study surveying Lake Tahoe's (USA) lakebed. In the study, scuba divers collected litter from a lakebed – counting 673 plastic items. Attenuated total reflection Fourier transform infrared spectroscopy was used to characterize the plastic polymers – data that the researchers believe can be used in conjunction with microplastics data to determine their source.

Octopus-inspired camouflage. Researchers from the University of California, Irvine, USA, drew inspiration from the unique blue rings of the Hapalochlaena lunulata octopus – which can camouflage itself by changing the size and color of the patterns on its skin – to develop a camouflage system with tunable spectroscopic and fluorescent properties. The researchers characterized the materials using a combination of NMR spectroscopy and mass spectrometry.

Fashionable recycling. Despite the efforts to implement "fiber-to-fiber" recycling, most clothes are difficult to process because they are made up from various materials – especially elastane, which causes blockages and other issues during recycling. That is why researchers from the Institute of Chemical, Environmental and Bioscience Engineering, Austria, developed a spectroscopy-based sorting technology to detect elastane – to eventually dissolve it with a non toxic solvent and isolate pure materials like cotton and polyester.

References available online

IN OTHER NEWS

Functional near-infrared spectroscopy confirms that visual-motor illusion (VMI) aids early stages of motor learning – which could lead to treatment and rehabilitation for hemiplegic stroke patients.

Scientists analyzed infants' brains with functional magnetic resonance imaging (fMRI) and near-infrared spectroscopy (NIRS) to explain how different molecules change when babies react to touch.

Researchers develop a rapid method to identify bacteria (Pseudomonas aeruginosa) using Raman spectroscopy.

Greek research group reveals how electrical impedance spectroscopy could enhance cervical cancer diagnosis – thanks to higher sensitivity than traditional methods.

Enter the METRIX

We plug into the (RAMAN) METRIX with Juergen Popp, who discusses clinical spectroscopy's exciting AI-enabled future

By Markella Loi

Spectroscopy has great potential to improve clinical diagnostics, but has yet to be incorporated into routine clinical workflows. Here, Juergen Popp, Scientific Director of the Leibniz Institute of Photonic Technology, Germany and chair for Physical Chemistry at the Friedrich-Schiller University Jena, Germany argues that the combination of multimodal spectroscopy and AI is set to change the face of clinical research.

How could multimodal spectroscopy change clinical research?

Intelligently combining multiple spectroscopic methods leads to a significant improvement and increase in the density of information that can be obtained from spectroscopic data. Many existing needs in medical diagnostics cannot be met by a single modality and instead require the interplay of multiple spectroscopic modalities (one modality can often elucidate only a single detail).

Each spectroscopic modality has its strengths and its limitations, but what if we combined several techniques to exploit their best features? "Multimodal" spectroscopy enables the simultaneous production of signals for more than one spectroscopic modality, yielding improved acquisition speed, penetration depth, sensitivity and molecular selectivity.

Research in this field in recent years has demonstrated this impressively, and numerous proof-of-concept studies exist that show the added value of multimodal spectroscopy for improved medical diagnostics and therapy. A prime example – pursued in our group – is the use of nonlinear multimodal CARS/TPEF/SHG imaging to display the morpho chemistry of tissue for improved intraoperative diagnostics.

You have designed RAMANMETRIX for the automated analysis of Raman spectral data in clinical settings, how does it improve spectroscopic analysis?

In recent years, Raman spectroscopy has developed into one of the most powerful spectroscopic methods with an incredibly broad range of applications. Raman spectra – displaying characteristic frequencies of molecular vibrations – is a kind of "molecular fingerprint" of the sample under investigation that enables the identification of chemical molecules or changes in tissues or cell components caused by metabolic or pathophysiological processes.

Using machine learning-based approaches for an automated analysis of Raman spectra can enhance the process. However, Raman spectra of biological samples must be pretreated to remove interfering signals prior to the analysis of their Raman spectra. Working on this problem in recent years led to the development of a new software, RAMANMETRIX – an online platform for the automated analysis of biomedical Raman spectroscopic data.

