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Born Too Soon?

Why we are not "the middle children of history"

It isn't often an anonymous internet quote is remembered for more than a decade, but this one seems to have an enduring resonance: "We are the middle children of history. Born too late to explore earth, born too early to explore space."

How reports of eyeglasses, crocodiles, and paper money must have fascinated 13th-century readers of Marco Polo's Travels. And imagine finding out, like Columbus, that there's an entirely New World out there – full of new peoples and strange exotic beasts. It is interesting that, as Earth receded in size, our imaginations turned to extraterrestrial worlds – Francis Godwin's The Man in the Moone was published in 1638, for example. Once it became clear that the moon was devoid of life, sci-fi writers looked to the Red Planet in the late 1800s. Then, when, thanks to spectroscopy, scientists found the same was likely true of Mars, the space opera was born – featuring far more speculative and distant worlds.

"Born too soon" reflects a disconnect between what might be out there in the wider universe and the inadequacy of our current technology. But what if we don't need to voyage to far-away star systems to answer the big questions…

On page 16-29, meet the pioneers developing the tools and methods required to discover if there's anything hidden beneath the thick icy crust of oceanic moons like Europa, Titan, and Enceledus.

"I believe it's a short bet there is extraterrestrial life in our solar system," says NASA scientist Desmond Kaplan on page 29. "It's just a matter of whether we'll discover it in our lifetime or not."

In fact, exploring new frontiers may simply be a question of knowing where – and more importantly, how – to look. As Adam Hollerbach puts it on page 34: "We still only know the complete chemical structure of around 5 percent of all the molecules we believe to exist. This number is staggeringly low and needs improving." Hollerbach has combined SLIM with Orbitrap mass spectrometry to tackle the problem. His early findings are exciting, but further work is needed – and Hollerbach believes new computational technologies could play a crucial role.

Speaking of which, I will leave you with a twist on the classic quote from Open AI Founder Sam Altman that went viral earlier this month on Twitter/X: "Born too late to explore the earth, born… at the absolute coolest time in history, about to be able to explore absolutely everything else. The scientific discoveries of the coming few decades will be breathtaking."

James Strachan
Editor

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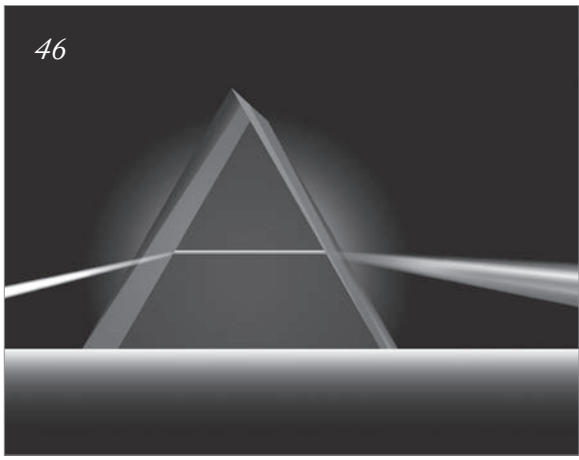

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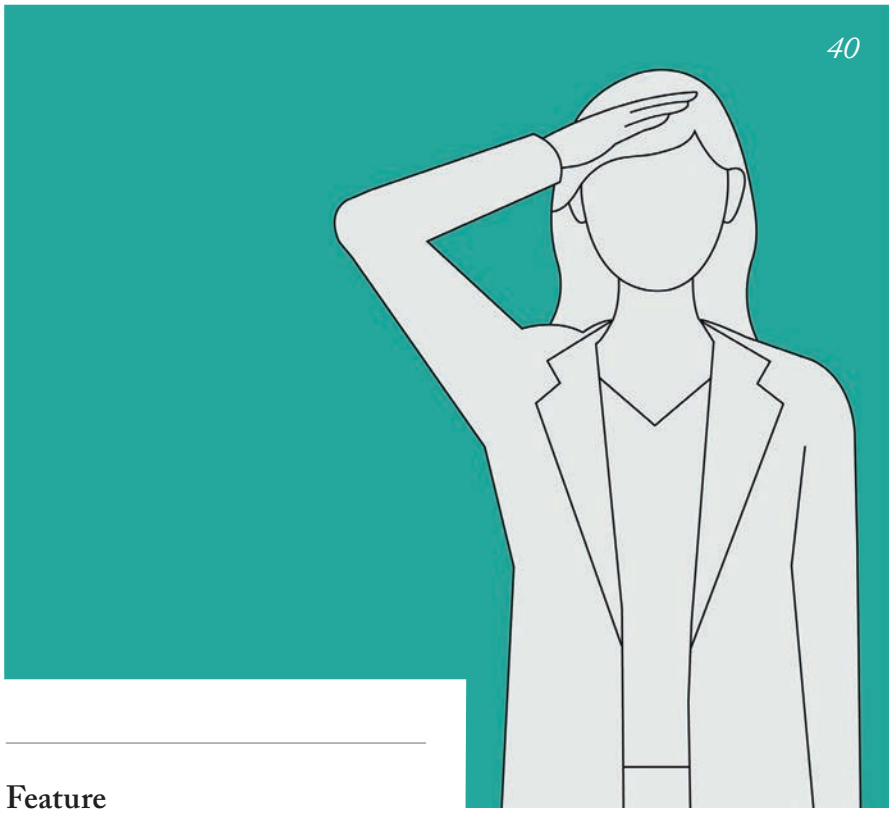

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the Analytical Scientist

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A Lollipop a Day...

How a sweet-looking saliva collection system could replace traditional throat swabs

At-home testing became a necessary and routine aspect of the COVID-19 pandemic, but many people – especially children – experience discomfort and difficulty performing these tests. And let's face it, no one likes swabbing the back of their own throat. Now, researchers from The University of Washington have developed a more enticing saliva sampling device, called CandyCollect, which is similar to a lollipop (1).

"As parents, we struggled getting our children to cooperate with sample collections or medical procedures in general," says corresponding author Ashleigh B. Theberge. "We also know that most children like lollipops, so instead of fighting their nature, we leverage a lollipop design to encourage children's compliance."

CandyCollect is a device made from sugar-free candy (isomalt) and a plastic structure, replicating the appearance of a lollipop. The researchers incorporated a spiral groove into the plastic stick to allow accumulation of microorganisms, like *Streptococcus mutans* and *Staphylococcus aureus*, a feature simultaneously preventing scraping by the tongue.

When compared with regular commercial oral swabs, the candy collection kit successfully and efficiently detected the target bacteria in 100 percent of the participants who previously tested positive on the conventional swabs. "The eluting solution has to remove most of the captured pathogens off the CandyCollect while minimally interfering with the qPCR sample processing. We tested several elution solutions and selected carefully until we achieved our goals," says Sanitta Thongpang – another corresponding author on the study.

The study participants were asked about their preferences for different sampling devices and methods; 87 percent said it was the "least disgusting and uncomfortable."

"These results demonstrate that CandyCollect – as a saliva collection device that is simple to fabricate, easy to use, and sufficiently sensitive for the detection of common respiratory diseases – has great potential for at-home or clinic saliva collection in humans, especially in children," says Thongpang, adding that easy access to diagnosis plus early treatment can reduce disease severity and complications.

What's more, say the researchers, at-home and patient-centric diagnosis using remote collection systems like CandyCollect could facilitate decentralized clinical trials in the pharmaceutical industry.

Reference

1. *WC Tu et al., ACS Publications, 95, 27 (2023). DOI: doi.org/10.1021/acs.analchem.3c00462.*

INFOGRAPHIC

Rising Retractions

What proportion of chemistry paper retractions over the past 20 years are due to misconduct?

Source: Y Sevryugina and R Jimenez, ACS Omega (2023).

Retraction in time:

The number of retractions has increased by **20%** since **1980**.

37% of manuscripts were retracted within a year.

The median retraction time during this period is **1.7 years**.

Fraud related manuscripts held the shortest peer-review time with an average of **43 days**.

BUSINESS IN BRIEF

A roundup of this month's business news – from partnerships to product launches, including a new in-line spectrometer for bioprocess control

- **908 Devices** has launched a Raman spectroscopy-based handheld device – Maverick – for in-line, real-time bioprocess monitoring and control. Maverick's de novo models automatically process Raman spectra data to direct process control actions, while the hub can monitor up to six bioreactor modules simultaneously, with independent analog/digital control of feed systems for each.
- **Leica Microsystems** has partnered with the Department of Biochemistry at The **University of Oxford** to launch a new Centre of Excellence for cutting-edge microscopy. The Centre, which will be hosted by Oxford's Micron Bioimaging Facility, will provide a place for experts to share knowledge through workshops and seminars. "We aim to accelerate scientific discoveries and inspire the next generation of scientists," said Darin Stell, Senior VP Global Commercial Operations at Leica Microsystems in the press release.
- **Shimadzu** has released a new gas chromatography instrument, the Brevis GC-2050. The 2050 uses the same techniques for sample injection and detection and gas control as its predecessor, the 2030, but in a smaller package. The GC-2050 also allows users to simultaneously analyze two lines with standard capillary columns, and comes with a touchscreen display.
- **The Advanced Cell Therapy and Research Institute, Singapore** (ACTRIS) will install and operate **Agilent's** xCELLigence real-time cell analyzer and Seahorse XF technology in its largest cell and gene therapy bioprocessing facility, as part of a three-year collaboration.
- **Curio Bioscience** has announced Curio Seeker 10x10 – a high-resolution, whole transcriptome spatial mapping kit. The model enables tissue imaging up to one square centimeter by detection and mapping of RNA molecules using next-generation sequencers.

Saliva Sampling Reveals All

Quantifying THC in oral fluid by turning convention on its head

A simple but effective workflow for reliable quantification of THC and its metabolites in oral fluid samples has been developed by researchers from the Institute of Legal Medicine of the Medical University Innsbruck, Austria (1).

The team took an unconventional approach, extracting the cannabinoids from the solid pellet produced by centrifugation ahead of liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis. "We demonstrated that processing of the pellet represents a valuable alternative for cannabinoid quantification in oral fluid," says lead author Herbert Oberacher.

When comparing these results to those from typical blood analysis, individuals with THC present in their blood were identified with an accuracy of 97.9 percent.

But there is a slight saliva snag. Unfortunately, the Greiner Bio-One Saliva Collection System (GBO SCS) – used to rinse the oral cavity and collect the samples – has since been discontinued…

Reference

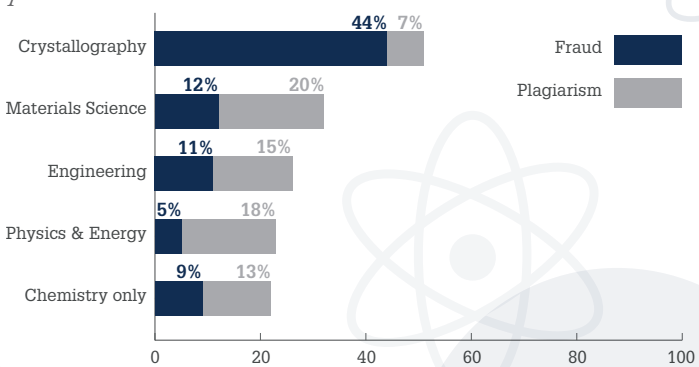
1. *V Reinstadler et al., PubMed (2023). DOI: 10.1002/bmc.5651.*

Reasons for retractions:

- ✖ Misconduct: **58.5%**
  - Self-plagiarism: **40.5%**
  - Fraud: **36%**
- ✖ Errors unrelated to misconduct: **26.2%**
- ✖ Reason unclear: **3.9%**
- ✖ Organization issues: **0.9%**

Interdisciplinary manuscripts:

81 percent of manuscripts were interdisciplinary with additional subjects. The fields with the highest proportion of misconduct-related retractions are as follows:



Credit: Images sourced from Unsplash.com

Saving the Dollar

How a unique combination of microscopic and spectroscopic techniques unveiled Benjamin Franklin's innovative approach to printing paper money

Benjamin Franklin was a statesman, scientist, and inventor – best known for creating bifocals and the lightning rod. But Franklin also printed nearly 2,500,000 banknotes for the American Colonies using what scientists have now found to be innovative and original techniques to prevent counterfeiting (1).

Researchers from the University of Notre Dame's Nuclear Science Lab analyzed approximately 600 notes made by Franklin during the 18th century, using a combination of high-resolution transmission electron microscopy (TEM), Raman and electron energy loss spectroscopy, as well as other non destructive and micro-destructive methods.

The team found that Franklin implemented sophisticated features – such as natural graphite pigments, colored fibers, translucent muscovite fillers, and his own unique designs of "nature-printed" patterns and paper watermarks – that could be used to distinguish original from counterfeit notes. "These features and inventions made early American paper currency an archetype for developing paper money for centuries to come," says first author Khachatur Manukyan.

Manukyan and his colleagues collaborated with chemists and historians to ensure the historical specimens remained intact. "There is always a challenge working with museum objects; due to the historic and artistic value of these objects, we face multiple technical difficulties to analyze them," says Manukyan. "We developed new imaging procedures to reduce electron irradiation damage – providing us with the best signal-to-noise ratio by combining several innovative imaging techniques. By monitoring and measuring the electron dose and incorporating additional images, we were able to achieve the necessary resolution for imaging light elements such as oxygen, aluminum, and silicon in low-dose conditions. This has allowed us to capture important information without damaging the tiny specimens."

The team's approach could aid other researchers working across a number of disciplines, according to Manukyan: "The new methods and procedures developed here could be used in art conservation, preservation sciences, and the investigation of other sensitive materials."

Reference

1. *K Manukyan et al., PNAS, 120, 30 (2023). DOI: 10.1073/pnas.230185612.*

Biomonitoring Goes Global

"Game-changing" approach for ecosystem surveillance has been right under our noses – and could open the door to global biodiversity monitoring

UK and Canadian scientists have unearthed a trove of biodiversity data – over 180 representative taxa of flora and fauna – after extracting and sequencing airborne environmental DNA (eDNA), collected from air pollution sensors that can now double as biodiversity monitors.

"These machines have been collecting these samples for decades, despite us only just finding it! It's a ready-made source of information that could prove invaluable for measuring biodiversity at continental scales," says co-author Elizabeth Clare, York University, Canada.

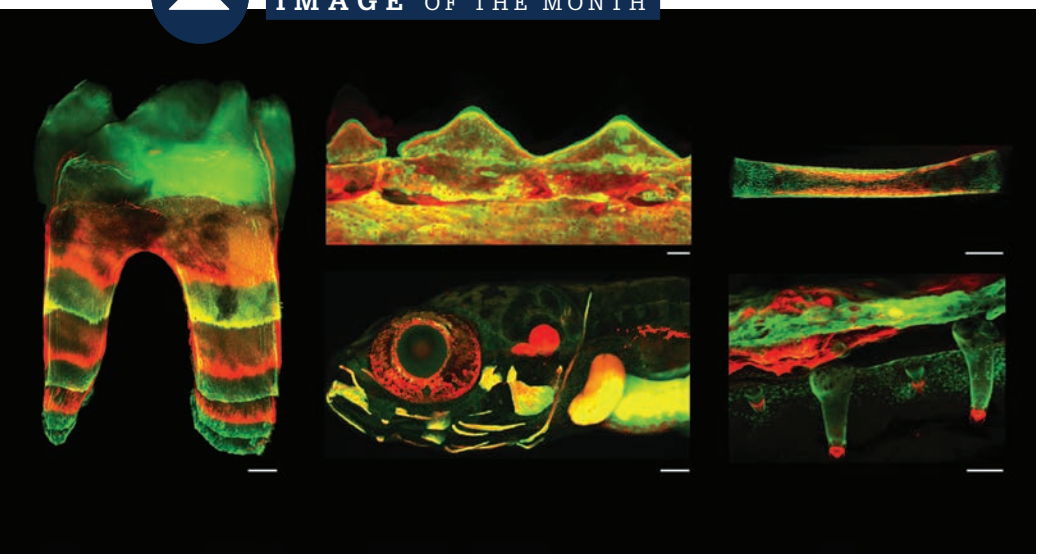
With little modification, they could be repurposed to scale up eDNA sequencing for large scale networks. "This idea is game changing for monitoring national, continental, or even global biodiversity," says Clare. "In a time where our climate, environment, and biodiversity loss is rapidly changing, such measurements could prove fundamental."

