

# the Analytical Scientist®

## Upfront

Radiocarbon dating  
Africa's "tree of life"

06

## In My View

Taking ICP-MS to the  
next level

12

## Feature

Native MS: Rewriting the  
immunology textbooks

34 – 42

## Sitting Down With

Analytical Neuroscientist,  
Jonathan Sweedler

50 – 51



## The Innovation Awards 2021

From imagination to innovation:  
who made this year's top 15?

18 – 29

# Exploring the hidden depths of open access publishing?

Dive deeper into the  
benefits with our support

[rsc.li/open-the-future](https://rsc.li/open-the-future)

Fundamental questions  
Elemental answers

# What Exactly Do Our Innovation Awards Celebrate

– and Why?

*New technologies with the potential to solve real-world problems – ultimately, making the world a better place. Now, that's innovation!*

Editorial



What do The Analytical Scientist Innovation Awards (TASIA) celebrate? You might quickly retort: “innovation!” But if you look up the definition in an economics textbook, you’ll find something along the lines of “the commercialization of technological inventions.” But is that what we’re celebrating here? I’d argue that innovation is the process that leads to new technologies and their subsequent commercialization.

But, as Rich Whitworth said back in 2013, that process is “ethereal” – we have no roadmap or formula. Einstein was a clerk when we came up with his theory of relativity; Mendel was a monk when he discovered genetics. Yet Tim Berners-Lee built the Web within the belly of a large organization: CERN. Steve Jobs is considered an “innovator” but also a “tweaker” – for improving the innovations of others, namely Xerox’s mouse. Innovation, like many concepts, is difficult to pin down. Suffice to say, we know it when we see it.

Whatever innovation is, we know it’s a good thing, right? Creating a more sustainable economy and tackling climate change are the two great challenges of our age. Is innovation for innovation’s sake – the drive for pure novelty – a help or a hindrance in this regard? Perhaps what we need is responsible innovation: new technologies with the potential to solve real-world problems that, ultimately, make the world a better place.

So how do this year’s TASIA winners stack up? Very well, I think. You won’t find novelty for novelty’s sake here. (I suppose it helps that analytical science exists to answer questions and solve problems.) Many of the technologies promise greater sensitivity, resolution, flexibility, and speed – with a broad range of possible applications. Others are more targeted, with the potential to create new opportunities in cancer research, environmental monitoring, biopharmaceutical development, ‘omics research, and more. Some take innovations from other fields and put them to good use. And a few are ground-breaking.

I’m confident you’ll see the results of genuine, responsible innovation when you browse through the winners of this year’s TASIA. And, who knows, one of you may embrace some of the technology showcased and apply it to a hitherto unimagined area, spurring further innovation. And thus onwards the cycle continues!

**James Strachan**  
*Editor*



50



29



09

03 **Editorial**  
What Exactly Do Our  
Innovation Awards Celebrate –  
and Why? By James Strachan

**Upfront**  
06 Reporting on recent  
breakthroughs, from fighting  
anti-fungal resistance with  
NMR to radiocarbon dating  
Africa’s “tree of life”

**On The Cover**



*It's the return of our annual  
Innovation Awards. See who  
made the cut on page 18*

**In My View**

- 12 **Norbert Jakubowski** discusses how to take ICP-MS to the next level: measuring dynamic processes in cells as they occur
- 13 **Calum Preece** reviews the role of stable isotope analysis in the ongoing search for evidence of our changing environment
- 16 Rather than rushing to the finishing post, **Meriem Gaida** argues researchers should all focus on the “four Cs” of data quality

Feel free to contact any one of us:  
[first.lastname@texerepublishing.com](mailto:first.lastname@texerepublishing.com)

**Content Team**

*Editor* - James Strachan  
 Lauren Robertson (Deputy Editor)  
 Frank van Geel (Scientific Director)

**Commercial Team**

*Publisher* - Lec Noyes  
 Gaurav Avasthi (Business Development Manager)  
 Nick Ransom (Business Development Executive Americas)

**Design Team**

*Creative Director* - Marc Bird  
 Hannah Ennis (Senior Designer)  
 Charlotte Brittain (Senior Designer)  
 Tea Hewitt (Junior Designer)

**Digital Team**

*Digital Team Lead* - David Roberts  
 Peter Bartley (Digital Producer Web/Email)

**Audience Team**

*Audience Growth Strategy Manager*  
 - Brice Agamemnon

**CRM & Compliance**

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

**Commercial Support Team**

*Internal Systems Manager* - Jody Fryett  
 Dan Marr (Campaign Reporting Analyst)

**Commercial Services**

*Commercial Service and Social Media Manager* - Matt Everett  
 Lindsey Vickers (Sales Support Project Manager)  
 Hayley Atiz (Sales Support Project Coordinator)  
 Julie Wheeler (Sales Support Project Coordinator)  
 Alike Zapties (Project Coordinator)  
 Lilly Pratico (Project Coordinator)  
 Sophie Hall (Social Media Executive)  
 Anna Harbottle (Video Producer)

**Marketing Team**

*Marketing Manager* - Katy Pearson  
 Jo Baylay (Marketing Executive)  
 Magda Brzegowy (Marketing Executive)

**Accounts Team**

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

**Human Resources**

*Human Resource Manager* - Tara Higby

**Management Team**

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

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

General enquiries

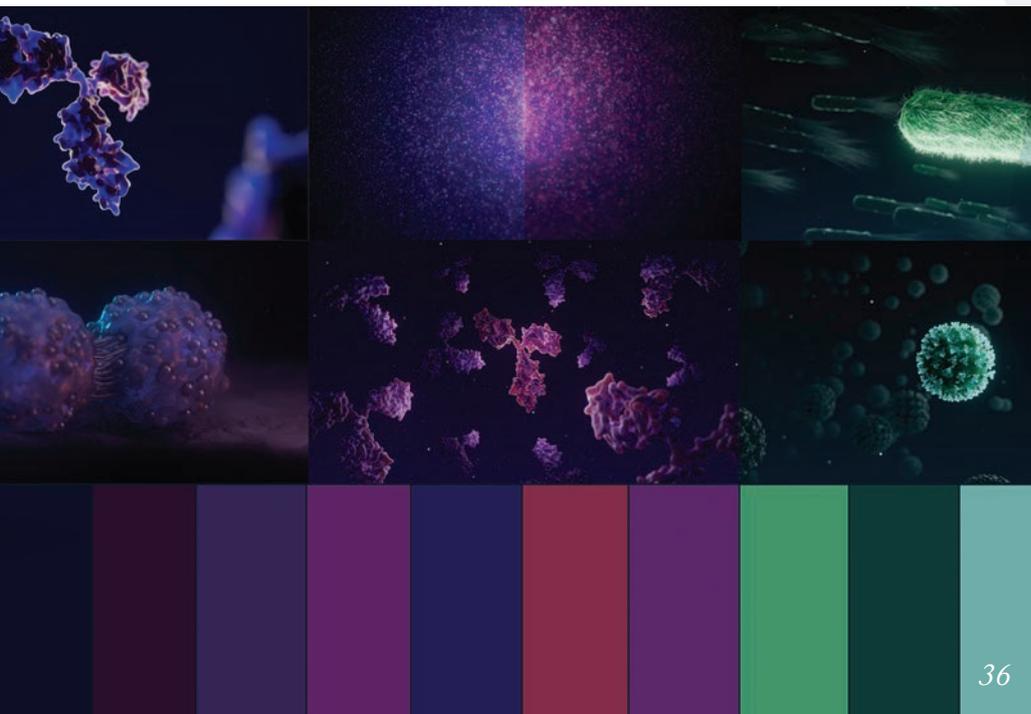
[www.texerepublishing.com](http://www.texerepublishing.com) | [info@theanalyticalscientist.com](mailto:info@theanalyticalscientist.com)  
 +44 (0) 1565 745 200 | [sales@texerepublishing.com](mailto:sales@texerepublishing.com)

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

Reprints & Permissions - [tracey.nicholls@texerepublishing.com](mailto:tracey.nicholls@texerepublishing.com)

The copyright in the materials contained in this publication and the typographical arrangement of this publication belongs to Texere Publishing Limited. No person may copy, modify, transmit, distribute, display, reproduce, publish, license or create works from any part of this material or typographical arrangement, or otherwise use it, for any public or commercial use without the prior written consent of Texere Publishing Limited.

The names, publication titles, logos, images and presentation style appearing in this publication which identify Texere Publishing Limited and/or its products and services, including but without limitation Texere and The Analytical Scientist are proprietary marks of Texere Publishing Limited. Nothing contained in this publication shall be deemed to confer on any person any license or right in the part of Texere Publishing Limited with respect to any such name, title, logo, image or style.



**Features**

18 **The Innovation Awards 2021**  
 Greater sensitivity, resolution, flexibility and speed; a broad range of applications, from cancer research, environmental monitoring, 'omics research, and more. The Innovation Awards are back!

36 **Talkin' 'Bout a (Protein) Revolution**  
 Albert Heck believes native MS will help rewrite the textbooks on immunology, and increase our knowledge of our wellness, health, and the planet - life itself, in other words

**Departments**

38 **Profession: Michael McGinley**  
 walks us through the Wild West of Oligonucleotide Analytics, where survival requires a good understanding of both chemistry and biology

**Sitting Down With**

50 **Jonathan Sweedler, James R. Eiszner Family Endowed Chair in Chemistry, Director of the School of Chemical Sciences & Professor of Neuroscience and Molecular & Integrative Physiology at the Beckmann Institute, University of Illinois, USA**

**Editorial Advisory Board**

Chris Harrison, San Diego State University, USA  
 Christina Jones, Research chemist, NIST, USA  
 Emily Hilder, University of South Australia, Australia  
 Frantisek Svec, University of

California at Berkeley, USA  
 Gary Hieftje, Indiana University, USA (Retired)  
 Hans-Gerd Janssen, Unilever Research and Development, The Netherlands  
 Ian Wilson, Imperial College London, UK  
 Jenny Van Eyk, Director of the Advanced Clinical

Biosystems Research Institute, USA  
 Luigi Mondello, University of Messina, Italy  
 Martin Gilar, Waters, USA  
 Michelle Reid, Cristal Therapeutics, The Netherlands  
 Monika Dittmann, Independent Analytical Scientist, Germany

Peter Schoenmakers, University of Amsterdam, The Netherlands  
 Robert Kennedy, University of Michigan, USA  
 Ron Heeren, Maastricht University, The Netherlands  
 Samuel Kounaves, Tufts University, USA



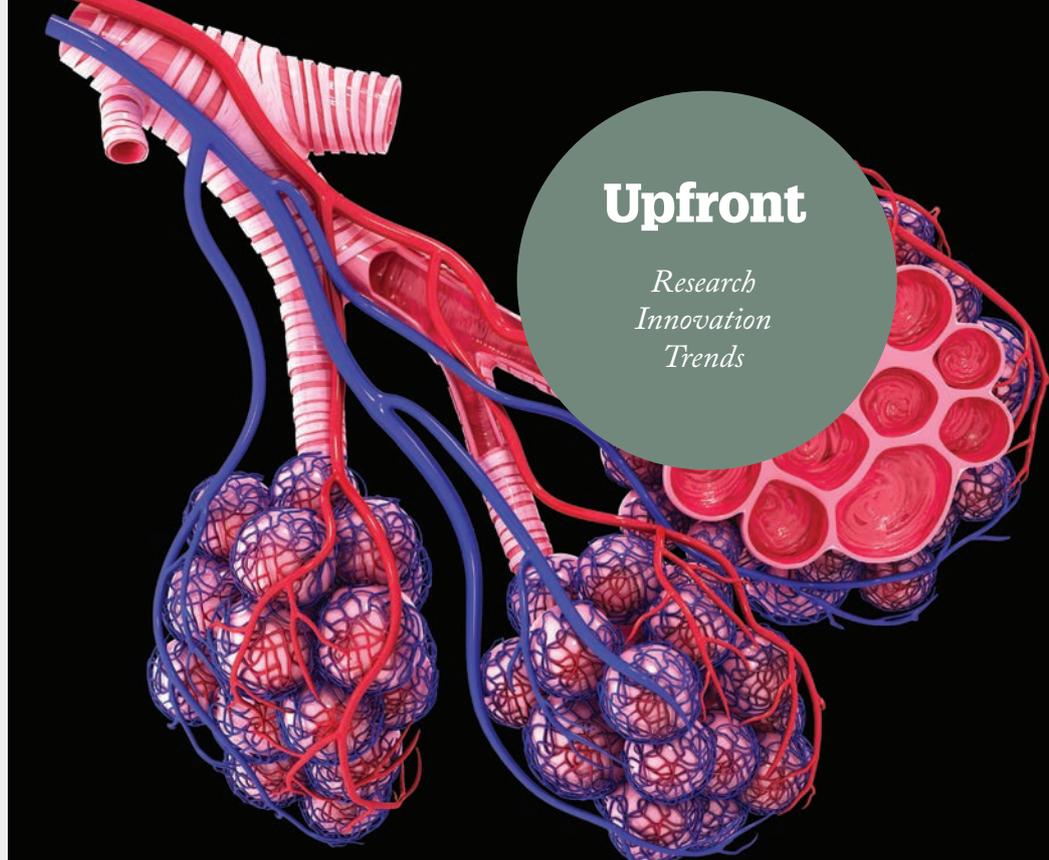
## The Phantom Lung

**How a gas spectroscopy technique could solve critical clinical challenges in respiratory diagnostics and treatment**

In recent decades, light-based technologies have grown in popularity among clinicians due to their ability to noninvasively provide detailed information on tissue functionality. In particular, gas in scattering media absorption spectroscopy (GSMAS) has emerged as a potentially useful tool for screening and monitoring respiratory conditions in neonates. However, the complexity of lung tissue – the alveoli in particular – has made it difficult to accurately study the technique’s feasibility for this application.

Andrea Pacheco and her team have managed to overcome this issue by creating an accurate lung tissue model with air-filled structures mimicking inflated alveoli. Their aim was to prove that GSMAS could successfully measure lung volume changes for neonatal respiratory care.

“We cannot go straight into the clinic and study GSMAS in patients,” says



Pacheco. “Therefore, we have developed a set of multi-layer anthropomorphic and functional phantoms to understand the technical limitations and advantages of GSMAS in simulating a clinical environment.” Previous studies have looked at sensing the absorption imprint of H<sub>2</sub>O and O<sub>2</sub> to quantify gas concentrations – but this is the first to sense volume changes directly.

“I am optimistic and I’d like to see GSMAS systems in neonatal care units within the next few years, making the surveillance of preterm babies less traumatic,” says Pacheco. So what are the next steps? “After successfully

completing tissue phantom studies, we are now starting a clinical study on healthy infants,” adds Stefan Andersson-Engels, co-author of the paper. “This will be the next step in assessing the possibilities of GSMAS. The plan is then to (for the first time) initiate studies on infants needing lung function monitoring.” After that, the challenge will be in studying the light penetration depth of GSMAS to scale it up for use in adults.

