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A Toast to Innovators of All Stripes

Whether you're grappling with the fundamentals, or putting the finishing touches on a new product – we salute you!

Welcome to our annual celebration of innovation in analytical science! Every year I can't help but wonder whether there'll be enough technologies worthy of our awards. And every year, I'm pleased to find that I had nothing to worry about – even amid political and economic headwinds. I'm ever impressed by the way in which developers are able to channel creativity towards the production of useful, commercially viable products – year after year. The key to making this happen, according to Chris Lock, R&D VP at SCIEX, is to create space for dissent, risk-taking, and failure (see page 22). And sometimes failure may be transformed, even years later, into success – that's one of Fabrice Gritti's key lessons learned bringing slalom chromatography back from the dead (see page 16).

To make that happen, Fabrice had to step outside of his comfort zone and immerse himself in the world of DNA physics in search of fundamental understanding. And there are, of course, researchers who spend most of their time grappling with the fundamentals – whose vital contribution we must acknowledge. On page 26, Scott McLuckey – whose work has influenced the development of commercial ion traps, for example – discusses his approach to cultivating creativity. He spends a good chunk of his time "turning over stones" – work that is likely to lead to new discoveries, even if there's an element of serendipity involved. "It takes all sorts," as my grandma liked to say. So, I'd like to raise a glass to innovators of all stripes.

James Strachan,
Editor

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Living the DreaMS

Transformer-based AI model "opens a new chapter in computational metabolomics," say researchers

A new AI model is helping scientists explore the molecular makeup of complex biological and environmental samples – without relying on extensive reference databases. Developed by researchers at the Czech Academy of Sciences and collaborators, DreaMS (Deep Representations Empowering the Annotation of Mass Spectra) outperforms traditional tools in predicting molecular properties, assessing spectral similarity, and identifying challenging compound classes, including fluorinated molecules (1).

To find out more about the technology – as well as its development story – we spoke with PhD student Roman Bushuiev and Group Leader Tomáš Pluskal, co-authors of the study.

Please describe how the DreaMS model learns from unannotated mass spectra?

Much like how large language models such as ChatGPT learn the structure of language without knowing the meaning of individual words, DreaMS learns to interpret mass spectra without prior knowledge of their underlying chemical structures. It's trained to reconstruct randomly masked signals from spectra and predict chromatographic retention order from randomly ordered spectrum pairs that originate from the same LC-MS/MS experiment. This self-supervised setup requires no molecular annotations, and can therefore be applied to millions of unannotated spectra from MassIVE. Our study demonstrates that this training approach leads to the emergence of molecular representations within the model.

What was the initial spark that led you to try a foundation model approach for mass spectrometry?

The vast majority of tandem mass spectra from untargeted metabolomics remain unannotated, mainly due to the limited coverage of current spectral libraries. We wanted to overcome this bottleneck by learning from the abundance of unannotated spectra directly – unlocking previously inaccessible regions of chemical space through self-supervised learning. We were also inspired by the success of protein foundation models such as Evolutionary Scale Modeling, which, once trained, can be adapted for diverse tasks such as structure or function prediction. We believed a similarly powerful and versatile model could be built for metabolomics, to address a range of computational challenges such as molecular structure prediction or molecular networking.

How might this approach influence future research?

We believe DreaMS opens a new chapter in computational metabolomics for two key reasons: versatility and scalability. It allows researchers to apply the same underlying model to a variety of metabolomics tasks – eliminating the need to design new tools for each specific challenge. And thanks to its efficiency, DreaMS can be scaled to hundreds of millions of spectra, enabling large-scale analyses in fields such as drug discovery and environmental monitoring.

What are the next steps?

On the methodological side, we're actively extending the DreaMS project in several directions, including the detection of structurally novel molecules using the DreaMS Atlas and support for multi-stage MSn data. Additionally, we've already developed an alpha version of DreaMS-Mol: a fine-tuned version of the DreaMS model to predict complete molecular structures – not just embeddings – which we plan to release next year.

On the application side, we're integrating DreaMS into biological applications in our lab. Our focus is on discovering plant natural products and their biosynthetic pathways, as well as exploring the chemodiversity of plants using the DreaMS Atlas.

Reference

1. *R Bushuiev et al., Nat Biotech (2025). DOI: 10.1038/s41587-025-02663-3.*

Automating Analytical Data Workflows in R&D

Scalable, web-based technology with self-serve automation to harmonize data and accelerate discovery across the enterprise

As R&D labs become increasingly digitalized and automated, analytical data remains difficult to manage due to its heterogeneity and complexity. Most scientific data management tools cannot harmonize diverse data types without losing essential chemical context. Automating and scaling these solutions can break down silos and enable real-time data access, but often demands heavy IT resources.

ACD/Labs addresses these challenges with a new generation of web-based technology that extends the Spectrus Platform's vendor- and technique-agnostic analytical data management capabilities into the browser. This modern, extensible architecture delivers scalability, accessibility, and enterprise-level integration.

Alongside these technologies, self-serve automation has emerged – enabling scientists and data engineers to design and implement automated data flows without extensive coding or IT support. This ensures analytical data is standardized, processed, and mobilized efficiently.

With rich web applications to provide intuitive environments to view, process, and analyze data, this new slate of technology meets scientists' immediate needs while simultaneously unifying data management and democratizing automation to establish a foundation for AI- and ML-driven discovery.

Ask the Expert

Richard Lee, Director of Core Technology, ACD Labs

What motivates you?
I'm inspired by the opportunity to bridge science and technology in ways that have a meaningful impact on how research is conducted. I'm driven by the challenge of transforming complex analytical data into knowledge that empowers scientists, accelerates decision-making, and fuels innovation. Seeing how our solutions enable organizations to work more efficiently today – and prepare them for the data-driven discoveries of tomorrow – continues to inspire my commitment to advancing this field.

How does your company embody "innovation"?
At ACD/Labs, innovation is embedded in how we approach the scientific and technological challenges of modern laboratories. We focus on developing solutions that not only address today's needs but also anticipate tomorrow's requirements. By combining deep expertise in chemistry and informatics, we deliver technologies that unify, standardize, and mobilize analytical data across diverse instruments and environments. Our commitment to innovation is reflected in advancements such as self-serve automation, scalable web-based applications, and integration frameworks that prepare organizations for an AI- and ML-enabled future.

What sets your company apart from other businesses in this space?
ACD/Labs' foundation in chemistry and pharmaceutical sciences, combined with decades of expertise in analytical data are a key asset. Unlike many vendors who provide generic data platforms, we deliver purpose-built solutions that are both vendor- and instrument-agnostic, capable of unifying raw data across diverse laboratory environments. Our technology not only manages data but also standardizes and enriches it for decision-making and advanced AI/ML frameworks. This deep scientific context, coupled with continuous innovation in modern technologies, including web-based and automated workflows, distinguishes ACD/Labs as the partner of choice for organizations seeking to transform laboratory data into knowledge and insight.

The "Dark Lab" Approaches

Why a fully automated analytical laboratory might be closer than you think

By Thorsten Teutenberg, Head of department of Research Analytics & Miniaturization, Institut für Umwelt & Energie, Technik & Analytik (IUTA), Duisburg, Germany

China is rapidly becoming the world leader in industrial automation. Take Xiaomi, for example, which has invested approximately $330 million in a fully autonomous "dark factory" that operates 24/7 to produce smartphones. In stark contrast, most analytical laboratories – at least the ones I know, primarily in Europe – function much the same as they did a century ago. The idea of a "dark analytical lab" might sound far-fetched, especially in the face of looming cuts to public research and development funding across much of the Western world, but I believe that a fully, or at least highly, automated analytical lab is closer than it seems.

My optimism stems from firsthand experience. About eight years ago, I read an article by a scientist who claimed that it was possible to program a robot using intuitive software. I don't remember the scientist's name or the journal, but I do recall being deeply impressed and enthralled. Eight years later, we have demonstrated that a domain expert in the field of analytical chemistry can actually automate a highly complex analytical workflow. This achievement is particularly gratifying given that one of our initial project proposals was rejected by a reviewer who questioned our core innovation – and our team's competence in lab automation altogether! Nevertheless, we managed to secure funding for this project in a subsequent call.

With that experience in mind, I am convinced that we can achieve a "dark lab" within the next decade, in both academia and industry. However, to make this a reality, we must address the connectivity issue. Instrument and software vendors need to embrace standardized communication protocols at scale. Thankfully, we don't need to wait – standards such as SiLA 2 (Standardization in Laboratory Automation) and LADS OPC UA (Laboratory and Analytical Device Standard Open Platform Communication Unified Architecture) are already available and built on non-proprietary frameworks. When devices support such universal standards, seamless data flow becomes possible – paving the way for the "AI party."

When we began exploring lab automation, we focused on building automated workflows using intuitive, drag-and-drop software. These systems are composed of modular building blocks – each one representing a specific task like moving a robotic arm or opening a gripper.

The next frontier? The ability to interact with the robot via a large language model (LLM). I really believe this is the future. I'd love to be able to talk to all my instruments and discuss my lab data with an AI lab agent! We could then also apply this concept to workflow orchestration. Currently, the lab execution system we use requires at least some basic programming and coding skills. But in the near future, it might become easier to create digital SOPs by simple drag-and-drop tools – or even by prompting an LLM.

Critics point out that this won't work because LLMs have inherent flaws, such as hallucination. While this is true, the same applies to human experts – their answers must be analyzed carefully, too! Rather than replacing experts, AI will help us accelerate and refine the insights we draw from our experiments.

In addition, some question whether full automation makes sense in dynamic environments like R&D labs, where methods are continuously developed and adapted. Although this complexity is real, we should not be content with the fact that some of our best-trained students and scientists are still scribbling notes in paper lab notebooks. Surely we can do better.

Let's work together to make the dark lab a reality – not to replace human scientists, but to free them from tedious tasks. Let's focus on the output and give more credit to the data produced by our high-end analytical instruments. Some may strongly oppose this, but I look forward to engaging in a lively discussion so that we can develop systems that are easier to use, more flexible, and offer a variety of options for assessing data quality based on their built-in sensors.