Reference

1. *J E Littlefair et al., Curr Biol, 5, 33 (2023). DOI: 10.1016/j.cub.2023.04.036.*

Credit: National Physical Laboratory, taken by Local Site Operator

IMAGE OF THE MONTH



Simply the BEE-ST

An international team of researchers have developed a technique for monitoring the development, growth, healing, and remodeling of calcified hard tissue in teeth and bones. Based on fluorescence, the Bones and Teeth Spatio-Temporal growth monitoring (BEE-ST) system allows scientists, for the first time, to observe and follow the dynamic processes in teeth and bone development in space and time – opening opportunities within developmental biology, bone healing, tissue engineering, and disease modeling across species.

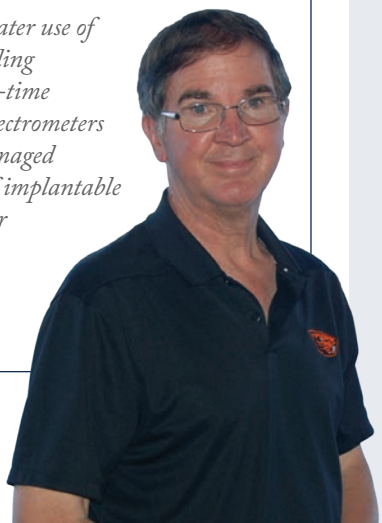
Credit: MG Lopez et al., SciAdv (2023)

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

QUOTE OF THE MONTH

"With this new era of medical mass spec, I envision greater use of MS in identifying risks for disease, diagnosis, and guiding treatment. Miniature devices will be employed for real-time disease diagnostics in clinics. During surgeries, mass spectrometers will become routine tools for identifying diseased or damaged tissue. There is also the potential for the development of implantable mass spectrometers – similar to pacemakers – to monitor therapeutic drug levels."

Richard van Breemen. See page 35.



Deadly Burn Biomarkers

Researchers use MS-based proteomics to identify three key proteins associated with mortality rates after life-threatening burns

Burns can cause severe circulatory, immune, metabolic, and coagulation problems – and can be deadly. However, the details behind many of these mechanisms are still unclear.

By applying an MS-based proteomics approach to the plasma of 10 healthy volunteers and 83 burn patients – 15 of which died within a 28-day period – researchers from Osaka University, Japan, were able to identify 10 proteins that were linked to mortality after statistical analysis (1).

HBA1, TTR, and SERPINF2 showed the highest association with mortality; patients with the highest mortality had higher levels of HBA1 (associated with hemolysis) and lower levels of TTR (an indicator of protein breakdown) and SERPINF2 (associated with blood clotting).

"These three proteins can function as important prognostic biomarkers for burn patients," said lead author Shinya Onishi (2).

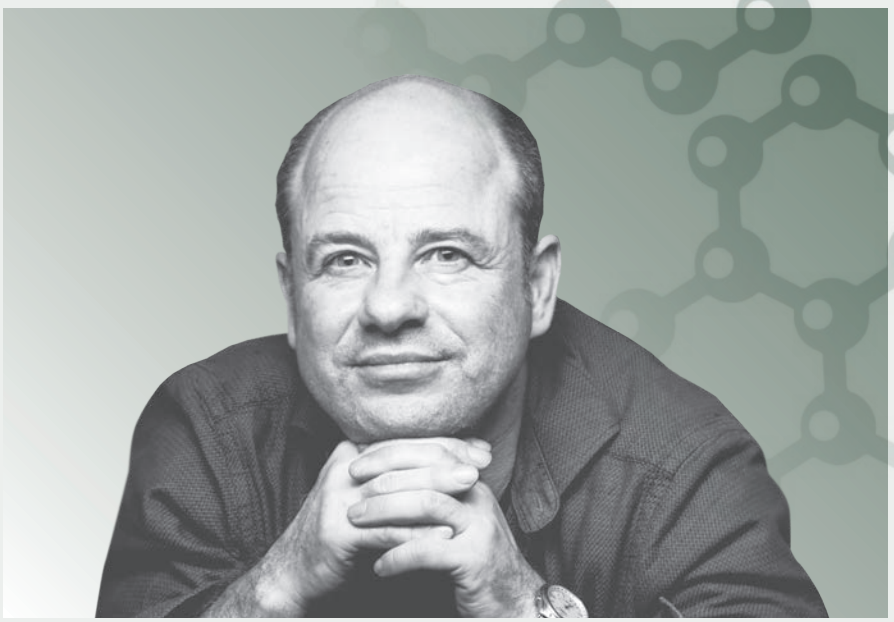
References available online

Credit: Bandaged hand by Guitarfoto from Shutterstock.com, adapted In House

Breaking Down the Complex Characterization Barrier

Polymeric drug delivery systems have enormous potential for personalized medicine, but their complexity and heterogeneity create real characterization challenges. Fortunately, there are analytical solutions available that enable developers to deliver – quite literally – for patients.

By Sam Dylan Moré



A drug's therapeutic potential depends on its bioavailability, which can be limited by low solubility, poor biodistribution, and rapid clearance from the body. Put simply, a drug must go where it's supposed to go and stay there long enough to elicit the desired effect.

Polymeric drug delivery systems use biocompatible polymers to enable targeted and controlled release of a wide range of encapsulated drugs. They can overcome or prevent passage through different biological barriers, reaching previously inaccessible sites to expand treatment options or reducing side effects – or both.

For the past 10 years, DendroPharm – the company I founded – has been developing novel nanomaterials for drug delivery systems. We produce them under GMP conditions for clinical trials and for customers. We have two main polymeric drug delivery systems. The first uses amphiphilic dendritic core-multishell-nanocarriers to deliver drugs through the skin. They have a polar core surrounded by an inner nonpolar shell, which, in turn, is in contact with a polar outer shell. This structure gives the nanocarrier its amphiphilic character, which allows the transport of both lipophilic and hydrophilic drugs through the skin. We have performed a pilot study using the nanocarriers for the treatment of feline hyperthyroidism, which found a 72 percent reduction in mortality in the first year – largely because delivery through the skin meant cats weren't vomiting the orally administered drugs (a common problem).

As well as facilitating passage through tissues, polymeric drug delivery systems can also prevent passage through biological barriers. DendroPharm has developed a second nanocarrier architecture that delivers opioid drugs intravenously or as depot to produce peripherical pain relief at inflamed tissues or tumors while, crucially, preventing passage through the blood-brain barrier, which reduces the chance of addiction and other side effects, such as nausea or constipation. We believe this system has real potential to help combat the opioid crisis.

These two examples illustrate how polymeric drug delivery systems allow for the development of more targeted, personalized treatments, reducing side effects and improving efficacy – even making certain previously unsafe treatments possible for patients. However, there is one key challenge that must be overcome: characterization.

Polymeric drug delivery systems are complex and exhibit size and structure heterogeneity related to variations in polymer composition, drug loading, and manufacturing processes. In short, it can be difficult to obtain a clear understanding of a given system's properties. Another critical factor for any drug delivery system is stability. Analyzing the stability of polymeric systems over time and under various conditions is challenging because changes in temperature, pH, and other environmental factors can lead to aggregation, precipitation, or degradation. Polymers and drug carriers can also undergo conformational changes in response to environmental conditions or interactions with biological molecules. These changes can affect drug release kinetics, biodistribution, and therapeutic efficacy – necessitating advanced techniques to monitor and understand them. Finally, accurately quantifying the amount of drug loaded within a polymeric carrier is crucial for determining the therapeutic dose. However, drug loading can be affected by factors such as solubility, compatibility with the polymer, and encapsulation efficiency – making quantification difficult.

This is why we partnered with Tosoh – a leading supplier of chromatography solutions for the purification and analysis of various macromolecules, including protein therapeutics and carriers such as AAVs or

VLPs – to address these characterization challenges. Doing so is essential to developing safe and effective drug delivery systems with predictable behavior and desired therapeutic outcomes; not least because this is what is demanded by regulatory agencies. Regulators want to see validated GMP-style synthesis of these novel excipients with smart quality control. Early-stage problems here can create bigger problems as drug-delivery developers attempt to scale up their systems. If boundaries and specifications are too narrow, it can create economic problems; if they are too wide, it can result in drug safety problems. Getting this window right is crucial to the success of the product.

The SEC-MALS solution

The gold-standard technique for polymeric drug delivery systems characterization is size exclusion chromatography (SEC) – a powerful technique that can separate and characterize macromolecules based on their size in solution. When coupled with advanced detectors, such as those based on multi-angle light scattering (MALS), SEC becomes even more valuable for characterizing complex polymeric drug delivery systems.

For example, MALS helps improve measurement accuracy by providing true molecular weight determination without relying on calibration standards; notably, molecular weight directly influences important properties, such as drug loading capacity, release rate, and stability. In addition, polymeric drug delivery systems often involve complex architectures, such as copolymers, block copolymers, and polymer conjugates, which can influence drug encapsulation, release, and interactions with biological systems. SEC-MALS provides insights into the molecular weight and size of different segments within the polymer, helping us understand the distribution of these segments and their impact on the overall behavior of the system.

SEC-MALS can also monitor changes in molecular weight and size distribution during stability studies, helping identify aggregation or degradation of the carrier system (which can affect performance and safety). And when developing different formulations of polymeric drug delivery systems, SEC-MALS can be used for comparative analysis to understand the impact of variations in polymer composition or processing conditions on the resulting system's size, molecular weight, and conformation. SEC-MALS can also serve as a valuable tool for quality control and process optimization during the development and production of polymeric drug delivery systems. By monitoring the size and molecular weight parameters, manufacturers can ensure consistent product performance and characteristics.

All in all, SEC coupled with MALS detectors enhances the characterization of polymeric drug delivery systems by providing accurate molecular weight determination, revealing complex structures, offering insights into conformational changes, and enabling comprehensive analysis of interactions and stability. This information is crucial for designing effective and safe drug delivery systems with desired properties.

In addition to SEC instrumentation, columns, and a MALS detector, Tosoh also recently introduced a viscometer, which measures the intrinsic viscosity of the polymer in solution. Intrinsic viscosity actually reflects the inverse of density; a polymer with an extended shape or low density in solution will show a higher intrinsic viscosity than a polymer with a compact structure or high density.

Combining light scattering (MALS) and viscometry provides a straightforward solution to complement standard refractometry detection systems to get the full picture of polymeric drug delivery systems. This triple-detection SEC approach reveals the structure, shape or conformation of polymers in solution, which may affect drug release kinetics and interactions with target sites.

In short, such advanced systems are vital for ensuring our nanomaterials are properly characterized. But DendroPharm isn't just a developer of new polymeric drug delivery systems. We also synthesize tailor-made nanocarriers, analyze and characterize compounds for clients, as well as offering other formulation development and contract manufacturing services. So we also see value in using the latest analytical methods – such as Tosoh's SEC-MALS solutions – to enhance our characterization capabilities for our customers.

I'm passionate about the potential of polymeric drug delivery systems to improve the efficacy of therapeutic drugs while also reducing potential side effects – enabling new personalized treatments for patients. At the same time, we all recognize that quality control – though challenging from an analytical point of view and heavily scrutinized by regulators – is vital to ensure patient safety and drug efficacy. Fortunately, there are solutions available to tackle those challenges and deliver – quite literally – for patients.

Sam Dylan Moré is Founder and CEO of DendroPharm

In My View

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

Bottleneck No Longer

It's time we really recognize sample preparation's crucial role as the cornerstone of analytical method development

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

Credit: Yannis Tsoyfidis

A quick literature search for articles introducing new sample preparation approaches, discussing the greenness of a method, or comparing methodologies will show that authors often refer to the sample preparation step as the "bottleneck" in chemical analysis – myself included. I penned an In My View article in 2017 (1) with the subtitle question: "Is sample preparation still the bottleneck of analytical chemistry?"

Six years later, it's time for a rethink. We must confront sample preparation from a different angle – not as an obstacle to analytical performance, but instead as a cornerstone – the solid foundation on which a good analytical method is constructed. The accuracy, precision, limits of detection and quantification, linearity, selectivity, robustness/ruggedness, stability, and applicability of any analytical method relies on good sample preparation. The reliability of the analytical results provided by any analytical laboratory is eventually based on the sample preparation used. It isn't simply an inconvenient stepping stone – a bottleneck – before the real work is done.

Samples should be handled with respect to their qualitative and quantitative consistency in such a way that results reflect the initial composition. There are various complex and tricky matrices, including food samples (of plant or animal origin), biological fluids, (bio)pharmaceuticals, environmental samples and so on, that must be analyzed – and each category has its own special features and poses its own challenges.

All challenges regarding matrix components, interferences, variety of target analytes, legislative criteria, presence in trace levels, variety of subsequent analytical approaches can be met using the sample preparation weapons in our arsenal. We can choose from traditional and/or modern extraction and microextraction techniques, solvent based or sorbent based, ultrasound or microwave assisted, in situ or in vivo approaches, fabric phase or paper-based sorptive extraction, selective materials and nanomaterials, molecularly imprinted polymers, metal organic frameworks, new extraction solvents

"I recognize that, by failing to prepare, we are preparing for 'method development' failure. And the only way not to fail? Using appropriate sample preparation in the most efficient way."

(ionic liquids), (natural) deep eutectic solvents, automated or hyphenated systems combining the benefits of two technologies, two dimensional analyses… The list goes on. But we're definitely moving in the same direction – providing reliable results in a fast and simple way, while also minimizing the negative effects to the environment and ensuring user safety (2).

Modern analytical methods must take into account the need for sustainability, greenness, practicality, and speed in providing the results without – or at least minimally – compromising performance. And there are many assessment tools able to evaluate a method's compliance with green analytical chemistry and green sample preparation demands to assist in selecting the most efficient and green(ist) approach (3–7).

I believe all analytical chemists should reconsider sample preparation and approach this crucial step from a different mindset – not as the tedious, error prone, difficult, time-consuming step, but as the cornerstone of a green and stable foundation.

My answer to the question I posed in 2017 was along the lines of: "Yes, the sample preparation step is still the bottleneck in chemical analysis, but we have many tools in our hands to make it easier and more efficient." I concluded with a Benjamin Franklin quote: *"By failing to prepare, we are preparing to fail."* Now, I recognize that, by failing to prepare, we are preparing for "method development" failure. And the only way not to fail? Using appropriate sample preparation in the most efficient way.

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The Analytical Lab of 2050: Data Management

How technology and data trends will shape the analytical lab of the future

By Gary Grecsek, Vice President/General Manager, PerkinElmer, OneSource

Many of today's labs are at an exciting inflection point as they move closer toward being a digital lab of the future. Some labs are just starting to embark on the journey, while others are making solid progress, making the most of intuitive technologies and instruments, streamlined workflows, automation, cloud-based informatics, and remote tools/resources.

This digital framework provides the volume and type of data needed to accelerate research and innovation. Converting this data and corresponding threads into true data-driven insights is more complex. In fact, laboratory leaders may have to change many of the ways their teams work with data, services, and strategic partners. Lab leaders will also have to shift the necessary skills of their laboratory personnel in order to support the digital framework.

Everyone seems to have a different opinion of what the lab of the future really means. My colleagues and I focus on three basic industry needs: simplification, optimization, and transformation. As labs across all sectors become increasingly complex, these three factors become central to increasing lab productivity and adding value.

During my 30 years in science and lab technology, I've seen firsthand how labs have evolved. In the early stages of my career, my focus was largely on instrumentation portfolios. I was able to appreciate how labs were using their instruments alone to handle increasingly complex scientific needs. However, about 15 years ago when I turned my focus to laboratory services, I saw firsthand the need for laboratories to change, with the core driver being to increase lab productivity. Today the industry has the additional challenge of generating such complex and large data that it now needs new data management approaches along with additional lab support and services.

Historically, service providers have mainly offered product-attached service

models (with an emphasis on selling products with services tied in). Though these models can support some elements of a lab's goals and help return precious time by off-loading support demands from scientists, labs can benefit from using a broader lens to think about the outcomes they really need the lab of the future to deliver.

Here, I present a few points that can help labs step into a digital future with more confidence.

First, you need to move away from the "break and fix" lab services mentality. A more holistic, vendor- and technology-agnostic partner can help address everything from IT and data management to scientific method development, and from workflow streamlining to regulatory compliance. It's also important to remember that digital transformation is, at its heart, a classic exercise in change management, which means that services should support and promote change in the lab by building a comprehensive roadmap.

Second, you need to set realistic expectations. Everybody wants to go from 0 to 100 in one jump, but that's rarely (if ever) possible. Labs should visualize where they want to be in the "long term" – a concept that in and of itself has changed in terms of timeline. A three-year horizon, for example, allows labs to strategically plan ahead but also navigate the fast-changing nature of digital technology. Use your broader vision as a guide but begin with small projects that can be used strategically to build momentum within the organization. Small wins in one lab or one building can and should lead to bigger wins.