#### Reference

1. A Pacheco et al., *J Biomed Optics*, 27, 074707 (2021). DOI: 10.1117/1.JBO.27.7.074707.

## INFOGRAPHIC

### A Picture of (Mental) Health?

**The world’s largest mental health survey of academics and researchers has revealed widespread discrimination, harassment and bullying**

the Analytical Scientist

**13,000** researchers were surveyed from

**160 COUNTRIES**



More than **37%** of researchers surveyed experienced some form of discrimination, harassment or bullying at work

*For mixed race respondents, this number jumps to 60 percent and for those in the LGBTQ+ community it’s 45 percent*





## BUSINESS IN BRIEF

*A round-up of the latest analytical science news, from key announcements at HUPO to partnerships aiming to improve the analysis of biomolecules*

- Amidst the 20th Human Proteome Organization World Congress (HUPO) program, a number of companies made key announcements. Bruker, for example, announced it was collaborating with partners in key areas such as single-cell proteomics, plasma proteomics and tissue proteomics to overcome some of the complexities of automating sample preparation protocols and increase adoption across the field. Chiefly, the partnerships will see Bruker's timsTOF system combined with an automated sample preparation system from Cellenion for single-cell 4D proteomics, Seer's Proteograph product suite for rapid detection of more than 3000 proteins in human plasma, and PreOmics' BeatBox technology for tissue homogenization (1).
  - Thermo Fisher Scientific followed a similar tact with a number of co-marketing agreements aimed at accelerating proteomics workflows. Thermo
- will also work with Cellenion to provide customers with a platform to effectively and efficiently analyze thousands of single cells using its TMT multiplexing technologies and Orbitrap mass spectrometers. Besides this, Thermo will build on its existing chromatography portfolio – namely the Vanquish Neo UHPLC system – through the acquisition of PharmaFluidics, who will provide its range of  $\mu$ PAC columns to enhance LC performance in biomarker, proteomics and drug research (2).
- Tosoh Bioscience has partnered with UGA Biopharma to exchange knowledge on upstream and downstream bioprocessing of biosimilar cell lines. Tosoh will gain access to UGA's library of ready-to-use cell lines, enabling the expression of mAbs, fusion proteins, and enzymes for biopurification and bioseparation research and development (5).

### References

1. Bruker (2021). Available at: <https://bit.ly/31iNkbp>
2. Thermo Fisher Scientific (2021). Available at: <https://bit.ly/31e6plp>
3. Tosoh Bioscience (2021). Available at: <https://bit.ly/3G16wdt>



## Dating the Big Tree

**How a new approach to radiocarbon dating has helped elucidate the age of Africa's "tree of life"**

Adansonia, or baobab trees, are among the longest-living (and largest) plants on Earth. Despite their extraordinary longevity, nine of the 13 largest trees and five of the six oldest have died since 2005 – a phenomenon scientists have linked to climate change. Understanding the age and growth of these plants has never been more important.

In a recent paper, a team of researchers used accelerator MS to radiocarbon date the historic Big Tree at Victoria Falls, Zimbabwe. Until now, this famous African baobab, which is over 25 meters high, has outwitted scientists who have attempted to determine its age. This is mostly because baobabs form a different number of tree rings each year, making traditional ring-counting methods obsolete.

The researchers' results indicate that there are three generations present in the Big Tree, with the oldest stem around 1,150 years old. In the future, this AMS-based approach to radiocarbon dating could help scientists date other trees with complicated growth or architecture.

### Reference

1. A Patrut et al., *Dendrochronologia*, 70, 125898 (2021). DOI: 10.1016/j.dendro.2021.125898.



Overwork is a key cause of poor mental health, with **6 in 10** saying they felt overwhelmed and a third saying their working week is over

**50 HOURS**

About half of respondents (**49%**) said they wouldn't feel comfortable discussing their mental health with relevant people in their organization, and

**46%**

stated they felt doing so would reflect badly on them.

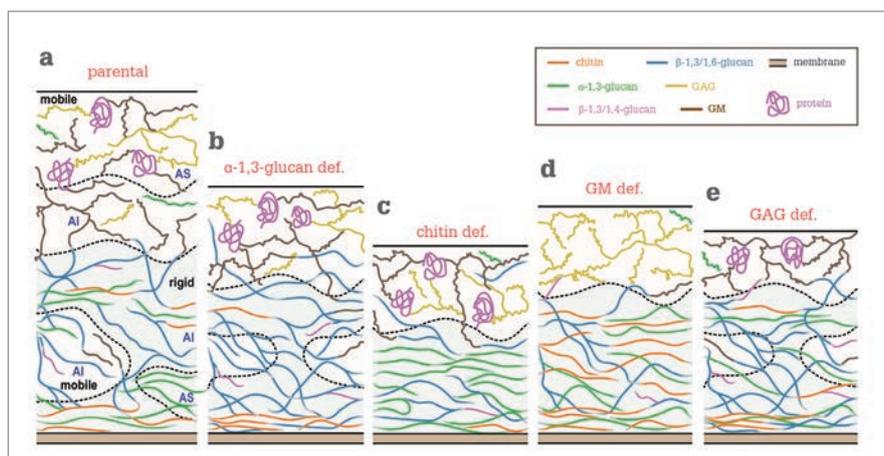
## A Closer Look at Fungal Armor

**By providing a detailed analysis of the cell wall, NMR spectroscopy could help scientists in the fight against antifungal resistance**

Bacteria get a lot of attention when it comes to discussing antimicrobial resistance – and, after the last couple of years, viruses really need no introduction. But it can be all too easy to overlook our eukaryotic cousins – the friendly fungi.

From bread to wine, beer to mushrooms, we humans have exploited these microbes for thousands of years. But they have a dark side; fungal infections can be life-threatening and, just like bacteria, fungi can develop resistance to the drugs we use to treat them. Given that there are only three types of antifungal medication in existence, this presents a problem.

In new research, Tuo Wang and his team from the Department of Chemistry at Louisiana State University have used NMR spectroscopy to uncover the



molecular architecture of fungal cell walls and their response to stress. “The structural information we’ve gathered could provide molecular-level rationale for the development of antifungal drugs that target unique molecules in the fungal cell wall,” says Wang.

The team combined biophysical methods (solid-state NMR spectroscopy of whole cells) with biochemical approaches to examine the structural dynamics of the cell wall polysaccharides present in *Aspergillus fumigatus* – a pathogen that causes life-threatening disease in immunocompromised individuals.

“This toolbox is widely applicable to structural investigations of a large variety of fungal pathogens, as well as their responses to antifungal compounds, mutants, and severe environments,”

adds Wang. “The approach also opens up the possibility of investigating the extracellular matrices in other organisms (such as algae, plants, and bacteria) using intact or even living cells with atomic-level resolution.”

In their paper, the team proposes a revised model of cell wall architecture including five categories of polysaccharides: chitin,  $\beta$ -glucan, mannan,  $\alpha$ -glucan, and galactosaminogalactan. Their results have also revealed greater plasticity of the fungal cell wall and its ability to implement different survival strategies in the presence of antifungal drugs. Ultimately, this could help scientists design new compounds to combat invasive fungal infections.

### Reference

1. *A Chakraborty et al., Nat Com, 12, 6346 (2021). DOI: 10.1038/s41467-021-26749-z.*

## Casting Light into Dark Unknowns

**Could NASA’s Roman telescope help scientists answer some of the most perplexing questions about the universe?**

NASA’s Roman Space Telescope is an impressive space observatory with a panoramic field of view 100 times wider than the Hubble telescope. The aim of the Roman mission? To answer mystifying questions within the areas of dark energy,

exoplanets, and infrared astrophysics – including the theories around cosmic expansion. In a recent study, scientists have evaluated the telescope’s impact in a bid to optimize the scientific returns of the cosmological data it will gather (1).

The onboard infrared instrument will not only survey large swathes of space in different wavelengths, but also measure light from a billion galaxies and find an estimated 2,600 exoplanets. It will work in conjunction with a coronagraph to perform high-contrast imaging and spectroscopy of individual nearby exoplanets – the first time an advanced coronagraph instrument has gone into space.

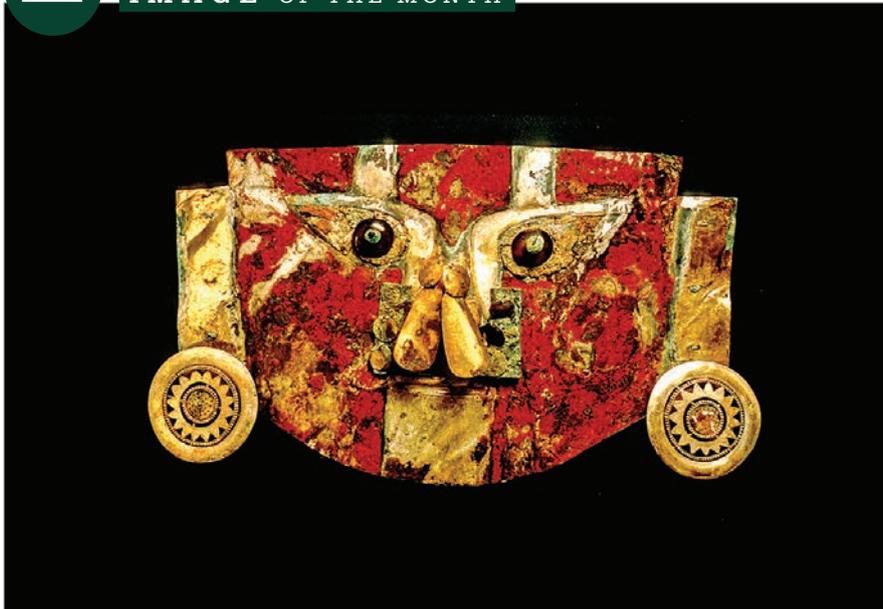
“Roman is designed specifically to solve mysteries such as cosmic acceleration, but its enormous view of the universe will reveal a treasure trove of data that could help explain other puzzles as well,” said Elisabeth Krause, co-author and assistant professor at the University of Arizona, in a recent press release (2). “The mission could even help answer questions no one has thought to ask yet.”

### Reference

1. *Tim Eifler et al., Mon Notices Royal Astron Soc, 507, 1746 (2021). DOI: 10.1093/mnras/stab1762.*
2. *NASA (2021). Available at: <https://go.nasa.gov/3HGwBoH>*



## IMAGE OF THE MONTH



*Egg on Your Face*

An analysis of the red paint preserved on the surface of a 1000-year-old gold mask excavated from a Middle Sican tomb in Peru finds human blood and bird egg proteins. The researchers used a combination of FTIR, lipid analysis, and proteomics by MS. “The presence of human blood would support previous ideas that red cinnabar paint may represent ‘life force’ intended to support ‘rebirth,’” wrote the authors.

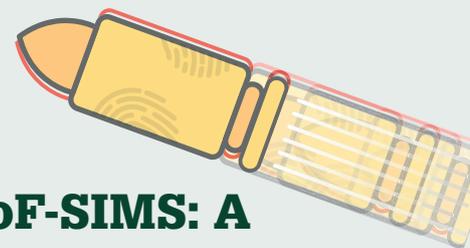
*Credit: Photo by Y. Yoshii & SAP*

Would you like your photo featured in Image of the Month?  
Send it to [james.strachan@texerepublishing.com](mailto:james.strachan@texerepublishing.com)

## QUOTE OF THE MONTH

*“To me, a (scientific) academic career is first and foremost all about maintaining and transferring knowledge. Teaching! Politically, we see all around the world that maintaining knowledge in society is a huge issue. I’d argue, based on what I have seen thus far during my limited career, that the same is true in science.”*

Bob Pirok, Assistant Professor at the University of Amsterdam, The Netherlands



## ToF-SIMS: A Secret Forensics Weapon?

**A new approach to imaging could help forensic scientists retrieve fingerprints from tricky bullet casings**

A team of researchers at the University of Nottingham, headed by James Sharp, have developed a unique ToF-SIMS method for imaging fingerprints left behind on curved objects, such as bullet casings (1). Traditionally, these objects pose a challenge for forensic scientists both because of their tricky shapes, but also the physical conditions the bullet is exposed to – like high temperature and pressure.

The team had already proven that ToF-SIMS provides much more accurate and detailed images than conventional forensic techniques, but they have now added a rotational stage that allows even more detail to be gained over the entire surface area of a bullet casing while crucially being non-destructive. The approach works by analyzing a thin strip and then rotating the object a few degrees, eventually stitching the strips together to form a complete image. The team were able to pick up ridge and sweat pore level detail on samples where no fingerprints had previously been detected.

“It’s really exciting to be taking this research a step further by adding the rotational stage,” said Sharp in a press release (2). “This could really pave the way for a new reliable way to analyze evidence, identify persons of interest and link them to the ammunition in a firearm.”

### References

1. CJ Lee et al., *Analyst* (2021). DOI: 10.1039/D1AN01768C
2. *EurekAlert* (2021). Available at: <https://bit.ly/3xLfy0e>

## Popular Reflections: The Rise and Rise of Metabolomics

**In 2018, Martin Giera, Mary E. Spilker and Gary Siuzdak shared their love of a special field in “Metabolomics: the Superglue of Omics” (1). Here, we catch up with Martin and Gary.**

Have there been any major developments in the field of metabolomics – especially related to systems biology and metabolite activity screening (systems-MAS) – since you wrote the article in 2018?

Absolutely. Firstly, we refined the topic quite nicely in our 2019 Nature Reviews in Molecular Cell Biology paper (1), now calling it “Activity Metabolomics” (more catchy!). Secondly, it is apparent in my daily work that there is increasing appreciation – and demand from both academic and industrial partners – for deciphering phenotypic observations and linking them to potentially bioactive metabolites. For example, my group is focusing on desmosterol – an endogenously formed precursor of cholesterol. Just recently we showed that its controlled accumulation by inhibiting its metabolism into cholesterol caused selective liver X receptor activation and thereby triggered an anti-inflammatory/pro-resolving phenotype (2). Importantly, others confirmed the anti-inflammatory/pro-resolving properties of desmosterol also in neurological disease settings (3, 4). It seems that boosting the accumulation of bioactive endogenous metabolites is becoming a cutting-edge therapeutic avenue. Recent examples from Gary’s lab include the identification of

microbiome derived bioactive metabolites influencing T cell-induced colitis as well as metabolites that modulate thermal regulation during calorie restriction (5, 6).

Is systems-MAS any closer to overcoming the challenges you posed, such as the need to develop effective approaches to identify active metabolites and generate libraries cataloging their bioactivity?

We feel a lot has happened. However, identifying bioactive metabolites remains a major challenge and tedious job. I believe one way forward might lie in starting out with identifying key pathways using CRISPR and iPSC technologies. For example, Martin’s group is involved in two exciting projects in this framework: one investigating the lipidomic disturbances in a library of CRISPR modified lipid transport proteins, and another (The Neurolipid Atlas, CZI funded) building a quantitative lipidomics atlas of hiPSC derived neural cells, including neurodegenerative disease-specific gene modifications. Both projects have the potential to identify novel disease-relevant lipid pathways, thereby leading to potential new targets and metabolic intermediates for bioactivity screening.

Consistent with Martin’s group, the Siuzdak lab is finding that metabolomics is the first step in identifying bioactive metabolites. And subsequent orthogonal technologies are required to complete these stories. For example, we (Siuzdak lab and collaborators) have been investigating two separate immunomodulators for years now, since their original discovery and identification.

Do you have any recent research highlights you’d like to share?

On the technical side I think that our recent work on employing enhanced in source fragmentation as a quantitative



bioanalysis tool on simple single quadrupole mass spectrometers has great potential enabling QqQ like quantitative analysis on a broad range of machines – and at a much lower cost, essentially democratizing MS (7). And the ever-growing METLIN database (now at 860K molecular standards with MS/MS and neutral loss data) is certainly helping on the identification side (8).

Overall, are we any closer to being able to “fix biology with biology” using metabolites?

Yes, we are. In general terms, it is extremely important that the perception of metabolites is changing. For years, metabolites have been considered as inactive biological bystanders. But this is starting to change and metabolites are becoming increasingly recognized as master controllers of biological phenotypes. If you think about it, whole scientific fields, such as immune-metabolism, are built on this



fact. Moreover, from several projects Martin is involved in, we are beginning to understand how the molecular composition of a cell determines its basic functions – consider immune cells and, in particular, immune cell subtypes, for example, M1, M2 macrophages or immunological phenomena such as trained immunity. Nevertheless, the translation of this knowledge into exploitable biological tools will be even more important – and that’s when we can talk about fixing biology with biology. Frankly, we expect novel therapies targeting the molecular composition of immune cells (in particular) to arise during the next decade. A recent example is the inhibition of 15-PGDH a prostaglandin E2 degrading enzyme (9). Moreover, neurological disorders, such as multiple sclerosis or even Alzheimer’s disease, might finally become treatable, if we understand how to molecularly control the function of specific neurological cells, a recent example is the involvement of post-squalene sterol

biosynthesis in microglia facilitated repair of demyelinated lesions (3).