Lessons Crossing the Valley of Death

Let's transform analytical chemistry into the hotbed of commercial innovation it ought to be

By Elia Psillakis, Professor, Aquatic Chemistry, TUCrete, Greece

Analytical chemistry should be a powerhouse of innovation. Yet, as it stands, much of the innovation happens within industry, whereas dynamic university spin-offs and successful entrepreneurs are rare. This is surprising, considering that research labs are hubs for knowledge creation, equipped with advanced facilities, and staffed by highly skilled scientists – constantly synthesizing new materials, developing cutting-edge technologies, and designing innovative analytical workflows. Despite this immense potential, most analytical chemistry innovations remain confined to academia, often published as research articles rather than being translated into patents and marketable products. The very few cases that manage to break through the academic sphere face significant challenges in securing adequate funding to support R&D and intellectual property protection services. In other words, they get trapped in the so-called "innovation valley of death."

Meanwhile, disciplines like biotechnology, computer sciences, and nanotechnology have successfully positioned themselves as leaders in innovation. These fields benefit from now-widespread innovation hubs and incubators, as well as funding opportunities from both governments and private investors that prioritize commercialization and public-private collaboration. Interestingly, analytical chemistry has access to many of these same resources but has not yet leveraged them effectively.

Analytical chemistry is far from achieving its full innovation potential, as opportunities to create tangible impacts beyond research are being missed. This disconnect arises from several barriers, including the absence of clear commercialization pathways for laboratory innovations and, more importantly, the lack of innovation culture, especially within research teams. Analytical chemistry is a relatively conservative and traditional sector characterized by a limited stakeholder collaboration. But for innovation to be successful, university-industry-government collaboration is essential. This collaborative framework should prioritize eco-friendly and cost-effective solutions that address routine analysis needs. Industry must focus on entrepreneurs and create space for change in their existing infrastructure. At the same time, innovation and entrepreneurship must become a core value in academia, with researchers developing the skills and mindset necessary to pursue these tasks.

We can see this existing cultural gap when new ideas are born in the lab. Faced with the choice between publishing their findings or protecting the idea's intellectual property, scientists often opt for the faster and more familiar route to secure their findings, and publish. But, before making that choice, scientists should consider a key question: would further development of this idea fill a gap in routine analytical practice? If the answer is yes, the idea may be a strong candidate for innovation. The next step is to refine the narrative around the idea. Is the validity of the underlying science confirmed? What concept development activities must be completed? What intellectual property protection should be in place? Once these foundations are laid, the next stage involves the technical evaluation of lab-scale prototypes and testing the innovation's performance. Prototypes are not final products, and several iterations are typically needed before reaching a viable, market-ready solution. Throughout this process, it is critical to have a thorough understanding of how the innovation will be used and focus on the industry as it is, not as one might wish it to be.

Spin-offs often struggle because their founders have limited experience in entrepreneurship and understanding of market trends, customer needs and competitive dynamics. From my experience with my spin-off company ExtraTECH Analytical Solutions, participating in incubators and innovation hubs can be transformative. These ecosystems provide invaluable mentoring by economics experts, as well as fast-track business training. More importantly, they create natural opportunities for networking, partnerships, and access to investors and funding. This support is key for crossing the valley of death and acts as a catalyst for transforming a research concept into a market-ready solution.

Crossing the valley of death is a long and complex journey that cannot be avoided. The goal is simply not to die there. My advice? Do not attempt to cross alone. A "ride-or-die" core team of problem-solvers, doers, and companions, with different skills, is needed to share the workload and help keep spirits high.

As an academic, I found that turning theory into a marketable product was extremely challenging. From the very beginning, we knew the odds were against us, as only few innovations survive the journey across the Valley. We are among the fortunate few who made it. But even if we hadn't, one thing is certain: despite the challenges, we would do it again and again. Innovation is like scientific experiments: they might not always work, but they show us what works and what doesn't in real-life scenarios. It is a powerful, self-developing experience that's shaped me not just as a scientist, but also as a person. It taught me to see science through a new lens – one that focuses on real-world impact and bold opportunities.

the Analytical Scientist

INNOVATION *Awards*

The products – and people – defining the next wave of analytical innovation

9 Nuvia wPrime 2A Media

Tunable mixed-mode chromatography for biomolecule purification

Produced by Bio-Rad Laboratories

Nuvia wPrime 2A Media is a tunable weak anion exchange-hydrophobic interaction (AEX-HIC) mixed-mode chromatography resin for challenging biomolecule separations. Its weak AEX functionality allows charge modulation through buffer pH adjustment, enabling greater control and milder elution conditions. The hydrophobic component adds complementary selectivity, combining two interaction modes in one medium. Built on a durable polyacrylamide bead matrix, Nuvia wPrime 2A Media maintains performance under high flow rates and harsh cleaning conditions, ensuring scalable, reproducible purification from lab to manufacturing scale.

Insights from Nuvia wPrime 2A Media Team

"The time we really knew we had something was when we had multiple customers ask us to be beta-testers because of the known need for a solution – and then when testers responded that they loved the product and asked when they could start ordering," says Daniel Yoshikawa, senior global product manager.

"The distance between 'problem' and 'solution' can be measured in curiosity," says Ian Harwood, senior global product manager. "Curiosity unlocks pathways to unexpected breakthroughs that lead to saving lives."

What the judges say…
"A good addition to the toolbox of biopharmaceutical analysis and purification."

10 timsMetabo

4D separation for small molecule analysis

Produced by Bruker Corporation

timsMetabo brings trapped ion mobility spectrometry (TIMS) to metabolomics and lipidomics, adding a fourth dimension of separation – orthogonal mobility – to conventional mass spectrometry. The system enhances resolution and sensitivity while improving annotation confidence for complex samples. Built specifically for small molecule analysis, timsMetabo enables confident differentiation of isomers, reduces matrix interferences, and improves reproducibility in metabolomic and lipidomic workflows.

Insights from Small Molecule Bioanalysis Lead Matthew Lewis

"The timsMetabo was born from a clear and deliberate ambition: to confront the conventional trade-offs in small molecule mass spectrometry head-on. We wanted to enable simultaneous sensitivity, selectivity, precision, accuracy, speed, and reliability."

"Innovation is not about perfection, it's about persistence. Stay close to the problem. Stay closer to the people. And never underestimate the power of a team united by purpose."

What the judges say…
"The new highest performance TIMS."

8 Veloci BioPharma Analyzer

Fast, column-free molecular fingerprinting for biopharma analysis

Produced by HORIBA

The Veloci BioPharma Analyzer is based on a fluorescence spectroscopy technique that involves the simultaneous acquisition of absorbance, transmittance, and fluorescence excitation emission matrix spectra in a single measurement. The team calls this new molecular fingerprinting technique A-TEEM spectroscopy, which enables rapid, real-time, high-resolution analysis – without the need for traditional column-based methods. The system supports real-time quality control and process monitoring, providing reliable molecular insights to improve efficiency and consistency across biopharmaceutical workflows.

Insights from Global Product Line Manager Cary Davies
"The biggest 'eureka' moment was our first pharmaceutical customer receiving FDA approval to implement this new tool as part of a drug packaging validation process."

"We believe that this innovation will allow the biopharmaceutical industry to develop new, faster and less expensive solutions in their drug production and/or validation processes."

What the judges say…
"Smart technique in PAT."

7 spectraMRR

Molecular rotational resonance for direct molecular analysis

Produced by BrightSpec

The spectraMRR is the first commercial platform powered by molecular rotational resonance (MRR) spectroscopy, enabling direct analysis of complex chemical mixtures without chromatography or sample preparation. By capturing the unique rotational "fingerprints" of molecules in the gas phase, it allows for rapid and confident identification and quantification. The integrated system combines high-resolution spectroscopy with advanced computing and user-friendly software, streamlining workflows and providing new insights across pharmaceutical, chemical, and academic applications.

Insights from co-founder and CTO Justin Neill
"To make the technique practical for analytical chemists, we had to engineer solutions from the ground up. This required major advances to achieve long-term stability and hands-off operation."

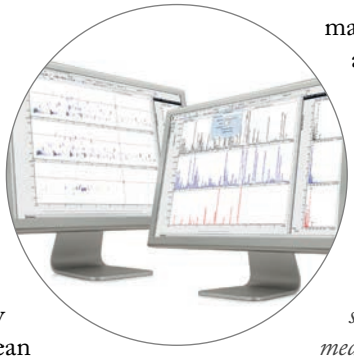
"Our goal for the spectraMRR is to allow users to confidently and unambiguously identify the structures of small molecules, while also dramatically simplifying user requirements for method development and reference standards."

What the judges say…
"New instrument for gas phase molecular identification based on a new principle: the spectral recording of the rotational fingerprint of molecules."

6 Smart Subtract

Probability-based subtraction for GC-MS and GC×GC-MS data

Produced by SepSolve Analytical



Smart Subtract uses a probability-based approach to reveal meaningful differences between GC-MS or GC×GC-MS chromatograms. By suppressing minor fluctuations, it generates clean subtracted chromatograms that highlight only significant changes while retaining full spectral information for downstream processing. The tool integrates with existing workflows for library searching and reporting – supporting fast, informed decision-making in sectors such as petrochemicals, flavors and fragrances, and recycling, where immediate detection of contaminants, off-odors, or formulation deviations is critical.

Insights from Principal Scientist Pete Grosshans
"Direct (or naïve) subtraction of two chromatographic datafiles never gives the straightforward results we expect. To generate meaningful subtractions, we had to understand and overcome the mechanisms that cause subtraction to fail."

What the judges say…
"Smart use of AI technology."

5 Agilent 1290 Infinity III Hybrid Multisampler

Feed Injection technology for enhanced HPLC/UHPLC performance

Produced by Agilent Technologies

The Agilent 1290 Infinity III Hybrid Multisampler introduces Agilent's Feed Injection technology to HPLC/UHPLC workflows. Feed Injection continuously infuses the sample into the mobile phase stream, directly at the point of injection – enabling precise control over sample delivery, while minimizing solvent effects, and improving chromatographic performance. The system enables accurate detection of trace-level compounds, such as PFAS, by maintaining peak integrity even with high-volume injections of strong solvents. And by eliminating the need for additional sample preparation, the Hybrid Multisampler aims to simplify workflows and enhance reproducibility.