Third, you need to think about identifying, standardizing and visualizing data. What are the various data threads within your digital lab that improve overall productivity? What best practices could be put in place to maintain and curate the data to support more data-driven decision making? Once you are able answer these questions, the real test and change management becomes: is your company prepared to act on what your data tells you?

"Building a comprehensive, yet agile data management and process strategy that reflects this rigorous pace is a chance to ensure you're moving forward with intent rather than being hampered by excessively long plans that don't consider unforeseen changes."

Post-COVID, we have found labs are much more receptive to digital technologies – so transformation is happening at a much faster rate, particularly around remote support and connected systems. Building a comprehensive, yet agile data management and process strategy that reflects this rigorous pace is a chance to ensure you're moving forward with intent rather than being hampered by excessively long plans that don't consider unforeseen changes. It also allows lab managers and scientists to consider how to best access and share data and how it can be used to unlock opportunities. One point to also consider in this regard – don't let perfection get in the way of good.

What's so exciting about analytical science is that the only real constant is change and evolution- in our processes, in our technologies, and in our insights and discoveries. The lab of today is very different from what it was at the beginning of my career and is very different from what it will look like in 2050.

As we look to the future, we will see labs increasingly adopt more and better automation, miniaturization, mobility and deeper use of AI and ML – all of which will only continue to accelerate. As we move ahead, labs may have more collaboration rooms than bench spaces where local and global R&D teams continually make real time, data-driven decisions. In the future, scientific instruments could fit on a single desktop that once filled entire rooms where all technologies naturally "talk" to one another with integrated operational and scientific data streams. Scientists and lab managers could run experiments and operations on smart devices from anywhere, anytime. This vision is becoming a reality faster and faster.

The unwavering constant, now and in the future though will be data and data-driven decision making will represent an unwavering constant! Smart data approaches and strategic services can act as a north star, helping steer your lab to the innovations, approaches, and skills that will help propel your science to reach new heights.

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FLY ME *to the* MOON(S)

We speak with five scientists developing the tools and methods required to make crucial measurements in far from ideal conditions

By Jessica Allerton

Humans ask questions and take risks to find answers – from playing with fire to deep sea exploration. Even before our species' first mission outside of Earth's atmosphere, we've wondered if there are others like us elsewhere in the universe – perhaps even within our own solar system. Such questions were once reserved for the pages of science fiction novels, but thanks to remarkable analytical advances in recent years, we may be at the precipice of huge discoveries.

Mars, our closest planetary neighbor, may have been habitable many millions of years ago; but scientists now believe that liquid water could be hiding beneath the surface of several moons further afield (including Europa, Titan, and Enceledus). Could there be anything else hidden beneath the thick icy crust of these oceanic worlds?

To find out, several missions have been launched into space to take samples of the outer atmosphere of these moons, providing tantalizing chemical hints of what lies beneath. At the core of these missions is analytical science – with mass spec in particular paving the way – and, of course, analytical scientists.

Why not meet them?

MASS SPEC TAKES TITAN BY STORM

NASA Astrobiologist Melissa Trainer discusses the DraMS mission to Titan – and the likelihood of finding extraterrestrial life on moons

How did you end up working in this field?

I was a chemistry major in my undergraduate studies and gravitated towards instrumentation and designing experiments. By the time I reached my PhD, I was drawn in by atmospheric chemistry – specifically the types of measurements you can make and how analytical techniques help. I started my studies thinking about Earth's atmosphere, but I happened to be working at the University of Colorado during the time it was partnered with the NASA Astrobiology Institute, which was exploring the multidisciplinary aspects of astrobiology. Being around these different studies and disciplines in the lab piqued my interest in Titan – Saturn's largest moon – and the potential similarities with ancient environments on Earth.

This led me to where I am today: the Goddard Space Flight Centre at NASA, designing instruments to send to planets within our solar system to learn more about habitability, prebiotic chemistry, and the potential of extraterrestrial life.

Which moons do you think are the most likely candidates for extraterrestrial life in our solar system?

The first thing we need to establish when looking for extraterrestrial life is habitable environments that can sustain living organisms. For example, there is a lot of focus currently on ocean worlds – planets within our solar system that have a subsurface ocean may seem inhospitable on the surface, but the surface boundary could have properties that are able to sustain life. With moons like Europa, there's high radiation hitting the surface alongside a thick, cold ice crust. However, underneath this crust is an ocean that's interacting with interior core rock. This rock water ice boundary could be a steady habitat for life. There are other locations that could sustain properties for life, but we're just breaching the precipice of possibilities for scanning the solar system for extraterrestrial life.

How do we currently look for extraterrestrial life – and are there any analytical challenges preventing progress?

Many people in the community think it's really important to have imaging that allows us to observe and estimate motility. We need to think about how we're interacting with the environment, whether we can sense chemical gradients, the possibility of using molecular measurements to find DNA in a sample, and so on.

To conduct so many different variations of analysis, we need to ensure the design of our system can handle the payload without collecting false positive data. The engineering challenges for these projects are complex – we need systems that can take detailed measurements with intricate images. Though this requires incredible power, there also needs to be a sterilizing system to ensure samples aren't contaminated or degrade past the point of usefulness. There's an incredible number of aspects to think about, and that's where I see a lot of our analytical challenges culminating.

"WE'RE JUST BREACHING THE PRECIPICE OF POSSIBILITIES FOR SCANNING THE SOLAR SYSTEM FOR EXTRATERRESTRIAL LIFE."

Could you give us an overview of some of the analytical technologies employed in this line of research?

Mass spectrometry continues to play an important role in these investigations. Because it's a generalized technique, you're able to look at the chemical content of an environment, look at potential molecular bio signatures, and explore the proteins and DNA of a cell.

There's also plenty of uses for microscopy in this field. As a visual society, we find it easier to use the analogy of seeing is believing – viewing the minute details provides an important contribution to this study of life. Through microscopy we can also use powerful selective analysis for different types of biomarkers – using DNA sequencing as a complement to mass spec gives us the potential to zone in on specific polymers.

Credit: Melissa Trainer

Environmental sensors can also be useful for looking at gradients and potential interactions with the environment. Such sensors allow us to monitor the local area and learn how nutrients are moving in and out. I see this as an incredibly important part of the science, but the question is: how do we do this analytically? There are plenty of analytical techniques available, but these stand out as some of the most commonly used in current practices.

Tell me about Dragonfly…

Dragonfly is a mission to Titan – due to launch in 2027. It is a chemistry mission, as opposed to a life detection mission, which is a very important distinction. What we really want to look at is Titan's potential for prebiotic chemistry.

Dragonfly is a quadcopter that carries a robust scientific payload, including the Dragonfly Mass Spectrometer (DraMS). Onboard Dragonfly, DraMS can be moved from location to location across Titan's surface to investigate the different environments. And that allows us to sample organic sands that have formed dunes, and look at the chemical composition of the ice crust. We can also go to a place where there was an impact melt in the past. By drilling into these spots, we can see the composition of trace molecules dissolved in liquid water before it truly froze over – providing us with evidence of really advanced chemical synthesis.

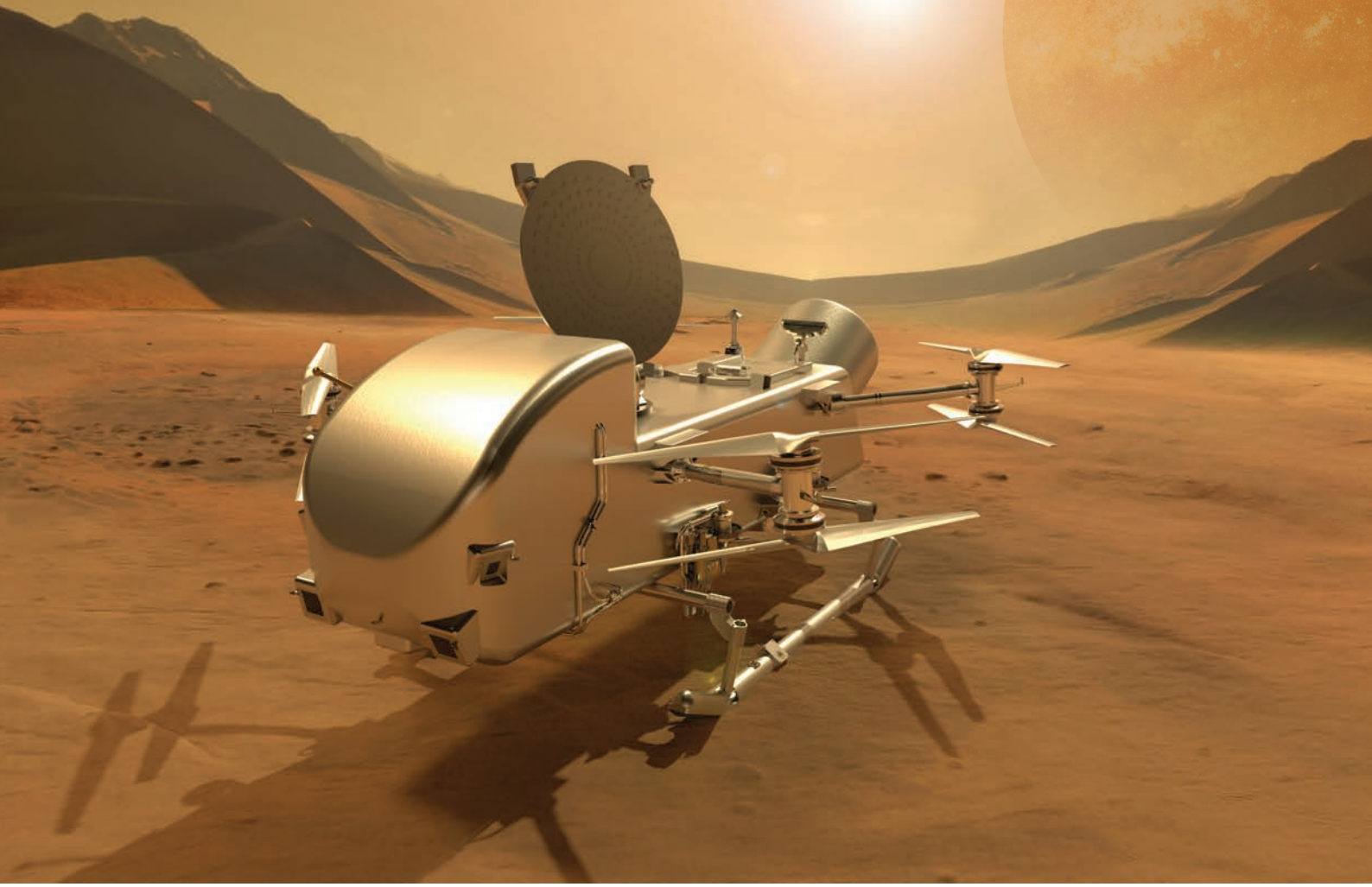
The system also uses a gamma ray spectrometer (GRS), which maps the chemical elements on the moon's surface. It measures how neutrons emitted by the spacecraft interact with different surface materials to determine the amounts and types of elements present.

Ultimately, we're hoping to understand what kind of molecules are present in an environment that has varying similarities and differences to what we understand is important in sustaining life on Earth.

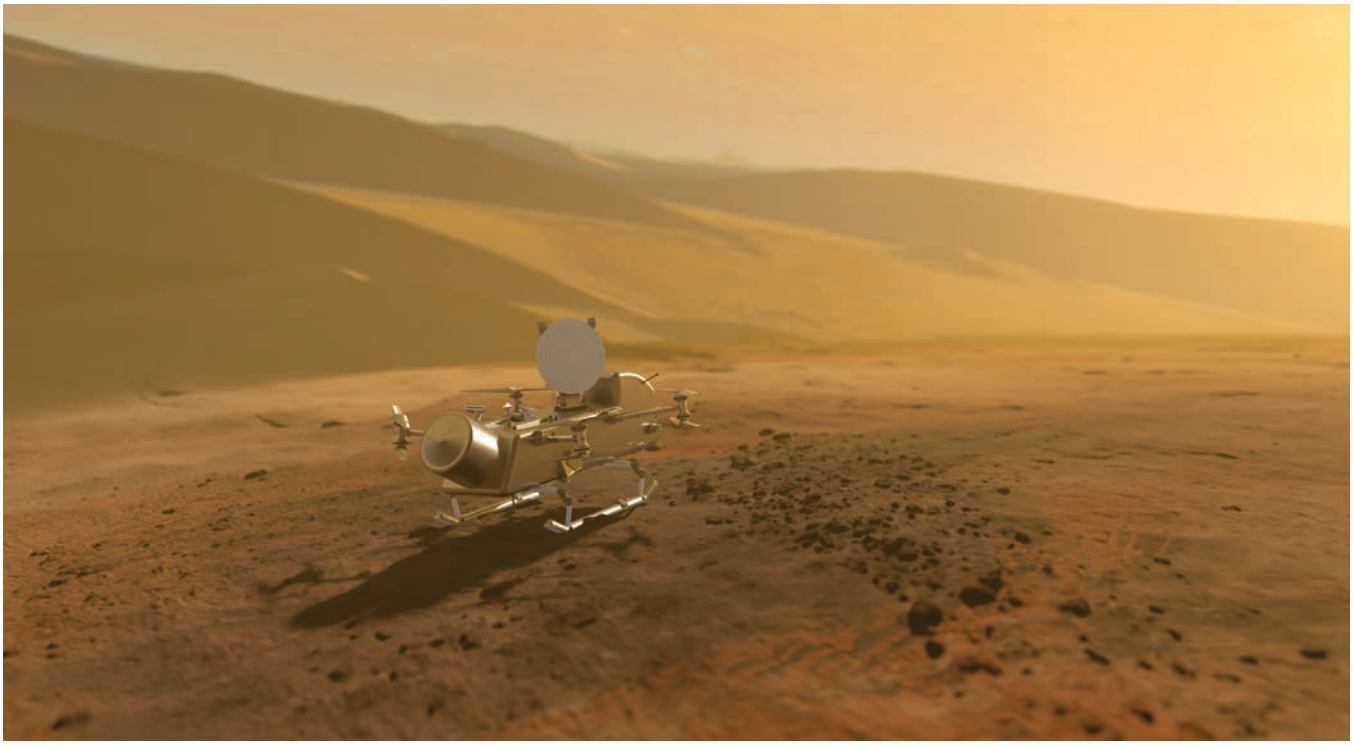
What challenges did you face while creating DraMS?

Working with Titan's thermal environment in particular presents various challenges. Titan's surface temperature is extremely cold at 94 Kelvin (-189 Degree Celsius) – most instruments and mechanisms won't function in this atmosphere. Because of this, we've added thick insulation around Dragonfly and used an MMRTG (multi-mission radioisotope thermoelectric generator) as the power source. This allows us to trap waste heat inside and circulate it to keep Dragonfly at an operating temperature. The MMRTG power source can also charge its battery on Titan's surface, allowing us to work here for multiple years.

Another issue with the atmosphere of Titan is in the process of taking samples. We have to be able to store different samples within Dragonfly in a way that doesn't alter their temperature



Credit: NASA/JOHNS HOPKINS APL/STEVE GRIBBEN



Credit: NASA/JOHNS HOPKINS APL/STEVE GRIBBEN

or integrity. By trying to keep Dragonfly warm, we could cause damage to samples taken from the surface. This meant we couldn't totally insulate the entire rover, so we've ended up with this medium stage that keeps the storage area cold even while being in close proximity to the power and heat source. Thermal management has definitely caused us some headaches.

Are there any similar missions planned for the future?

Next year, NASA is hoping to launch the Europa Clipper mission, which is a Jupiter orbiter that will complete flybys of Europa to learn more about the chemical environment – feeding our understanding of the likeliness of finding life in the moon's interior ocean. This will be a five-year project, and there will ultimately need to be further missions that allow us to land on Europa to sample the ice. But this is a long way into the future – we need more technological advancements to take these steps to get through the ice press and get into the ocean.

NASA's New Frontier proposals are coming up within the next few years, and I'm expecting some missions to be focused on Enceladus – another of Saturn's moons. Icy moons in general are extremely exciting locations for evidence of habitability and potential signs of life. We can also see some similarities between Enceladus and Europa – they both have active interior oceans – so in the future I expect several mission concepts for going through the water plumes of these moons and capturing fresh samples, or even landing on the surface.

Could you speak to the importance of collaboration in this line of work?