Thinking more broadly, what has been the most exciting advance in analytical science since you wrote the article in 2018?

There are a couple actually. The shotgun lipidomics assistant (SLA), recently published by Kevin Williams and colleagues (10), is a really cool platform allowing the quantitative-flow-injection-based analysis of up to 1400 individual lipid species (10). Martin is really happy that his group could partake in this development – it is one of the most frequently applied assays in my lab. Joshua Rabinowitz’s group published some remarkable papers on metabolic flux analysis (11) – a topic that will become increasingly important particularly when trying to fully understand metabolic homeostasis. The development of METLIN and more recently enhanced in-source fragmentation by Gary’s group has also

been a great contribution, particularly considering its potential impact. The quantitative application of this development, termed Q-MRM, could enable students and less fortunate colleagues around the globe to carry out triple-quad-like quantitative analysis on affordable single quadrupole machines with similar sensitivities.

#### References

1. *MM Rinschen et al., Nat Rev Mol Cell Biol, 20, 6, 353–367 (2019)*
2. *A Körner et al., Proc Natl Acad Sci USA, 116, 41, 20623–20634 (2019)*
3. *SA Beryboff et al., Nat Neurosci, 24, 1, 47–60 (2021)*
4. *RG Snodgrass et al., Cell Death Differ, 28, 4, 1301–1316 (2021)*
5. *JR Montenergo–Burke et al. Sci Signal. 14, 702, eabf6584 (2021)*
6. *C Guijas et al. Sci Signal. 13, 648, eabb2490 (648)*
7. *JXue et al., Anal Chem, 93, 31, 10879–10889 (2021)*
8. *JXue et al., Nat Methods, 17, 952–954 (2020)*
9. *AR Palla et al. Science, 371, 6528, eabc8059 (2021)*
10. *B Su et al., J Am Soc Mass Spectrom, in press (2021)*
11. *S Hui et al., Cell Metab, 32, 4, 575–688 (2020)*

## ICP-MS: Taking the “Gold Standard” to the Next Level

**Today, ICP-MS allows us to understand how cells interact with their environment – but we have a long way to go before we can measure these dynamic processes as they occur. What comes next?**

*By Norbert Jakubowski, Spetec GmbH, Germany*

Cells are the basic unit of all living organisms – “the building blocks of life” – so it isn’t surprising that analyzing cells and their constituents is central to life science research. One challenge for researchers is that cells vary considerably – even cells of the same culture behave differently at a chemical level because of their different life cycles (or cell status). ICP-MS is the only method that provides quantitative metal data in single cells with multi-element coverage and high sensitivity, which has led to its rise as the gold-standard tool for measuring how cells interact with their environment.

Elemental single-cell analysis comprises both the assessment of biomarkers through metal tagging of antibodies (denoted as mass cytometry or imaging mass cytometry), as well as the determination of endogenous/toxic metal accumulation and the up-take of nanoparticles from cell suspensions. Isolated cells and cell agglomerates in tissue samples have been investigated with laser ablation (LA)-ICP-MS in an imaging mode, which has focused on detecting metals – either directly or with metal tagged antibodies.

Though ICP-MS has been on the



### In My View

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

market since 1983, mass cytometry is a relatively young technology (commercially available since 2009, launched by DVS – Dimitry, Vladimir and Scott – under the brand name CyTOF Mass Cytometer). The basic idea is similar to fluorescence-based flow cytometry. Instead of using fluorescence to tag antibodies, single-enriched isotopes of rare earth elements (REE) are used. This approach overcomes the problem of “bleaching” or high-background interference associated with autofluorescence, while also allowing the use of a greater number of isotopes in a single assay. Then, to bind metal isotopes to antibody polymers, tags are applied, which mostly bind to surface receptors of single cells or, in the case of phenotyping, the antibodies bind to intracellular proteins after cells are permeabilized (the approach for cell functional assays). Because each polymer can bind up to 100 atoms, it is possible to amplify a single protein/receptor by the same factor. In fact, a cell can have up to 1,000 surface receptors of the same kind, which can really increase the amplification for extremely high sensitivity!

After incubation of the target cells with

different antibodies, which are tagged individually by enriched nuclides from lanthanide elements, the cell suspension

*“There have been a number of improvements in ICP-MS over the years. For example, higher sensitivity, higher time resolution, and dedicated sample introduction systems.”*

is transported to a pneumatic nebulizer. Stochastically spaced cells in the laminar flow are then delivered concentrically to the plasma core, where the cells get ionized. Since each cell generates ion signals of a few hundred  $\mu\text{s}$  peak width, a very fast mass spectrometer (a time-of-flight instrument) is required to measure each cell time resolved.

There have been a number of improvements in ICP-MS over the years. For example, higher sensitivity, higher time resolution, and dedicated sample introduction systems. For laser ablation systems, lasers have been developed with higher repetition rates (up to 200 Hz), the ability to wash out aerosols more quickly to achieve better lateral resolution at the sub-micrometer level.

With novel LA-ICP-MS devices, sub-micrometer resolution has been achieved, which is needed to compete with light microscopy! Early results have demonstrated multiparametric analysis of cancer tissues with up to 40 parameters measured in the imaging

mode by laser ablation. Indeed, such analysis has revealed the role of the neighboring community of cells in cancers – going some way to explaining why patients respond differently to cancer treatments.

There have been thousands of papers published on the use of ICP-MS, covering nano-particle interactions, metallo-drug research, various types of cancer research, and many more areas. However, some big challenges remain. For example, at the cellular level, we don't have reference materials, which holds true for imaging and mass cytometry. And that means we must use our own standards to calibrate devices – not an ideal situation. Validation reference materials and inter-lab comparisons are urgently needed. And concerning mass cytometry, we still wait for it to be accepted as a routine diagnostic tool for detection of cancer, inflammation or other diseases.

In the future, through improvements in reagents, it may be possible to detect single viruses or even single molecules.

Currently, we can measure the end-point of a disease, such as a cancer cell, or the toxification of a cell leading to cell death, but we cannot measure these dynamic processes as they occur (time resolved analysis). We would need multimodal spectroscopies to measure – in a time resolved manner – the complex chemistry underpinning living processes.

In fact, we know very little about the complex machinery of life, which is why we need more scientists – especially younger scientists – applying analytical chemistry to the complex reactions taking place within cells at the nano-meter level and at time scales of  $\mu\text{s}$ - or milli-seconds. Single cell analysis – including ICP-MS – can take us a long way, but we need to measure living processes in real time to truly understand what's going on. Who will step up to the plate?!

*Norbert will be chairing a session on elemental imaging and mass cytometry at the Winter Conference, Tucson, Arizona, USA, in January 2022*

## Stable Isotopes in an Unstable Climate

### The ongoing search for evidence of our changing environment

*By Calum Preece, Environment Product Manager, Elementar UK*

Since the 1860s, when physicist John Tyndall recognized the Earth's natural greenhouse effect, scientists have understood the insulating qualities of carbon dioxide and other greenhouse gases. A seminal paper written by Swedish



scientist Svante Arrhenius in 1896 was the first to predict that changes in the level of carbon dioxide in the atmosphere could substantially alter the surface temperature, further advancing our understanding.

Today, satellites and other technological

advances have enabled scientists to collect more information about the Earth, allowing them to analyze its climate on a global scale and to identify the signs of a changing climate.

How the Earth's climate responds to changes in greenhouse gas can be seen in ice cores drawn from Greenland, Antarctica, and tropical mountain glaciers. Bubbles of air in glacial ice trap samples of the Earth's atmosphere from as far back as 800,000 years ago, and the chemical makeup of the ice provides clues to the average global temperature. Additionally, the study of tree rings, ocean sediments, coral reefs, and layers of sedimentary rock all allow scientists to see the Earth's atmospheric conditions as they existed thousands of years ago.

Using these ancient records, scientists have been able to see how the Earth's

climate has changed over time, including past ice ages and periods where the climate was warmer than it is today. This paleoclimate record also reveals that current climatic warming is occurring more than 10 times faster than the average rate of ice age warming (1). The predicted rate of warming for the next century is at least 20 times faster.

But scientists studying climate change to determine future scenarios only have what has happened before to help their research. Stable isotope analysis works as a virtual paleo-thermometer, allowing readings of past Earth temperatures in a variety of materials. By combining this temperature information and extrapolating into the future, stable isotope analysis plays a crucial role in helping to understand how the worst outcomes can be avoided.

For example, Peter Wynn, a senior lecturer at Lancaster University, uses stable isotope geochemistry in glaciology and the reconstruction of paleoclimates. Wynn and his team conduct stable isotope analysis on a diverse range of sample types and across a broad range of environmental problems – from deep geology and pollution dynamics to wildfowl migration patterns (2).

The department specializes in analyzing sulfur isotopes and high-temperature oxygen pyrolysis. And they have established techniques to extract sulfur isotopic signals from paleo records, including speleothems, tree rings and carbonate rocks, and routinely use high-temperature pyrolysis to extract the isotopic record from oxygen-bearing molecules, including sulfates and phosphates. Future research for the department will focus on isotope analysis of greenhouse gases, including the analysis of methane C and H isotopes and nitrate N and O isotopic composition in a variety of environmental samples.

Another example: research engineers Michel Stievenard and Monique Pierre supervise a stable isotope laboratory of the continental paleoclimate section of the Laboratoire des Sciences du Climat

*“Stable isotope analysis works as a virtual paleo-thermometer, allowing readings of past Earth temperatures in a variety of materials.”*

et de l’Environnement (LSCE) (3). The group analyzes cellulose from tree rings for their carbon and oxygen isotopic composition – data that provides insight into past climates, especially humidity and temperature conditions. The team reconstruct regional climates of the past using trees from places all over the world; for example, living trees from Tibet and Morocco, Réunion island fossil trees, and massive wood beams from historical French castles. One project focused on finding a reliable paleoclimate reconstruction based on tree ring proxies (4).

The project compared the potential of the oxygen isotopic composition of the cellulose in two types of trees: *Fitzroya cupressoides* and *Nothofagus pumilio*, which are found in Patagonia. The *F. cupressoides* was favoured to assist in long-term climate reconstruction due to their longevity (they can grow up to almost 4,000 years old). However, due to a poor understanding of its complex physiology, it was difficult to determine the climatic signal recorded in its  $\delta^{18}\text{O}_{\text{cell}}$ . The results indicated that *N. pumilio* represented a more robust paleoclimate archive due to its

$\delta^{18}\text{O}_{\text{cell}}$  consistency between sites. Analyses of a 200-year-long  $\delta^{18}\text{O}_{\text{cell}}$  chronology are currently in progress.

Climate change is one of the greatest threats to human civilization, but determining future climate scenarios can only be built on the foundation of what we know has happened before. In order to achieve this, the world’s scientific community will need to make full use of all of the tools available to them – which is why elemental analysis, which has been long-established as a tried-and-tested method of long-term climate analysis, will be relied upon more than ever before.

Leading scientific organizations, such as NASA, have cited elemental analysis as one of the key tools they rely upon to extract the maximum amount of climate insight from the physical, chemical and biological materials used as climate proxies, meaning climatologists now have a strong idea of how global temperature trends have developed for millions of years into the past. Armed with this knowledge, it becomes possible to develop well-informed climate scenarios for the future, which in turn clarifies the actions that must be taken if the world is to avoid the worst possible outcomes.

As with all aspects of the current climate crisis, knowledge of these factors is only half the battle, and the world still faces many obstacles to making the necessary difference. However, by making use of the full range of technological solutions available, it will be possible to ensure that any future decisions are taken from the best possible scientific vantage point.

#### References

1. NASA (2010). Available at: <https://go.nasa.gov/3CBm4qX>
2. Elementar UK (2021). Available at: <https://bit.ly/3CHv0l0Y>
3. Elementar UK (2021). Available at: <https://bit.ly/3oKVcjB>
4. M. Stievenard, et al. (2020). Available at: <https://bit.ly/3nF4fTS>



## Best things come in small packages

The HIC-ESP ion chromatograph features the same low carry-over and excellent injection precision characteristics of Shimadzu HPLCs to ensure highly reliable results in quantitative ion analysis. The newly developed, low-volume anion suppressor minimizes band spreading to achieve the highest sensitivity, providing stable functionality even over long periods of use, while the system's small footprint offers more efficient use of laboratory bench space.

**High sensitivity, reliability and robustness**  
through use of the new patent-pending ICDS-40A anion suppressor

**Outstanding performance in a compact design**  
with optimized solvent delivery, low carry-over and fast injection speeds

**Seamless integration with LabSolutions software platform**  
simplifies analysis settings, data processing/review and reporting while ensuring data integrity

[www.shimadzu.eu/small-packages](http://www.shimadzu.eu/small-packages)



HIC-ESP Ion Chromatograph



## No Prize for Second Place?

**Rather than rushing to the finishing post, we should all focus on data quality by sticking to the four Cs: consistency, correctness, completeness, and credibility**



*By Meriem Gaida, PhD student in the Organic and Biological Analytical Chemistry (OBiAChem) laboratory, University of Liège, Belgium*

What does it take to provide good quality data in science? A rudimentary question and yet a profoundly important one – especially for young emerging scientists at the start of their careers.

In a world bouncing between two paces – quick and quicker – our self-worth can often be driven by our ability to produce and to deliver. And though this is a natural human reaction, one should still keep in mind that faster does not always mean better – particularly in science! We must ensure that we're producing high-quality data and not producing data for its own sake.

Good quality data entails good lab practices, and reflects the researchers' attitude, commitment, and ethic. As researchers, we are expected to critique our own research and the research of others. We must ask relevant questions

before starting any project to make sure we avoid common data pitfalls.

How can I certify the quality of my data? Well, it is simple! The data needs to satisfy the “four C's”:

- **Consistency:** compatibility within each collected data point and suitability of the dataset they form for the research question.
- **Correctness:** the dataset contains no aberration and is relevant to the value that is measured.
- **Completeness:** the produced dataset does not contain missing values.
- **Credibility:** the produced dataset is plausible and realistic.

The temptation to overlook one or more of these rules of thumb can be strong – especially when up against a deadline and intense competition for grants and academic positions. Unfortunately, tweaking study results to achieve a statistically significant outcome is not an uncommon practice in science. In fact, according to a Nature survey, 70 percent of researchers did not manage to reproduce other scientists' experiments and 52 percent of the participants to the survey attest to a significant reproducibility crisis in science (1).

Some practices are far too common: cherry picking, ruling out data that do not seem to reinforce the starting hypothesis; P-hacking, testing, arranging, filtering, tweaking and/or tuning of the dataset to obtain a statistically significant result; and outcome switching, altering a protocol to rule out inconclusive or negative results. The data must lead to the conclusion and not the opposite!

Recently, a Nature investigation (2) raised concerns about the manipulation of the publishing process via “paper mills” – firms that produce falsified research. The study revealed that in January 2021,

68 papers were retracted from the RSC advances journal due to allegations that they may be linked to paper mills. By March 2021, 1300 articles were identified as being fraudulent and 26 percent of them were already pulled back or stamped with expressions of concerns. This comes with no great surprise since the number of retracted articles had increased 10-fold during the previous 10 years, with fraud accounting for about 60 percent of these retractions (3). In a Nature statement, Elsevier and other publishers expressed their deep concern over paper mills, saying that what they are currently witnessing is only the tip of the iceberg – but that they're doing their best to combat falsified research. Many journals are now implementing a stricter review process by demanding that the editors ask for the raw data and by training and hiring people to stamp out suspicious manuscripts.