Insights from Product Manager Juan Liang-Schenkelberg
"The inspiration came from listening to users – their pain points sparked the idea to bring this advanced capability of Feed Injection into a format that's practical, scalable, and solves everyday problems."

"This project taught us that the most impactful innovations come from creatively addressing problems that lack good answers."

What the judges say…
"Versatile autosampler, supporting both routine and research labs."

"Provides the first integration of multiple important LC injection modes."

4 Aurora Series Capillary Flow Column Range

Capillary flow columns combining proteomic depth with long-term stability

Produced by IonOpticks

The 150 µm Aurora Series Capillary Flow Column Range aims to resolve the long-standing trade-off between sensitivity and robustness in proteomics. These columns deliver strong separation performance and wide dynamic range while maintaining consistent stability over extended use. Designed for capillary flow LC-MS workflows, they provide comprehensive proteome coverage with reliable performance, supporting high-throughput and long-term studies in drug discovery, clinical proteomics, and bioprocessing.

Insights from the Aurora Series team
"I'd really like to shout out our Production team," says Andreia Almeida, Senior R&D Scientist. "They pivoted seamlessly from manufacturing established products to validating new protocols, stress-testing prototypes, and managing the final release, all on an accelerated timeline.

"Allowing failure to happen quickly rather than over-engineering to avoid it proved crucial," says Greta Briedyte, R&D scientist.

What the judges say…
"Industry-leading integrated capillary column electrospray cartridge."

3 BioResolve Protein A Affinity Columns with MaxPeak Premier Technology

Protein A columns delivering earlier, more precise antibody quantification

Produced by Waters Corporation

BioResolve Protein A Affinity Columns with MaxPeak Premier Technology combine non-porous 3.5 µm particles with bioinert hardware to improve sensitivity in antibody titer quantification. These columns enable accurate measurement at lower concentrations and earlier in bioprocess development, reducing time-to-result during clone selection and process monitoring. Compatible with multi-attribute methods, they streamline workflows by supporting simultaneous titer and aggregate analysis in a single run – enabling earlier decision-making in upstream development and faster optimization in downstream processes.

Insights from Senior Principal Scientist Beatrice Muriithi
"We went out and listened to everyone from loyal Waters

customers to labs that had never used our products. We even did blind interviews so people could speak honestly. They told us what frustrated them, what they wished for. That feedback shaped everything."

"I ran the experiment and saw a signal so sharp I thought I'd made a mistake. I checked everything three times. When I realized it was real, I went to my technical advisor and said, 'You have to see this.' It was a moment of pure disbelief before it turned to joy."

What the judges say…
"A well-designed innovation – particularly valuable for 2D workflows combining affinity LC and SEC."

"An important advancement in the quality of affinity chromatography columns."

2 Orbitrap Astral Zoom Mass Spectrometer

Next-generation Orbitrap platform accelerating large-scale proteomic discovery

Produced by Thermo Fisher Scientific

The Thermo Scientific Orbitrap Astral Zoom mass spectrometer delivers faster scan speeds, higher sensitivity, and greater throughput over its predecessor. With scan rates up to 270 Hz and enhanced multiplexing capability, it supports deeper proteome coverage and large-scale biomarker discovery. Designed for precision medicine and omics research, the system facilitates high-throughput analyses across proteomics, single-cell studies, and biopharmaceutical development.

Insights from Technical Lead Johannes Petzoldt
"The biggest hurdle that the team faced was balancing the many ideas that we brought together. We had to prioritize the specific innovations that would be the most beneficial to our customers given the time that we had to finalize the instrument before launch."

"We believe this will equip scientists in large translational research studies for diseases like Alzheimer's to reach new treatments and therapies at a faster rate than ever before."

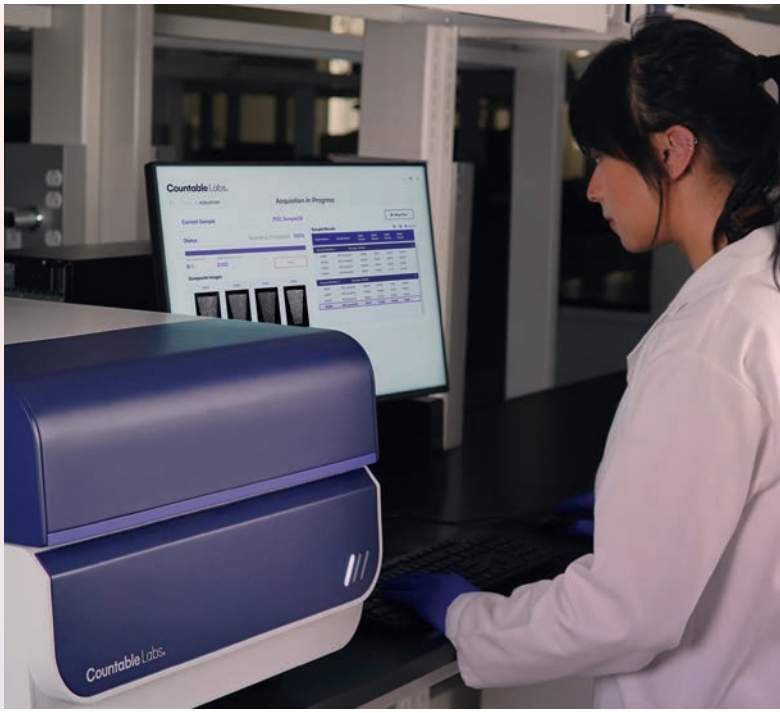
What the judges say…
"Breakthrough in resolution, speed, and sensitivity for MS."

"Numerous possibilities on this instrument thanks to parallel analyzers and hybrid acquisition modes. It looks like the perfect tool for proteomics applications, which has the power to drastically extend the amount of information obtained."

1 Countable PCR

Single-molecule counting for unbiased genomic quantification

Produced by Countable Labs



Countable PCR is the first platform to directly count every molecule without sample loss or amplification bias, advancing precision in genomic quantification. Using 30 million reaction compartments and 3D light-sheet imaging, it achieves single-molecule measurement across a broad dynamic range. The system overcomes the limitations of qPCR and digital PCR, offering ultra-sensitive, reproducible nucleic acid detection in a simple, scalable workflow – enabling the development of more sensitive assays that can lead to earlier disease detection, faster treatment monitoring, and more accessible translational testing.

Insights from CTO and co-founder Christina Fan

"Our goal is to take the single-molecule precision of next-generation sequencing methods and develop a technology that's simple to use, scalable, and accessible so that advanced molecular counting is as routine as running PCR."

"We had to make a deliberate decision to abandon the idea of improving on existing methods. Instead, we built Countable PCR from the ground up – starting with a clean slate."

"By lowering cost and complexity, it brings high-sensitivity genomics to any lab – not just large sequencing centers – helping accelerate precision medicine where it's needed most."

What the judges say…

"Truly innovative single-molecule counting technology bringing a new standard in the precision of PCR measurements with a very broad application range."

"Ideal for ultra-sensitive detection of rare variants – this could become a game-changer in the near future, as the principle of operation is quite different from what is already on the market."

SPECTROSCOPY

Spectroscopy in the Clinic: Ten Years On

As CLIRSPEC turns ten, co-founder Peter Gardner assesses the progress made – and the work still needed to bring spectroscopy to patients

Founded in 2015, the International Society for Clinical Spectroscopy (CLIRSPEC) aims to promote the translation of spectroscopy into the clinic for the benefit of patients. To mark its 10th anniversary, the society published a perspective reflecting on how far the field has come – and where it needs to go next (1).

To reflect on the past decade and explore what the next ten years may hold, we spoke with Peter Gardner, Professor at the University of Manchester, UK, and co-founder of CLIRSPEC.

Looking back over the past decade, how do you feel about the pace of progress in clinical spectroscopy?

There have been a number of significant changes over the last 10 years that I think demonstrate how the field has really matured and is now much closer to clinical impact.

The most obvious one which has impacted all areas of life is the explosion in machine learning and AI analysis. AI just wasn't on our radar 10 years ago – and we were one of the more advanced groups at the time. Back then, most people were using PCA and maybe random forests; today, deep learning methods are much more common and are making a difference – we can extract much more information from large data sets, which can greatly help pathologists. It must also be noted however that in the field of digital pathology, AI methods applied to the study of H&E images have also moved forward very rapidly, meaning that some of the "easy wins" for spectroscopy can be achieved with existing technology. We therefore need to focus on problems where that additional chemical information can make a real difference to the eventual diagnosis.

In terms of new technologies, the introduction of IR QCL was just beginning in 2014, and there were a few early pioneers. However, the field seemed to stagnate a little partly due to the fact that you see coherence effects when using lasers that you do not get with FTIR. Things have changed dramatically this year with the developments of Bruker's new ILIM system that has coherence reduction. We have shown that the system can provide the same diagnostic information as the FTIR but at least 20 times faster. This is a real game changer, since it now means that measurements that used to take many hours now only take minutes and thus are fast enough for a clinical laboratory.

In addition, the Optical Photothermal Infrared (OPTIR) microscope had not been invented back in 2014. It was developed in 2016 and versions of it have continued to develop rapidly ever since. To be able to obtain IR spectra at 500 nm spatial resolution without interference from scattering is a major breakthrough – and only now is it being exploited. Its utility in the clinical setting is likely to be limited, but much of our work in understanding disease is done at the single-cell level. This is a major new tool in our analytical armory.

I'd also highlight the rise in the number of groups using spectroscopy for liquid biopsies, which has taken me by surprise. Pioneered by Matt Baker and his team initially in Strathclyde and then at Dxcover, they have really moved the agenda forward and have gone into significant clinical trials.

In your view, is there a single most impressive advance over the past decade?

As mentioned, there have been many advances on many fronts. But sometimes it is the combination of things that come together that enables you to move forward.