One thing I love about planetary science is how interdisciplinary it is. It's impossible to do what we're doing without having input from a large number of people across a range of disciplines – the DraMS project is a perfect example of this. There are those of us who are trained in chemistry, looking at the molecules within the planetary environment, physicists to figure out how we can get across the solar system to reach Titan, nuclear scientists to create the GRS instrumentation used within Dragonfly, thermal engineers to ensure the project survives in extreme temperatures, geologists and oceanographers to interpret observations from the spacecraft once they arrive at target destinations… I could go on and on.

What most excites you about working in this area?

Overcoming the challenges really excites me, even if this does make my job a lot harder. I could easily analyze a sample with an instrument by going down the hall in the lab – but doing this autonomously on a moon in space has all these weird environmental features that require a lot of problem solving and difficult choices.

I've spent years and years in the lab trying to guess what the organics on Titan are made of – and now we're going to be able to actually measure them. That's a huge breakthrough and I'm very excited about it. From seeing the images and measurements from the touchdown of Dragonfly on Titan, we're going to completely rewrite everything we thought we knew – and that's what makes planetary exploration so fun. We can design the most robust system, make lots of predictions and nice graphs, but we really have no idea what it'll be like until we get there. We want to be proven wrong because it's what makes discoveries all the more exciting.

Finally, if you were a betting person, how confident would you be putting money on extraterrestrial life in our solar system?

I would probably be comfortable placing a bet that there is life beyond Earth, but I don't think that I will be around to see it firsthand. As time goes on and technology improves, the odds increase. I don't think it will happen within my lifetime, but I would love to be proven wrong!

THE LAST STEPPING-STONES FOR SUSTAINING LIFE

The exciting discovery of phosphates originating from Enceladus – and what it means for the prospect of finding life elsewhere in the solar system

Evidence of all six bio-essential elements for life, including the elusive phosphorus, has been found on Saturn's moon Enceladus (1). We spoke to one of the researchers behind the discovery, Frank Postberg, Professor of Planetary Sciences at the Institute of Geological Sciences, Freie Universität in Berlin, about his work on the Cassini-Huygens mission and what their recent discoveries could mean for the prospect of discovering life elsewhere in the solar system.

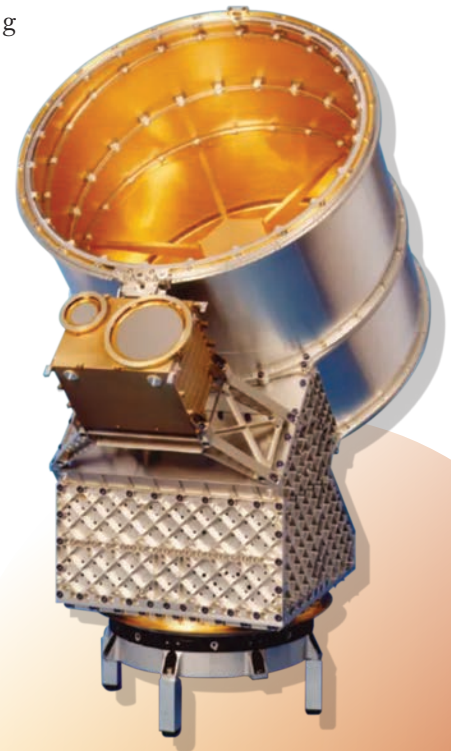
Where might we find extraterrestrial life in our solar system?

Within our solar system, there are a few places that have the potential to harbor life. As scientists, we must assess the probabilities, statistics, and conditions of these environments to learn how favorable they are for habitation. We only have Earth as a datapoint for the existence of life and, with a long timeline and high funding requirement to explore other planets, we must demonstrate a high probability of finding useful information before projects will even be considered.

We're already looking at the potential for life within samples of Mars – a planet that had very good conditions to develop and sustain life four billion years ago and may still hold evidence of such. However, research shows that the availability of both organic and inorganic carbon in the outer solar system is generally much higher than in the inner solar system, where Earth and Mars reside. Over the past 20 years, we've also discovered a number of subsurface oceans in the outer solar system – on moons and dwarf planets – some of which have a relatively strong chance of being able to sustain life.

What is the Cassini–Huygens mission?

Cassini-Huygens was launched in 1997 and has been orbiting Saturn from 2004 to 2017. The mission was a collaboration between NASA (who built most of the Cassini orbiter) and the European Space Agency (who built most of the Huygens probe). Planetary science by definition is multidisciplinary – and this mission is no exception. To go beyond Earth, we must also go beyond the horizon of our own perceived capabilities. Connecting insights from multiple instruments and multiple fields of expertise is the best route to exciting scientific discoveries with a space mission. It was an extremely rewarding experience for me to be part of the Cassini-Huygens team – it was such a vibrant and inspiring international scientific community.



The Cosmic Dust Analyzer (CDA) before it was mounted onto the Cassini spacecraft.
Credit: Frank Postberg

What were the main findings of this mission?

Since the mission's arrival at Saturn in 2004, there have been a series of discoveries that placed Enceladus higher on the potential habitability scale. This started with cryo volcanic eruptions shooting out into space through cracks in the moon's thick, icy crust – which, as we discovered later, concealed subsurface liquid water. Once we confirmed that Enceladus has a global subsurface ocean, we became even more interested in what this tiny moon has to offer. It was so unexpected for such a small moon to create enough energy to maintain a liquid ocean, and somehow, the surprises kept coming!

While flying past Enceladus, the Cosmic Dust Analyzer instrument on the spacecraft had the ability to analyze individual dust and ice grains emitted by Enceladus' cryovolcanic plume that hit the instrument at high velocities. These samples were then analyzed by time-of-flight mass spectrometry to reveal information about the subsurface ocean. Another instrument aboard the Cassini orbiter was the Ion and Neutral Mass Spectrometer (INMS) – a quadrupole mass spectrometer – designed to probe the composition of volatiles and analyze the gasses emitted by Enceladus. We found substances that gave information about the composition of the ocean and pointed towards hydrothermal activity at Enceladus' ocean floor. Being so far from the sun, Enceladus needs an alternative energy source, and these hydrothermal vent systems could allow ecosystems to utilize energy independently from sunlight.

The mission ended in 2017, and I applied for funding to form a research group that would allow us to identify and analyze the ice grains from Enceladus with greater precision. This funding also allowed us to better replicate the mass spectra from space with laboratory analogue experiments. After finding evidence for a rich and complex organic chemistry inside Enceladus' ocean in 2018 and 2019 (2,3), we were delighted and amazed to reveal the presence of sodium phosphates – which we published in June, 2023.

After detecting such a vast amount of phosphate (100 to 1000 times what is present in Earth's oceans), we connected with our partners in Tokyo, Japan, to use their sophisticated geochemical lab and stimulate the environment at the bottom of Enceladus' ocean. Cassini's measurements gave us a good idea of the composition (the salinity, a high amount of carbonates, pH values, and presence of ammonia) – strikingly different to Earth's ocean. To learn more, we used an Enceladus ocean simulant together with carbonaceous chondrite as an analogue of Enceladus' rocky material and we monitored how the chemical composition of the ocean simulant changes in this environment, until equilibrium is reached. We discovered that the high amount of carbonate and the high pH of about 10 in the ocean allows high concentrations of phosphates to dissolve from the rocky material.

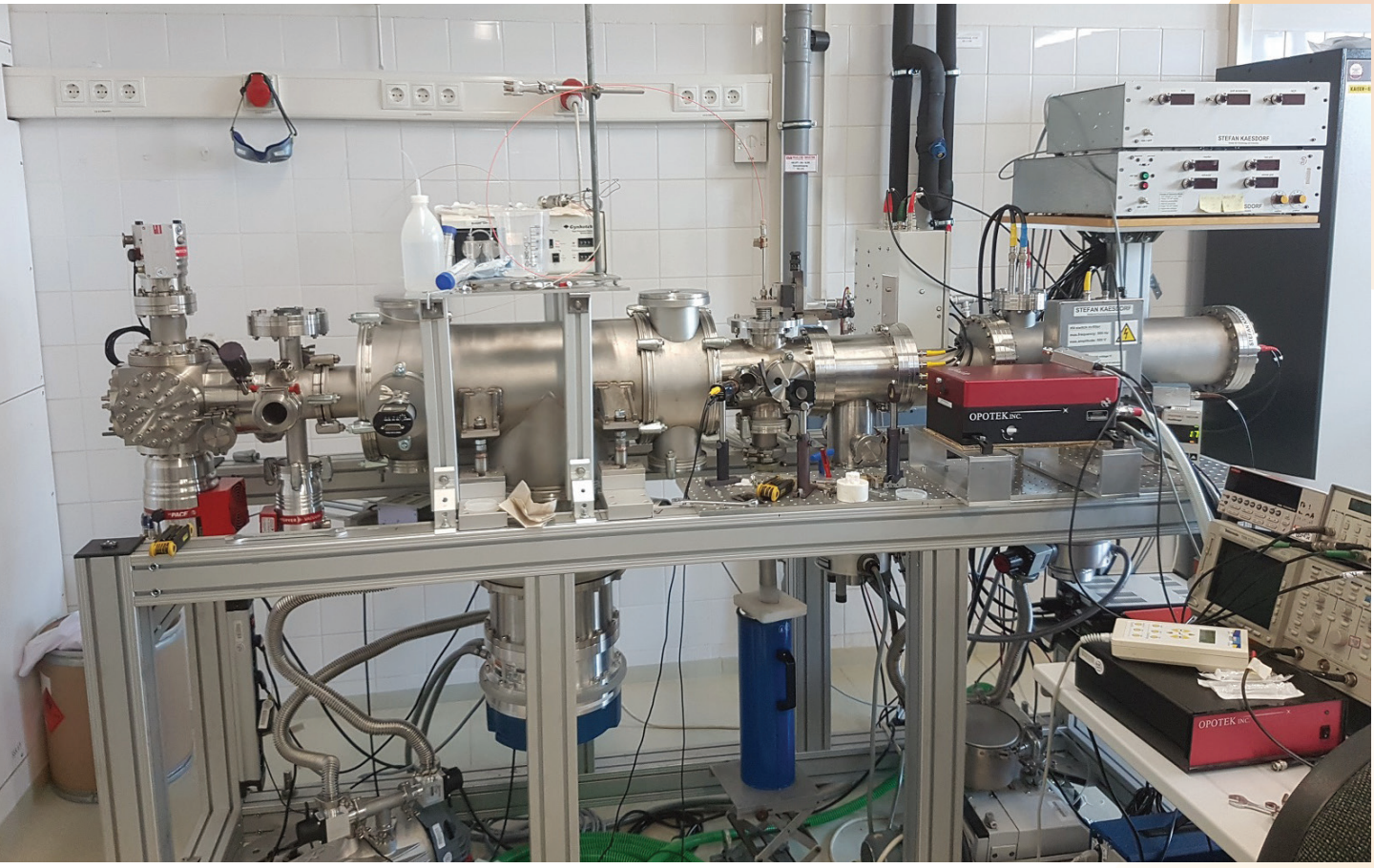
> "WE'RE SATISFIED THAT ENCELADUS HAS FAVORABLE CONDITIONS TO DEVELOP AND SUSTAIN LIFE."

Why is this discovery of phosphorus so important?

There are six bio-essential elements required for life to form (carbon, hydrogen, nitrogen, oxygen, sulfur, and phosphorus). Previous studies of Enceladus' water vapor and ice grains had shown definite or tentative evidence of five of these elements, but we were still missing one crucial element for life: phosphorus.

Often seen as a bottleneck for life, phosphorus is the rarest of cosmic abundances. It doesn't easily dissolve in water – further eliminating bioavailability – but it is essential for the creation of DNA and RNA, energy-carrying molecules, and cell membranes. A publication in 2018 based on geochemical modeling (4) predicted that phosphate and phosphorus levels on ocean moons such as Enceladus would be depleted much more than on Earth, which would drastically limit the prospect of life. Our findings suggest otherwise. And having, for the first time outside of Earth's atmosphere, found evidence for phosphorus in a liquid water environment, we're satisfied that Enceladus has favorable conditions to develop and sustain life.

Artist impression of the Cassini spacecraft traversing Enceldus' plume. *Credit: NASA/JPL*



The lab setup used to simulate the mass spectra from space. *Credit: Frank Postberg*

What's next for detecting life on moons – what are your hopes for the future?

From our research, we believe the conditions of this subsurface ocean are not unique to Enceladus – there could be a number of bodies that harbor oceans with high phosphate availability.

There are two missions coming up to the Jovian ocean moons. The ESA JUICE (JUpiter Icy Moons Explorer) mission is already on its way to take detailed observations of Jupiter and its three large ocean-bearing moons – Ganymede, Callisto, and Europa. In 2024, NASA will be sending the Europa Clipper to explore the habitability of this moon in more detail – which ranks close to Enceladus in terms of its potential for sustaining life.

From the Cassini-Huygens mission, we now know that complex organic chemistry is present on Enceladus, but we need another mission to see if this is an indication for life or prebiotic chemistry. We have the instrumentation ready to launch these "life finder missions," we just need to fund, assemble, and launch the spacecraft to Enceladus. However, this all takes time and it will probably be another 20 years before the next mission arrives there. Despite this, I'm quite optimistic that it will become reality in the near future – the possibilities of what we could find there are just so exciting.

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MASS SPEC IN SPACE

NASA scientists discuss the role of mass spectrometry in life detection within our solar system

There are many analytical techniques that contribute to the search for extraterrestrial life beyond Earth's atmosphere. But, according to Desmond Kaplan, Consultant Research and Development Scientist, Xiang Li, Research Scientist at Goddard, and Ryan Danell, MS Research Scientist, mass spectrometry is set to play a crucial role. We spoke with Kaplan, Li, and Danell to find out more.

How did you end up working in mass spec at NASA?

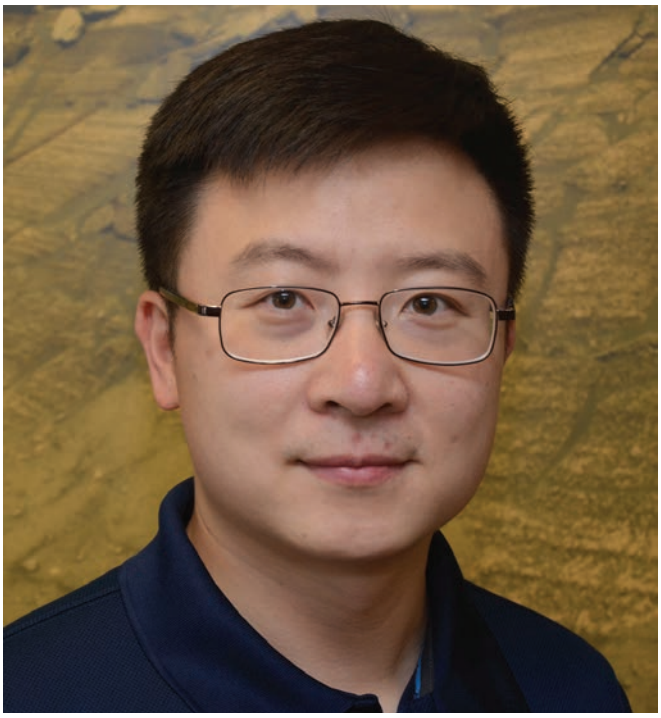
Desmond Kaplan: I grew up in Maryland spending a large portion of my childhood around the Goddard Space Flight Center at NASA and going to space camps. While I never envisioned myself working at Goddard, it just happened to be a natural evolution in my life. The golden age of space projects in the 1980s fascinated me greatly; from traveling to the moon, to watching ring structures form into biospheres – I couldn't keep my eyes off it!

From this, I went into analytical science and worked in industry getting involved with mass spectrometry and instrument development. An opportunity presented itself to work on mass spec for spaceflight missions, which I enthusiastically accepted. Since being at Goddard, I've been a part of some really exciting missions, hoping to discover life in a frozen world – seeing if a biological environment could exist in the ocean beneath the thick ice crust on Europa or Enceladus.

Xiang Li: My PhD in experimental physical chemistry was focused on mass spec. I focused on instrumentation development and sample analysis, which overtly led towards my interest in research at Goddard Space Flight Center at NASA. Now, I'm actively engaged in the development of compact mass spectrometers for space exploration and life detection.

Ryan Danell: Similar to Xiang, my analytical chemistry PhD was centered on the measurement of different chemical properties and focused on building and optimizing instruments – specifically mass spectrometers. After grad school, I worked for an instrument company developing commercial mass spectrometers, which led to consulting on the development of these instruments. Through this process, I was connected with NASA to help them with a Mars project. Now, I am developing mass spec instrumentation, techniques, and technology for various space exploration missions.