What potential hurdles do you expect before AI-driven spectroscopy is more widely adopted?

The main obstacle in the wider adoption of AI-driven biomedical Raman spectroscopy is the optimal pretreatment of Raman spectra for model training. It is essential to adopt pretreatment routines generating Raman spectra for building a "generally applicable" model. In this context we made a big step forward by developing the online software platform RAMANMETRIX.

> *"One big challenge comes down to the actual application of deep learning methods in Raman data analysis – specifically about the amount of Raman data available."*

One big challenge comes down to the actual application of deep learning methods in Raman data analysis – specifically about the amount of Raman data available. Deep learning requires large independent Raman data sets, since small sample sizes lead to poor deep-learning algorithm performance. We also need to ensure the generalized ability of trained deep-learning-based models, meaning a model performing well on one dataset should not lead to a bad performance for another dataset. This again depends on the adoption of generalized pretreatment routines.

To overcome all these challenges, we must expand beyond proof-of-concepts studies for a rather limited patient cohort. For example, this can be achieved by initiating large open-source Raman datasets in an international ring trial study. The more popular Raman in medical diagnosis becomes – which is also triggered by advances in AI – the more Raman data are generated worldwide.

But the path of translating a research idea into a product is a rocky one, and here we must cross the so-called valley of death. We have now reached the stage where we can test our Raman approaches in clinical trials on a large cohort of patients. There are regulatory hurdles to overcome here, such as compliance with the EU Medical Device Regulation (MDR) 2017/745 in Europe, which is often difficult if not impossible for research institutions. Industry, on the other hand, often only gets on board once reliable data from such MDR-compliant clinical trials on many patients are available, clearly demonstrating the added value. This essentially creates a "vicious circle."

Funding is needed here to enable solutions that have been verified as functional in principle to be further developed as medical devices. Only through such MDR-compliant research and development is it possible to translate research solutions into everyday clinical use and thus also later in industrial utilization.

Another prerequisite for promoting the translation of research ideas into medical products is special infrastructures that offer user-open platforms (for example, under the umbrella of a university hospital) and bundle the expertise of renowned players from science and industry to accelerate the translation of new diagnostic and therapeutic procedures in the long term. The Jena located "Leibniz Center for Photonics in Infection Research (LPI)," which was recently included by the German government in the national roadmap, shows what such translational research could look like in concrete terms. LPI will become a translation infrastructure that accompanies new solutions from idea to validation, while significantly shortening development time. LPI will become a translation infrastructure that accompanies new solutions from idea to validation, while significantly shortening development time – serving as a blueprint for other medical conditions, such as cancer and neurodegenerative diseases.

"Only through such MDR-compliant research and development is it possible to translate research solutions into everyday clinical use and thus also later in industrial utilization."

What other spectroscopic trends are you excited about?

The second quantum revolution by non-classical light sources is definitely an emerging approach I see becoming a trend. The measurability of new characteristics of a light field, beyond the intensity distribution, opens new conceptual and technological possibilities. The use of non-classical light (quantum entanglement) for linear and non-linear spectroscopy will allow researchers to exploit new temporal and spectral windows that cannot be reached with classical light. This will boost the sensitivity, selectivity and speed of molecular spectroscopy to new dimensions, allowing us to address questions that cannot be answered at the moment.

Additionally, the application of new materials, such as metamaterials or photonic nanomaterials, in spectroscopy would offer new possibilities in terms of boosting, for example, non-linear light matter interaction down to a single molecule level with highest spectral and temporal resolution.

Separation of a Complex Carotenoid Isomer Mixture

Carotenoids tend to form geometric isomers, so they can occur as all-trans (all-E) or as cis (Z) isomers. They can arise from the effects of light or heat, but also occur naturally or are formed in the human body.

This application note demonstrates the separation of up to 48 carotenoids by detection at different wavelengths (285, 347 and 450 nm) [1]. Standards of lutein, zeaxanthin, β-cryptoxanthin, α-carotene, β-carotene, lycopene, phytoene and phytofluene dissolved in ethanol were heated at 80 °C for 30 min to achieve stereomutation. A mixture of these extracts was used to optimize the separation (Fig. 1).