Managing data responsibly and with integrity makes findings easier to share, reuse, and, most importantly, to reproduce – and data reproducibility is a cornerstone of good quality research. Finally, good quality data helps scientists improve their visibility and facilitates collaborations. It can also help speed up innovation and, perhaps even more importantly these days, restore the public's faith in science.

Just remember: science is not meant for quick fixes!

### References

1. M Baker and D Penny, “Is there a reproducibility crisis?”, *Nature*, 533 (2016). DOI: [doi.org/10.1038/533452A](https://doi.org/10.1038/533452A).
2. H Else and R V Noorden, “The fight against fake-paper factories that churn out sham science”, *Nature*, 591, 516–519 (2021). DOI: [doi.org/10.1038/d41586-021-00733-5](https://doi.org/10.1038/d41586-021-00733-5)
3. J Brainard and J You, “What a massive database of retracted papers reveals about science publishing's ‘death peanalty’”, *Science*, (2018). DOI: [doi: 10.1126/science.aav8384](https://doi.org/10.1126/science.aav8384)

GOLD  
OPEN  
ACCESS

# Energy Advances

## Embracing research at the nexus of energy science and sustainability

Your ideas could help tackle  
global energy problems.  
Open for submissions now.

[rsc.li/energy-advances](https://rsc.li/energy-advances)

 @ees\_journal

Fundamental questions  
Elemental answers



<sup>the</sup>  
**Analytical Scientist**  
**INNOVATION**  
**AWARDS**

**BE NOT  
AFRAID OF  
GREATNESS!**

*After open nominations and scrutiny from our expert judging panel, we showcase 15 trailblazing technologies that cut the mustard in this year's TASIAs*

15



## DPiMS QT

Probe electrospray ionization (PESI) is combined with a quadrupole time-of-flight mass spectrometer for the analysis of small samples

*Produced by Shimadzu Corporation*

Shimadzu's DPiMS QT allows researchers to analyze small quantities of sample (liquid or solid) without sample preparation and without LC separation with HRMS. Moreover, thanks to the ease of switching between probe electrospray ionization (PESI) mode or LC-ESI-MS mode, it can provide a wide range of analytical methods – from rapid screening to quantification (using LC-MS analysis).

### Potential impact

DPiMS QT will be useful for quick screening in the forensic toxicology field, as well as in the food industry. It reduces the time required to analyze blood, urine, and other biological samples with conventional methods by approximately 50 percent, according to Shimadzu.

### What the judges say...

*"An exciting sampling interface that reduces sample usage and speeds up analysis times."*

14



## BIOPHASE 8800 SYSTEM

The BioPhase 8800 is the only multi-capillary system for CE-SDS analysis on the market – and it aims to help biopharma companies shorten development timelines

*Produced by SCIEX*

The development of increasingly sophisticated biopharmaceutical therapies, such as monoclonal antibodies (mAbs), mAb variants, and gene therapies, requires rapid measurement and monitoring of critical quality attributes throughout the development continuum. The SCIEX BioPhase 8800 is a multi-capillary system for CE-SDS analysis that processes eight samples simultaneously – helping scientists understand molecular liabilities more quickly in their efforts to develop and manufacture robust and stable biologics.

### Potential impact

Biopharmaceutical manufacturers are transitioning to more innovative biologics; samples are becoming more numerous and more complex – but results are still needed quickly. By processing eight samples simultaneously, the BioPhase 8800 can, according to SCIEX, reduce experiment design times from one month to as little as a week. How? Because researchers are able to rapidly quantify critical quality attributes for large sample sets, which delivers consistent, comparable data throughout the pipeline – from R&D to bioprocessing to QA/QC.

### What the judges say...

*"A nice, higher throughput CE-SDS system incorporating multi-capillary analysis."*

13



## ORBITRAP IQ-X TRIBRID MASS SPECTROMETER

Combining mass analyzer tech with intelligent acquisition, intuitive software, and hands-free calibration for small molecule identification

*Produced by Thermo Fisher Scientific*

Thermo Fisher Scientific's Orbitrap IQ-X Tribrid MS features software that enables real-time library search to address the complexities of small-molecule identification. The local and customizable library can be used to selectively detect and characterize unknown compounds that are structurally related to known compounds. There's also an ultraviolet photodissociation option, which provides insights on lipid double-bond localization and site specific glucuronidation; while the 1,000,000 resolution option enables fine isotope detection and improved confidence in results.

### Potential impact

The Orbitrap IQ-X Tribrid MS aims to allow small molecule researchers – both in academia and the pharmaceutical industry – to confidently perform a range of applications, including metabolomics and lipidomics research, leachable/extractable impurities identification, and forensic toxicology. The real-time library search technology provides simultaneous spectral searching to increase confidence in metabolite identification and characterization, and improve the structural analysis of isomeric species. Overall, the technology should reduce the number of compounds without MS<sup>n</sup> spectra and increase the number of compounds identified.

### What the judges say...

*"This is probably the best platform currently for untargeted metabolomics as the IQX enhances metabolite identification – one of the bottlenecks in metabolomics."*

12

## CRYORAMAN

A Raman microscope that enables measurements at a supercool 1.8 K, in high magnetic fields, and with full polarization control

*Produced by WITec GmbH and attocube systems AG*

WITec and attocube's cryoRaman makes Raman microscopy at the edge of absolute zero a possibility for the first time by integrating a Raman imaging system with a cryogenic sample chamber. The technology offers VIS to NIR excitation lasers, 1.8–300 K operating temperatures, high magnetic fields of up to 12 T, cryogenically compatible Raman-specific objectives, and a precise piezoelectric scan stage. Other options include precise software-controlled laser power adjustment, automated switching between optical microscopy and spectroscopic imaging, multi-wavelength excitation capabilities, automated spectrometer calibration light source and routines, time-correlated single photon counting (TCSPC) modes, low-wavenumber Raman peak detection, and full polarization control in excitation and detection.

### Potential impact

Interest in cryogenic Raman imaging has expanded beyond the initial core of graphene and carbon nanotube research groups, which drove the development of cryoRaman. Research on phase-transitions and emergent properties of novel low-dimensional materials will benefit from cryoRaman's high magnetic field options, which are ideal for investigating transition metal dichalcogenides (TMDs) and van der Waals heterostructures. Possible applications of these materials include the new generations of transistors, photo detectors, light-emitting diodes and photovoltaic cells.

### What the judges say...

*"Looks interesting for analysis at cold temperatures – it will be good to see what info comes out of this!"*



## MH VERIFY

A LAMP-based test for HLVD: RNA that can cause disease in many plants, including cannabis

Produced by *KAYCHA LABS*

Hop Latent Viroid (HLVd) is a single-stranded, circular strand of RNA that can cause disease in many plants, including cannabis/hemp. Plants infected with HLVd may or may not show symptoms and the disease can be dormant in a plant for extended periods of time prior to showing symptoms. Kaycha Labs' HLVd test uses a type of PCR called loop mediated isothermal amplification (LAMP), which, when tagged with carboxyfluorescein (FAM) and biotin, creates dual-labeled products that can be visualized with lateral flow assays (LFA). If a sufficient number of dual labeled products are present, a

test line becomes visible within 5-10 minutes.

### Potential impact

HLVd greatly reduces the quality and quantity of the flower in the infected plant. During the vegetative stage, plants grow shorter with smaller leaves and tighter node spacing. Flowering plants will have smaller buds with much fewer trichomes. Over time, yields can be reduced up to 70 percent, with a loss of potency and terpene production up to 35 percent. MH Verify's field test kit makes it easier for growers to detect plant pathogen contamination rapidly.

### What the judges say...

*"This technology could benefit the economics of the cannabis/hemp industry. And it seems to be fairly simple, easy to implement technology."*

11



## PROTEOME DISCOVERER 3.0 SOFTWARE

Artificial intelligence and deep learning for proteomics research

*Produced by Thermo Fisher Scientific*

Proteome Discoverer 3.0 is a piece of MS software that, when combined with MSAID's CHIMERY search engine, uses artificial intelligence (AI) and deep learning to substantially increase peptide identification and quantitation capabilities for proteomics researchers. Instead of assuming that all peaks in a tandem mass spectra are derived from a single peptide, as most software does, Proteome Discoverer identifies a minimal set of peptides that can explain the acquired tandem of mass spectra.



### Potential impact

AI allows deeper mining of proteomic data, not only improving proteomic coverage, but also expanding the possibilities for scientists to acquire and apply their data. According to Thermo Fisher Scientific, the software provides a 1.7-fold increase in the peptide identification rate and 1.3-fold increase in the protein identification rate, which should enable more efficient data acquisition, helping scientists generate more biological insights from their data.

### What the judges say...

*"This appears to be a first generation proteomics software platform based on AI technology for more efficient and accurate protein identification. Proteome Discoverer is already an industry standard for the field; I expect many customers will upgrade their systems to version 3.0."*

## SPECTRUS JS

Spectrus JS is the first browser-based NMR data processing software on the market

*Produced by ACD Labs (Advanced Chemistry Development, Inc.)*

Spectrus JS brings the ACD Lab's popular NMR data processing tools from the desktop to the browser, providing a complete toolset for processing 1D and 2D NMR data without the heavy CPU requirements and lengthy installers needed to use modern desktop NMR processing software. The easy-to-access interface makes Spectrus JS suitable for casual users and expert spectroscopists alike. For the first time, organizations can host vendor-agnostic NMR processing applications and deliver them to users over their network – all individual users need to do is type the URL into their browser and log in.

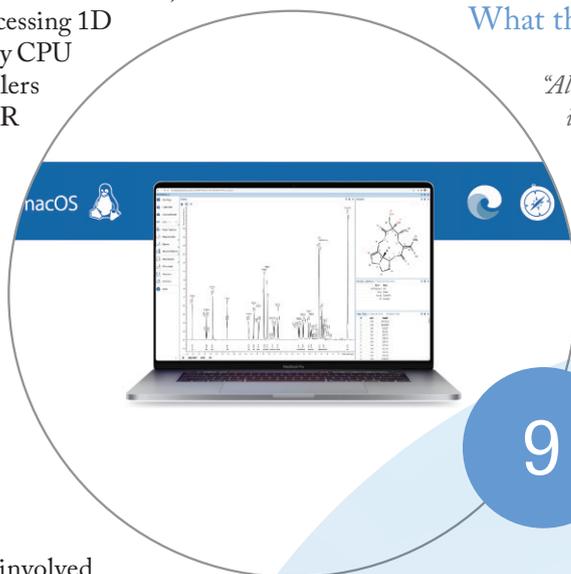
### Potential impact

For facility managers and those involved

in the management of open access labs, Spectrus JS will allow easy deployment on a single hosting server/computer. Additionally, being able to access the software remotely will allow for better use of instrument time – enabling a shift to more flexible work environments. In academia, students can access Spectrus JS on their own devices or shared public computers, enabling educators to better equip their students by providing hands-on experience processing NMR data.

### What the judges say...

*"All-in-one software is always appreciated in core facilities. And this will be a popular NMR software system for academic and other large facilities because of its flexibility."*





## ORBITRAP EXPLORIS GC 240 MS

A high-resolution GC-MS system with the mass resolving power to expand research capabilities

*Produced by Thermo Fisher Scientific*

The Orbitrap Exploris GC 240 MS has a resolving power of 240,000 that, in combination with its wide dynamic range, should deliver increased flexibility, speed, and accuracy in a variety of research applications. The system offers MS/MS capability for compound structural information, and both electron and chemical ionization without system venting – for fast and accurate analysis.

### Potential impact

The Orbitrap Exploris GC 240 MS aims to accelerate scientific discovery in academic, industry research, government, and omics laboratories. The system provides the flexibility to tackle a diverse range of analytical challenges, including identification of unknown compounds across a spectrum of applications – from extractables and leachables studies to metabolomics.

### What the judges say...

*“An integrated GC system coupled to high resolution Orbitrap mass spectrometry is a nice advancement over previous generations. It is better integrated than previous generations too – and in a smaller footprint. I expect that this will be a popular instrument.”*

7



## SELECT SERIES MRT

A high-resolution quadrupole time-of-flight mass spectrometer that delivers 200,000 Full Width Half Maximum (FWHM) resolution and part-per-billion mass accuracy independent of scan speed

*Produced by Waters Corporation*

The 200,000 FWHM resolution achieved by the SELECT SERIES MRT is the result of multiple reflections of the ion beam, which increase the length of the flight path to 47m, while maintaining a manageable instrument footprint. This, in combination with multi reflecting time-of-flight (MRT) technology, results in high resolution over a broad mass range and routine ppb mass accuracy, enabling highly detailed structural characterization. The system was introduced for MS imaging and can be equipped with enhanced desorption electrospray ionization (DESI) and matrix-assisted laser desorption ionization (MALDI) imaging sources. Together, these technologies enable scientists to explore molecular structure and function through the precise identification and localization of individual molecules in samples.

### Potential impact

SELECT SERIES MRT aims to help scientists increase their understanding of the spatial localization of molecules and their mechanisms of action in various scientific fields, including pharma, biomedicine, natural products research, and materials research. For example, a researcher trying to understand how an investigational oncology drug interacts with its intended target, such as a specific brain tumor receptor, could use the SELECT SERIES MRT to do so much faster – at speeds up to 10 Hz without compromising mass accuracy or resolution.

### What the judges say...

*“This is a really exciting multi-reflecting ToF mass spectrometer that not only allows higher resolution, but does so in a compact space. This is one instrument to watch.”*

## BIOACCORD SYSTEM WITH ACQUITY PREMIER

Enhancing biotherapeutic monitoring through improved analyte recovery and increased assay-to-assay accuracy and precision

*Produced by Waters Corporation*

With pre-defined analytical methods, guided workflows, auto-calibration and auto-tuning, analysts can use Waters' BioAccord System with ACQUITY Premier to monitor critical quality attributes of biotherapeutics and assess the processes that make them, while decreasing risk. The system incorporates the ACQUITY Premier LC inlet featuring MaxPeak high performance surface (HPS) technology, which eliminates analyte/surface interactions and thereby improves recoveries of hard-to-detect sample analytes. The result, according to Waters, is improved assay-to-assay reproducibility.

### Potential impact

Biologists and chemists who once had to send samples to a laboratory and await results can, with Water's system, instantly monitor critical quality attributes of challenging biotherapeutics in development. With this information, drug companies may be able to cut costs and delays. Additionally, the system automatically monitors its own performance, improving productivity by maximizing system uptime and minimizing re-analysis.

### What the judges say...

*“The BioAccord has been a popular platform for biopharma analysis. This improved platform appears to be a nextgen system with improved systems capabilities – closer to plug-and-play for biopharma.”*

6



5



## MULTI-GAS ENABLED THERMAL DESORBERS

Thermal desorption instruments that can operate with hydrogen, helium, and nitrogen

*Produced by Markes International*

Markes' multi-gas enabled system has been independently certified for use with hydrogen as well as helium and nitrogen carrier gases. Switching to hydrogen produces the same data quality as helium, but at a greatly reduced cost. The implementation is straightforward too, as commercially available software can be used to translate the GC method from helium to hydrogen.

### Potential impact

Switching from helium to hydrogen carrier gas protects

laboratories against future helium shortages and is more sustainable because high-purity hydrogen can be generated from water. Hydrogen offers faster chromatographic separations, shorter thermal desorption methods and lower-temperature separations than helium, increasing laboratory throughput, extending consumables' lifetimes and extending maintenance intervals. Finally, switching from helium to hydrogen saves up to 90 percent per cylinder and a hydrogen generator eliminates the costs of cylinders.