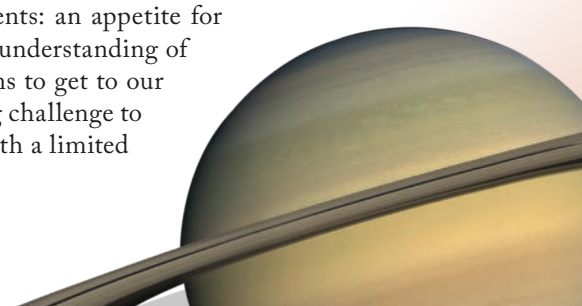
Desmond Kaplan



Xiang Li

Could you talk about some of the analytical challenges associated with detecting life elsewhere in the solar system?

Kaplan: At the core of achieving these goals are two elements: an appetite for exploration, and an understanding of the high expectations to get to our destination. One big challenge to tackle is working with a limited



Ryan Danell

budget – we need to be able to fund these explorative projects to learn more about what's out there beyond our little bubble in our atmosphere.

There are also analytical challenges in getting data back. Regardless of the actual measurement techniques, we need these to survive the extreme temperatures of space travel and exploration on the moons themselves. These practical challenges require finer details before the system is perfected for leaving the lab.

Ultimately, we need to ensure that the instrument is autonomous and can fix any issues itself. Building this intelligence takes a lot of documentation and testing, but it is crucial for any space mission to work.

Danell: As Desmond alludes to, there is such a high-volume of challenges in this field, and I struggle to fully appreciate it all myself! To have an instrument performing optimally, you have to pay attention to many details. Ultimately, we desire high sensitivity and analytical performance from a fairly compact and robust device. Unfortunately, detecting extraterrestrial life is not like landing in a garden and seeing a bug walking along in front of your spacecraft. Unlike performing analysis on Earth, when we're going into space, a lot of the time we don't know exactly what we're looking for – i.e. what does life on another planet look like? This forces us to generalize what we send into space, while ensuring that it can cope with the harsh environment of space and still perform analysis that will generate the results we need.

Li: Yes, as Desmond and Ryan say, there are many challenges to address. One particular obstacle I'd like to draw attention to is in identifying traces of biosignatures. We need to develop sophisticated analytical techniques and refine our understanding of nuances that distinguish extraterrestrial biomarkers from other sources. This obviously takes expertise, time, and funding that further complicates the process.

> "AS ARROGANT AS IT SOUNDS, MASS SPEC CAN SOLVE ALL THE PROBLEMS IN CONJUNCTION WITH SPECTROSCOPY."

What analytical techniques hold the most promise for facing these challenges?

Li: There are two examples that initially come to mind. Firstly, the Dragonfly mission to Titan uses laser desorption – a new technique that targets higher mass, non-volatile species. This technique has the ability to detect relatively complex organics, including biomarkers. It is non-destructive and has the potential to identify intact large organics, providing a more thorough analysis of a complex sample. As for the Europan Molecular Indicators of Life Investigation (EMILI) mission, the subcritical water extraction capillary electrophoresis (CE) technique has high sensitivity to detect amino acids, which is a crucial group of compounds directly related to life detection (at least as we know it here on Earth).

Danell: Yes – they are both superb techniques, and there's a lot more on the table. The mass spectrometers that have already been sent into space have provided a lot of useful

GESI TO THE MOON(S)

Desmond Kaplan at NASA discusses the GESI system and its uses in life detection missions – with analytical science at the forefront

GESI is a capillary electrophoresis mass spectrometry interface which takes ions from the liquid to the gas phase through nano electrospray ionization (nano-ESI). This, in turn, is tied to Ocean Worlds Science Exploration and Analogs (OSEAN) – a capillary electrophoresis system. The team at OSEAN are responsible for pioneering the miniaturization and portability of the system, and we take care of the interface and mass spec.

What we're attempting to do with GESI is take measurements and understand more about Europa, Enceladus, and other moons' capabilities for sustaining life at an amino acid level. Most measurements and chemical analysis that we'd take would provide indirect measurements, whereas mass spec provides a direct measurement of weight. This allows us to put the pieces of the puzzle back together to figure out what the components are and if there are any similarities with Earth.

The best way to deal with ice is by melting it down and to use nano-ESI – because gas chromatography doesn't work to its best abilities on polar compounds. ESI's strength is in polar compounds, which is why developing this system for space provides the strongest applications. In simple terms, GESI is a ESI system with an atmospheric interface consisting of a standard setup – ion funnel and ion multipole into a small linear ion trap.

This is the same design concept that's used on the Dragonfly system (DraMs) to Titan, the Rosalind Franklin (ExoMars) Rover, and the Exo Mars Organic Molecular Analyzer (MoMA) instrument. Taking these analytical techniques into space isn't for the faint of heart, but I do enjoy taking these challenges and figuring out how to simplify and parameterize them for spaceflight missions.

At the core of GESI is multidisciplinary collaboration – which goes for other systems and projects across Goddard and NASA. When you see the group sizes for these projects, you can see it really does take a village to get things done.

information about many astrobiological targets. Their applicability to analysis of unknown samples is what makes them so compelling and powerful. However, we can't send untested technology into space due to the excessive cost and time it takes to execute these missions. We need to take proven instrumentation and techniques that have been developed and vetted here on Earth and adapt them to operate in space. One example is the technique of MS/MS, which allows us to accurately identify or map a chemical through the analysis of its fragments. For life detection, this sort of detailed information, i.e. the specific chemical structure that we are observing, is key to the ultimate conclusions we can draw from the data.

Speaking of mass spec, what benefits does it bring to this area of research?

Li: Mass spec is a powerful analytical instrument with multiple advantages: fast analysis, direct measurement of molecular weight, high sensitivity, and ease of coupling with different ionization techniques to name a few. I believe that mass spec plays a crucial role in life detection and astrobiology research.

Danell: Agreed! There are a lot of techniques available, but if you want the most powerful answer, mass spec is the way forward. It is very complicated, which makes it resource intensive (both cost as well as mass and power), as well as requiring highly trained individuals to work on the hardware. However, the generality of mass spec allows us to handle unknown samples, providing results from a single analysis without necessitating additional techniques and instrumentation. The detailed information provided by mass spec can be very informative, helping us advance our knowledge as we explore further into the universe.

Kaplan: Yes, as arrogant as it sounds, mass spec can solve all the problems in conjunction with spectroscopy. These two pieces give confirmatory, tangential information that positively identifies if something has a molecular complexity that indicates life. In my opinion, without mass spec, every other technique would be a bit of hand waving rather than a direct measurement to the system. Everyone has a mass spectrometer, so it's only fitting that we should also have mass spec in space.

Do you have any hopes for the future of life detection on moons?

Li: I hope we can explore areas we've never been to before (specifically the icy moons with hidden oceans) and uncover bio-signatures – or even signs of life itself. I believe this information will reveal entirely new scientific insights about life that exceed our imagination. I'm particularly excited about surface missions on ocean worlds.

Danell: I couldn't agree more. If we continue on the path that we're currently on, there is great potential for exciting discoveries. Of course, there will always be challenges and setbacks working in these unique environments, but the excitement of the unknown pushes us onwards.

Kaplan: I also believe it's a short bet that there's extraterrestrial life in our solar system – it's just a matter of whether we'll discover it in our lifetime or not. It wasn't too long ago when we were scraping rocks together to make fire, so we're pretty young as a species and we've accomplished a lot in that time. Just imagine what the next 1,000 years hold for us – hopefully our planet lasts long enough for us to experience it!

EMPOWERMENT THROUGH PERFORMANCE

Tackle the PFAS problem head-on with the single-digit parts-per-quadrillion sensitivity from the Xevo™ TQ Absolute MS

For Waters, customer collaboration is at the core of its innovation efforts – and its latest generation of tandem quads. The goal? To continue to refine and improve solutions that scientists around the world need to keep our food and water safe, and our bodies healthy.

One problem when looking for a solution is the threat posed by per- and polyfluoroalkyl substances (PFAS). PFAS are synthetic chemicals that, due to their extreme stability, physical, and chemical properties, are heavily used in industrial and consumer products, including nonstick coatings and waterproofing materials. Numbering in the thousands and highly persistent in humans, animals, and the environment, PFAS are increasingly regulated to reduce harm in ecosystems and society.

To better understand the impact of PFAS – in terms of their persistence and toxicity – and to assist governments as they develop plans to remove them from our environment, detection at low concentrations is key. That's why Waters has developed a comprehensive solution for PFAS analysis, which includes QC-tested sample preparation, the ACQUITY™ Premier UPLC™ System, the Xevo TQ-MS Family, waters_connect™ for Quantitation, MassLynx™, Professional Services PFAS specific training, and PFAS certified reference materials and proficiency testing.

In particular, the Xevo TQ Absolute MS with enhanced negative ionization aims to strengthen analytical game plans with PFAS detection levels as low as single-digit parts-per -quadrillion (ppq) in a compact and sustainable tandem quadrupole mass spectrometer.

Absolute performance

The Xevo TQ Absolute MS empowers customers to achieve lower limits of quantitation with up to 15 times more sensitivity for

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challenging negative ionizing compounds than the previous Xevo TQ-XS product, helping analysts confidently meet regulatory requirements.

In fact, the negative ion performance of the Xevo TQ Absolute – along with the Waters QC tested Oasis™ WAX for PFAS and the use of the Waters PFAS Kit – allow users to achieve as low as 0.001 ng/L sensitivity. Meanwhile, waters_connect for Quantitation alleviates data review bottlenecks and reduces training burden – not only improving productivity but also boosting confidence in PFAS analysis. Customers are able to push beyond the current boundaries of PFAS analysis by accelerating time-to-results and capabilities with on-site PFAS-specific professional services consultation and training support. Additionally, with Waters ERA proficiency testing and certified reference materials, you can demonstrate competency, ensure quality in your workflow, and confidence in your data while keeping pace with evolving analytical methods.

In addition, many businesses are trying to actively address environmental sustainability while also reducing operational costs. The Xevo TQ Absolute achieves 50 percent lower electricity consumption, gas consumption, and BTU/hr output – lessening the need for air conditioning and lowering costs, while allowing users to meet their sustainability goals. The Xevo TQ Absolute also provides more analytical capability per square foot of lab space by minimizing the LC-MS/MS footprint, so laboratory managers can fully optimize their facilities and increase efficiency.

Absolute impact

The 2022 US EPA Health Advisory Levels (HALs) regulation for PFAS detection sets limits as low as 0.004 ng/L in drinking water. This requires a carefully designed and executed workflow, an analyte enrichment step, ultra high-performance liquid chromatography, and a highly sensitive mass spectrometer.

Waters has demonstrated that a combination of water sample enrichment using SPE extraction (with Oasis WAX), analysis (performed on a Waters ACQUITY Premier UPLC and Xevo TQ Absolute MS), and data analysis (using waters_connect for Quantitation software) can reach quantification limits of 0.001 ng/L for PFOA, PFOS, and PFBS, and 0.004 ng/L for GenX (HFPO-DA) – all of which outperform the US EPA updated 2022 interim HALs.

CUSTOMER TESTIMONIAL

By Stephan Lebertz, Operational Laboratory Manager at SGS INSTITUT FRESENIUS GmbH

As a contract lab, we need to offer analyses that differentiate us from other labs on the market. With the Xevo TQ Absolute – which we purchased alongside the Premier LC System in December 2022 – we are able to meet our customer's challenging LOQ requirements thanks to the excellent sensitivity in negative mode – especially for *m/z* values below 200, which is essential for PFAS analysis. The UniSpray™ ion source boosts sensitivity further while maintaining great robustness – even with complex samples.

The Premier LC and Premier columns are an added benefit and help to solve chromatography challenges that result not only from the large suite of PFAS compounds that we need to be able to run in one method, but also from the very complex matrices that require maximum separation power to avoid interferences. And besides the great performance and design, the Waters system also saves the lab energy costs and space efficiency – helping us to optimize from a carbon footprint point of view.

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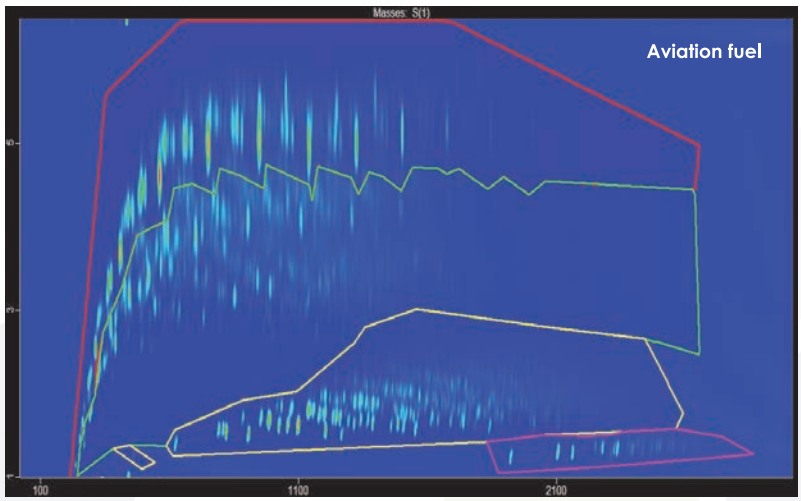

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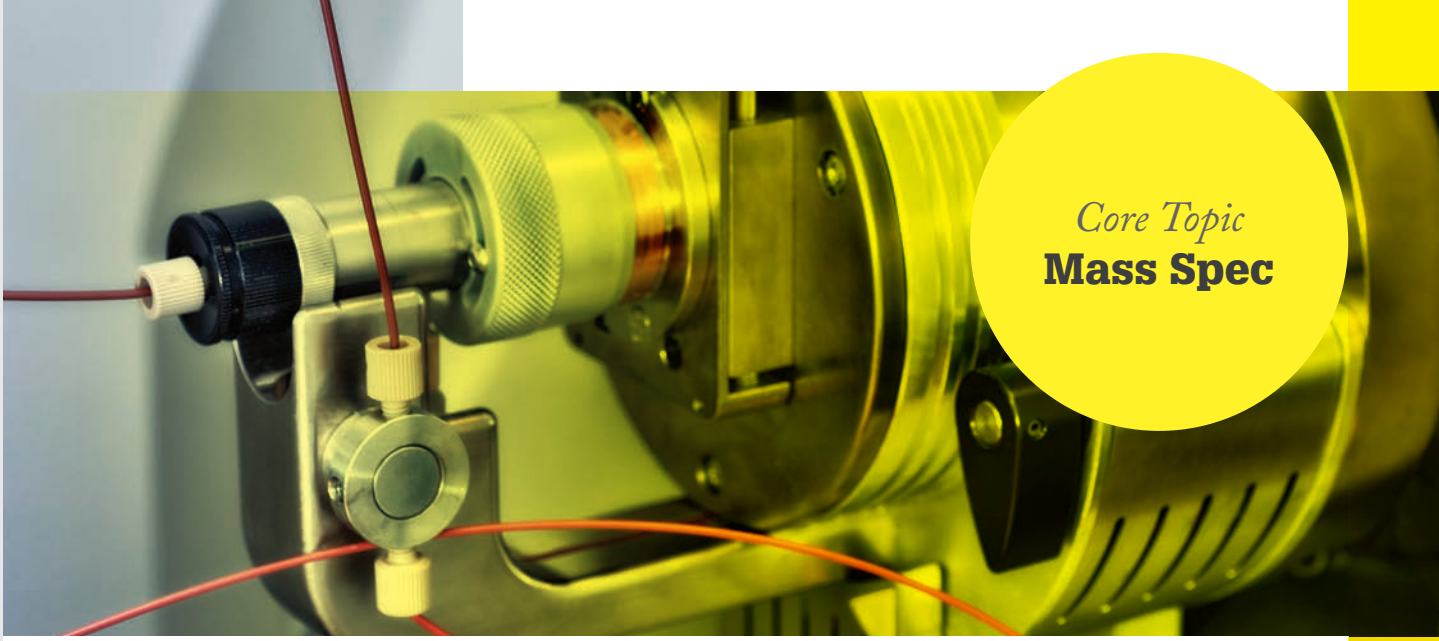

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Core Topic
Mass Spec

No eraser needed. Distinguishing between thyroid, parathyroid, and lymph node tissue during surgery can be very challenging, due to their localization and physiological similarity. With this in mind, the medical mass spec team from Texas assessed the performance of their MasSpec Pen during endocrine surgery. The study demonstrated the pen's ability to distinguish between and identify tissues with more than 90 percent accuracy. Analyzing the sample in real time with this device enabled instant feedback on its pathology, aiding surgical decision making and decreasing procedure time and costs.