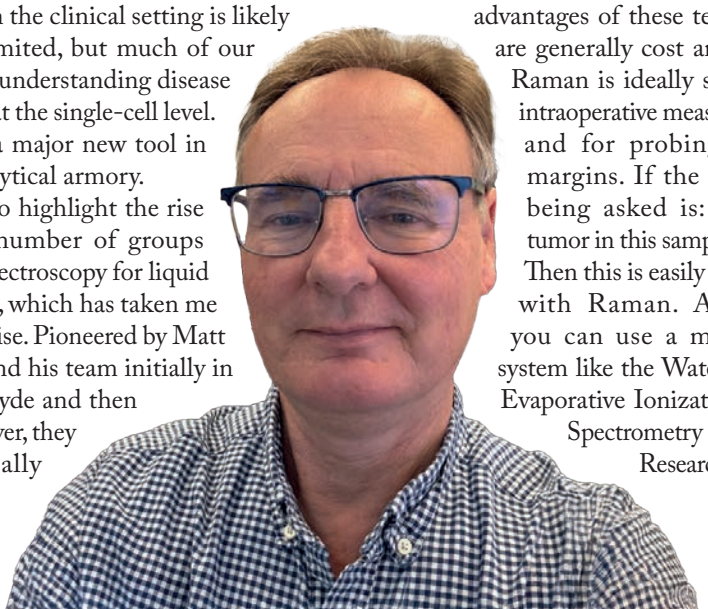
For example, a breakthrough in our own work came about due to (i) having access to 1,500 biopsy samples with 20 years of follow up data, (ii) developments in AI that enabled us to analyze the data, and (iii) the development of a very rapid QCL imaging system. Without any one of these components, we could not have done what we have done.

How would you summarize the current "state of play" in clinical spectroscopy?

I think that the field of clinical spectroscopy is in good shape. There are significant developments taking place in both infrared and Raman imaging, as well as in AI. There is also a vibrant community working in the field. However, as with many areas we need significantly more funding to take a lot of promising developments to the next stage.

How does clinical spectroscopy compare with clinical mass spectrometry?

In CLIRSPEC, we have a focus on infrared and Raman spectroscopy in the clinic. The advantages of these techniques are generally cost and speed. Raman is ideally suited for intraoperative measurements and for probing tumor margins. If the question being asked is: is there tumor in this sample or not? Then this is easily answered with Raman. Although you can use a mass spec system like the Waters Rapid Evaporative Ionization Mass Spectrometry (REIMS) Research System



"We have to make sure that what we want to introduce solves a real problem and has real clinical utility."

with iKnife, the Raman will do just as well.

In the pathology lab, infrared is much faster than mass spec and can provide the pathologist with significant additional information. Mass spec, generally, is more information rich and can be molecule specific, but it is more expensive and has poor spatial resolution compared with imaging IR. However, there is considerable interest in using both IR and mass spectrometry in tandem. There are examples of rapid IR imaging being used to target MALDI imaging of tissue, and this is going to be an important area of research.

You're developing a spectral pathology roadmap that connects spectroscopy, digital pathology, and AI. Can you tell us more about the goals of that project?

The EPSRC in the UK funded a Health Technologies Network with the aim of bringing together the spectral pathology community with digital pathology and AI communities. This network, "CLIRPath-AI," was a great success and introduced new academic and clinical groups. After four years we wanted to take stock to see where we are up to and how to move forward. The idea is to produce a road map that might influence policy makers and perhaps help us secure funding in vital areas. Although the Roadmap is UK centric, due to the funding, the themes are directly relevant to all members of the CLIRSPEC community.

What are the biggest technical or cultural hurdles we still need to overcome before spectroscopic tools become routine in hospitals and labs?

We have to make sure that what we want to introduce solves a real problem and has real clinical utility. We then need to make sure that it is cost effective. If we can demonstrate these two things then the technology will be adopted. The cultural barriers are gradually being eroded. This is where the rise of digital pathology has been helpful. Pathologists like their optical microscopes, and there was a lot of resistance to the introduction of digital pathology. However, they are starting to see the benefits, and with the explosion of AI it is becoming increasingly apparent how this can help them. As a result, pathologists are becoming much more used to looking at a large monitor rather than staring down the microscope binoculars. This helps us because infrared or Raman images are just a different modality of imaging providing additional information. The digital pathology revolution in the UK, driven by pathologists such as Daren Treanor at Leeds, has really made a difference – it is no longer such a step-change to adopt a new technology.

Finally, if you were to imagine the field of clinical spectroscopy ten years from now, what do you hope will have changed the most?

I hope that the new generation of very talented spectroscopists take up the mantle and accelerate the field far more quickly than we have done.

Over the 10 years of the CLIRSPEC society, the thing that I am most proud of is our International Summer School held in the Lake District, UK. About 250 students have come through this program and it is always a pleasure to see how they are starting to move the field forward. In 10 years time they will be the new leaders in the field and it is up to them to shape it. Hopefully by that time we will also have commercial companies offering vibrational spectroscopy-based solutions to certain clinical problems. Ultimately, I would like to see vibrational spectroscopy used routinely to benefit patients – enabling them to get faster diagnosis and better, more personalized, treatment. I can see the emergence of such companies and so I am optimistic this vision will be realized.

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MASS SPEC

The State of Mass Spectrometry Innovation in 2025

Three leaders explore how instrument design, AI, and multiomics are reshaping the field

David E. Clemmer: Each year, I believe I understand the scope of mass spectrometry-based measurement, yet the field never fails to surprise me.

Nowadays, we have advanced ionization sources that enable us to generate ions in so many different ways. If you can imagine it, chances are there's a way to ionize it. There are still some molecular classes we're stumbling around with, but we have so many more options – and so many gentler ones. This allows us to preserve structure and begin using mass spectrometry in different ways, including in structural biology.

It's also worth mentioning all these new "sniffing devices," similar to what you might have seen used in an episode of Star Trek. A recent example is Graham Cooks' DESI source, which enables direct probing of an environment with atmospheric pressure ionization. There are some – my former postdoc Sarah Trimpin, for one – who don't believe you even need voltage to make ions anymore. Steve Valentine (one of my first graduate students) has a droplet-generating vibrating tip that can create ions across a continuum of potentials used in positive and negative ion electrospray taking advantage of differences in ionization that we never would have imagined would generate ions years ago.

It's fair to say that the ion source revolution is here – that's something we now have at our disposal.

Susan Richardson: It's rare in this field to see a completely new ionization technique or a brand-new type of mass analyzer, but the pace is still fast in terms of improving instruments – letting us detect lower levels, work faster, shrink the size, and make them more robust.

Bringing mass spec technology to the field is a key goal – in the environmental world especially, there's definitely a growing need for portable, field-deployable mass spectrometers. And while miniature mass specs aren't new – they've been developed for many different purposes over the years – we're seeing more and more progress. I mean, we've even sent one to Mars! NASA had a great exhibit this year in Baltimore, as the Goddard Space Flight Center is right there too.

The other major trend I've noticed is, of course, AI. It's being used to do everything now, it seems, with use in data analysis, and even in the planning of experiments. I'm sure there was a little bit on show at ASMS last year, but there appears to be a lot more integration with mass spec now, and definitely more to follow. It's a big, exciting development, and I'm looking forward to seeing what happens.

Boone Prentice: The increasing availability of multiomics approaches in biomedical research is really exciting. I think it's well poised to influence areas like personalized medicine and biomedical research in general. With regards to technical challenges, the biggest right now are probably in data integration. There are all these data streams coming from different types of experiments – some from mass spec technologies, some from others – and integrating them into a cohesive framework to push forward personalized medicine is unexpected, interesting, and challenging, all at once.

In terms of speed and innovation, I would say mass spec research is moving at an excellent pace. Innovation seems to be trending toward these exciting new applications and integrations with other mature technologies. There's still a good amount of research on fundamental instrumentation and methods – you definitely still see that at ASMS – but the technology has matured to a point where it's more broadly accessible, even to practitioners who may not have deep expertise in mass spec. That's really promising, as it broadens the influence of mass spectrometry into other fields, which has been exciting to watch.

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Susan D. Richardson is the Arthur Sease Williams Professor of Chemistry at the University of South Carolina and a Distinguished Professor in the Department of Chemistry and Biochemistry.

Boone Prentice is an Assistant Professor in the Department of Chemistry at the University of Florida.

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CHROMATOGRAPHY

What I Learned Bringing Slalom Chromatography Back from the Dead

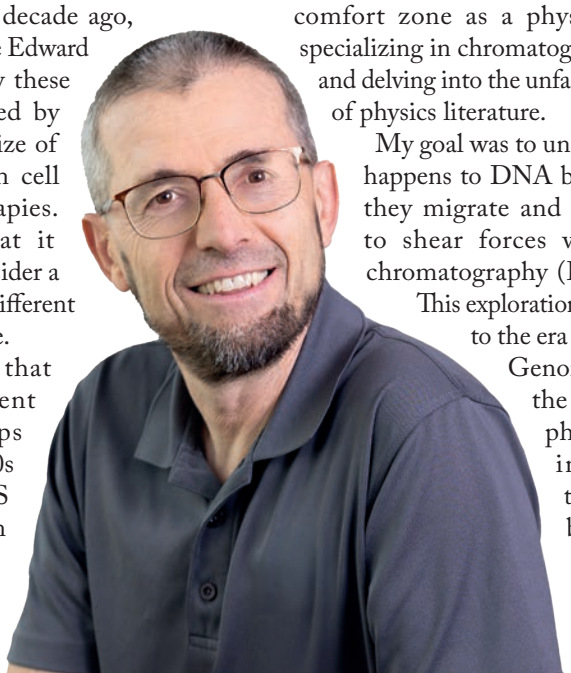
Fabrice Gritti spent a year immersed in the world of DNA physics to resurrect a long-abandoned technique to solve modern challenges in cell and gene therapy analysis

With Fabrice Gritti, Principal Consulting Scientist, Waters Corporation, USA

You never know when a dead end might open up

A central challenge when separating DNA and RNA macromolecules – essential during cell and gene therapy development – is the pore sizes of the particles used in modern chromatography columns. Often, they simply aren't large enough. As a result, developers face a choice between poor selectivity or having to adopt slower and more complicated techniques.