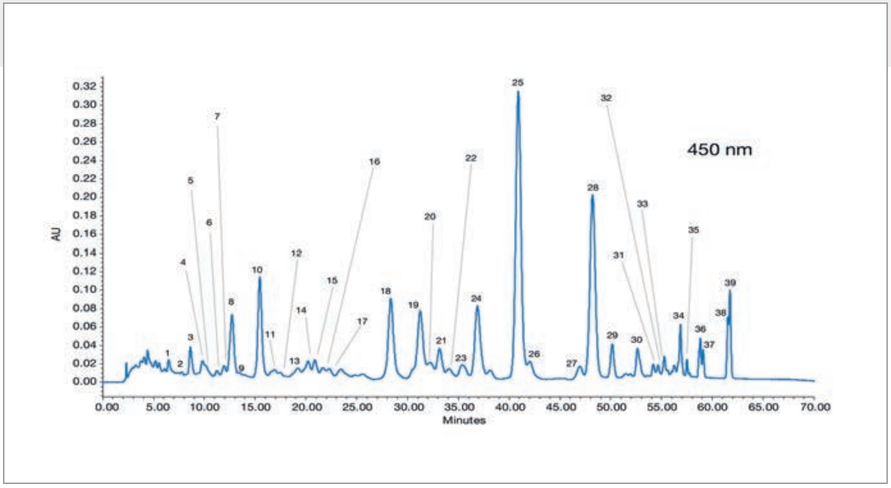


Figure 1: Chromatogram corresponding to the mixtures of isomers obtained by thermal stereomutation detected at 450 nm (1).

With this method, a human plasma sample 24 h after the consumption of carotenoid containing vegetables and fruits was analyzed. Several previously studied carotenoids were found as well as three unidentified peaks.

Reference

1. *A. J. Melendez-Martinez, C.M. Stinco, C. Liu, X.-D. Wang, Food Chem, 138, 1341-1350 (2013).*

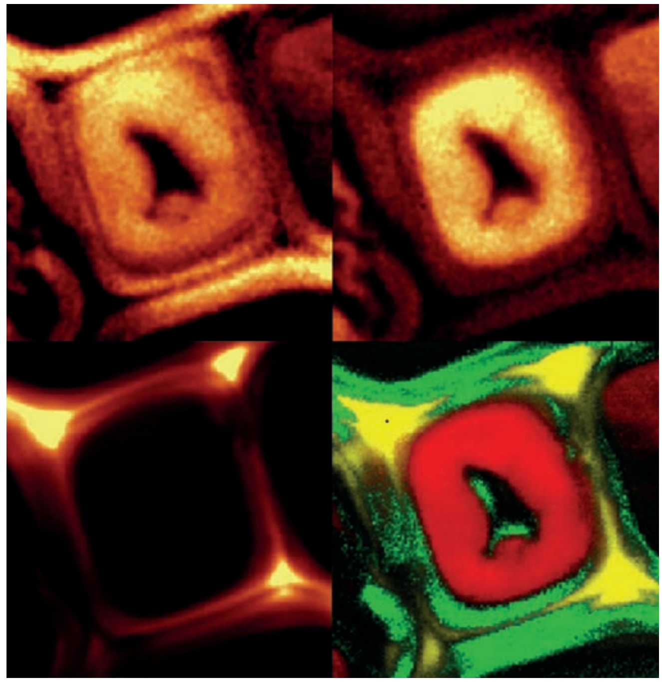
Full method details can be accessed here: https://ymc.eu/d/brDpA

