JULY 2019 # 78

the Analytical Scientist™

Analyte at the Museum

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Image of the Month

Bringing Art to the Table

These delicate shapes form part of one of the more unusual depictions we've seen of the periodic table of elements – an art installation titled "Divining Nature: An Elemental Garden," by artist Rebecca Kamen. Kamen spent three years working on the sculptures, each of which represents one of the 83 naturally occurring elements in the periodic table. The number of rods in each sculpture represents the atomic number of the element. The artwork translates the periodic table into a "garden of sculptural elements based on geometry and atomic number," says Kamen.

Read more about the installation and listen to the accompanying soundscape (based on the vibration of atoms) at tas.txp.to/kamen. *Photo credit: Angie Seckinger*

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

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A combined photo and radiograph of Buddha (dated 17th–18th century) from the RMAH collection
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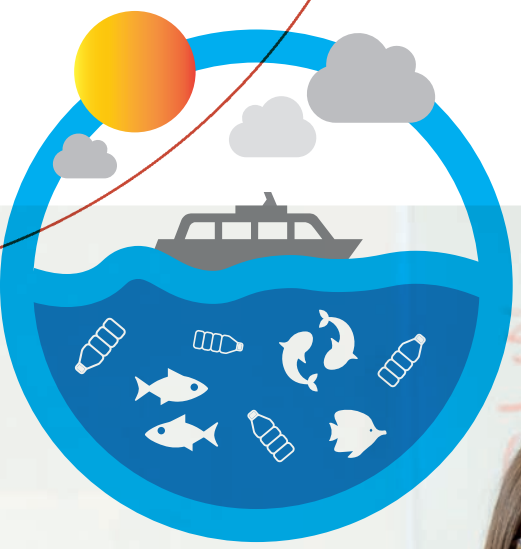

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Remarkable Technology, Amazing People

ASMS and HPLC 2019 showcase why the field of analytical science is so special.

It's rare for The Analytical Scientist to publish back-to-back editorials on the same topic. But having read Charlotte Barker's opening question – "Are conferences still worth it in the digital age?" – in June, I felt compelled to add weight to her conclusion. Why? Because, in that same month, I attended the 67th ASMS in Atlanta and the 48th HPLC in Milan.

Tiring (and, at times, too hot)? Yes. Worth it? Absolutely.

The two conferences had more than a few things in common; the powerful combo of LC-MS was (unsurprisingly) dominant in presentations and posters, as was "omics" of one form or another (alongside associated challenges). In short, the caliber of science was high. But it was the advanced technology on display and the intense yet friendly discussions on every corner that reminded me of how great it feels to be part of this special community.

Though it is true that we can access information about new products online, there's something rather wonderful about seeing the technology unveiled before your very eyes. At ASMS, real innovation was unleashed, satisfyingly, in two distinct directions, each widening the reach of mass spectrometry: i) better (higher sensitivity, higher resolution, faster) and ii) simpler/smaller (increased accessibility). "Smarter" was a common theme. Instrument manufacturers at both conferences pulled out all the stops to wow crowds with slick presentations, emotional videos and VR experiences. Actual experts were on hand to help savvy scientists understand the advantages – and, perhaps more crucially, the limitations – of the latest systems. The energy of an exhibition is hard to replicate online.

And then there are those moments when you find yourself part of something special. At HPLC, I was honored to be in esteemed company as a jury member for a new event: the Separation Science Slam. Sponsored by KNAUER, Merck and The Analytical Scientist, the upbeat session invited six young scientists to present their research in the most creative way – and it proved to be extremely entertaining. I was taken aback by the flair – and, in some cases, audacity – of the next generation of analytical heroes. Congratulations to all six finalists – and especially to the three winners Pascal Breuer (bronze), Simona Felletti (silver) and self-professed "regular, everyday chromatographer" Nándor Lambert (gold), who delivered his project through the medium of rap.

Being part of a 300-strong crowd, clapping and cheering along to a track about the extraordinary insulation properties of polyurethane foam? Well, you had to be there.

Rich Whitworth
Content Director

Upfront

Reporting on research, personalities, policies and partnerships that are shaping analytical science.

We welcome information on interesting collaborations or research that has really caught your eye, in a good or bad way. Email: charlotte.barker @texerepublishing.com

A human whipworm (*Trichuris trichiura*).