Where the wild things are. The growing demand for wild salmon – along with the higher price tag – has led to instances of food fraud, where farmed salmon is sold as wild salmon. It can be nearly impossible to differentiate between the two once they've been processed. This led an international team of researchers to develop a method – which combines matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-ToF MS) and chemometric analysis – to differentiate between wild and farmed salmon. The researchers achieved 100 percent classification accuracy.

Spinal tag. A newly-developed fluorescent technology can tag lipoprotein subspecies in small volumes of human cerebrospinal fluid and could be used by clinicians to learn more about what's happening in Alzheimer's disease. The researchers engineered an ultrasensitive fluorescent detector into a high-resolution SEC system, which they combined with liquid chromatography-tandem mass spectrometry (LC-MS/MS)-based proteomics. The mass spec analysis identified 303 proteins across the populations, over half of which have not been reported in plasma high-density lipoproteins.

The forever problem. Researchers from the Yale School of Public Health, USA, coupled a high-resolution orbitrap mass spectrometer to an ultra-high-performance liquid chromatography system to study the relation between thyroid hormone levels (crucial for normal growth and development) and PFAS concentrations after birth from dried blood stain samples. They found some "exploratory, potential relationships" between thyroid hormones and PFAS exposure. "These findings should be examined in a larger cohort with a broader range of thyroid hormone measurements to more thoroughly describe potential patterns of association," concluded the authors in their pilot study.

References available online

IN OTHER NEWS

Julia Laskin and colleagues develop an integrated microfluidic probe for mass spec imaging of biological tissues – with both high spatial resolution and high throughput.

Tandem-MS-based metabolomic analysis demonstrates significant correlation between metabolism of arginine, methionine, and tryptophan, and inflammatory cytokine release and insulin resistance in HIV/AIDS patients.

Antarctic research stations are contaminating Antarctica's marine waters, which contain high amounts of metals (lead, copper, zinc, tin, cadmium), hydrocarbons (TPH) and PBDEs, according to GC-MS/MS analysis.

Silver-109 and gold nanoparticles improve the performance of high-resolution laser desorption/ionization mass spectrometry (LDI-MS) and mass spectrometry imaging (MSI) of steroid hormones.

Exploring the Deep Sea of Unknown Compounds

How high-resolution ion mobility-mass spectrometry holds the answer to unraveling the structures of the many molecules we know must exist

By Adam Hollerbach

Despite all the scientific advancements over the years, we still only know the complete chemical structure of around 5 percent of all the molecules we believe to exist. This number is staggeringly low and needs improving so that we can learn more about how molecules react within the environment – and what role they play in biological pathways. With this in mind, my team and I decided to create a new instrument to improve the identification rate of unknown molecules.

Many compounds have similar structures, which makes identification complicated. This is especially true for complex biological mixtures. Another common issue is that many unknown compounds only exist in low concentrations, and this means we might not even see them, much less identify them. All these issues must be considered when trying to identify unknown molecular structures.

Two common approaches used by researchers to identify unknown molecules are nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS). NMR is considered a definitive structural measurement, but a fairly pure concentration sample must be obtained for it to be used. On the other hand, MS is widely used to analyze mixtures, but it doesn't typically provide enough information to definitively determine a chemical structure – especially when used alone. Other gas-phase analysis techniques, such as infrared (IR) spectroscopy, ultraviolet photodissociation (UVPD), and ion mobility (IM) spectrometry can be paired with MS.

However, we believe that the combination of high-resolution MS and high-resolution IM spectrometry shows tremendous promise in identifying the chemical structures of unknown ions. And that is what the SLIM-Orbitrap is designed to do.

The Orbitrap mass spectrometer was developed by Thermo Fisher Scientific to measure an ion's mass electric charge and how the ion breaks apart – providing insights into an ion's constituent atoms, and helping us determine the ion's chemical formula. The second instrument used in our study is known as SLIM: structures for lossless ion manipulations – which is an ion mobility spectrometer that measures the size and electric charge of ions. SLIM addresses the challenge of differentiating ions with identical mass and fragmentation patterns, but differing atomic bonding (structural isomers).

We cannot measure an ion's mass with this instrument alone, which is why we combined SLIM with the Orbitrap for a more detailed analysis. The combination of these two instruments allows us to measure multiple different properties of ions with very fine details, and we use all these fine details to help us determine the structure of an unknown ion.

To couple these machines together, we used the dual-gate scanning technique, which involves pulsing a small number of ions into the ion mobility spectrometer and letting the ions separate. Instead of releasing all the ions at once, only a few at a time are allowed to exit the instrument based on their arrival speed. Two ion gates are used to make a "dual-gate" setup, and "scanning" the second ion gate allows us to send ions with slightly lower speeds to the mass spectrometer until all the ions are analyzed.

There are a few known disadvantages to this technique (for example, sample wastage and long experiment times) but, overall, SLIM-Orbitrap provides us with high-resolution results that effectively distinguish and analyze ions with high precision.

Our main findings revealed that a combination of high-resolution SLIM and Orbitrap measurements can assist in distinguishing ions that cannot be achieved with other techniques. One instance of this was shown through the analysis of a lipid mixture – the Orbitrap couldn't tell the difference between two lipid structural isomers, but the SLIM instrument could. Though we couldn't fully tell what these two lipids were, the Orbitrap identified them as phosphatidylcholines, and SLIM revealed that they were slightly different in size.

Though these results are exciting, the system is quite new and further work is required. We've already explored compounds in many samples (such as lipids, dyes, and metabolites), but we want to push this machine to its full potential. These systems can analyze almost every ion that you put into them – expanding our research capabilities even further.

Moving forward, we're hoping to use the SLIM-Orbitrap to fully identify unknown compounds that challenge other researchers. And though we aren't yet sure on the role of AI, computational models are sure to play a big role in decoding the data acquired from the SLIM-Orbitrap.

Predicting unknown ion structures based on many different high-resolution measurements could revolutionize sample analysis and save time, effort, and money. We believe that the SLIM-Orbitrap is part of the solution to achieving this goal.

Adam Hollerbach is a Chemist at Pacific Northwest National Laboratory, Washington, USA

The full length version of this article is available online

The Third False Dusk of Mass Spec

Has the current era of biomedical mass spec crossed the finish line? Naysayers be warned: we've been here before…

By Richard van Breemen

The field of mass spectrometry has evolved through three major eras since its invention. As the current field of biomedical mass spectrometry reaches maturity, challenges arise regarding how the next generation of mass spectrometrists should focus their efforts. By looking at the history of mass spec, we can estimate what the future will look like and plan accordingly.

Mass spectrometry was invented at the turn of the 20th century by physicists, physical chemists, and analytical chemists to measure the masses of the elements and prove the existence of their isotopes. As additions were made to the periodic table, many believed mass spec's utility for expanding knowledge was ending, and some professors began advising their students to pursue other fields. As we now know, this advice missed the mark as the new field of organic mass spec was born in the 1940s.

Analytical and organic chemists developed organic mass spec to characterize and quantify organic chemical constituents in petrochemical products. Organic molecules were characterized in part by determining their elemental compositions using accurate mass measurements. By applying fundamental principles of organic chemistry to interpret the fragmentation patterns contained in the mass spectra, structural information could be determined to help identify unknown organic molecules.

These studies used electron impact and chemical ionization techniques, but they were only suitable for substances that could be turned into vapor before ionization – typically weighing less than 1,000 Da. By the 1970s, university chemists were once again advising their students to avoid pursuing careers in mass spec because the fundamentals had been determined and they believed that the most significant applications had been thoroughly explored. However, once again this advice was premature; the next generation went on to establish the field of biomedical mass spectrometry.

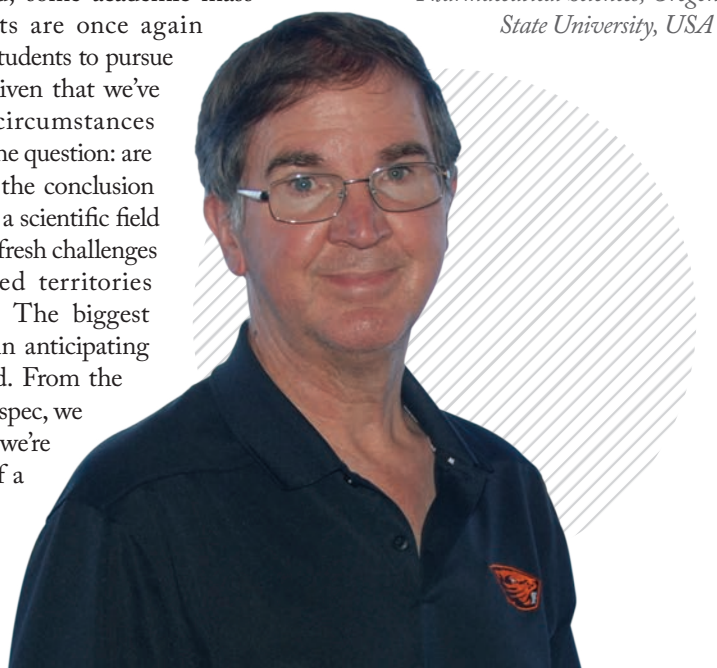
The invention of desorption ionization techniques (such as field desorption, laser desorption, and fast atom bombardment) in the 1970s and 1980s are widely used today as matrix-assisted laser desorption ionization and electrospray. These ionization techniques enabled the creation of intact gas-phase ions of polar and nonpolar large organic molecules, surpassing 1 million daltons in size. These advancements created opportunities for biomedical applications of mass spec, such as proteomics, metabolomics, and lipidomics. As a result, many biochemists and biologists gained interest in the field of biomedical mass spec, which was previously dominated by analytical chemists.

With the maturity of the biomedical mass spec field, some academic mass spectrometrists are once again advising their students to pursue other fields. Given that we've seen similar circumstances before, it begs the question: are we witnessing the conclusion of mass spec as a scientific field or will there be fresh challenges and unexplored territories to delve into? The biggest challenge lies in anticipating what lies ahead. From the history of mass spec, we can predict that we're on the brink of a new era.

I would like to believe that the next era for mass spec is around the corner – and may focus on medical applications. With this new era of medical mass spec, I envision greater use of MS in identifying risks for disease, diagnosis, and guiding treatment. Miniature devices will be employed for real-time disease diagnostics in clinics – supporting annual checkups and enabling on-site diagnostics, such as urinalysis, breath analysis, hair analysis, biopsy analysis, and blood analysis with minimal waiting time. During surgeries, mass spectrometers will become routine tools for identifying diseased or damaged tissue.

There is also the potential for the development of implantable mass spectrometers – similar to pacemakers – to monitor therapeutic drug levels and important molecules like insulin. An implantable mass spectrometer could also control the release of drugs to maintain good health. We're already seeing the initial use of mass spectrometers in operating theaters, LC-MS is used routinely for therapeutic drug monitoring, and proteomics mass spectrometry is already monitoring health and predicting disease risks. Perhaps the new era of medical mass spec has already begun…

Richard van Breemen is Professor of Pharmaceutical Sciences, Oregon State University, USA



Nipping Nitrosamines in the Bud

Nitrosamines are carcinogenic at low concentrations, able to form in medicines over time, and difficult to detect affordably and with high throughput using conventional techniques. Fortunately, there is a quick, reliable, sensitive, cost-effective screening method that identifies at-risk samples containing nitrites and nitrates: The Automated Total Nitrosamine Analyser.

By Jonathan Angove

Nitrosamines are carcinogenic compounds that demand close monitoring in a number of industries, including food, brewing, rubber, tobacco products and, of course, the pharmaceutical industry. There are a wide range of products with the potential to form nitrosamines – some of which are commonly prescribed. Indeed, the recent global withdrawal of ranitidine (a widely-prescribed antacid medication) showcases the negative fallout of detecting the presence of nitrosamines – in this case, NDMA.

The main challenge for pharmaceutical companies stems from the carcinogenic nature of nitrosamines even at very low concentrations. The FDA and EU have listed a number of nitrosamines and their maximum permissible daily exposure limits; NDMA has a daily intake limit of 96 ng, but other nitrosamines drop to as low as 8 ng.

Another challenge is that nitrosamines can form over time, so pharmaceutical companies have the difficult task of predicting the nitrosamine concentration that could exist by the expiration date of the product; notably, the rate of nitrosamine formation increases at elevated temperatures or under acidic conditions. In the presence of a source of nitration, any amine-based active pharmaceutical ingredient (API) is at risk of nitrosamine formation, which brings us to the focus on nitrites and nitrates.

Nitrites and nitrates can be found in excipients – the substances used alongside the API in solid drug formulations to add bulk or boost stability. When the API and excipient are mixed together and pressed into tablets or placed within capsules, we create an excellent recipe for nitrosamines – especially in a product with a designated shelf life of several years. Because nitrites are less stable than nitrates, they are considered to have a higher risk of forming nitrosamines.

There are several techniques used to detect nitrosamines, including GC-MS/MS and LC-MS/MS, but throughput is low, MS/MS instruments are typically expensive, and standards are required for every nitrosamine that has the potential to form. Moreover, because MS/MS methods rely on fully resolving analytes, the detection of an ion of interest through the first set of quadrupoles and the commencement of daughter/grand-daughter ion experiments, may result in the first quadrupole missing subsequent nitrosamines. For example, if the first analyte detected is a contaminant and not a nitrosamine, the system could generate a false negative – arguably the worst outcome for a pharmaceutical company.

ICP-MS can also be used to detect nitrites and nitrates with high throughput, but again the equipment is expensive. GC-thermal energy analyzer (TEA) can be used to detect volatile nitrosamines with high specificity, but throughput is low.

In short, mainstream technologies tend to be expensive, do not test for the presence of nitrites, nitrates, and nitrosamines, or have low throughput, so screening of incoming ingredients and excipients is not feasible.

A total solution

Fortunately, technological advances present a solution. For several years, Ellutia has sold a system that uses a chemical reaction to screen for the total presence of nitrites, nitrates, and nitrosamines. The system uses Ellutia's TEA as the detector, but it is configured for non-speciated detection because it is not connected to a GC. In fact, there is no chromatography performed at all. A chemical reaction cleaves NO (the nitrosyl radical) from any nitrite, nitrate, or nitrosamine molecule in the sample. The NO is injected into Ellutia's TEA Inlet, where it passes into the reaction chamber. Here, the NO reacts with ozone to form an excited state of NO_2, which then releases a photon of light, which can be detected.

This process has now been further developed and automated in the form of the Automated Total Nitrosamine Analyser (or ATNA for short). The same chemical reaction is used, but the throughput is six samples per hour. The system has a typical capacity of 120 standards, blanks, and samples, resulting in 20 hours of unattended use. ATNA is capable of analyzing NDMA standards to a concentration of 1 ppb (1 ng/mL) to meet the legislative requirements for sensitivity, but because the TEA is a molar detector for the nitrosamine molecule, any nitrosamine standard may be used to calibrate the system.

The main benefits are speed, cost, and versatility, which facilitates the screening of incoming ingredients and excipients for the presence of nitrites, nitrates, and

nitrosamines. Of course, it is possible to only screen the finished product for nitrosamines, but a positive result here would mean the wastage of an entire batch of medication. Equally, if a company has no control or knowledge of the nitrite or nitrate concentration within a given excipient, nitrosamines may form at concentrations that exceed regulatory limits down the line, resulting in product recalls and fines in the millions of dollars.

Screening excipients also allows pharmaceutical companies to selectively use any excipients with high concentrations of nitrites or nitrates with APIs that do not contain an amine.

The ATNA system has a low cost per sample, high throughput (therefore a quick return on investment), a low limit of detection, and is simple enough for screening purposes. Indeed, it has been successfully implemented in food, brewing, rubber, tobacco, cosmetics, and pharmaceutical companies for many years.

No screening method will replace the need for qualitative identification of the nitrosamine present to ensure that the concentration is within regulated limits. However, a proactive approach to nitrite, nitrate, and nitrosamine screening that identifies "at-risk" samples, reduces waste and costs, while boosting product safety.

Jonathan Angove is Senior Applications Chemist at Ellutia

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Core Topic
Chromatography

A sticky solution. As more SARS-CoV-2 "variants of concern" emerge, so too does the much-debated question of face mask effectiveness. But what if a long running problem in liquid chromatography, whereby proteins tend to "stick" to silica (in columns), could improve face mask efficiency and better protect against viral airborne transmission? Researchers from the University of Liverpool, UK, incorporated liquid chromatography (LC) silica microspheres into face coverings to achieve an average filtration rate of 93 percent, without affecting comfort and breathability.