More than a decade ago, my late colleague Edward Bouvier foresaw these challenges posed by the increasing size of biomolecules in cell and gene therapies. He argued that it was time to consider a fundamentally different separation mode.



He recalled that two independent research groups in the late 1980s (one in the US (1) and one in Japan (2)) had successfully separated large plasmid digest fragments exceeding 1 MDa in mass. They coined the term "slalom chromatography" (SC) to describe the phenomenon, likening the movement of DNA molecules through packed particles to a skier weaving through slalom gates (the fixed packed particles). While the concept was visually compelling, the underlying separation mechanism remained poorly understood, and SC was eventually abandoned because of limitations in particle purity, market demand, and mechanistic clarity.

Fast forward to 2022 and the problems Ed foresaw had not gone away. Myself and colleagues at Waters – Matthew Lauber and Kevin Wyndham – began thinking: could we bring slalom chromatography back from the dead?

Step outside your comfort zone to seek fundamental understanding

If we were serious about developing and commercializing the first SC column in the history of chromatographic separation science (and hopefully in 2 to 3 years), we first needed to understand the mechanistic foundations – something that remained elusive as of 2023. I was given full freedom to pursue both theoretical and experimental investigations. I began by trying to understand the fundamentals, which meant stepping outside of my comfort zone as a physical chemist specializing in chromatographic science and delving into the unfamiliar territory of physics literature.

My goal was to understand what happens to DNA biopolymers as they migrate and are subjected to shear forces within liquid chromatography (LC) columns. This exploration took me back to the era of the Human Genome Project in the 1990s, when physicists were investigating the relationship between the elongation of a single DNA polymer chain and the mechanical force applied to one of its ends. From there, I had to understand the magnitude of forces required to stretch, overstretch, and even break a double-stranded DNA chain.

The next step was to build a conceptual bridge between the world of DNA quantum physics and our own classical world of shear rate in chromatographic separation science. This effort laid the foundation for the first publication we produced on the fundamentals of SC (3). Altogether, it took me nearly a full year of intensive searching and reading to gather the most relevant physics literature related to the core principles of SC.

We discovered that within our LC column, entropic elastic stretching, the process of uncoiling the random DNA coil without enthalpically stretching or breaking chemical bonds, was occurring for double-stranded DNA, but not for single-stranded DNA polymers. This insight revealed a significant opportunity in the field of cell and gene therapy: the potential to separate and purify single-stranded RNA (such as mRNA vaccine products) from their double-stranded RNA impurities.

But the real magic happens when theory meets experiment

However, many practical questions remained unanswered: What mobile phase composition should be used? What organic content, salt concentration, or pH? What particle size, temperature, flow rate, or static pressure would be optimal? None of these questions could be resolved through existing literature or by relying on user intuition alone.

I then had to return to the lab and systematically investigate, through experimentation, the intrinsic role of various chromatographic parameters on the retention and efficiency of an SC column. This was not a trial-and-error approach, but rather a quality-by-design methodology, where only one parameter

is varied at a time to assess its specific impact on DNA separation. The empirical insights gained from this process led to our second and third practical publications on SC, focused on method development and performance optimization (4,5).

As a result of our initial research efforts, two years later – now in 2025 – we have developed a solid understanding of the separation mechanisms governing DNA and RNA biopolymers as they migrate through chromatographic columns packed with spherical particles. This knowledge has enabled us to streamline the development of an efficient, selective, and robust SC column for separating large DNA/RNA biopolymers. Ultimately, Waters became the first company to commercialize an SC column, marking a significant milestone.

We see this as just the beginning. As customers begin to share feedback, highlight current limitations and suggest new applications, we anticipate further advancements. Our hope is that this technology will contribute meaningfully to the development and delivery of next-generation biopharmaceuticals in cell and gene therapies.

Embrace childlike curiosity – undergirded by a broad scientific education

Having embarked on this exercise of stepping outside my own core area of expertise, I'd like to reflect on what it required from a mindset perspective, and offer some advice for others who might like to try something similar.

The main challenge we faced, as is often the case in interdisciplinary research, lay in adapting to different scientific terminologies and ways of thinking. Physicists don't think like analytical chemists, and the same holds true for physical chemists and chemical engineers. Yet, breaking down the barriers between these disciplines is incredibly rewarding – provided we're not discouraged by unfamiliar concepts and are willing to navigate confidently across these scientific domains.

Overall though, I have to say that I had a great time getting to grips with the fundamentals. It didn't require materials, chemicals, or lab time, only mental engagement through thought experiments. For instance: What happens when DNA chains are exposed to shear forces? Can they remain extended within LC columns? What if we change the flow rate or temperature? What if the particles are negatively charged? What if the ionic strength is altered? We sought answers by exploring relevant physics literature and then transposing those insights into our LC column systems.

My mindset here was reminiscent of a child constantly asking teachers and parents why things happen or how they work – to the point of getting on their nerves! But, like children, researchers exploring new terrain need support. I'm fortunate to work with top-level

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"Our hope is that this technology will contribute meaningfully to the development and delivery of next-generation biopharmaceuticals in cell and gene therapies."

managers who understand what scientists need to make meaningful progress and deliver impactful results for our customers.

However, for many researchers in industry, it can be difficult to make translational or cross-disciplinary jumps. Professionals are typically assigned to specific technical tasks aligned with the domain for which they were hired. Also, the pressure to deliver results quickly, often "yesterday," combined with internal review systems tied to career advancement, can discourage scientists – especially those early in their career – from venturing into unfamiliar fields or spreading themselves inefficiently. It's also difficult because such exploration often demands significant investment in education and scientific development. Not all companies have the resources or flexibility to train their scientists and engineers across multiple disciplines – despite the fact that fostering this kind of intellectual agility can be incredibly valuable for innovation and long-term impact.

My advice, especially for those early in their career, would be to gain a broad scientific education, one that encompasses the core principles of chemistry, physics, analytical chemistry, and physical chemistry, and, most importantly, fosters an understanding of how these disciplines interconnect. This integrative approach is often lacking in the US, where students tend to specialize immediately while completing their master's degrees. Education delivered as a series of disconnected and independent "islands of knowledge" can significantly hinder the ability of early-career researchers to think holistically and make cross-disciplinary connections.

Analytical science will increasingly require ideas from across disciplinary boundaries and from unexpected angles

My view is that, given the complexity of the new biomodalities designed in the pharmaceutical world and the deep level of characterization required, we will need researchers capable of exploring different disciplines. An expert in liquid chromatography cannot survive alone without complementary expertise in novel detection techniques (light scattering, mass photometry, electrochemistry, some spectroscopy, flow cytometry, etc.) besides classical optical and mass spectrometry. This should naturally be encouraged.

But that isn't to say that all scientists should attempt to become experts across many different disciplines. Instead, we need researchers capable of interfacing efficiently between all these different disciplines to collaborate with other relevant experts. And some scientists may be more inclined to interdisciplinary working than others. For me, I just enjoy being slightly less ignorant. Learning new concepts in physics and biology, especially when this knowledge is directly applicable to my own work, brings great satisfaction – especially when I get the opportunity to share this new knowledge within our specialized field of separation science, whether through publications or presentations at international meetings.

Ultimately, stepping outside my comfort zone in liquid chromatography to better understand slalom chromatography has reinforced my conviction that novel and impactful ideas often originate when someone thinks differently, outside the box, and views things from a completely unexpected new angle. This is possible when a person can comfortably navigate across different scientific disciplines. So, if we want to avoid stagnation, we need cross-disciplinary thinking; and my message to any research manager is: ensure that most of your scientists are multidisciplinary.

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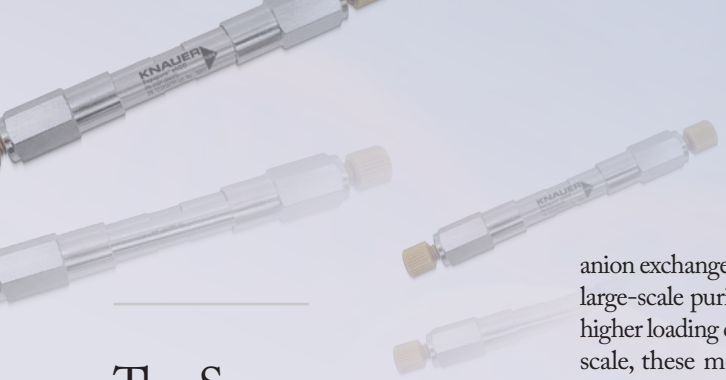


The Sepapure Solution

Dr. Kristin Folmert, Analytical Product Manager at KNAUER, showcases how Sepapure oliGO is raising the bar for affordable, high-performance oligonucleotide analysis

How would you describe the oligonucleotide development – and analysis – landscape?

Since the coronavirus pandemic, oligonucleotides have been one of the hottest topics in molecular biology and therapeutic research. The ability to design customized DNA or RNA strands, specifically for a molecular target or individual patient, sounds almost like a sci-fi-esque concept that is now becoming reality. Whether it's personalized cancer therapies, or mRNA as a basis to synthesize proteins at the site of action, the number of versatile applications is growing exponentially.

Given that many applications arise in regulated environments, where quality and safety are key issues, it is essential to analyze oligonucleotides both precisely and reliably. This isn't always a simple task, however, as the extremely polar and often long-chain oligonucleotides often differ by just a single base in length or single modification of synthesis by-products. UHPLC-MS is usually the most appropriate method to analyze the impurities, both qualitatively and quantitatively.

What limitations do researchers face with traditional columns for oligonucleotide analysis?