Coprolite Parasite Insight

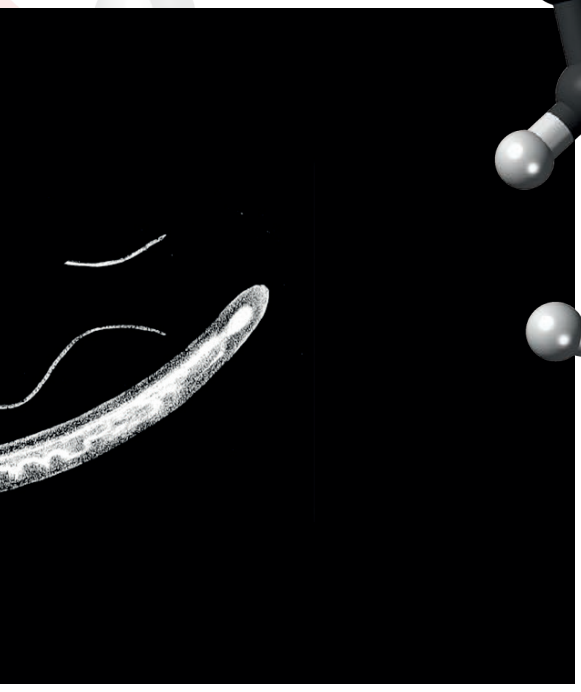
Lipid profiling of fossilized feces highlights the spread of intestinal infections in ancient Turkey

The increased spread of infectious disease during the Neolithic period is attributed to agricultural and population expansion as humans transitioned from hunter-gatherers to farmers and herders. Intestinal parasites in particular are thought to have adapted in response to altering human behavior at that time.

Marrisa Ledger and colleagues honed in on parasite infections in the village of Çatalhöyük, Turkey, by analyzing four samples of coprolite (fossilized feces) from 6410-6150 BCE (1). The samples were first ground and analyzed by digital light microscopy to confirm the presence of parasite eggs; next, the total lipid extracts of the infected samples were subjected to GC-MS to determine levels of sterols (including those used as fecal biomarker compounds) and bile acids (produced by the organism of origin).

Two of the four samples tested positive for whipworm eggs (*Trichuris sp.*), most likely human whipworms (*Trichuris trichuria*), and lipid analysis indicated samples of human origin; sterol profiles were typical of omnivores (high coprostanol, low cholesterol and numerous phytosterols) and bile acid profiles were primarily deoxycholic acid, with few lithocholic acids. The results appear to provide the first evidence for intestinal parasite infection in this region at this time. Additional pelvic soil samples were also collected from nearby burial sites as a control – but all tested negative for parasite eggs.

The researchers plan to use the method to study additional compounds from coprolite samples in studies that go beyond simply confirming the species of origin. "We are developing a more holistic approach," says investigator Ian Bull.



"Many compounds derive from diet, so we hope that we can gain more information about the way people lived, as well as the commodities used."

How much more information can be uncovered from such samples? The answer is, of course, tied inextricably to the team's method, which has been evolving in line with instrumental innovation since the early 2000s. "Greater sensitivity is always appreciated but, certainly for us, better workflows and mining of data obtained from time-of-flight and Orbitrap MS systems is now key," says Bull. "We can already collect vast amounts of information using such platforms – we just need to improve and simplify methods for us to interrogate such datasets. And that moves us very much in the direction of lipidomics and metabolomics."

Reference

1. *ML Ledger et al., "Parasite infection at the early farming community of Çatalhöyük", Antiquity, 93, 573–587 (2019). DOI: 10.15184/aqy.2019.61.*

Pot Cemetery

Residue from an ancient burial site in Eastern Asia – and the cannabis use that time forgot

Who inhaled in East Asia circa 500 BCE? Yimin Yang and colleagues applied GC-MS analysis to ten wooden braziers bearing burning traces from the Jizankal Cemetery of the Pamir Plateau to find out (1). The team certainly had a hunch – but would the samples be viable? "We were afraid that all the biomarkers would be completely burned or degraded following 2,500 years of burial," Yang says. Fortunately for the researchers (and their study), most of the samples had stood the test of time, bearing relevant compounds.