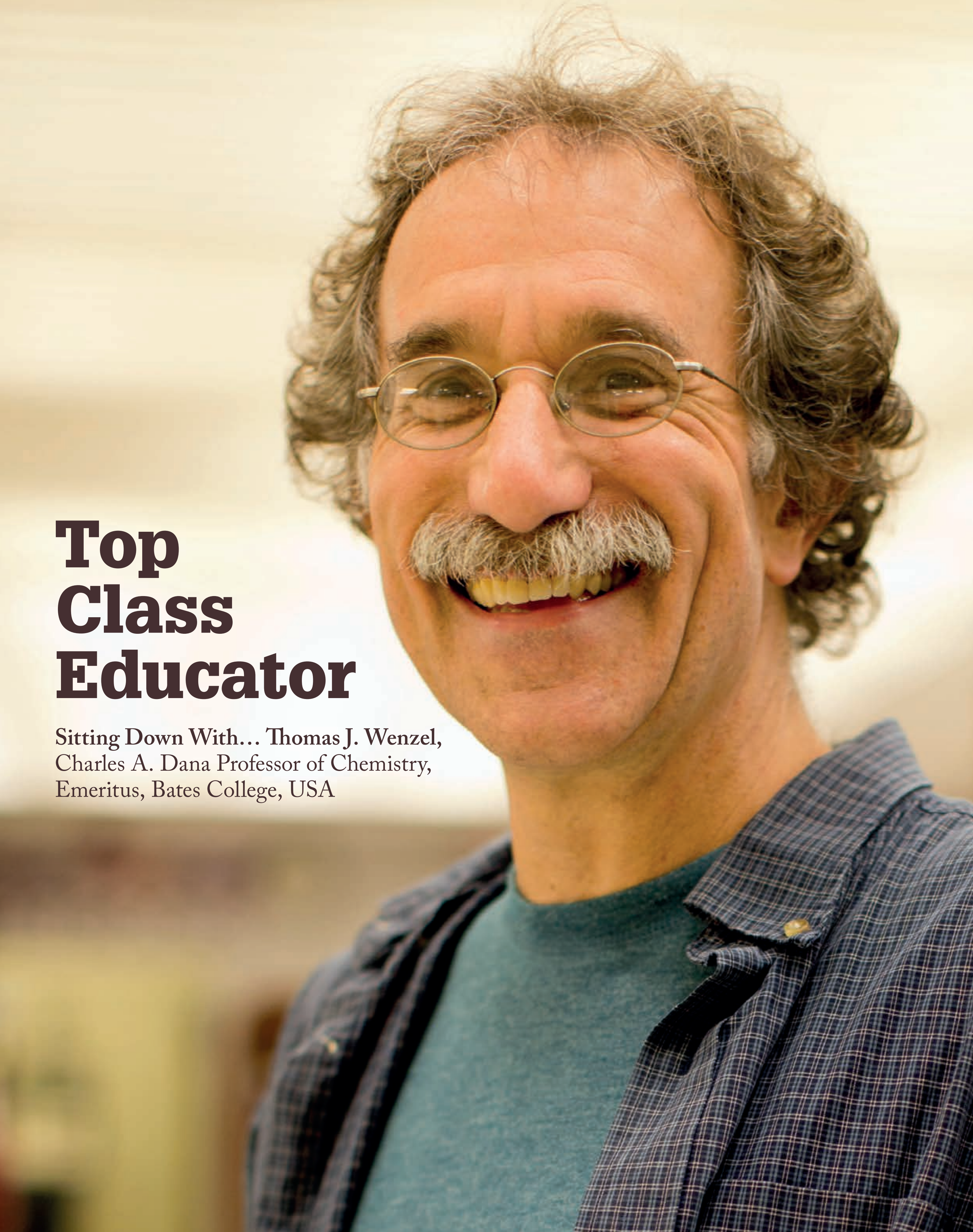
Raman Imaging & Correlative Techniques in Life Sciences

Raman imaging is a versatile, label-free and non-destructive microscopy technique that is ideally suited for characterizing life science samples. It provides information about their properties such as chemical composition and compound distribution. Correlative Raman imaging, which includes combinations of Raman with fluorescence microscopy or SEM, among others, delivers a more comprehensive understanding of a sample than any single approach.

This study shows how Raman imaging and correlative microscopy can be used to investigate living cell components and plant cell walls, characterize atherosclerotic human aorta tissue, differentiate malignant from healthy cells, monitor lipid uptake in macrophages, and identify phenotypic heterogeneity in bacteria.