Due to their polarity, classic reversed-phase separations do not work on oligonucleotides. Therefore, the negatively charged phosphate backbone is exploited and separation is instead achieved via the charge. Classic anion exchange (AEX) columns are used for large-scale purification because they have a higher loading capacity – but on an analytical scale, these methods are often too time-consuming, as well as inaccurate. Poor MS compatibility also makes AEX less attractive for analysis. HILIC enables very high precision for complex separation problems, but the methodology is neither robust, nor particularly effective. Additionally, HILIC columns have limited pH stability in the alkaline range, which often makes them an unattractive option. For several years now, ion pairing reversed phase (IP-RP) chromatography has been recognized as the "gold standard." It combines the robustness and effectiveness of RP with the precision of ion chromatography.

Could you explain how the ion-pair reversed-phase (IP-RP) mechanism works and why it's especially suited to oligonucleotide separations?

IP-RP chromatography uses hydrophobic ion pair reagents to mask charge positions in the oligo backbone, thereby enabling hydrophobic interaction with the stationary phase. Quaternary or tertiary ammonium compounds such as tetraethylammonium (TEA) are typically used for this purpose. To ensure solubility, a basic eluent mixture of hexafluoroisopropanol (HFIP), TEA, and water as a gradient against methanol has proven to be a robust and well working method. This enables very precise and rapid separation, as retention is linked directly to the charge density. Additionally, differences in individual functional groups can affect retention through classic hydrophobic interactions, meaning even small deviations from the desired synthesis product can usually be detected by UHPLC-MS.

What inspired the development of the Sepapure oliGO column?

The reagents used in IP-RP chromatography, TEA and HFIP are rather aggressive, and many conventional silica gels have a limited shelf life – especially when used with basic eluents. HFIP also puts a lot of strain on the entire HPLC system. In addition, the high pressures involved in UHPLC lead to rapid system wear-and-tear and clogging of the silica gel. Therefore, we sought after a material that would enable high resolution and selectivity using an IP-RP method, while also being robust enough against the reagents. It was also important to us to develop a material that would enable high-throughput even without high pressures. We are proud to say that we have achieved exactly that with the Sepapure oliGO column.

Can users transfer existing methods directly from other column brands – and how easy is that process?

Of course, there's no general answer to this question. However, we have directly transferred methods from a well-known manufacturer of IP-RP oligonucleotide columns, and in no cases did we have to adapt the method. We tested synthetic raw products, some of which were thiolated, with different chain lengths and sequences and achieved excellent results – even with structures that were really complex. The only difference is that the back pressure is significantly lower, extending the lifetime of the entire system.

What benefits can labs expect to see when switching to Sepapure oliGO?

Oligonucleotide columns are among the most expensive columns currently on the market – though unfortunately, their durability is often suboptimal. We repeatedly hear from users that their columns clog or performance declines rapidly, meaning they have to be replaced regularly. It is important to us that significant research on oligonucleotides is affordable for all laboratories. For this reason, we wanted to ensure Sepapure oliGO columns are available at an affordable price. We hope that by combining high quality, specialization, and robustness in a single column offered at a fair cost, we can help further advance oligonucleotide research.

KNAUER

PROFESSION

The Psychology of Innovation: How to Build a Fearlessly Curious Team

Creating space for dissent, risk-taking, and failure is key to innovation, says SCIEX's R&D VP Chris Lock

You started out as a scientist and now you've moved into a leadership role. Was that what you always intended to do?

Honestly, I did not expect to be in this role; it's something that just evolved over time. Early on, I remember my parents saying I was always asking "why" – to the point of annoyance, I think. Why is that? How does this work? I used to constantly take things apart, always interested in how and why things worked. That kind of natural curiosity drew me into the sciences. The scientific process – the constant challenging of the status quo and the discovery of new truths – really appealed to me.

I always assumed I'd end up in a lab, working as a bench scientist. That was the career I pictured. But as I progressed, I also developed a deep interest in human behaviour and psychology. I started reading a lot on those topics, and it sparked an interest in how to build and structure innovative teams.

I've always been comfortable taking educated risks. I've taken on some quite challenging assignments – things that others might have seen as risky – but I saw them as opportunities. One of those was stepping into a management role. When I was offered the chance to leave the lab and become a manager, I spent an entire Christmas thinking about it. My boss at the time was surprised – I think he expected me to jump at the opportunity. But I knew it was a pivotal moment, a fork in the road for my career, and I wanted to be sure.

Ultimately, I felt I could have more impact in a leadership role than I could by staying at the bench. It gave me a chance to combine my passion for science and innovation with my growing interest in psychology and team dynamics. That combination has really shaped my career and brought me to where I am today.

Are you more driven by raw curiosity or by the desire to have an impact on the world – and has that changed over time?

From the very early stage of my career, I wanted to do something that had an impact – that's always been a driving force for me. I want to do work that matters. I have two daughters now, and I want them to be proud of what I do, to be excited to tell their friends, "Hey, my dad's working on this."

And I find what we do as an organization incredibly motivating and impactful. When I talk to our customers – scientists – and hear about the challenges they're trying to solve and the potential that has for improving human health, it's deeply motivating. That impact is a huge part of what drives me, and I think it drives the team I work with as well.

That said, individual curiosity still plays a strong role. When I took on this role, I made it very clear to my boss at the time that I didn't want to just sit in an office and shuffle paperwork. That can easily happen to senior leaders as they move up in an organization – suddenly all you're dealing with is budgets and admin. I said no, what drives me is the science, the technology, and the impact, so I want to stay close to that.

THE TRICORDER MOMENT: MASS SPEC IN THE AGE OF AI

Could AI soon allow users to operate instruments using natural language, without understanding how to build a method or process data?

Are there any emerging trends on your radar?

Probably not surprisingly, I'd say AI is the big one right now. Pretty much every time I speak publicly, I get asked about what we're doing with AI – and internally, too, it's something the team brings up regularly. I really believe it's going to be transformational.

The speed at which AI is evolving right now is incredible. Sure, there's the fun side of AI – people using it for entertainment – but I believe this is one of those step-change moments in human development. You could compare it to the advent of the personal computer, or the cell phone, or the shift from analog to digital photography. AI is on that level.

One of the big impacts is how it can democratize complex technologies. When I started my career, the people buying mass spectrometers often had PhDs specifically in mass spectrometry. The instruments were complex and required deep expertise to operate. But over the years, that's changed. Mass spec has become more accessible, easier to use, and now people from a much wider range of backgrounds – like biotechnology, food science, or engineering – are using it not because they're experts in mass spectrometry, but because it helps them get answers they need to move their work forward.

AI has the potential to take that further. It can compress the time it takes to go from problem to answer. It can provide deeper insight into complex data and reduce the need for highly specialized expertise in every use case.

We're moving toward a future where someone can use natural language to describe what they want to learn from a sample. Ideally, they wouldn't need to understand the inner workings of the instrument, how to build a method, or how to process the data. They could simply walk up, load the sample, and the instrument would figure it out.

I often think of the mental image of the tricorder from Star Trek. You walk up to something, scan it, and it tells you what's there and in what quantity. That's what I think a lot of customers would love. They want to put in a sample and just have the system say: "Here's what's in it, here's how much, and here's a report you can use." AI absolutely has the potential to deliver that. There's still work to do, but the trajectory is clear – and it's exciting.

This applies not just to mass spec, but to a whole range of analytical technologies. AI could fundamentally change how we understand biology, how we approach precision medicine, how we develop drugs – both biopharmaceutical and small molecule. We're already seeing AI used extensively in pharma, including with some of our partners who are applying it to transform their internal capabilities.

The pace of innovation in AI is what amazes me the most. It feels like every week there's something new. I don't see that pace slowing down anytime soon, and we're going to be part of that transformation with the tools we're developing.

What is missing today from the mass spec toolkit? Are there any major problems that we can't fully address with the current technology?

First, something that's been interesting to observe throughout my career – I've been working in mass spectrometry for more than 28 years now – is what I'd call an "arms race" between technology developers and customers. As we evolve the technology, customers immediately find new ways to use it and then run into new bottlenecks. That cycle continues – we push the technology, and then they push the boundaries of what they want to do with it.

A good example of that is high-resolution accurate mass technology. Initially, customers used it to identify what was in their sample – say, a protein digest. Then they quickly moved to asking, "How much of these proteins are there?" Once they had ID and quantification, they wanted to know how things changed under different conditions – so they wanted to run multiple samples, get IDs, quantitation, and do it with high precision and repeatability. And they wanted to do it faster, more robustly, and at scale.

Every time we've thought that increased performance might mean fewer instrument purchases or reduced sample throughput, it's been the opposite. Customers find more questions to ask, go deeper into their samples, and extend their research. So that continual drive for deeper insights – faster, more quantitative, more robust, more reliable – that's very much still alive. We're not done yet. There's still lots of innovation needed.

Accessibility is another big theme. As we discussed earlier, customers increasingly don't want mass spec to be the focus – they want easy, intuitive access to results. That's where AI has huge potential, by lowering the barriers to entry and making the technology more approachable to non-specialists.

The second major gap I'd point to is data integration. Many customers are using multiple analytical technologies in their workflows, and at some point, they need to bring that data together. There's no single, dominant tool that does that really well today – nothing that seamlessly integrates all those different modalities into a coherent whole.

Ironically, what we see most often is that people are still using Excel and Word as makeshift integration tools. They're flexible, familiar, and can pull in different types of information, but they're clearly not purpose-built for this kind of scientific data integration. So there's a big opportunity there: how do we combine multimodal results – mass spec, chromatography, spectroscopy, imaging, whatever it may be – into one unified platform that gives scientists a "single source of truth" they can actually use to make decisions? That's a big challenge still waiting to be solved.

"Some people really excel in that startup-style environment, while others thrive in the execution and quality-focused mindset. You shouldn't treat those as interchangeable roles."

I still take part in brainstorming sessions with our technical team. I still get into the details of technical barriers we're trying to overcome. I enjoy getting in the mix and thinking through ideas with the team.

A while ago, I had the chance to meet the CEO of NVIDIA at a Danaher conference. He gave a talk and afterward we chatted one-on-one. That conversation really stuck with me. He said that every week, no matter what, he made time to talk with the scientists and engineers working on key projects – just to hear directly from them about what they were doing, what challenges they were facing. He wanted to stay connected to the heart of the work.