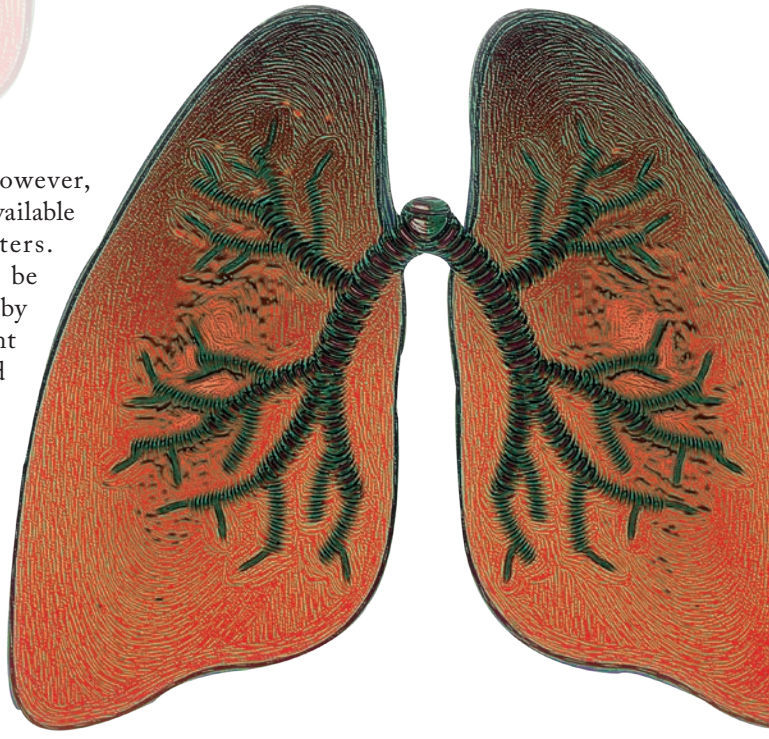
Using ancient cannabis (dated 790-520 BCE) from another site to provide reference signals for cannabis metabolites cannabinol (CBN), cannabidiol (CBD) and cannabicyclol, researchers were able to identify CBN – an oxidative metabolite of THC – on all but one of the wooden vessels exhumed from the burial site. Other cannabis markers were also identified but, interestingly, one was suspiciously absent. "CBD and its degradation products were not detected in the burning residues, indicating that the burned cannabis plants expressed higher THC levels than typically found in wild plants," says Yang.

The investigating team believes that the high altitude of the site was more conducive to the growth of high-potency cannabis of this evolutionary group, and that the stronger cannabis may have been actively selected by the people smoking it – perhaps explaining the prominence of ritual sites in such locations. Alternatively, the high CBN:CBD ratio could hint at domestic hybridization to select for potency.

With plenty of scope for further study, Yang says the team will next analyze human tissue or other artifacts, such as pottery, to confirm exactly how these ancient people consumed psychoactive plants. Answers to such questions will enhance our understanding of this ancient culture and their practices – and of humankind's longstanding relationship with a plant that still causes so much discussion around the world.

Reference

1. *M Ren et al., "The origins of cannabis smoking: chemical residue evidence from he first millennium BCE in the Pamirs", Sci Adv, 5, eaaw1391 (2019). DOI: 10.1126/sciadv.aaw1391.*



Diagnosis: Asthma

Inflammatory asthma classification is complex, but mass spectrometric-based breath analysis may guide the way

MS-based applications in the clinic are expanding, and the recent "BreathPrint" study suggests its reach could extend into asthma classification (1). Of seven tested volatile organic compounds (VOCs), five were confirmed as biomarkers capable of classifying asthma to the same degree as currently used tests, which typically examine induced sputum and/or blood and exhaled nitric oxide (FeNO).

Here, we speak with Jean-François (Jef) Focant to find out more.

Why are new markers needed for asthma phenotyping?

When a patient is diagnosed with asthma, it is necessary to accurately determine the inflammatory phenotype to guide therapeutic approaches. There is not a single fully accurate test that can do this. Nowadays, clinicians use induced sputum (mucus from the lower airways) for inflammatory phenotyping. The cells present in the sputum are counted and characterized on the basis of their morphology. Based on the number of neutrophilic and eosinophilic cells present in the sputum, two thresholds have been established, and four phenotypes have been proposed, including eosinophilic asthma (high number of eosinophilic cells) and neutrophilic asthma (high number of neutrophilic cells). However, sputum analysis is not available in most medical centers. Sputum cell count can be supported or replaced by blood eosinophil count or fractional exhaled nitric oxide (FeNO) measurements, but the accuracy of these tests can still be improved. New markers are needed to support clinicians in their phenotype diagnosis – ideally using a non-invasive approach, given that a patient's phenotype may change over time and require repeated tests.