### What the judges say...

*"Moving from helium to hydrogen for TD makes economic sense, with helium prices increasing rapidly. Many labs who have become frustrated with helium availability will find this product to their liking."*

## VIRSA RAMAN ANALYSER

A flexible, fiber-coupled system that allows real-time analysis of irregular surface samples

*Produced by Renishaw Plc.*

Renishaw's Virsa Raman analyser allows users to analyze samples away from the confines of the laboratory microscope, using remote fiber-optic probes, thereby expanding the use of Raman spectroscopy to new samples, applications, and environments. The Virsa system has LiveTrack focus-tracking technology and a new Monitor software module, which together enable real-time analysis on large samples with irregular surfaces – such as those that move (on production lines for example) or change shape as they undergo phase changes.

### Potential impact

The Virsa Raman Analyser is portable, allowing users to analyze samples in their native environment. Large or immovable samples that can't be placed under a microscope, or those contained within vessels, can be measured with laboratory-grade performance, high sensitivity, and high spectral and spatial resolution. Renishaw hopes that the system acts as a bridge between research/laboratory Raman measurements and in-field applications – expanding the range of applications and uses of Raman spectroscopy.

### What the judges say...

*"Raman often suffers because the sample must be flat. This solution builds on previous innovations to allow automatic real-time analysis on samples with irregular surfaces."*

*"A remote sampling probe for Raman spectroscopy is a welcome addition for many labs."*



3



## MOBIE

MOBIE is a SLIM-based high-resolution ion mobility product aimed at biotherapeutic drug development and multiomic biomarker discovery

*Produced by MOBILion Systems, Inc.*

MOBIE is MOBILion's first SLIM-based (structures for lossless ion manipulation) high-resolution ion mobility (HRIM) product on the market – and it aims to accelerate and simplify the workflows of challenging analyte classes, including peptides, proteins, lipids, and glycans. SLIM stands out from other ion mobility platforms with its 13-meter path length and serpentine electrode patterns (on standard printed circuit boards) – in a benchtop instrument. The longer path length enables a much higher resolution and the separation of highly similar molecules, greatly improving reliability and reproducibility in the lab.

### Potential impact

There's a growing demand for instruments that can characterize more complex therapeutic systems and identify biomarkers in the biopharma drug development space. And according to MOBILion, MOBIE can analyze 5-60 times faster than conventional separation methods, such as LC. MOBIE is integrated with Agilent Technologies' 6500 line of Q-TOF mass spectrometers, which combines high ion mobility separation performance with mass spectral fidelity.

### What the judges say...

*"The SLIM system has the potential to offer high resolution gas phase separations in small footprints compared with conventional systems. The applications are very broad and could impact a large number of areas."*

*"One of the true innovations in ion mobility based separations."*

2

## HYPERION II FTIR MICROSCOPE

FT-IR and infrared laser imaging (ILIM) microscopy are combined in a single device for the first time, offering all three measurement modes: transmission, reflection, and ATR

*Produced by Bruker Optics*

The HYPERION II FTIR QCL Imaging Microscope maintains the versatility of the original HYPERION microscope and expands its list of features with quantum cascade lasers (QCLs) and an optimized beam path for imaging applications. The HYPERION II can be equipped with a low magnification objective (3.5x) to enable fast imaging on large areas (for example, in tissue imaging or surface analysis). And the addition of a TE-MCT allows for sensitive MCT-measurements without the need for liquid nitrogen. Finally, the design has been streamlined to better represent the new features and match the style of the INVENIO-platform.

### Potential impact

The combination of FT-IR and QCL technology in one instrument should create new opportunities for researchers in a wide range of industries, including pharmaceuticals, forensics, microplastics, polymers and plastics, semiconductors, and more. Users simply need to collect an FT-IR spectrum and select the wavelengths for investigation using QCL to rapidly create chemical images.

### What the judges say...

*"A great combination of IR and ILM that should open up some interesting opportunities for combinatorial analysis of a range of materials."*

*"Access to a quantum cascade laser for imaging microscopy appears to be a powerful combination!"*



## ZENOTOF 7600 SYSTEM

A new QTOF mass spectrometer that includes a Zeno trap to increase duty cycle and EAD (electron activation dissociation) for alternate fragmentations and improved structural characterization

*Produced by SCIEX*

The ZenoTOF 7600 mass spectrometer is an orthogonal quadrupole time of flight (QTOF) mass spectrometer with a Zeno trap. With the new trap/release setup, ions at the end of the collision cell are trapped in a short linear ion trap. Voltages are then applied, causing the ions to be released so that lower  $m/z$  ions entering the TOF accelerator catch up with heavier ions at higher  $m/z$ , allowing all ions to meet before they get pushed in the TOF extraction region. The result is a substantial gain in sensitivity ( $\geq 90$  percent duty cycle) without the loss of mass resolution or accuracy – leading to improvements on MS/MS spectral quality. In addition, SCIEX's new reagent-free EAD (electron activation dissociation) cell offers an alternative fragmentation strategy, which preserves labile modifications.

### Potential impact

The improvements in MS/MS sensitivity offered by the Zeno trap coupled with the benefits of tunable modes of fragmentation with EAD should help scientists address analytical challenges across many markets. According to

SCIEX, the ZenoTOF 7600 can quantify up to 40 percent more proteins and analyze samples five times faster for large biobank studies. Moreover, EAD fragmentation could allow researchers to better understand how proteins are post-translationally modified – an important but challenging area in biomarker research. The system can also be used to fully characterize an individual lipid from a single spectrum using EAD fragmentation, which may enable the discovery of novel lipid markers for cancer and inflammatory disease.

### What the judges say...

*"This is a new generation QTOF mass spectrometer from one of the industry leaders in QTOF technology. The improvements in speed and sensitivity are clearly huge leaps over previous generations – as is the new EAD cell to generate fragment ion mass spectra."*







<sup>the</sup>  
**Analytical Scientist**

# THE INNOVATORS

SHOWCASING THE  
PRODUCTS AND  
COMPANIES MAKING  
A DIFFERENCE IN 2021



## HYPERION II: A BREAKTHROUGH IN FTIR IMAGING TECHNOLOGY

*The HYPERION II (FTIR, FPA, IR) Laser Imaging Microscope*

The HYPERION II Laser Imaging Microscope is breaking new ground in FTIR imaging with unmatched flexibility in integrating QCL technology with traditional IR source-based imaging down to the diffraction limit. The HYPERION II is the only IR microscope that combines infrared laser imaging (QCL) and FTIR microscopy in a single device empowering the user to get the best data possible.

With the HYPERION II, you are prepared for any application challenge. Whether you want to combine ATR, transmission, or reflection with single element MCT-, FPA-, or laser-imaging measurements, take control and let the HYPERION II work for you.

Its focal-plane array (FPA) detector takes IR imaging to the next level, providing unmatched spatial resolution and peak sensitivity for all analytical tasks. By incorporating both QCL technology and FTIR into the HYPERION II, the infrared laser imaging module (ILIM) offers limitless opportunities

for new and exciting discoveries.

But above all, the HYPERION II is all about having complete control of the instrument on a software platform that make even the most demanding analyses quick and easy. Taking FTIR measurements in single point mode, mapping or full imaging with various detectors and objectives is easily done. The Hyperion II also utilizes special sample stages like heating and cooling stages with full software control of temperature ramps and data analysis. With the OPUS Wizard software platform, you readily select and optimize the outcome of your results.

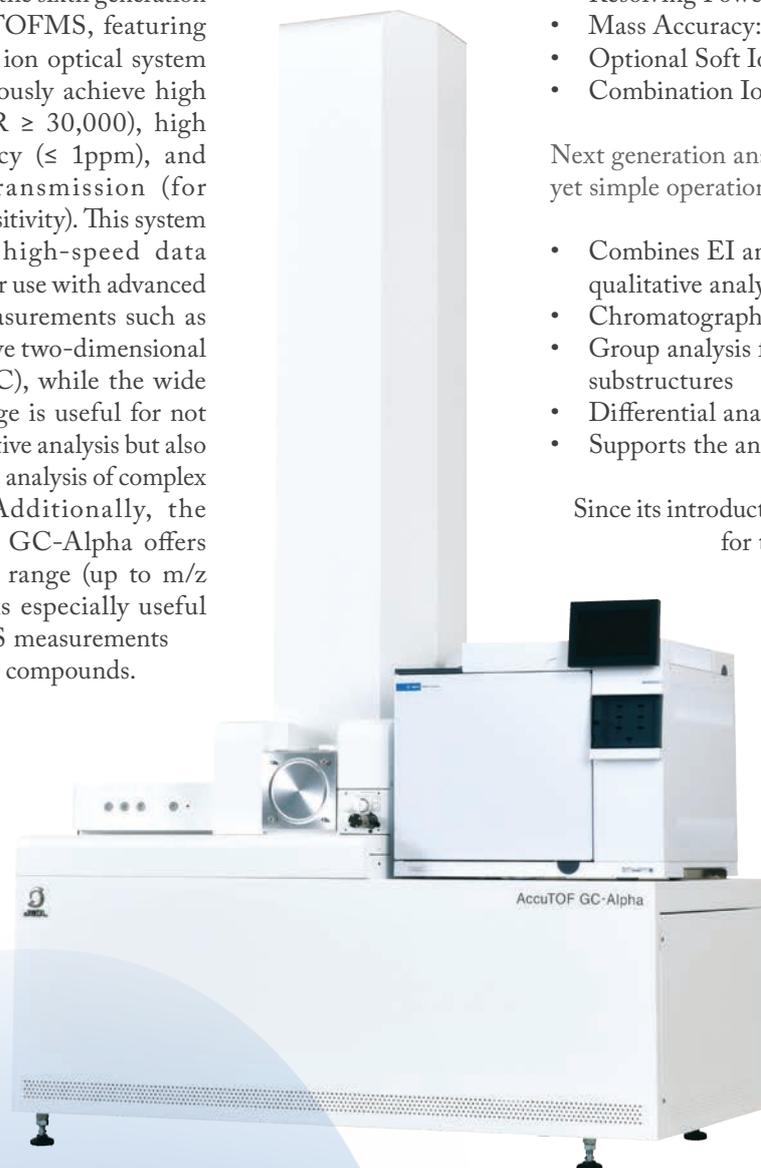
Only a practical combination of both FTIR and QCL in one easy workflow achieves the best results. Fortunately, the HYPERION II is both an unrivaled FTIR imaging microscope and a groundbreaking QCL microscope.

To learn more, please visit: <http://www.bruker.com/HYPERION>

# JMS-T2000GC ACCUTOF™ GC- ALPHA

*Two key technologies to revolutionize your workflow using high-resolution GC-MS monitoring for GMP cleanroom compliance by integrating innovative features “all inside the box”*

The JMS-T2000GC AccuTOF™ GC-Alpha is the sixth generation JEOL GC-TOFMS, featuring a redesigned ion optical system to simultaneously achieve high resolution ( $R \geq 30,000$ ), high mass accuracy ( $\leq 1\text{ppm}$ ), and high ion transmission (for increased sensitivity). This system also offers high-speed data acquisition for use with advanced GC-MS measurements such as comprehensive two-dimensional GC (GCxGC), while the wide dynamic range is useful for not only quantitative analysis but also for qualitative analysis of complex mixtures. Additionally, the AccuTOF™ GC-Alpha offers a wide mass range (up to  $m/z$  6,000) that is especially useful for direct MS measurements of nonvolatile compounds.



The AccuTOF™ GC-Alpha also features new data analysis software: msFineAnalysis. The msFineAnalysis software is a new generation of automated data analysis software that provides qualitative results by combining data acquired by EI and soft ionization (FI, CI, or PI) in a simple, speedy and automated way. Additionally, the latest version of this software offers a comparison feature to identify differences between samples.

Aiming for high performance while keeping it simple, the AccuTOF™ GC-Alpha uses two new key technologies:  
New high-performance hardware

- Resolving Power:  $\geq 30,000$
- Mass Accuracy:  $\leq 1\text{ppm}$
- Optional Soft Ionization: CI, PI, FI
- Combination Ion Sources: EI/FI/FD and EI/PI

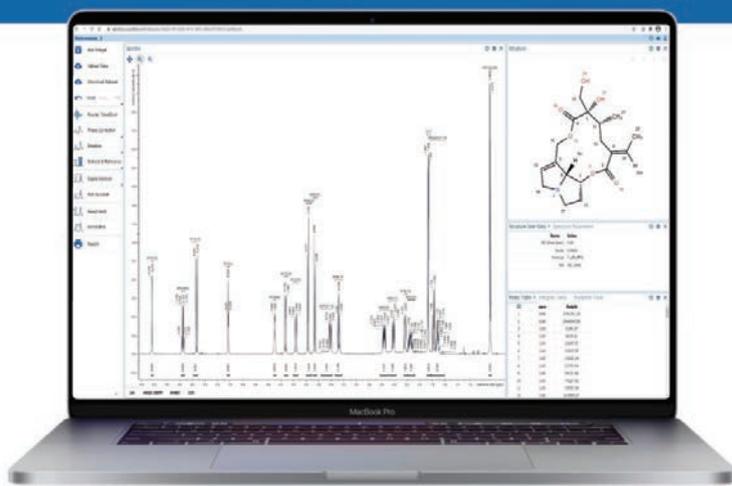
Next generation analysis software (msFineAnalysis) for fast yet simple operation

- Combines EI and soft ionization data for automatic qualitative analysis
- Chromatographic peak deconvolution
- Group analysis for extracting compounds with common substructures
- Differential analysis for directly comparing 2 samples
- Supports the analysis of EI data alone

Since its introduction in 2018, the msFineAnalysis software for the AccuTOF™ GC series has been well received as an innovative software solution for the automatic qualitative analysis of unknown compounds. This software makes full use of the high-quality data obtained by the AccuTOF™ GC-Alpha, thus providing a new approach to qualitative analysis for identification of unknown compounds.

The AccuTOF™ GC-Alpha is truly a high-performance GC-MS system that removes limitations in chemical analysis.

*To learn more, please visit:  
<https://go.jeolusa.com/AccuTOF-TAS-Innovators-Issue>*



## BROWSER-BASED NMR DATA PROCESSING

*With Spectrus JS, the NMR data processing tools you know and love are in your browser*

Spectrus JS is a first-of-its-kind software providing a complete toolset for processing 1D and 2D NMR data in your browser.

Spectrus JS lessens the load on you and your computer with:

- minimal CPU demands
- no required downloads or installations
- no requirement for a specific computer attached to an instrument or with a licensed software installed

All you need to do is type the URL into your browser and log in to access the highly intuitive and configurable interface!

Whether you're a facility manager, research scientist, educator, or student, Spectrus JS makes every NMR user's data processing workflow more accessible and convenient.

*Try Spectrus JS free for three weeks: [www.acdlabs.com/SpectrusJSTrial](http://www.acdlabs.com/SpectrusJSTrial)*



## ASK THE EXPERT

*Andrew A. Anderson, Vice President  
Innovation & Informatics Strategy,  
ACD/Labs*

*What sets your company apart from other businesses in the space?*

In this era of digital transformation, organizations are still struggling to deal with the variety and volume of data generated by their analytical instrumentation. The following capabilities set ACD/Labs apart from other informatics vendors:

- Breadth of native analytical technique and format support
- Range and scope of analytical data processing and analysis capabilities
- Capability to store and manage all analytical data, and the ability to associate "digital representations" of scientists' and algorithm-based interpretation/analysis results to such data.

*How do you plan to continue innovating in 2022 and beyond?*

We are currently expanding the capabilities of our Spectrus Platform to include utilities for Edge computing. This should further assist our customers in managing heterogeneous analytical data more effectively. In 2022, and beyond, we will release utilities that support:

- Automated Data Marshalling – from the source to the cloud
- Extended technique and format support for our browser-based client applications, including Spectrus JS
- Enhanced data storage, query, and access capabilities – for both scientific end-user and machine learning applications.