Fluorescent improvements. Conventional ion exchange chromatography is a reliable analytical tool for the diagnosis of metabolic disorders, such as aminoacidopathies, but it is time consuming and costly. A research group from the National Institute for Biotechnology and Genetic Engineering, Pakistan, successfully developed a reverse-phase HPLC assay, using a low-cost C18 symmetry column and a fluorescence detector to quantify amino acids at low level (ng/mL) concentration in biofluids. "This assay could be applied for the analysis of human plasma to identify aminoacidopathies in newborn screening programs, and other metabolic disorders," wrote the authors.

A purer BEV. Bacterial extracellular vesicles (BEVs) have emerged as a promising new class of vaccines and therapeutics, but are hindered by a lack of efficient and scalable purification methods. But scientists from The University of Maryland have developed a protocol combining high performance anion exchange chromatography with tangential flow filtration to successfully isolate BEVs from *E. coli* and LAB probiotics – with increased BEV purity, which could enhance therapeutic efficacy. The team are hopeful their approach could be used in large-scale manufacturing.

A meat-free solution. Plant-based meat substitutes, such as tempeh and quorn, have grown in popularity in recent years. But for food producers, replicating the flavor and aromas of meat is an evolving challenge – often involving synthetic processes that cannot be labeled as "natural." In search of a natural alternative, researchers at the University of Hohenheim, Germany, developed a platform to generate meaty flavors from onions, chives, and leeks through fermentation with common fungi. They then used gas chromatography-mass spectrometry-olfactometry to reveal several key meat aroma compounds. Onion ferments, in particular, resulted in an intense meaty and liver sausage-like flavor.

References available online

IN OTHER NEWS

Gas chromatography sheds light on insect behavior, as researchers identify aphrodisiac chemical in male moths during courtship.

Newly-designed screening method employing hydrophilic interaction liquid chromatography-tandem mass spectrometry (HILIC-MS/MS) successfully identifies 520 differential lipid features related to COVID-19 severity.

Japanese scientists analyze flower scents with gas chromatography and MS to reveal that plants adapted and developed pollination syndromes to attract pollinating fungus gnats.

Scientists optimize gas chromatography-electron capture detector for decreased solvent consumption and "greener" pesticide monitoring in various fruits, vegetables, and cereals.

From Military Brat to Analytical Chemist

On the occasion of her retirement, Apryll Stalcup, former Professor of Chemical Sciences, Dublin City University, considers the past – and what she'd do with a lottery jackpot

How did your academic career begin?
My first academic position was at the University of Hawaii (UH). I was the first woman hired into the department in 40 years. I was hired at the same time as a marine natural products scientist, Brad Davidson. Beginning an academic career can be very stressful – there are so many expectations, but often not a lot of guidance on the mechanics of being an academic, such as purchasing, submitting proposals, drafting budgets, etc. Thankfully, Brad and I shared information – which was a real lifesaver. Another lifesaver was the campus-wide mentoring program for women that I was invited to join. I shared everything I learned from the mentoring program with Brad.

I became a single parent while at UH, and managing childcare and professional travel was very difficult in Hawaii. Eventually, I had an opportunity to move to Cincinnati, which had a more robust research support infrastructure, although traveling to conferences still wasn't easy.

You said HPLC was your first scientific love…
My first post-BS job was working in an environmental lab outside Washington, DC. I was hired with four guys who all went into a nice, clean lab, but I worked by myself in a huge lab that was used for solvent storage and contained several pieces of scientific equipment with no manuals. There was no air-conditioning, not all the lights worked, and there were signs with skulls and crossbones all over because of the dioxin work that had been done there. One of the few bright lights in the lab was shining on this brand-new Altex orange-and-black pump with a Schoeffel variable wavelength UV detector and an injection valve that looked like a stick shift on a car. It had these cute little wrenches that I could use for connecting and disconnecting columns. This was a new technique to the company and during the installation, I was able to ask all the questions I wanted of the person installing the instrument.

What have been your career highlights?
I am still experiencing them. A former postdoc contacted me recently to tell me that he had been invited to speak at an International Women's Day event about a person who had been particularly influential in his life and career – he selected me.

On another occasion, when I was attending a talk by a prominent separation scientist, he said that they were going to do a particular experiment, but that Stalcup already did it! Another highlight was being selected as Director of the Irish Separation Science Cluster. And the time our research was recognized by the Dal Nogare and Benedetti-Pichler awards. I have been very fortunate in terms of highlights.

What motivates you?
Curiosity, a streak of independence, and a desire to solve interesting problems. It became much easier for me to ask questions at conferences once I made the decision to focus on satisfying my curiosity – rather than worry what the audience or the speaker thought of my questions. One of the reasons I left the environmental lab was because I was pulled off a project just when it became interesting to me. The company had a "good enough" answer, but my curiosity had not yet been satisfied!

You call yourself a military brat – how did this impact your life and career?
My father spent 32 years in the US Navy. The military permeates family life more than most other professions – and one consequence is having to move frequently. I went to eight different schools between kindergarten and high school. Military

brats grow up in a culture that is generally more heterogeneous than the average civilian neighborhood – which means they can be quite adaptable and have seen a lot of different ways that systems can be set up or messed up.

I knew from the frequent moves experienced as a child and then later as an adult that they wouldn't kill me. Indeed, they would likely bring interesting new opportunities, experiences, and people into my life. In fact, my professional moves have been primarily driven by what best facilitates my science.

But it was also a life filled with separations. I was continually thrown into situations in which I knew no one in the room. I watched how other people interacted with each other and imagined a backstory for them. Molecules do the same thing both in solution and in the gas phase, but in solution the liquid moderates the interactions, much like the environment can moderate the interactions between people. In my work, I just tried to understand the molecular backstory.

How does this impact your approach to your students?

My perception is that people sometimes limit themselves by geography or any number of other things – like other people's expectations. In high school, I was told that women don't do science. But it was really the only thing I wanted to do.

On another occasion, at PittCon, I once overheard two recruiters for a large pharma company talking about some recent job interviewees trained in a prominent separation scientist's group. One of the recruiters was obviously impressed with the candidates, but the other recruiter was less so – noting that students coming out of that group only knew about one thing. I vowed no one would ever say that about my students.

Throughout my career, I used understanding of separation mechanisms as an excuse for the students to learn other approaches – for example, using NMR to understand interactions between ionic liquids and phenols to understand capillary electrophoretic separations of polyphenols.

You recently retired from your role as professor. What are you looking forward to?

In 2001, I was being recruited for a position at one of the funding agencies in the US and I was seriously considering it. I was having difficulty getting funded and I was afraid I would never have another idea. I submitted a "Hail, Mary" pass of a proposal and the funding agency gave me twice the amount of funding I asked for. I realized then that there was still some science that I wanted to do. Flash forward to 2023 and I'm retired, but I have about four or five ideas that I would love to pursue. I keep buying lottery tickets – if I hit it big, I am hiring a few postdocs!

Apryll Stalcup, former Professor of Chemical Sciences, Dublin City University

Greening LC

The steps we can take to reduce liquid chromatography's impact on the environment

By James Grinias

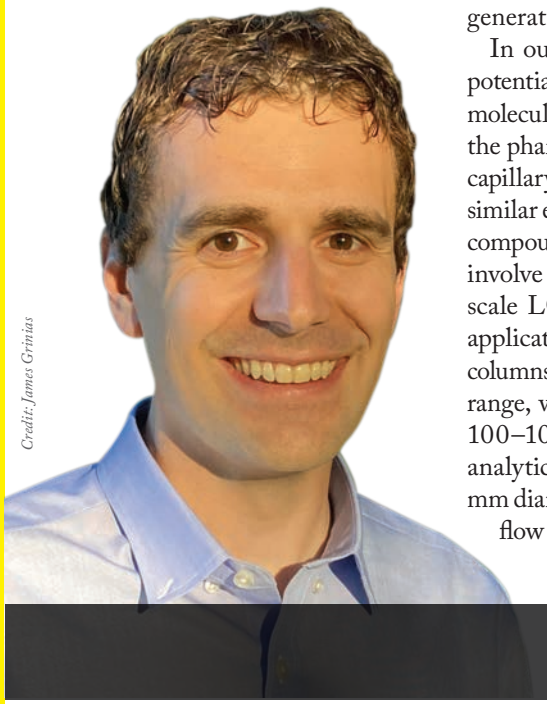
As we all do our part to combat climate change and protect the environment, every aspect of life should be considered to some extent – including our jobs. For those in science careers, not only should we be considering the materials we use and how they are produced, but also the full life cycle – transport and disposal included. Together, we can bring about colossal change through many small efforts.

Many researchers are focused on developing greener approaches to sample preparation, primarily through the use of alternative solvents with lower toxicity and lower carbon footprint. And I have also heard of efforts to recycle metals in consumables (column hardware, tubing, and so on), but this may not be an option available to all chromatographers.

The overall development of compact instrumentation for traditional LC-UV analysis has greatly improved the sustainability of chromatography. There have been similar efforts in the area of MS, but there are a number of significant challenges to overcome in making compact MS instruments. Further efforts to reduce the overall size, power consumption, and consumable needs of a complete LC-MS system would greatly enhance the ways in which this technique could be applied…

To further improve the sustainability of liquid chromatography (LC), we can develop faster methods, which reduces the time instruments spend in full power mode. But we can likely have the biggest impact by considering solvent consumption – and that's arguably the most easily addressed. In my view, we need to more actively make the shift to smaller column diameters, which allows instruments to be operated at lower flow rates, consuming less mobile phase and generating less waste.

In our lab, we've been exploring the potential of translating the typical small molecule analytical methods used within the pharmaceutical industry down to the capillary scale. We're currently exploring similar experiments on biopharmaceutical compounds. In fact, many of our projects involve advancing the use of capillary scale LC columns in a broad range of application areas. We typically employ columns in the 0.150–0.300 mm diameter range, which brings the flow rates down 100–1000 times lower than typical analytical scale columns in the 2.1–4.6 mm diameter range. With this decrease in flow rate comes a reduction in the need for mobile phase – as well as the carbon footprint of shipping and the generated chemical waste. For cases where there is no access to capillary scale instrumentation, we have also started exploring the use of 1.5 mm diameter columns – which are useful in generating results that are comparable to typical 2.1 mm diameter columns but at half the flow rate.



Credit: James Grinias

"I am hoping that our work can demonstrate that there are many routine LC applications that can be performed with smaller diameter columns."

Capillary LC has long been seen as a tool primarily for biomedical researchers conducting LC-MS analysis on very complex samples. I am hoping that our work, and that of others investigating similar topics in the field, can demonstrate that there are many routine LC applications that can be performed with smaller diameter columns. We all just need to make the effort.

James Grinias is Associate Chemistry and Biochemistry Professor, Rowan University, New Jersey, USA

Confronting Cannabis' Mycotoxin Maze

Top tips to overcome common pitfalls and challenges associated with mycotoxin testing of cannabis products, including sample preparation, regulatory changes, and method sensitivity

The presence of mycotoxins, regardless of the matrix, can cause adverse health effects in humans and animals – ranging from gastrointestinal and kidney diseases to immunodeficiency and cancer. Contamination can occur in a variety of food commodities, animal feed, crops, as well as herbal medicines and other natural pharmaceutical products. And with the increasing legalization of cannabis and hemp products, mycotoxin testing is becoming increasingly important in the cannabis industry.

To find out how to overcome the analytical and regulatory challenges associated with mycotoxin testing – with a focus on cannabis products – we spoke with Juliane Kramer, Senior Application Specialist at KNAUER.

Can you give me an overview of the regulatory landscape for mycotoxin testing?

There is a lack of regulatory harmonization for mycotoxin testing – each country or region typically has its own regulatory framework. But there are also international standards that serve as a reference for national regulations and provide guidance on test methods and limits. These regulations may include allowable limits for specific mycotoxins in various commodities, including food, feed, and sometimes cannabis or hemp products – there are no specific regulations for cannabis and its products in the EU, for example, but the limits for mycotoxins in food and animal feed are used as a guideline.

What are some of the analytical methods used in mycotoxin testing for cannabis products?

At present, the routine methods used to ensure the quality and safety of cannabis products are underdeveloped compared with those used in the food and pharmaceutical industries. Indeed, developing a method that is fast, robust, but also simple can be a quest! In the context of cannabis, mycotoxin testing typically involves the detection and quantification of specific mycotoxins, such as aflatoxins (G2, G1, B2, B1) and ochratoxin A. Samples may be analyzed by HPLC or ELISA, for example. For HPLC determination, fluorescence detection (FLD) or mass spectrometry (MS) is usually chosen.

How important is sample preparation for mycotoxin testing?

Sample preparation is a critical step in mycotoxin testing because it directly affects the accuracy and reliability of the results. Sample preparation for cannabis is especially challenging because the matrix composition is complex and contains many compounds from different classes in addition to the cannabinoids, including terpenes, hydrocarbons, and others at various concentrations. Matrices range from fresh marijuana plant material to medicinal oils and ointments. Cannabis materials embedded in edible matrices, including baked goods and beverages, are also appearing on the commercial market.

In addition to sample complexity, we must also consider homogeneity, matrix effects, sample size/representativeness, and extraction efficiency. Depending on the analyte and sample matrix, different extraction techniques are used; for example, solvent-based extraction, solid-phase extraction (SPE) or QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe).

How important is customization – and how can KNAUER help?

Customization in mycotoxin testing is essential because different industries have unique requirements and challenges. KNAUER can assist in the development and optimization of analytical methods for mycotoxin testing in different matrices by selecting appropriate sample preparation techniques, optimizing instrument parameters, and selecting the most appropriate detection method. In addition, our customized application support ensures that customers receive support specific to their industry and testing requirements. We also offer a range of advanced analytical instruments that can be tailored to meet industry-specific needs. These instruments can include high performance liquid chromatography (HPLC) systems, mass spectrometers, and related accessories, such as custom switching valves. Customized instrument configurations can be designed to meet the unique requirements of mycotoxin analysis in different industries.

Please tell me about KNAUER's LC solutions for mycotoxin quality control…

KNAUER offers solutions that are well suited for mycotoxin quality control, including applications in the cannabis industry. KNAUER's LC systems, such as the AZURA® HPLC/UHPLC systems, are designed to provide selectivity, robustness, and ease of use for mycotoxin analysis. The HPLC systems can be combined with various detection technologies, including fluorescence detectors and triple quadrupole mass spectrometry, for the precise identification and quantification of target compounds in cannabis samples. We develop applications for the detection of target mycotoxins, even at concentrations below 20 ppb, which are specified in most regulations. In spiked hemp flour samples, we have even detected mycotoxins down to 0.5–2.0 ppb.

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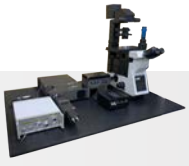

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Core Topic
Spectroscopy

Are we alone in the universe? In a recent research, a team of astronomers shed light to the question – literally – with NASA's spectroscopy based James Webb Space Telescope, unveiling the potentially habitable properties of a newly discovered exoplanet, K2-18 b, approximately 120 light-years from Earth. James Webb's near-infrared imager, slitless spectrograph, and near-infrared spectrograph detected methane and carbon dioxide, without noting any signs of ammonia – implying the presence of liquid water. More tantalizing still, the team found signs of dimethyl sulfide (DMS), which on Earth is only produced by life. "This result was only possible because of the extended wavelength range and unprecedented sensitivity of Webb, which enabled robust detection of spectral features with just two transits," said principal author Nikku Madhusudhan in a press release.

Spectral assistant. Nerve repair surgery could be enhanced with multispectral photoacoustic imaging, according to the findings of a study conducted by researchers at The Johns Hopkins University, USA. The researchers were able to visualize and differentiate lipid-rich nerves from surrounding water-containing and lipid-deficient tissues and materials, which could aid surgical decision making.

Talking trees. It might be celtic folklore that trees can whisper, but a research group from the University of Cambridge "spoke" with plants to uncover their biomolecular processes. Highlighter – a biosensor conveying a synthetic, light-gated gene expression system – was developed to trigger and translate optogenetic signals of protein expression in plants under stress – providing insights into plant immunity. The photoswitching technology was evaluated and adapted following spectroscopic analysis to define the light conditions necessary for optogenetic gene expression control.

Dinosaur or the egg? Modern day birds have evolved from dinosaurs, but several questions remain unanswered as to what molecular changes occurred to enable this transition. Researchers from the University College Cork, Ireland, employed infrared and sulfur X-ray spectroscopy coupled with controlled taphonomic experiments to analyze Mesozoic feathers. They found that feather corneous beta proteins (CBPs) gradually adapted to α-helices. This molecular alteration ensured the survival of CBPs against thermal maturation – indicating that dinosaurs had similar feathers to modern birds.