What analytical methods did you use – and what were the results?

The BreathPrint study was accomplished in two phases. First, a set of seven potential asthma phenotyping biomarker VOCs were selected through a discovery study (276 patients) at Maastricht University in the Netherlands, using GC-Time-of-Flight MS (GC-TOFMS). Second, we performed an independent validation study (245 new patients) in Liège using GC×GC-high-resolution TOFMS (GC×GC-HR-TOFMS). We confirmed five biomarkers that can be used to phenotype asthma with the same degree of accuracy as induced sputum, blood eosinophil count, and surrogate FeNO breathing tests. Furthermore, when blood eosinophil count, FeNO measurement, and biomarker VOCs were used together, an unprecedented classification model performance was obtained for eosinophilic asthma diagnosis. In future, complex mixtures of biomarker VOCs could eventually improve asthma phenotyping and could become a new gold standard, next to induced sputum cell count.

What were the main challenges – and your solutions?

Exhaled breath analysis is challenging in itself. Moreover, large-scale GC×GC-HR-TOFMS studies are not common and the analytical framework needed to be designed. First, we had to be sure that our method of sampling the breath would allow us to isolate putative biomarkers despite being present at potentially low levels amongst non-relevant exogenous molecules, while maintaining a simple sample collection procedure.

In addition, every step of the analytical workflow had to be optimized to produce high-quality data matrices to ease data processing as much as possible. Compound identification was confirmed using the two retention times, specific electronic ionization mass spectra, and HR-MS information. Instrument performance (for example, linearity and limit of detection) was evaluated for the different targets. Sample batches included quality control standards to account for possible instrumental variations and to ensure data integrity.

The same care was applied in the optimization of the preprocessing and processing workflow to ensure complete control of the analytical

process. The classification models were built using random forest – a machine-learning algorithm based on a forest of decision trees. Each model was based on bootstrapping cross-validation and data splitting between training and test sets.

What are the next steps for this research?

So far, we have been using GC×GC-HR-TOFMS to confirm a set of five biomarkers using a targeted approach. What we are doing now is to reconsider the entire validation set (245 patients) using a non-targeted approach. As a matter of fact, we have created a composite image template containing more than 700 analytes that can be used to highlight subtle differences in the breath fingerprint of asthmatic patients. Such a non-supervised volatilomic approach has the potential to link specific VOC profiles to subsets of patients based on a number of factors, including current medication, food habits, environment, toxicant exposure, and so on. These VOC fingerprints certainly hold a significant amount of information that could be revealed… From an analytical point of view, because of the availability of HR-MS data, we could also investigate other data-mining approaches, such as Kendrick Mass Defect classifications.

What impact do you expect the work could have in the clinic?

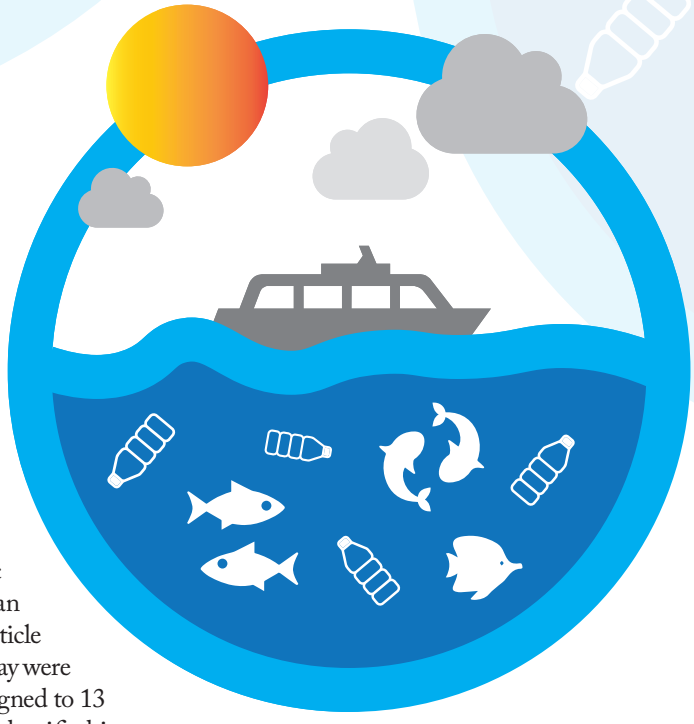
We hope that this unique approach will be positively received by the medical community, which desperately needs better ways of phenotyping asthma. We have already been duplicating selected sample measurements with selected-ion flow-tube MS analyses to evaluate the possibility of transposing the method to simpler instrumentation that could be used directly in hospitals for the screening of the five biomarkers molecules – or to create pattern-based patient classification methods. Direct sample introduction into selected-ion flow-tube MS would also help eliminate the need for the transfer procedures prior to measurement. Such a move would be the logical next step in the line of making this VOC approach usable by practitioners in the hospital environment – and perhaps even in doctor's offices.