Dimensions: 95 x 68 x 20 mm



## AVASPEC COMPACTLINE – MINIATURE SPECTROSCOPY REDEFINED

*How high resolution and speed ensure unsurpassed inter-instrument reproducibility*

Spectroscopy redefined – this is what we consider our AvaSpec-Mini spectrometers to represent.

In cases where size matters, the AvaSpec CompactLine of spectrometers offers one of the smallest form factors on the market. This compact spectrometer enables easier integration into original equipment manufacturer (OEM) and handheld devices. But don't be mistaken – squeezing down the size does not compromise the performance of the AvaSpec-Mini. And with multiple configurations available, this spectrometer can be used for numerous applications across various industries.

As the AvaSpec-Mini is produced using a semi-automated production process – called AvaMation – we can ensure unsurpassed inter-instrument reproducibility. Equipped with CMOS detectors, and advanced electronics and communications these miniature spectrometers offer high resolution – speed – and they are suitable for harsh environments.

*Curious how our AvaSpec-Mini can improve your application? Visit our website for more information:  
[www.avantes.com/future-proof](http://www.avantes.com/future-proof)*



## ASK THE EXPERT

*Ger Loop, Product Manager for Avantes BV, the Netherlands*

I'm most proud of our recent automated manufacturing process – or "AvaMation," as we call it. Historically, our spectrometers have been assembled by hand with great precision, care, and expertise, but this new way of manufacturing yields many benefits for our customers. AvaMation provides unsurpassed inter-instrument reproducibility, scalability in production, and enables data analysis for further product innovation. With AvaMation we are ready for a future with an increasing demand for high-quality spectrometers.

*How does your company embody "innovation"?*

We continuously invest in the future, company-wide. Innovating, together with our customers, is an important belief within our company. And that's why we invest in in-house application know-how. Our sales team, for example, consists of engineers and physicists with specific knowledge of the areas our customers operate in. Thanks to all this in-house knowledge, we can offer our customers the optimum solution to their application challenges.

*What sets your company apart from other businesses in this space?*

We believe in a partnership approach, tailoring our solutions to meet the needs of the end user. We are passionate about the success of our customers, so we like to go the extra mile in everything we do. We follow a discovery journey with our customers to ensure we create their most suitable setup. Furthermore, we offer extensive feasibility studies, demo equipment, and expert advice – all to support our customers in finding their most valuable setup.



## ASK THE EXPERT

*Andrea Krumm, Product Manager Analytical Columns, Tosoh Bioscience GmbH*

### *What motivates you?*

I am excited about new therapeutics for diseases that were barely treatable just a few years ago. My motivation is to help those at the forefront of this work – the people developing, producing and controlling drugs, and biopharmaceuticals in particular. I feel this is true for everyone I work with at Tosoh Bioscience. In concrete terms, as an analytical scientist this means making analyses faster, more precise, and adding further critical quality attributes.

### *What development are you most proud of?*

It relates back to speed and critical quality attributes: Tosoh developed an affinity chromatography column that analyzes the interaction between a monoclonal antibody (mAb) and a receptor that is responsible for mAb's functionality. We hoped to reduce the time it took to investigate the function and structural changes of mAbs and indeed, we received positive feedback from researchers that the elimination of sample preparation facilitates their workflows. We are all very proud of this.

### *What collaborations are you excited about?*

All collaborations that share our goals are inherently the most interesting for me. We are currently collaborating with academic partners who are working to obtain more information about therapeutic samples in a short timeframe; for example, by using 2D-LC or mass spectrometry approaches. This work will ultimately help support our biopharma partners as they move forward with new developments.



# TSKgel: THE BENCHMARK FOR CHROMATOGRAPHY COLUMNS

*Celebrating 50 years of HPLC innovation*

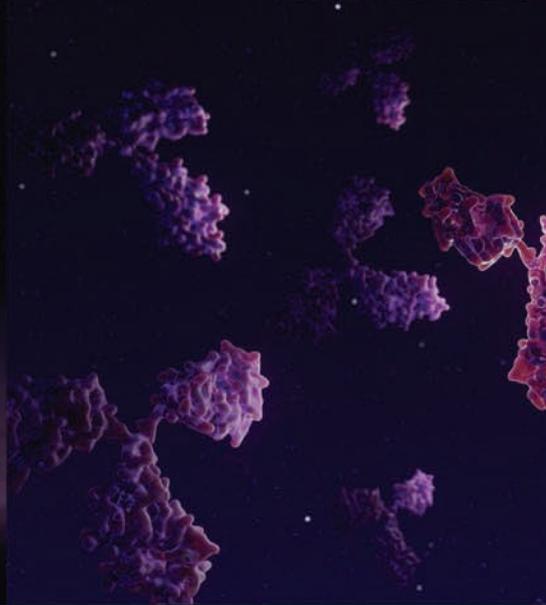
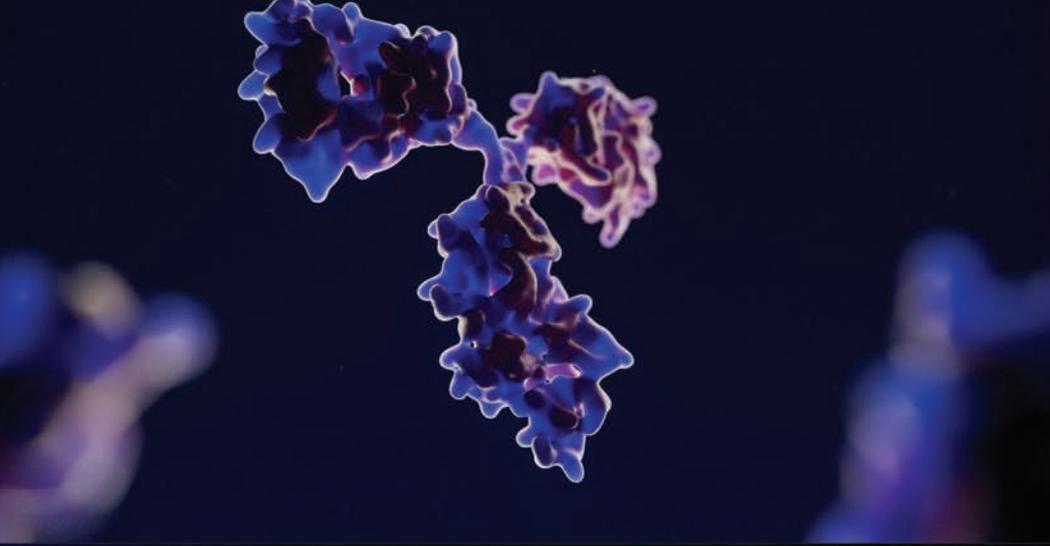
In 1971, the first TSKgel column was launched for polymer analysis (a TSKgel S-type polymer-based gel permeation chromatography [GPC] column); which was just five years after the first articles on fast liquid chromatography (later HPLC) were published. Since then, Tosoh has become a world leader in the analysis of proteins and the development of columns for size exclusion chromatography (SEC).

TSKgel – top in SEC development

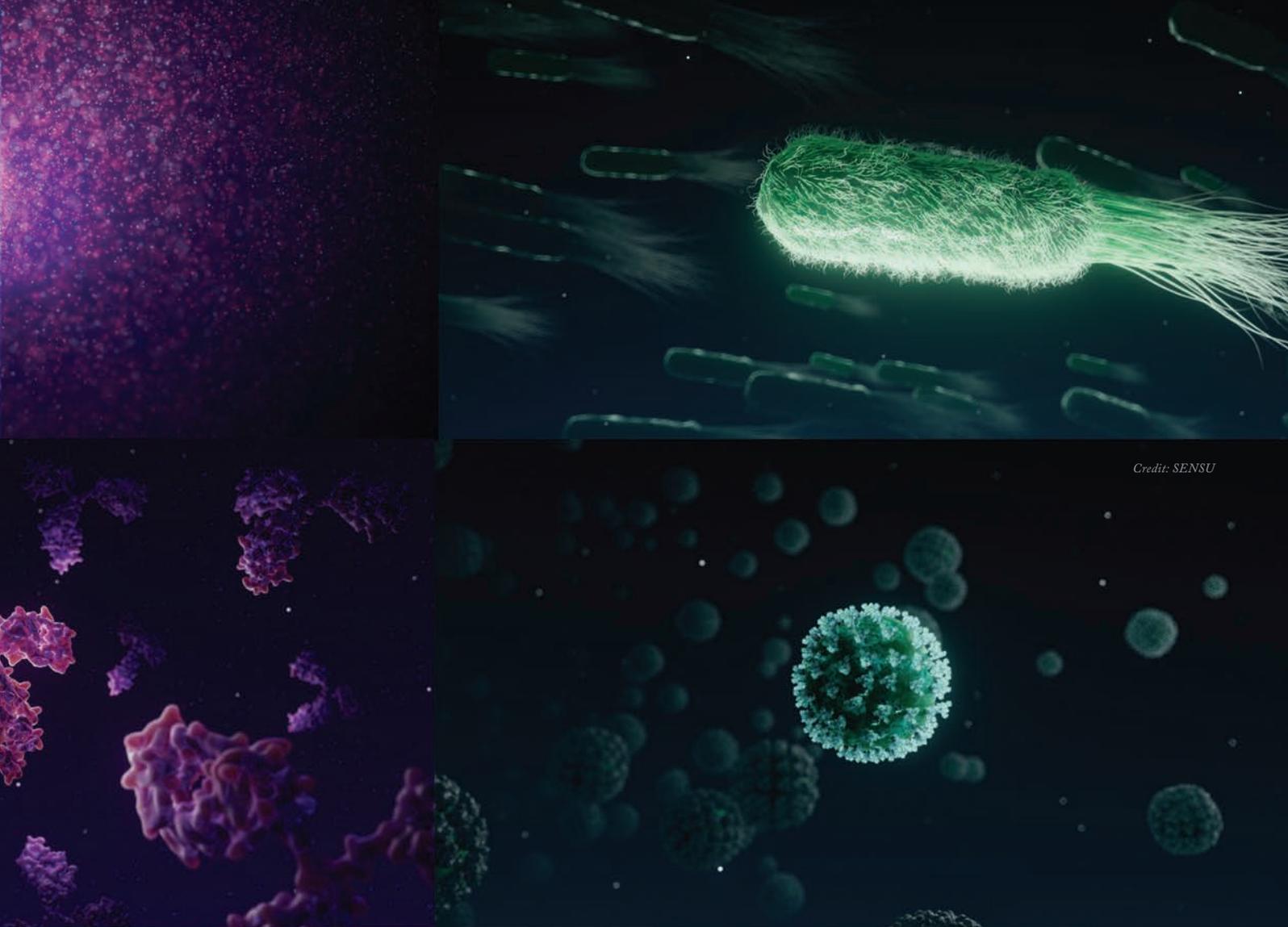
TSKgel S-type columns paved the way for an entire suite of columns in nearly every mode of liquid chromatography. TSKgel biochromatography columns became increasingly popular as they were already established when biotherapeutics, such as proteins, antibodies, and nucleic acids, emerged.

SEC remained a special focus in Tosoh's product line, with TSKgel SW columns becoming biopharma's first choice for therapeutic antibodies. The most recent developments include UHPLC versions of the stationary phases for biomolecule analysis and affinity columns mimicking biological processes for fast functional characterization of antibodies.

*Find more information at: [www.tosohbioscience.de](http://www.tosohbioscience.de)*



TALKIN'  
'BOUT A  
**(PROTEIN)**  
REVOLUTION



*Credit: SENSU*

How native MS  
may help rewrite  
the textbooks  
on immunology  
– and life itself

*By Albert Heck, Chair, Biomolecular  
Mass Spectrometry and Proteomics Group,  
Utrecht University, The Netherlands*

For researchers in the life sciences, the “protein revolution” happened quite some time ago. But for the general public, proteins are still somewhat of an alien concept – unless you’re talking about counting your “macros” as part of the latest dieting trend. Though most people are well aware that DNA carries genetic information and that this has an effect on our lives – from the color of our hair to our predisposition to certain diseases – most do not fully understand the vital role proteins play in every living process.

One of the few positive things to come out of the COVID-19 pandemic is that people have (in general) gained extra understanding around concepts like viruses, antibodies, and vaccines – and, in turn, the action and function of proteins. As scientists, we should welcome the public’s newfound (non-literal) appetite for proteins with open arms – not only is it a sign of how far we’ve come, but of how much there is still left to explore and understand.

As we learn more and more about our proteins, scientists around the world are making fascinating discoveries. My own team recently uncovered evidence that we are even more unique at the proteome level than was ever previously thought – and that this can explain a lot about how and why we all react so differently to diseases, drugs and vaccines. But more on that later...

First, I hope to bestow upon you all the same passion I have for native mass spectrometry – an exciting technique that could help us write the next chapter in the protein revolution.

### *Going native*

So what is native mass spectrometry? Native MS is a term that we initially coined here at Utrecht University. (There’s a similar well-known technique in biochemistry called native gel electrophoresis, where non-denaturing gels are used to analyze proteins and protein complexes in their folded state – and that’s partly where the name came from...)

In contrast to traditional MS, with native MS we try to keep the structures of the proteins and protein complexes that we analyze as close to what they were in their native environment of the cell. To do this, we use special solvents that not only

maintain the integrity of the protein interactions, but are also compatible with the electrospray ionization process that transfers molecules from the liquid to gas phase. By using this unique set-up, it means even non-covalent complexes can remain intact for analysis. In the words of the Nobel Laureate John Fenn, through electrospray under these pseudo-physiological conditions, we can make elephants fly (1).

By keeping proteins and protein complexes intact in the mass spectrometer, we’re able to accurately measure the masses of interesting biomolecular machineries, such as intact antibodies, viruses or ribosomes. It also allows us to confirm the composition of these systems; for instance, do

we have a monomer or tetramer (the tetramer will have a mass that is four times as great as the monomer). Even when a protein complex consists of about 20 different proteins and RNA; as for instance in an intact ribosome, with a mass close to two million Daltons, we are able to accurately measure its mass in a native state and observe changes in its composition.

Accuracy is the real key to native MS. After all, we are only measuring the masses of the complexes, but we do it so accurately that we are able to learn about their composition and whether this changes over time – like when they exchange or add new subunits. And that

means we’re also able to learn a lot more about the function of these macromolecular complexes. For example, a change like a phosphorylation or glycosylation, which also induces changes in mass, may either activate a protein or inhibit a protein’s function. By discovering whether a protein is modified or not, you can learn how to activate or deactivate a protein. In turn, this means you could aim to regulate entire biological processes. And that’s just one reason why measuring these masses so accurately is important – there are also many other incredible applications (see for instance our work on a bacterial biological clock).

### *Gene therapy*

When my team and I first started using native MS, we looked at virus-like particles (VLPs). VLPs resemble viruses; they form beautiful, very rigid spheres made up of self-assembling

“One of the few positive things to come out of the COVID-19 pandemic is that people have (in general) gained extra understanding around concepts like viruses, antibodies, and vaccines – and, in turn, the action and function of proteins.”

## *What's the Deal with Antibodies?*

Our data shows that, when you receive a COVID-19 vaccine, your body doesn't just make one antibody against the spike protein – it makes 10–20 different antibodies in what's called a polyclonal response. Now, most of these antibodies are probably pretty good at their job – blocking the spike protein and stopping the virus from entering host cells. However, if a new variant pops up, it's a different story; for example, out of the 12

antibodies that were initially effective, six may not be effective against the new variant. By producing a range of antibodies, your body is better prepared for any changes (mutations) the virus might undergo – and this is partly why we think our bodies don't just produce a single antibody.