References available online

IN OTHER NEWS

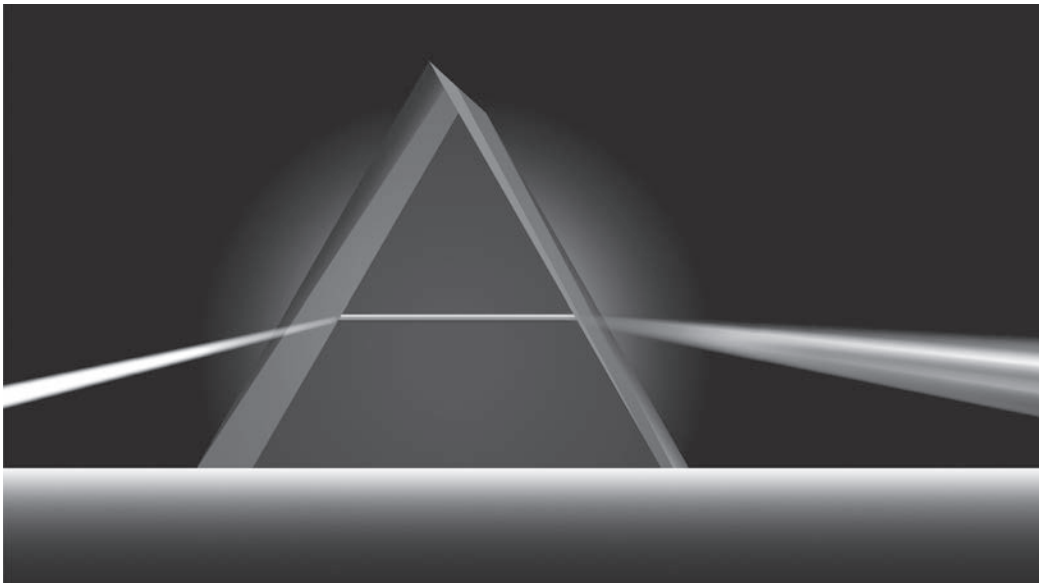
Diamond materials are, in principle, suitable for use as photoelectrodes that could use sunlight to convert greenhouse gasses into less harmful compounds, according to analysis involving four different X-ray and UV-vis spectroscopy methods.

High-resolution NMR spectroscopy coupled with computer simulations enables scientists to simultaneously characterize dynamic and structural properties of multi-domain proteins for the first time.

Researchers at Aston University, UK, use a benchtop NMR spectrometer to analyze pyrolysis bio-oils – demonstrating that NMR analysis can be "easier and more accessible to potential users."

Study employing protein spectroscopy, electron microscopy, and chromatography unveils the role of the ancient protein family serum amyloid A (SAA) in host defense and lipid clearance in pathologic amyloid formation.

The (Dark) Art of Spectroscopy



What is the single biggest challenge facing spectroscopists in 2023? We present answers from six SciX speakers.

Xiaoyun (Shawn) Chen: Others may come up with some highly technical challenges facing spectroscopists. Instead, I'll mention a rather mundane and yet important one: how to engage and cultivate the new generation of spectroscopists. The breadth of spectroscopy applications is growing – ranging from cancer and infectious disease diagnosis to microplastics. And artificial intelligence is playing a more prominent role in converting highly complex spectral data into actionable information. The danger? As more and more people start to treat spectroscopy as a black-box, they risk reaching wrong conclusions or confirming their own biases. A solid understanding of spectroscopy and the myriad of tricks associated with the art of spectroscopy is indispensable. I hope the next generation of spectroscopists will spend time and effort learning, mastering, and appreciating the art of spectroscopy.

John Wasylyk: From an industrial point of view, the biggest challenge spectroscopists face is hiring new graduates in the chemistry field who lack basic understanding how spectroscopy can aid in their research. This applies to chemical engineers and synthetic chemists who are not familiar enough with the various instruments and instead rely on traditional labor-intensive techniques, which often provide only snapshots of data. Those chemists should be made aware of where spectroscopy fits in and who the subject matter experts are in their company.

C. Derrick Quarles Jr: I completely agree with John here… Graduate programs in the United States are not focusing on atomic spectroscopy, partly due to a shift in the type of funding that is being offered to the universities. There also seems to be a sense that these types of instruments are just used for routine analysis. For example, there is a lack of understanding of how an ICP-MS fundamentally works, leading to – as Shawn said – the black box concept. Alternatively, the universities in Europe are still doing a great job teaching the fundamentals of atomic spectroscopy, which is leading to more job opportunities when these students graduate.

Sian Sloan-Dennison: I think the biggest challenge facing spectroscopists, especially those using SERS measurements, is absolute quantification. To build reliable and quantitative assays, which use SERS analysis to produce the concentration of a biomarker present in a sample, we must investigate new approaches that standardize the measurements and minimize the variation between samples. This could be as simple as including internal standards in the assay, creating robust calibration models that take into account sample matrix and background interference, or using complementary analysis methods such as IC-MS to characterize the SERS active material. However, this all starts with synthesizing stable and monodispersed nanoparticles, which can be a dark art!

Alexis Weber: As a young spectroscopist, still in graduate school, I find that the largest challenge is engaging students/researchers to be self-motivated in developing their own skills and network. As students are approaching the end of their doctoral degrees, they have been within the academic community for 9–14 years – sometimes without ever having an industry job within their field. This can lead to a lack of external connections – connections that are extremely beneficial when finally exiting the academic environment. If students do not attend conferences, network, or join professional societies, they will be at a disadvantage when looking for a job. Meeting with and learning from professionals outside of your lab provides you with insights and connections that you would not otherwise have. However, in my discussions with fellow students, they do not see the importance of this until it

"Though spectroscopy can be thought of as a single science, it must work with multiple disciplines."

is too late. What's worse is that there are opportunities available for students in the form of professional organizations, but they do not see the value in it because it is not specifically research oriented. Finding a way to break this stigma is one of the larger challenges faced in 2023 because it affects the spectroscopists of the future.

Roy Goodacre: Though spectroscopy can be thought of as a single science, it must work with multiple disciplines. As well as the biological question one is trying to address, there will be experimental design and data processing steps that are needed to turn spectral data into some sensible answer. Thus, I think the main challenge is to have multidisciplinary groups that are in it for the team and not the individual – so they are invested in the research question rather than the techniques, both analytical and computational. A common dialogue towards the central aim/objective is necessary and this starts with designing the experiment.

Today, there is a reproducibility crisis in science – this has been highlighted by a series of opinion articles published by the Nature publishing group. A big problem is that many experiments are designed incorrectly; please note, this is not a deliberate act, but the samples chosen to be analyzed very rarely address the problem that one is wanting to answer. For example, cancer is in general a disease that tends to be found in the elderly (I know there are exceptions, but if we think of pancreatic, prostate or bowel cancer, these are usually found in more elderly populations), therefore, one needs to look at the match controls in studies to make sure there are no age differences, no gender differences, nor any differences in other demographic or clinical information. In addition, it is worth noting that people with disease are usually self-medicating before they seek help from a doctor and thus the use of over-the-counter medicines might also correlate with people who are ill. All of these confounders need to be considered during the sample selection and design phase – this is often difficult. But it is pointless designing a spectroscopic experiment that tells you the age of the person or about the drugs or supplements they are taking – rather than whether they actually have disease!

So my thoughts on the biggest challenge come down to capturing enough information about the patient and mining this to check if there are any confounding variables that one needs to be aware of and then adjust for.

SciX took place on October 8–13 in Sparks, Nevada, USA. For more information about the conference, visit: scixconference.org

MEET THE SPEAKERS

Alexis Weber is a PhD student within the Chemistry Department at the University at Albany, SUNY, where she focuses on the spectroscopic analysis of biological fluids and trace evidence in forensics. Alexis is also COO of SupreMEtric LLC. She is a SciX session chair for contemporary issues in analytical science and early career researchers.

John Wasylyk is Associate Scientific Director at Bristol Myers Squibb. At SciX on October 9, he spoke about spectroscopic applications for pharmaceutical development. John's presentation covered a range of studies spanning in-line and off-line polymorph transformations as well as reagent stability studies, both of which are key to driving sustainability in analytical analyses.

Sian Sloan-Dennison is a Research Associate for Pure and Applied Chemistry at the University of Strathclyde, UK. She specializes in SERS and point-of-care. She is a SciX session chair for Raman spectroscopy.

Xiaoyun (Shawn) Chen is a senior research scientist at Dow Chemical Company, where he focuses on vibrational spectroscopy – especially for in-situ reaction monitoring. He is a SciX session chair for process analytical technology.

Roy Goodacre is a Professor of Biological Chemistry at University of Liverpool, UK. Roy's research interests include mass spectrometry-based metabolomics and developing Raman spectroscopy approaches for bioanalysis.

C. Derrick Quarles Jr. is a Sr. Scientist working for Elemental Scientific in the areas of automation for ICP and ICP-MS, elemental speciation (LC-ICP-MS and LC-ICP), and laser ablation (LA-ICP-MS). He is a SciX session chair for Atomic spectroscopy.

How Chelating Agents Can Easily Be Analysed Using Truly Inert Column Hardware!

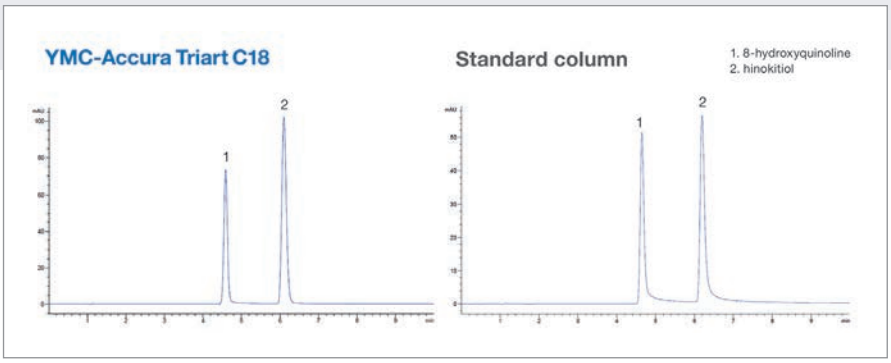


Figure 1: Analysis of the metal coordinating compounds 8-hydroxyquinoline and hinokitiol using the bioinert coated YMC-Accura Triart C18 column compared to a conventional column with stainless-steel hardware.

Metal-coordinating compounds such as chelating agents can interact with the metallic surface of the column body, which can adversely affect the analysis. The interaction can lead to loss of recovery, deterioration of peak shapes and sample carry-over. The YMC-Accura column hardware with a strict bioinert coating of the column body and frits is designed to prevent these unwanted interactions.

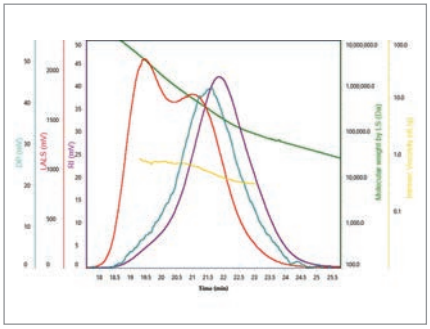
In this application the analysis of two typical examples of chelating agents, 8-hydroxyquinoline and hinokitiol, using the bioinert YMC-Accura Triart C18 is compared to the analysis using the corresponding column with stainless-steel hardware.

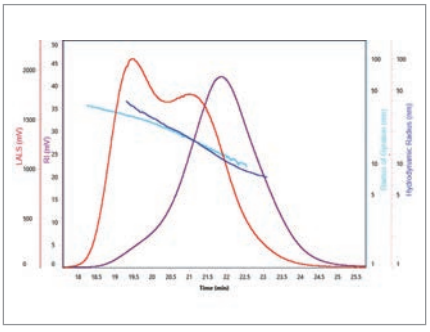
Both metal-coordinating compounds showed strong peak tailing when using the standard stainless-steel column. In contrast, the use of the bioinert coated YMC-Accura Triart C18 column resulted in higher peak intensities and superior peak shapes. Virtually no tailing was observed with the bioinert hardware.

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

Branching Analysis in Polymers via Triple Detection SEC/GPC

Branching in polymers significantly impacts their material properties, such as flexibility, impact resistance, and processability, making them highly adaptable across a wide array of applications. To comprehensively understand the structure, shape and conformation of polymers in solution, size exclusion chromatography (SEC) together with advanced detectors such as multi-angle light scattering (MALS) and viscometry are indispensable. In a triple detection SEC setup, the refractive index (RI) detector gauges concentration, MALS provides true molecular weight and radius of gyration (Rg), while the viscometer measures intrinsic viscosity (IV). A polymer with an extended shape or low density in solution will show a higher intrinsic viscosity than a polymer with a compact structure or high density. A branched polymer will have a compact structure compared to a linear polymers, resulting in a reduced IV and Rg.





Following My Own Path

Sitting Down With… Koen Sandra, CEO and Co-owner, RIC group; Visiting Professor, Ghent University, Belgium

Did you always see yourself following in your father's footsteps?

I was always fascinated by all the old fashioned GC instruments in my father's garage – where the Research Institute for Chromatography (RIC) started. But honestly, I never thought of doing anything chemistry related – or getting involved with the company at that time. In fact, as a young boy, I wanted to become a pilot!

I initially studied engineering because that leaves all options open. I finally decided to do a PhD in biochemistry after being encouraged by my professors. Then, I joined a startup company, focusing on biomarker discovery. Eventually, after having become a bit of an entrepreneur in my own right, I ended up joining RIC, bringing something completely new to the mix – a focus on life sciences. I remember my father being very happy to pivot to life sciences – not only from a scientific point of view, but also because we could do it together. My father has always been an ideal sparring partner. He was (and still is) very aware of trends and quickly realized that it was a good domain to go into. In hindsight, it was a no brainer.

How did the shift to life sciences influence the growth and culture of the company?

When I joined, the main goal was to work on metabolomics and lipidomics, since I had a background in biomarker discovery. We steadily began working on those principles and suddenly, we got all these requests from the biopharma industry to characterize their products – and that's when we really started growing fast.

We've gone from employing 10–15 people to a family of 75 in around 10 years. The biopharma domain has been an important driver. Originally, we grew organically – mainly through word-of-mouth recommendations. When you continue to deliver quality, you create a bond with the clients and gain respect – and that has allowed us to continuously grow. But we have to be very careful to preserve our culture – our DNA, which is, I would say, a genuine passion for analytics. That passion guides us and makes us good at what we do – educating people, sharing knowledge, addressing the toughest analytical problems and shaping the analytics of the future. We feel comfortable in our niche, which somehow sits between a company and an academic institute.

How do you see the next decade of biopharma analysis shaping up?

There will be new types of molecules, which we will have to analyze. Proteins will continue to dominate the market, but cell and gene therapies as well as mRNA vaccines and therapeutics are emerging. Given that the analytics here are in a similar state to antibody analytics 20 years ago, we'll need to drastically sharpen and re-invent the toolbox; a heavy duty that we will for sure take up with enormous enthusiasm, dedication, and pride.

I also think we will see more and more automation – for example in data analysis – and the adoption of artificial intelligence. In fact, both automation and miniaturization will be increasingly important in all sectors – especially in terms of sustainability. Everything needs to be smaller and more efficient – and, fortunately, that's a trajectory we're already on.

What keeps you motivated?

First, I recognize there is no limit to learning – and I am always keen to learn new things, which keeps me focused. At RIC, there is certainly always scope to do that! But the most rewarding part of my job is making a difference in the market and having an actual impact on society. For example, one of our customers recently received FDA approval for a molecule we worked on extensively. I often meet people at events that share how our research has been beneficial for their activities. This direct impact is what drives us to keep doing what we do best. What more do you want than happy coworkers and a smile on your client's face?

"I'm very happy that I could work on completely different areas of science to make a name for myself."

How has your father's name and legacy influenced your career?

I decided I had to follow my own path and I'm very happy that I could work on completely different areas of science to make a name for myself. If I had worked in gas chromatography – a field where Pat Sandra did pioneering work – it would have been impossible for me to achieve the same things as him. I am pleased and proud that I had the opportunity to explore my own field and grow in that domain.

Of course, the older generation may recognize me as "the son of," but it's funny – others sometimes ask if he's "the father of…" Now that he has taken a step away from the company, it is a pity that he's not able to experience all the wonderful changes here first hand. But he keeps supporting us. And we carry on doing everything with his level of passion. My father is very proud of what my brother and I have achieved with RIC – both as a scientist and a father.

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