I've taken that with me ever since. No matter where I am in the organization, I want to stay grounded and connected to the people doing the work – to understand their challenges and help where I can.

What is the role of innovation in an established company like SCIEX – as opposed to a startup instrument business, for example?

I think it goes back to culture – you have to create the right environment for the type of work you're trying to do. I've had many opportunities to explore how you integrate what is essentially a startup mentality into a more established organizational framework. You want that innovative mindset – creative, agile behavior that enables new ideas and fresh approaches. You want to capture the value that brings. But you also have to couple that with a regimented product development process that delivers reliable, high-quality products that meet customer expectations. Those are very different processes.

And what you come to realize – and this ties into my interest in human behavior – is that some people really excel in that startup-style environment, while others thrive in the execution and quality-focused mindset. You shouldn't treat those as interchangeable roles.

As you work with more and more people, you begin to recognize that everyone is wired differently. We all have different strengths and weaknesses. Some people are comfortable with risk and ambiguity, while others are better suited to detailed execution and structured environments. Some are highly creative; others prefer having clear guidelines.

Understanding where people fit along that innovation continuum is critical to structuring an effective R&D organization. That's a big part of talent management: recognizing how someone is wired and identifying the best place for them to contribute. It's like assembling a jigsaw puzzle – when you get it right, all the pieces fit together, and you end up with something cohesive and complete.

Just because two people have the same title – say, mechanical engineer – doesn't mean they should be treated the same. They may be fundamentally different in how they work and what environment allows them to thrive. So figuring that out and aligning people with the right roles is essential.

That's been a passion of mine over the years – understanding that range across the innovation pipeline and, as we hire or develop people, making sure we place them where they can bring the most value. That's how you capture both the startup mentality and the structured, high-quality execution required to bring a great product to market – because those are radically different skill sets.

Are there any other lessons from psychology that you've implemented in how you build your team?

The idea of psychological safety is really important to me. It's a core tenet of how I lead. I want the team to feel comfortable bringing up ideas or expressing contrary opinions. I've always told them: I'll never get upset if someone tells me they think something's a bad idea. But I will be frustrated if no one says anything in the moment – and then several months later says, "Yeah, I knew that wouldn't work."

We need to be able to talk openly about concerns and risks, and get the data around those concerns so we can make informed, logical decisions together as a team. That openness is critical. Many of us have worked in environments where people were afraid to speak up or challenge the status quo – where they felt like they couldn't say something that might go against what the boss had said.

Creating an environment where people feel safe to speak their minds is incredibly empowering – not just for individuals, but for the team as a whole. It fosters a lot of creativity. You'd be surprised at the ideas people come up with when they feel safe and supported. That sense of psychological safety and mutual respect has become a real strength of our culture, and I think it plays a huge role in driving our innovation mindset.

Easy Encapsulation Efficiency Determination of mRNA in LNPs via AEX

This Application Note, based on the publication and data of the University of Geneva and Sanofi's mRNA Center of Excellence in France, presents an AEX method for determining the encapsulation efficiency as a refined and more robust alternative to commonly applied analytical workflows (1).

By Ann Marie Rojahn

To enhance intracellular delivery and preserve mRNA integrity against RNase-mediated degradation, therapeutic mRNA can be encapsulated in lipid nanoparticles (LNPs). The encapsulation efficiency (EE) defines the proportion of mRNA that will eventually be delivered into the cells. Therefore, RiboGreen (Thermo Fisher Scientific), a fluorescent dye which binds to free mRNA is often used. However, this method is prone to matrix effects, the binding is highly sensitive to environmental factors and the structure of the LNP can be affected by dilution. As LNPs exhibit neutral charge, anion exchange chromatography (AEX) offers a targeted strategy to separate free mRNA from unretained drug product.

Encapsulation efficiency determination

To determine the EE, the sample must be analyzed twice. First, it is analyzed undiluted and under native conditions to determine the concentration of free mRNA. For the second analysis, the sample must be disrupted with a surfactant to evaluate the total mRNA concentration. Figure 1 shows the chromatograms of these two analyses demonstrating how the amount of mRNA is increased for the disrupted LNP (green).

The comparison of both analytical approaches reveals consistent results in many cases, however the RiboGreen method occasionally reports a notably lower EE. Figure 2 displays the chromatograms of two selected samples where the outcomes align (blue) and where both methods diverge significantly (orange). The blue sample produces a peak exclusively for free mRNA, while the orange sample additionally reveals a pre-mRNA signal, which is assumed to be some kind of surface-associated mRNA. The data suggest that the RiboGreen dye binds to surface-associated mRNA, which falsely contributes to the free mRNA signal and results in a reduced EE.

Conclusion

This AEX method compared to commonly used spectrofluorometric approaches provides:

- Fast analyses
- Cost efficiency
- Additional structural insights of the LNP

This makes it a viable alternative for determining the encapsulation efficiency.

Link: https://ymc.eu/d/brDrl

Reference

1. *Athanasios Tsalmpouris, Sofiane Mahjoubi, Camille Malburet, Chamsan Daher-Hassan, Marc François-Heude, Jean-François Cotte, Davy Guillarme, and Jonathan Maurer Analytical Chemistry 2025 97 (35), 19275-19282; DOI: 10.1021/acs.analchem.5c03299*

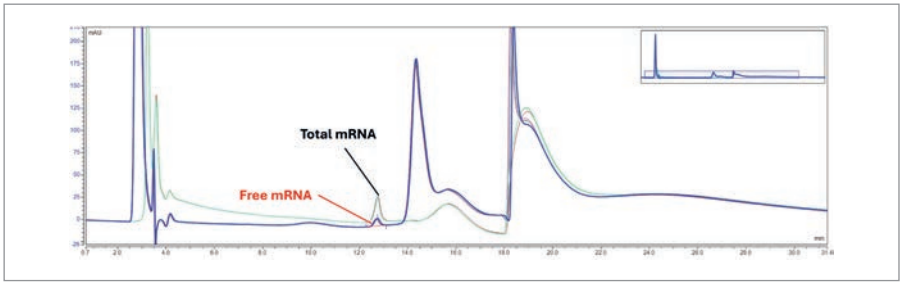


Figure 1: Analysis of the intact drug product (blue) and the disrupted LNP (green) using a bioinert coated YMC Accura BioPro IEX QF column to determine the amount of free mRNA vs. the total amount of mRNA included in the LNP.* Method details: Column: YMC Accura BioPro IEX QF (3 µm) 100 x 4.6 mm ID; Eluents: A) 25 mM glycine (pH 10.1), B) 25 mM glycine + 1.5 M NaCl (pH 10.1), C) 25 mM glycine + 3 M NaCl + 0.05 % Triton X-100 reduced (pH 11.0); Gradient: 50 %B (0–2 min), 50–53 %B (2–2.25 min), 53 %B (2.25–4 min), 50–100 %B (4–6 min), 100 %B (6–8 min); Washing step: 100 %B (8.01–12 min); Re-equilibration: 50 %B (12.0–22 min); Flow rate: 0.2 mL/min; Temperature: 25°C; Injection: 2 µL; Detection: UV at 230, 260 nm; Sample: mRNA (in-house), LNP (in-house), Disrupted LNP with 4 % reduced Triton X-100 (T4TE20x) (1). *Courtesy of University of Geneva, Institute of Pharmaceutical Sciences of Western Switzerland (ISPSO)

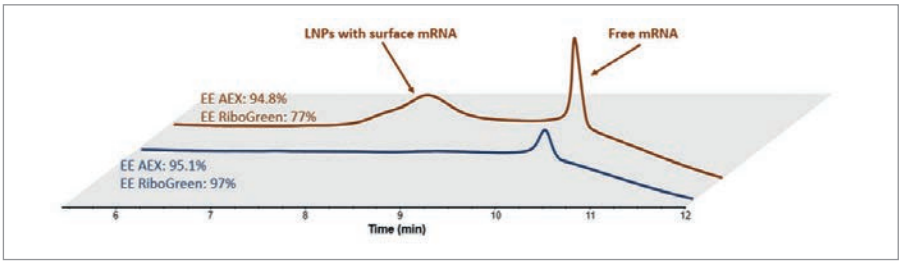
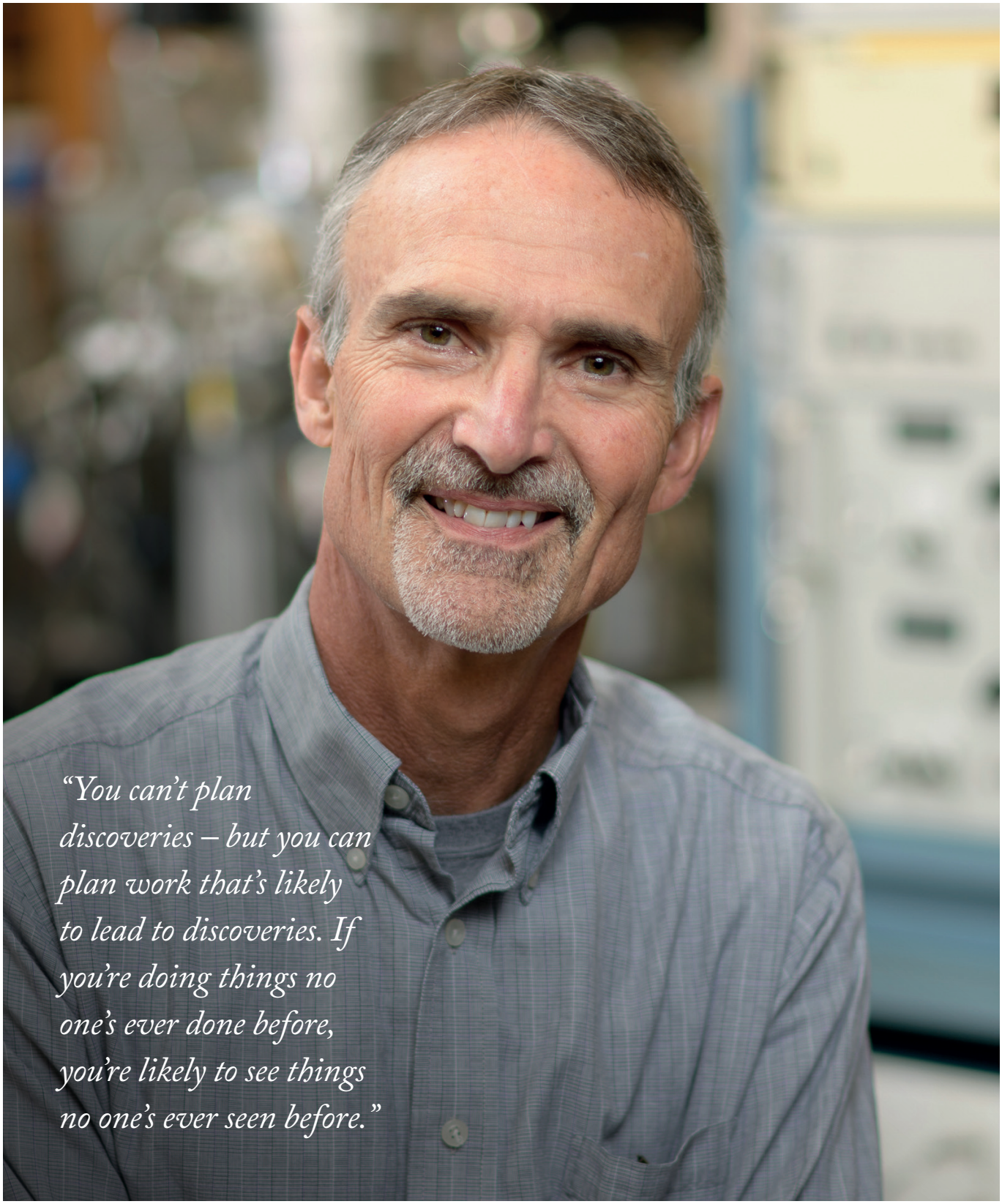