In other words, a polyclonal response helps prepare our bodies for the unexpected. I sometimes like to think about a theoretical question: What would happen if a pathogen landed on Earth from somewhere else in the universe? Would it wipe out the human

species? Or would we be able to harness the power and flexibility of our immune system to create antibodies against something so very foreign? Clearly, I have no concrete proof, but I think the answer lies closer to the latter. I think at least some of the population would be able to mount a good response against such a pathogen.

We've managed to survive a long time on planet Earth thanks to the millions of years that have been spent designing a complex and beautiful immune system. And modern research is still only scratching the surface.

## RESTEK | ADVANTAGE

See What It Can Do for You and Your Lab



Sign up today to access Restek's years of chromatography knowledge at [www.restek.com/advantage](http://www.restek.com/advantage)



proteins – this is known as the capsid. However, these VLPs lack the genetic information needed to infect a host cell, making them safer to analyze. On the other hand, intact or “native” viruses contain not only the capsid, but also all the genetic information that enables the virus to reproduce within the host. One well known example of a native virus – and one that is not harmful to humans – is the adeno-associated virus (AAV). In recent years, biopharmaceutical companies have used AAV as a vector for delivering certain genes into human cells by replacing part of the viral genome – the basis for gene therapy. A notable example of this is Zolgensma; a prescription approved AAV vector-based gene therapy for the treatment of children less than 2 years old with spinal muscular atrophy introduced by Novartis.

Even more recently, adeno-virus (ADV) vectors have garnered attention because of their use in the AstraZeneca, Janssen and Sputnik vaccines for COVID-19. Without a doubt, these gene-loaded viral particles are an exciting class of emerging biopharmaceuticals. However, they are also extremely complicated to produce and structurally very heterogeneous and

therefore raise huge and specific novel analytical challenges.

We work with several pharmaceutical companies to help them overcome some of these challenges by analyzing virus-based gene delivery vectors using native MS. Why do they need our help? First of all, it’s about sensitivity. It’s very hard and laborious to produce these particles, so you never have many of

them available to analyze – unlike recombinant antibodies where you can produce grams. There are also further complications because these particles are huge – we are talking 4–5 million Dalton. And they are extremely heterogeneous, containing several different proteins and gene products, which makes them difficult to analyze with a single technique.

We pioneered the use of a particular type of native MS – charge detection MS – for this exact purpose (3). This technique’s big advantage is

its ability to count, while accurately measuring the mass of, single viral particles. And it’s really opened up a whole new avenue of analysis, allowing us to look closely at gene vectors and discern whether or not the genome of choice has been successfully loaded. Understanding whether the gene has been

**"Charge detection MS has opened up a whole new avenue of analysis, allowing us to look closely at gene vectors and discern whether or not the genome of choice has been successfully loaded."**

incorporated is vitally important for the biopharmaceutical companies producing these particles. As such, I foresee that native MS will play a crucial role in the quality control of gene delivery factors for this exciting new field of medicine.

### *Rewriting the textbook on immunology*

More recently we also started to focus on antibodies, as they are naturally present in huge quantities in our blood. According to the textbooks, antibodies are made by certain cells in our body called B cells. The number of different B cells in our body is enormous – we're talking 10<sup>15</sup>, which to put it in perspective is several times more than the number of people on the planet. I had been wondering myself already for some time: how many (and which) antibodies does the human body really produce that end up actually circulating in our blood to counteract invading pathogens? The commonly accepted answer within immunology was that this could be an almost infinite (or at




**NEW**  
SLD2020

# GPC/SEC Light Scattering Detectors

- static and dynamic, stand-alone and GPC/SEC light scattering detector solutions
- from 1 angle multichrom to 20 angles multi angle
- suitable for all major LC instruments
- empowered by PSS WinGPC software for highest data integrity enabling full compliance with FDA 21CFR 11



Your samples in the  
right light and angle



**PERFECT SEPARATION SOLUTIONS**

[www.pss-polymer.com](http://www.pss-polymer.com)

least, immeasurable) number. When we suggested measuring them all, many within the field thought it would be impossible. We've now published research that proves the task was not as insurmountable as people thought (4). To our surprise, we found that just a couple 100 different antibodies dominate the repertoire in each person's blood – a number so low in comparison to what was previously believed, that we knew these findings were already very exciting. But then we also discovered that each person had their own personal repertoire of antibodies – equally exciting.

You might be thinking that such a finding is somewhat obvious; “Of course we would make different antibodies against every virus or pathogen we encounter,” you say. “I'd expect there to be a unique signature to align with this fact.” However, we observed that, even if people are exposed to exactly the same pathogen – or vaccine in the case of COVID-19 – they still make their own personal repertoire of antibodies against it. Fascinating. This clearly implies that every person reacts to incoming pathogens differently. We can see this working on a grand scale when we look at how everyone has reacted to the COVID-19 vaccines; some people get ill, others don't, and the vaccine works better at protecting some people from the virus than others. We now know that these differences are at least partially due to the specific antibodies each person makes. (For more information, see the sidebar: What's the deal with antibodies?)

In the long run, I hope that we will be able to measure and identify the antibodies that each person makes against a certain pathogen using MS. This would open up the possibility of taking antibodies from someone who does mount a good response, and using them to help those who don't. In this case, we'd be using recombinant molecular biology to produce the best antibodies against the disease and treat someone who has a sub-par response. Such treatment could be used against all COVID-19 variants, but I'm equally eager to see how this could be applied to any other viral or bacterial infection – or even other diseases, such as rheumatoid arthritis and cancer. Basically, new understanding in this arena could be applied to any disease to which our bodies respond with antibodies – and that's quite a few! Ultimately, it could open a new way of producing personalized biotherapeutics.

Our finding was extremely exciting and totally unexpected – and one that is bound to find its way into the textbooks in the

coming years. It's not often you get to make such discoveries, so I'm extremely proud that our team of about ten researchers, who worked on this for a couple of years, was able to achieve this.

### *The horizons of MS*

MS has come a long way since its inception more than 100 years ago, but some challenges seem to always remain the same. Can we get faster? Can we get more sensitive? Can we get higher mass resolution? Can we get better mass discrimination? Though many great advances have been made, the answer to all these questions is yes, we could and should. It's incredible to think that we now only need tiny amounts of material to run our analyses, which means we can uncover the entire proteome of a single cell. This

is an enormous sensitivity jump from where we were. However, the cell is still made up of billions of proteins. The area I'm most excited about for the future – and an area we've also contributed to ourselves – is in increasing the sensitivity of MS to measure single molecules.

My ultimate dream is to take a single cell, take out every molecule one by one and measure its mass. And though it might sound like a pipe dream, it's already theoretically feasible. Practically, I'm not sure when we'll manage it – but, because I can imagine how it might happen, I'm sure someone will figure it out

soon enough, and of course we hope to contribute to that.

For me, progress is all about understanding, fundamentally, how life works. In turn, we increase our knowledge about our wellness, health, and the planet. The horizons of MS are already beautiful. But beyond that horizon, there are undoubtedly new and wonderful stories – applications that many of us haven't even dreamed of yet.

*Albert Heck will be presenting his talk “New Horizons in Mass Spectrometry: Sizing and Counting Particles by Native Mass Spectrometry” at the 2022 Wallace H. Coulter Lecture at Pittcon. Learn more here: <https://pittcon.org/pittcon-2022-keynote-lecture-announced/>*

#### References

1. JB Fenn, *Angewandte Chemie* (2003). DOI: 10.1002/anie.200300605
2. TP Wörner et al., *Nat Methods*, 17, 395 (2020). DOI: 10.1038/s41592-020-0770-7
3. A Bondt et al., *Cell Systems*, 12, 1 (2021). DOI: 10.1016/j.cels.2021.08.008

“It's incredible to think that we now only need tiny amounts of material to run our analyses, which means we can uncover the entire proteome of a single cell.”

# How to Avoid Extraction Exasperation

Keep your Soxhlet sample prep running smoothly with a handful of simple troubleshooting tips

By Mohan Nimmagadda,  
Product Manager, Cytiva

Soxhlet extraction is a simple, user-friendly way to get the components you're interested in out of your sample. Since its discovery in 1879, Soxhlet extraction has been routinely applied in almost every analytical laboratory – up to this day. One might think the standard Soxhlet technique would have been perfected over the past 140 years, but minor hiccups remain common – especially when setting up a new extraction.

Fortunately, most issues can be solved with relatively simple fixes. Here, I offer a few tips and tricks to help keep your extractions running smoothly.

No (or not enough) solvent evaporates  
If there is little or no evaporation from the solvent reservoir, the problem usually lies in the solvent or the heating element. First, check whether the heating element is functioning correctly; is it reaching the temperature you need for your extraction?

If you require faster evaporation without altering the temperature, then a change of solvent could be an option. There are several commonly used solvents for Soxhlet extraction, all with different properties and boiling points. If a solvent with a lower boiling point is suitable for your application, it will likely improve evaporation speed.

I'm not extracting the right compounds  
The compounds you extract from your sample depend almost entirely on the solvent, and each commonly used solvent

comes with its own benefits and drawbacks. Hexane, for example, is a popular choice, because it readily dissolves polar compounds. It is also easy to retrieve after the extraction is complete.

Ethanol, on the other hand, has the ability to dissolve both polar and nonpolar molecules thanks to the combination of a polar hydroxyl group and a nonpolar "tail." Ethanol can also break the tough cell walls of plant samples, which helps in the extraction of intracellular compounds.

The solvent is not syphoning back  
If, after passing through the sample, the solvent does not syphon back into the reservoir, a simple solution is to heat up the syphoning tube slightly – a hairdryer usually does the trick. If this has no effect, the most likely cause is a blockage.

To prevent sample-material blockages, make sure to use a thimble that precisely fits inside your Soxhlet extraction apparatus. (Soxhlet extraction thimbles are available in a range of sizes to fit different extractors and prevent blockages.)

But I'm not even sure which thimble to use...

Soxhlet extraction thimbles can be made from different materials – and there's a lot to consider. If the wall is too dense, the thimble might not empty fully, which reduces efficiency as more cycles are needed to complete the extraction. Conversely, if the wall isn't dense enough, the thimble loses its structural integrity.

Excessive variation in wall thickness and therefore external thimble diameter, may cause issues with insertion and removal of the thimble into/from the Soxhlet apparatus. High-quality, focused manufacturing process ensures uniform dimensions along the body



of the thimble, which positively impacts ease of use and avoids, for example, significant "flare" at the open end of the thimble.

While most scientists use high-purity cellulose or glass fiber thimbles; Cytiva's thimbles are made from pure alpha cellulose or borosilicate glass. Both materials have broad solvent compatibility and suit many common applications of Soxhlet extraction.

To confirm solvent compatibility when using a new protocol or a new type of thimble, you can carry out a blank run with an empty thimble. Blank runs help to check for "extractables" – compounds that could be released from the thimble itself, potentially interfering with analysis.

If extractables are a concern, prewashing the thimble is an option. Prewashing with a small amount of pure solvent is also a rapid way of removing potential contaminants from the thimble before starting the extraction. However, the need for a prewash step can be minimized by choosing high-quality thimbles with broad solvent compatibility (and thus low levels of extractables).

Figuring out exactly which thimble is right for your Soxhlet extraction needs can be tricky. But remember there is always help close at hand; filtration experts with troubleshooting experience (such as those within Cytiva's filtration team) will be able to offer sage advice.

A word on complacency

You may be thinking my tips seem almost too straightforward. But, in my experience, it's actually remarkable how often the simple aspects are overlooked, leading to extraction delays and, ultimately, additional cost.



**Solutions***Real analytical problems  
Collaborative expertise  
Novel applications*

# Taming the Wild West of Oligonucleotide Analytics

For oligonucleotide therapies to realize their huge potential, analytical scientists need to have a good understanding of the biology, while also keeping pace with constantly changing chemistries

*By Michael McGinley, Senior Manager of Global Technical Support Department, Phenomenex*

“Take him home; love him; take a lot of pictures,” the doctor said to Eric’s parents\* (1). “There’s nothing you can do.” The couple’s infant son had been diagnosed with spinal muscular atrophy (SMA) type I. And, without treatment, Eric probably wouldn’t see his second birthday (2). Until five years ago, there was no cure for SMA – the most common genetic cause of death in infants. But a new therapy based on oligonucleotides (oligos) called Spinraza (nusinersen, approved by the FDA in December 2016) has profoundly changed the outcome for SMA patients (3,4). In addition, we have also seen widespread use of oligonucleotides – specifically the use of messenger ribonucleic acid (mRNA) in vaccines – for a far more common illness: COVID-19 (5).

Oligonucleotide therapeutics are a new frontier in drug development, pushing boundaries in the treatment of cancer and genetic diseases in particular. Yet despite more than two decades of pharmaceutical research, widespread usage of oligo therapeutics has typically been hindered by inefficient delivery, preclinical toxicology,



or lack of clinical efficacy. All that said, the rapidly growing number of oligo drugs receiving regulatory approval – and a number of recent developments – have renewed interest in the field.

Modifying oligos stabilizes them but also makes them more difficult to analyze. The field of oligonucleotide development

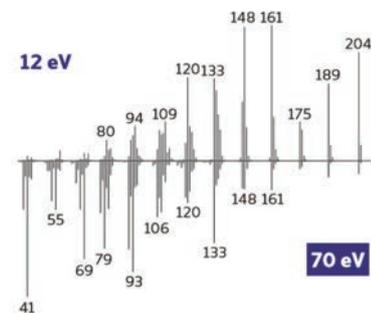
is now expanding rapidly, with many new platforms and methodologies for targeted delivery. Within this range of new therapeutics is a wide array of modifications that enhance oligo stability. But these modifications also present additional obstacles in characterizing the oligonucleotides and their closely-related impurities. The rapid growth of the sector

# NEW

## TOF MS for GC and GC×GC



**BenchTOF2™**



**with Tandem Ionisation®**

Powered with ChromSpace® software



- Enhanced sensitivity
- Superior spectral quality
- Improved selectivity
- Extended dynamic range
- Hydrogen carrier capability
- Both hard- and soft- EI

**Discover more**  
[chem.sepsolve.com/TAS/BenchTOF2](http://chem.sepsolve.com/TAS/BenchTOF2)



A company of the **SCHAUBENBURG** International Group

and the novel challenges posed by oligo therapeutics are creating a significant need for complementary technology and increasingly sensitive instrumentation that will help to address analytical obstacles.

In the past, only oligo-focused biotechnology companies were working on these issues. Today, most major pharmaceutical companies have an oligo group, and credible biologists and chemists are building out their experience with the aim of becoming oligo experts. In the last five years, at TIDES Oligonucleotide and Peptide Therapeutics – the main conference for oligo therapeutics and peptide development professionals – the number of attendees has gone from around 600 to more than 1,500. And whereas in previous years the majority of people represented specialty oligo start-ups, now attendees include more traditional pharma companies that are licensing or developing oligo drugs. What has really changed mindsets towards oligos was COVID-19 and the use of mRNA as the principal active ingredient in some vaccines.

Oligonucleotide therapeutics are moving into the mainstream

Vaccine development is shifting toward mRNA, given its incredibly short drug development timeline and relatively straightforward development process. Considering their ease of development and product stability, there is even some talk of moving toward mRNA therapeutics instead of protein therapeutics.

Yet the opportunity extends beyond vaccines. Many scientists have not lost sight of where oligo therapeutics have traditionally been a big player: untreatable diseases, such as SMA; indeed, oligos have the potential to reach previously undruggable targets. Better still, some companies are combining antibody therapeutics with oligonucleotide therapeutics by attaching a piece of oligonucleotide onto a monoclonal antibody. This method uses the

monoclonal antibody as a delivery device to get the antisense RNA into a cell to then target and activate or disrupt it. Done well, similar methodologies could offer a new frontier with oligo therapeutics completely displacing some of the recombinant drugs already on the market.