Read the Application Note here:
https://raman.oxinst.com/assets/uploads/raman/materials/WITec_AppNote_LifeSciences_2024.pdf





Top Class Educator

Sitting Down With… Thomas J. Wenzel,
Charles A. Dana Professor of Chemistry,
Emeritus, Bates College, USA

Did you always want to be an educator?

Though I enjoyed my courses at university, I often felt like there was a better way to teach – but I wasn't sure exactly how at the time. With this interest, I pursued education courses that allowed me to teach high school chemistry. After a single semester in the classroom, my eyes were opened to how differently students learn, develop, and perform. I then worked through graduate school with the goal of teaching at an undergraduate level.

Pointed question: are we in need of an analytical science education revolution?

I believe so – although this is true across the sciences. When I was an undergraduate back in the 1970s, I soon realized that there was a severe lack of student engagement. Classes involved copying notes from the board, and time in labs was reduced to following recipes where the outcome was known beforehand. This passive and traditional learning style doesn't give students the opportunity to fully immerse themselves in science. I hated the first undergraduate analytical course I took for this reason – it emphasized titrations and gravimetry and didn't give me the appreciation of the relevance of the topics we were learning about. Nevertheless, it seems as though this outdated approach is still being used in educational institutions across the world.

In the mid-1990s, I was invited to address participants at an analytical science curriculum workshop led by the late Ted Kuwana at the University of Kansas. The goal of this meeting was to examine the curriculum and promote strategies to improve student learning outcomes. Many industrial participants said graduates weren't equipped with the knowledge required for problem solving in industry. After we discussed problem-based, collaborative, hands-on teaching methods – something I have been passionate about for several decades – the group fully endorsed the use of these strategies in analytical courses.

It's clear that, the more we discuss these issues, the more likely change becomes. I strongly believe that by creating an environment that empowers and engages students, we'll be giving the next generation of analytical scientists the tools they need to follow their curiosity all the way to new discoveries that exceed our current understanding.

It's clear you are a big advocate of active learning…

Yes. And it has other benefits. When I first started teaching, there also wasn't much of an emphasis on teaching in a manner that promotes inclusivity – attracting students from historically underrepresented groups into the sciences. Over the years, this has changed – arguably driven by a rise in active learning strategies that put student engagement at the forefront.

The smallest changes can boost engagement. When students in the lab asked me, "What do we do?" My usual response was, "Well, I'm sure there's some journal articles out there that cover it." By allowing students to explore unknown avenues in a supported environment, we help prepare them for the real world. Not only did my active approach give students the freedom to develop, learn, and explore – to experience – it also allowed me to actively engage with each student as they navigated different phases of their project.

What are the standout moments of your career in analytical chemistry?

I've been fortunate to receive two national awards from the American Chemical Society: Research at an Undergraduate Institution Award in 2010 and the George C. Pimentel Award in Chemical Education in 2020. These awards are gratifying in validating the substantive work I've done over my career to develop educational approaches that enhance student learning beyond lectures and recipe-based experiments.

Additionally, making the The Analytical Scientist Power List 2023 as the only person from an undergraduate institution is the best way to cap off my career. I'm very grateful to have received these three major honors.

What advice can you offer the next generation of analytical scientists?

Get as much experience in a broad range of topics as possible. Pursue opportunities during undergraduate studies for research or industrial lab work – take all the courses your program offers. Visit conferences to network with as many scientists as possible. The more you know, the better you can apply yourself to the field. Curious students with a willingness to engage are more likely to succeed in their career.

Since receiving your PhD in 1981, what are the biggest changes you have seen in the field?

The most dramatic change is improvements to instrumentation. Back when I was a student, the only time you would hear "mass spec" and "proteins" in the same sentence was when someone said, "Mass spec cannot be used to analyze proteins." From silica capillary columns for gas chromatography to inductively coupled plasma instruments, there is so much more that an analytical scientist can do. With these technological advancements, we need to ensure that our courses – and the students we teach – are up to date rather than being 20 years behind!