Figure 2: Comparison of two samples where the EE outcomes align (blue) and where both methods diverge significantly (orange) (1).


"You can't plan discoveries – but you can plan work that's likely to lead to discoveries. If you're doing things no one's ever done before, you're likely to see things no one's ever seen before."

The Thrill of Discovery

Sitting Down With… Scott A. McLuckey, John A. Leighty Distinguished Professor of Chemistry, Purdue University, West Lafayette, USA

How did you end up in the mass spectrometry field?
Early in my senior year at a small liberal arts college, one of my professors asked me where I was going to go to graduate school. That wasn't on my radar at all – I thought I'd just get a job. He said, "Unless you want to wash test tubes for somebody else, you really want to have a PhD." That January I took an industrial internship, and the only person who really seemed to be having fun was the PhD – he was deciding what people in the lab should do and was genuinely excited. That convinced me to go to graduate school.

From there I looked at different groups, and it just so happened that Graham Cooks became my advisor. I visited his lab at Purdue, where he was doing mass spectrometry research. I knew nothing about it – my undergrad institution didn't even have a mass spectrometer – but everyone in his lab seemed really excited about their work. Even though I didn't understand it at the time, I thought, "I want to be that excited."

What are some of the biggest lessons you learned from Graham Cooks?
I think people outside science don't realize just how important creativity is – and how creative scientists must be to do original work. That really hit home for me being around Graham, joining conversations with senior grad students, and seeing how they thought.

But creativity is just one side of the coin; the other side is discipline. Graham is a very disciplined scientist – he's the hardest-working person I've ever met and I could see how that paid off. He once told me, "If you and I both have 50 ideas a day, and I pursue 10 of them while you pursue one, I will win." That stuck with me. There's just no getting around hard work.

How do you cultivate creativity?
We all know that word, serendipity. You can't plan discoveries – but you can plan work that's likely to lead to discoveries. If you're doing things no one's ever done before, you're likely to see things no one's ever seen before. The challenge is: are you a good enough scholar to figure out what's going on?

In my lab, a certain fraction of what we do is just turning over stones – trying something out and seeing what happens. There's usually some kind of hypothesis or goal, but around 25 percent of the time we're just exploring. Another 25–30 percent is following up on something we've found and turning it into a project. The rest is developing an idea toward some useful end.

So, for example, I might discover a new reaction, then try to understand the underlying principles. Once we know what's going on, we ask: how could this be useful? Could it solve a measurement problem? Those stages – discovery, understanding, and application – are always going on in parallel in my lab. It's a process that's kept me going for more than 40 years. I can't tell you what I'll be doing five years from now, but I know there will be plenty to do as long as we keep turning over stones.

Are you solely driven by curiosity and discovery – or does potential impact factor in?
I think impact follows from curiosity. But the extent of that impact is really hard to predict. One of the great things about the university model is that it allows single investigators to go off in left field and do work that nobody asked for – and it can turn out to be very important.

On a personal level, I once took a Myers–Briggs personality test when I was working at Oak Ridge National Lab, and it came back that I was a "thrill seeker." I didn't see that in myself at all, but my supervisor said, "Of course you are – look at the way you do research." And he was right. I'm always looking for the next discovery, and when I find it, I feel like I'm not even touching the ground.

The truth is, most of the time experiments don't work. You're struggling, things don't pan out. But then one day you come across a result or a phenomenon you don't yet understand – and it's exciting. That intermittent reinforcement makes it all worthwhile.

How do you approach mentoring your students?
Communication is extremely important. We have group meetings where everybody presents what they did that week. That way, younger students see what the older students can accomplish in a week, and that motivates them. They also see how I, as someone who has been doing this for a long time, reacts to data when I see it for the first time – the kinds of questions I ask, the critical thinking involved. The older students, in turn, become good mentors themselves.

My philosophy has been to try to get most of my work done with graduate students rather than postdocs, whom I can mold into independent scientists – which is my primary goal. I've found that if I can get a graduate student up the learning curve quickly, by the time they're senior students, they're essentially working at the level of postdocs.

Do you still feel that sense of fun and excitement around discovery that you felt in Graham Cooks's lab?
Oh, absolutely. I really feel super privileged to have been a scientist during the period of my career. I really got started in the late '70s, and from then until now I've had way too much fun – more than I deserve, doing what I do. Discovering something, or realizing something new, is just a tremendous high. I feel it as much now as I ever did – maybe more.

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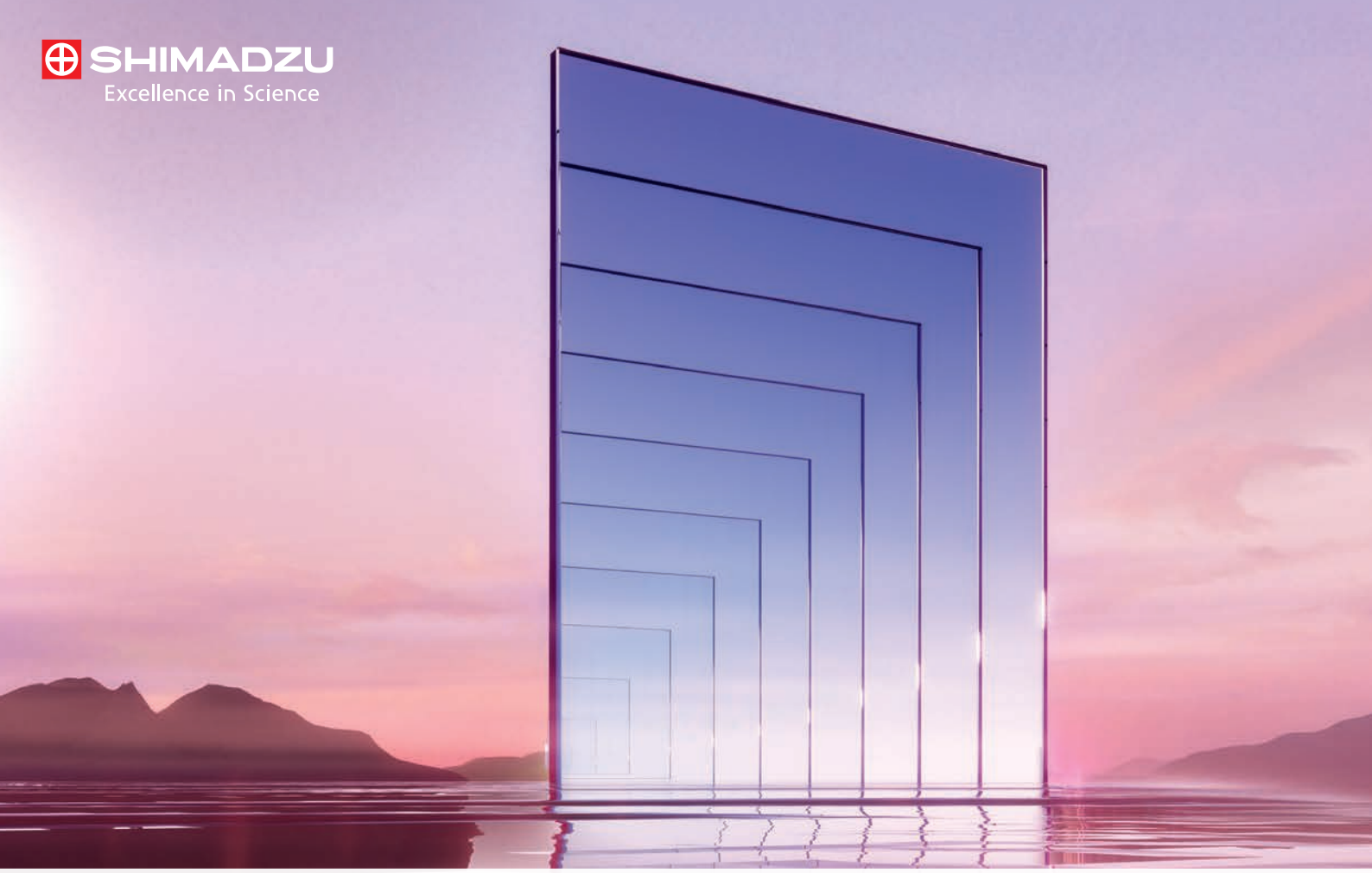

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