The novel challenges of oligo analysis We continue to witness an influx in the oligo business; many of these players have been our customers for a long time and were previously protein therapeutics professionals or even small molecule pharmaceutical scientists. Many of them are asking for oligonucleotide separation

applications that allow scientists to isolate oligonucleotides from biological fluids and biological tissues. One of the key challenges in drug discovery and drug development is determining the pharmacodynamics and pharmacokinetics profiles. Oligos are often difficult to isolate from biological tissues, but separation is critical for analytical methods based on MS or even molecular biology techniques.

The drugs themselves also look different. It is never one chemistry – and the chemistries are constantly changing. Over the last 20 years, all traditional oligonucleotide companies have been constantly trying to improve oligo chemistry to increase the

half-life and bioactivity of therapeutics. Part of that involves making the oligos more nuclease-resistant, which requires a great deal of chemical modifications. And other modifications are made to increase the uptake of the oligonucleotide into cells and the cytosol, where the oligos are bioactive. Oligo drug developers often need to increase the potency of their therapeutics with chemical modifications; for instance, we saw the addition of phosphorothioates, which involved adding a sulphur atom onto the phosphate backbone. But now we are seeing the use of modified nucleic acids.

Even subtle modifications can make a difference – not only to the oligo but also to the way we need to approach analysis. Indeed, it would be a mistake to think that, as the chemistry changes, the molecule largely remains the same – especially in terms of the analytical methods needed for characterization. In fact, each time chemistry changes are made, the tools and methods we use to perform the oligo analysis must be re-tested and potentially modified or even swapped out for a new set of methods.

In short, thanks to the ever-changing chemistry of oligos, there is always a method development step. And that's why most companies developing oligos are likely to face multiple challenges, including the lack of practical expertise to perform the various complex separations required or the chemistry knowledge to even understand how to get to the right separation. Separation scientists are in demand!

The Wild West of analyzing oligos  
We have seen that there can be fundamental knowledge gaps in the oligo space – biologists who struggle with the chemistry or chemists who struggle with the biology. And that's because they sit somewhere between a small molecule and a protein therapeutic. Oligos for the most part are biological molecules that are chemically synthesized (as with antisense therapeutics) or are recombinantly

synthesized (as with mRNA- or AAV-based therapies). Given that oligos live in a world where both chemistry and biology are involved, it stands to reason that associated analytical method development and application require a knowledge of both sciences. And there lies the problem: most pharmaceutical analytical scientists come from either small molecule or protein therapeutic backgrounds, and they tend to import not only knowledge but also biases from their previous field.

For instance, protein purification is so good these days that we consistently approach 99 percent purity – which wasn't the case in the past. For protein therapeutics, such a difference is minor and results in low analytical variability. Thus, protein therapeutic analytics have evolved from a wide-open field to one with set expectations and standardized methods – including USP methods with set ways of performing them. Similarly, with the small molecule industry, there are set standards and standardized methods, with clear definitions of purity – what is good or acceptable, what is bad, what makes for a good molecule or a bad one, and so forth.

It is a very different story with oligos. The nature of oligos – and how they are synthesized – means that obtaining 100 percent purity is nearly impossible. With oligos, we are back in the Wild West, where we're still learning and figuring out what's "pure" and "not pure" – what's good enough and what's not. This uncertainty is compounded by regulatory requirements that vary from country to country, agency to agency. The approach to oligo purity and activity requires a whole different mindset.

Working together to develop bespoke analytical solutions for oligos  
Chromatography and separation rules are profoundly different for oligonucleotides when compared with small molecule or protein separations. And for my global technical support group, education is

part of the solution. We have first explain to our partner why their older methods cannot be applied to analyze oligos with sufficient robustness. We have to share data and research, as well as the benefits of our ever growing experience. With every case, there is always some (and often a significant) element of method development before we land on the right chromatographic solution. Sometimes the molecules we are working on are completely new, in which case we find ourselves in a true collaboration with our customers – one that relies on our chromatography knowledge and their knowledge of the molecule.

To summarise – and contrary to the section within which this article sits (Solutions!) – there is no one solution for oligo analysis. There is no set playbook or formula. Instead, there are many discussions – and some trial and error – on the way to the right solution for each molecule. It's challenging, but when we get there – and we very often do get there – it's incredibly rewarding. After all, both sides know they are working towards radical new therapies that may treat or even cure diseases for individuals like Eric – now that's what I call a solution.

*\*Not patient's real name; scenario adapted from caregiver answers to polling questions at a public meeting hosted by Cure SMA (1).*

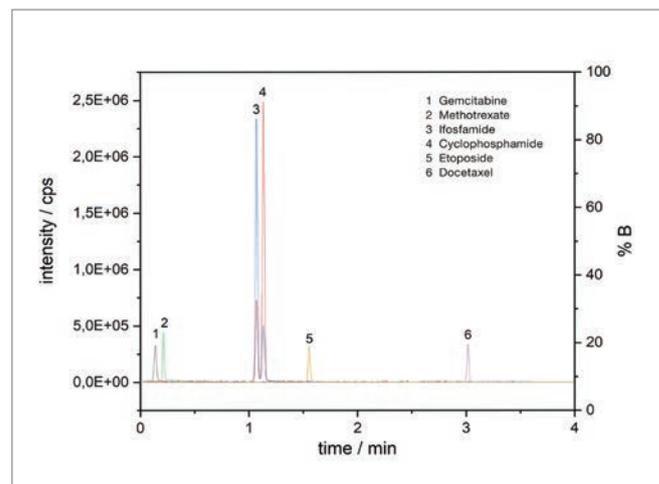
#### References

1. Cure SMA, "Voice of the Patient Report" (2018). Available at: <https://bit.ly/3kJfjyf>.
2. NINDS, "Spinal Muscular Atrophy Fact Sheet" (2021). Available at: <https://bit.ly/3qmRuPx>
3. Biogen, "How Spinraza works" (2021). Available at: <https://bit.ly/3bY7DCt>
4. FDA, "FDA approves first drug for spinal muscular atrophy" (2016). Available at: <https://bit.ly/3qoV9wj>
5. TK Le et al., "Nucleic Acid-Based Technologies Targeting Coronaviruses," *Trends Biochem Sci*, 46, 5, 351–365 (2021). DIO: doi: 10.1016/j.tibs.2020.11.010

## High Sensitivity Screening of Antineoplastic Drugs Using a 1 mm UHPLC Column

Antineoplastic drugs are commonly used for the treatment of cancer. On the one hand they are life-saving for affected people, on the other hand they can be harmful to people who are exposed to them, including pharmacists, nurses and other staff members. Due to their adverse health effects, a reliable and highly sensitive detection process is very important. Even low residual concentrations – for example, on surfaces in hospitals or pharmacies – need to be reliably monitored.

Here, a 1 mm ID YMC-Triart C18 UHPLC column was used for LC/MS screening of six antineoplastic drugs. Due to the need for high sensitivity, where even the smallest amounts of these drugs need to be detected, a small internal column diameter is the ideal choice. By coupling it to MS, it becomes



the perfect fit in order to detect low sensitivity compounds or low sample amounts with high sensitivity.

You can download the application note with the full method details following this link:  
<https://ymc.eu/d/brDmF>

**YMC**  
EUROPE GMBH

**Experts in  
Reproducibility**



- Robust Bio-RP (U)HPLC
- High Recovery IEX
- Highly Efficient HIC & SEC



**Discover more at [www.ymc.de](http://www.ymc.de)**



# Spotlight on... Technology

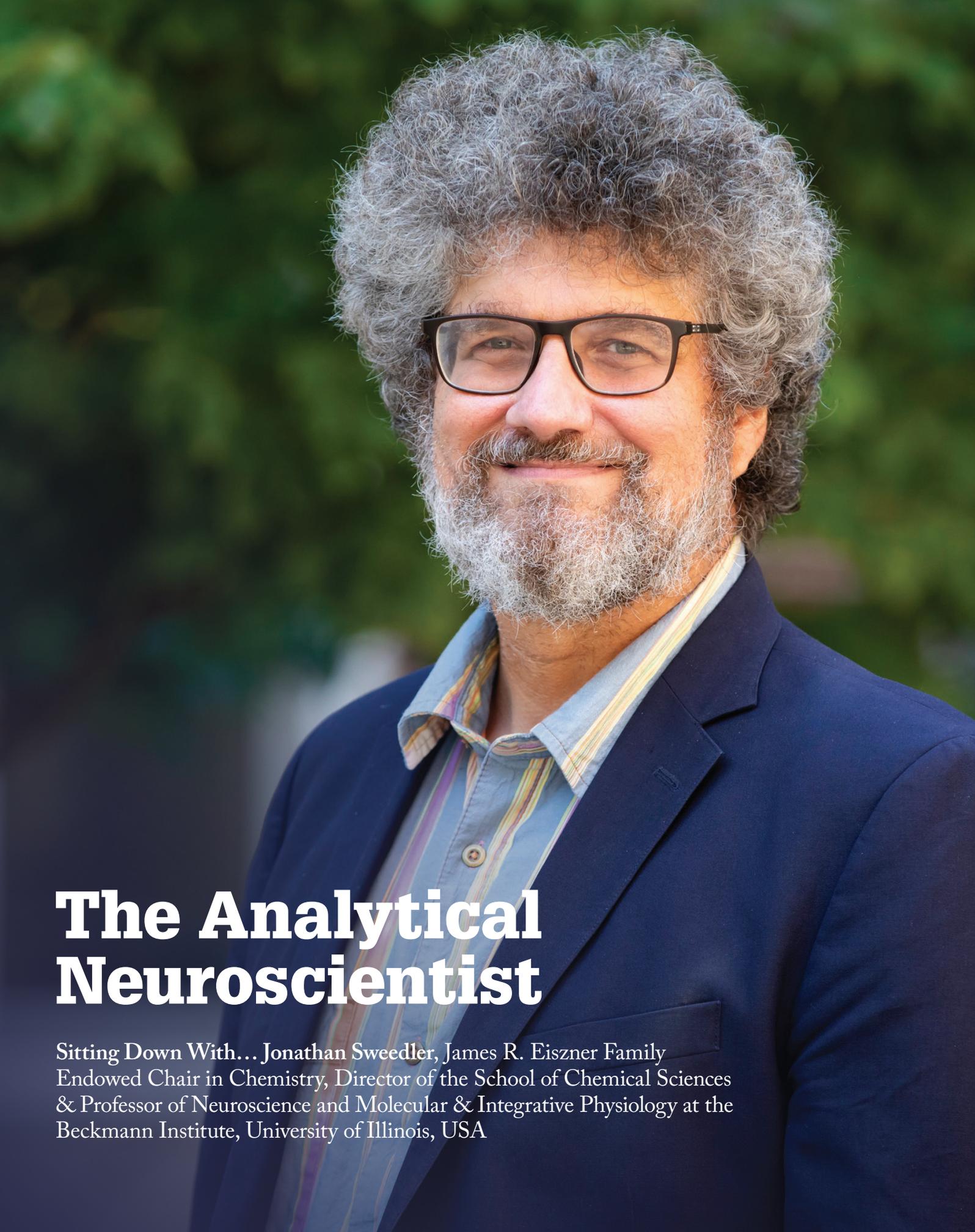
## WITec alpha300 Ri – Inverted Confocal Raman Imaging Microscope

The alpha300 Ri offers 3D confocal Raman imaging through an inverted beam path to enable sample investigation from below. This is a great advantage when working with aqueous solutions, oversized samples and environmental enclosures. All modular components and upgrade possibilities for the alpha300 series are compatible with the Ri version.

*Find out more at <https://bit.ly/3ojkFkX>*







# The Analytical Neuroscientist

Sitting Down With... Jonathan Sweedler, James R. Eiszner Family  
Endowed Chair in Chemistry, Director of the School of Chemical Sciences  
& Professor of Neuroscience and Molecular & Integrative Physiology at the  
Beckmann Institute, University of Illinois, USA

How did you get into analytical science? I was always into science – be it using a ham radio or making model rockets. In fact, in California, when I grew up, they had a ban on model rockets, so I was busy writing to state legislators to try and change the law – at about 12 years old. Soon after I became honorary first president of the local rocket club (which was mostly adults). I had around seven years' worth of science courses in high school having changed my schedule around to accommodate the extra classes. I was always going to study science in college, and I guess I liked exothermic reactions, so chemistry was the one I went for. Though I did also study classical Greek as a minor...

The hard part was figuring out what I actually wanted to do as a career. I was interested in applying chemistry to biology and the brain, but I ended up getting a fellowship to work at the Lawrence Livermore National Lab as an undergraduate. Livermore is one of the two main weapons labs in the US – though I was working on analytical projects, which is what made me decide to stay in analytical chemistry. But I remained interested in neuroscience and, once I finished my analytical chemistry PhD, that's what I decided to focus on during my postdoc at Stanford.

The Livermore Lab – is that where you met Tomas Hirschfeld?

Yes. He was my first mentor and, really, the reason I am an analytical chemist. He was the only person I've ever met who genuinely had a photographic memory. You could ask him a question and he'd tell you to look up a paper – he'd know the journal, year of publication, the page number and even where on the page the relevant paragraph was. It was remarkable. And yet he'd sometimes forget to meet you after lunch! More importantly, he was a truly creative thinker with a broad knowledge base who always had a unique

perspective on any given problem – and he'd encourage his students to explore new and crazy ideas. (It helped that the budget at Livermore was limitless, as far as I was concerned; I was working with FTIR and MS instruments back in the early 1980s, which just wasn't possible anywhere else.) Creative problem solving is something I've valued throughout my career – and often just asking myself “What would Tomas have done?” does the trick!

Has your career ever taken a serendipitous turn?

In planning my postdoc, I was trying to figure out how I could study the brain from the point of view of a chemist – a daunting prospect. One way would be to simplify the problem by working on a simpler organism. So I started looking into researchers working on things like sea slugs, which have around 10,000 neurons, a number I can comprehend. I also needed to find a chemist to support this idea, something I was able to do at Stanford with Richard Zare and Richard Scheller. At UIUC, I continued this research area. I was discussing these research ideas with a physiology professor who suggested I go to Friday Harbor Marine Lab, San Juan Island, Washington, to learn about some of these organisms. I even ended up doing a sabbatical at Hopkins Marine Station in California learning fundamental neuroscience of marine organisms. I got paid to learn, be on the beach, and to scuba dive – it was great! A lot of people said I was crazy trying to learn new skills at the stage in my career when you're supposed to be your most productive, but it was invaluable. I've used the practical skills I learned throughout my career and it also redefined me as a researcher.

Your lab is known for combining different perspectives...

Yes, you could say that. I'm in my 30th year at the University of Illinois and my

*“Working across traditional disciplines and boundaries is something I enjoy – and I think it does foster original thinking.”*

group is half analytical chemistry and half physiology/neuroscience – with many sub-niches. People have left my group and become professors of neuroscience, and I don't have a degree in neuroscience, which is pretty unusual. And it is funny to think about the fact that I'm training the next generation of teachers in a field I have no (formal) credentials in! But working across traditional disciplines and boundaries is something I enjoy – and I think it does foster original thinking.

What legacy would you like to leave?

I wonder if any of my students have asked themselves, “What would Jonathan do?” – just as I have done in the past with Thomas Hirschfeld – that would be quite the legacy. I keep in contact with almost all of my former graduate students and postdocs. Every once in a while, we have reunions. There are over 100 now and that's an incredible number of lives to have touched. And it's great when someone comes up to me and says, “You don't know me but I work for your former student, so you're my academic grandfather” – great grandfather in some cases. Which is a little strange... Fortunately, academic generations are relatively short!

**Call for papers**

# Every open call. One place to check

Find the perfect home for your research in a journal portfolio that is transforming publishing culture, as well as sharing brilliant science with the world.

**[rsc.li/explore-calls-for-papers](https://rsc.li/explore-calls-for-papers)**

**Fundamental questions  
Elemental answers**