Do you expect such applications of MS to become more commonplace?

Time will tell. But I am quite sure that there is room for MS-based diagnostic strategies that rely on VOC patterns in the medical field. Will we see GC×GC-HR-TOFMS instruments blooming in hospitals? I'm not sure at this point. Will medical staff domesticate these complex instruments? I guess it depends if the trend goes in the direction of target analysis of validated biomarkers or towards exhaustive breathprinting of patients. In any case, current instrumentation in the GC×GC-MS domain will definitely play some role in medical diagnosis based on volatilomics in the future – and it will go far beyond breath analysis…

Reference

1. *FN Schleich et al., "Exhaled Volatile Organic Compounds are Able to Discriminate between Neutrophilic and Eosinophilic Asthma", Am J Respir Crit Care Med (2019). DOI: 10.1164/rccm.201811-2210OC.*



Life in Plastic, It's Not Fantastic

Raman spectroscopy highlights the presence of an invisible pest lurking below the ocean's surface – microplastics

You'd have to live under a rock to be ignorant of the plastic pollution problem (see page 14). Though the first evidence for plastic debris in the Atlantic and Pacific oceans surfaced in the 1970s, studies of deep pelagic waters – which provide the largest volume of space for inhabitation of all environments on Earth – have been lacking, leaving us with a shallow understanding of the issue.

Anela Choy and colleagues set out to change that. The team modified the filtration equipment on a remotely operated deep-diving vehicle to collect microplastic measurements using Raman spectroscopy (1) – despite many challenges; for example, investigator Kyle Van Houtan notes the substantial differences between sample and reference spectra: "The reference library used near-pristine industrial samples, while samples had been subjected to wind, waves, sun, biofouling and potentially repeated digestion by marine species."

A second library of Raman spectra was curated based on degraded fishing gear of known materials, and statistical differences between the two spectra were used to calibrate microplastic analyses. Using microscopy and Raman spectroscopy, samples from depths of 0–1000m and from biological samples (pelagic red crabs and giant larvacean sinkers – chosen for their particle feeding habits) in Monterey Bay were identified, quantified and assigned to 13 plastic polymers commonly identified in environmental studies.

Microplastics were identified at all depths – with the highest concentration (15 particles per m^2) observed 200m below the surface – and across all biological samples studied. The results shocked the researchers; "There are higher concentrations of plastic at depth in Monterey Bay – a success story of ocean protection – than have been reported at the surface of what's perceived to be one of the dirtiest places in the ocean: the Great Pacific Garbage Patch," says Van Houtan. Polyethylene terephthalate was the most common plastic in all instances, followed by polyamide, polycarbonate and polyvinylchloride.

Having established the presence of microplastics in marine species capable of transporting them into food webs and to the ocean bed, lead investigator Choy says that she is keen to examine whether some microplastics are more readily transferred through marine food webs than others. Such an understanding of plastic distribution mechanisms in marine ecosystems could provide crucial information for identifying sources of pollution, informing policy, and supporting conservation.

We can all play our part in protecting the environment at home – or in the lab – so please don't forget to reduce, reuse and recycle.

References

1. *CA Choy et al., "The vertical distribution and biological transport of marine microplastics across the epipelagic and mesopelagic water column", Sci Rep, 9 (2019). Doi: 10.1038/s41598-019-44117-2.*

A SMArter Way to Diagnose Diabetes

Could a polymer that "biopsies" living cells lead to improved diabetes diagnosis and monitoring?

Diabetes – a disease so common that almost everyone knows someone who has it, but so comprehensive that few members of the public are fully aware of the risks it can pose to patients. For example, the disease can cause severe damage to blood vessels throughout the body – and that damage begins early on. The silver lining? A method of detecting the blood vessel damage could also offer a route to earlier diagnosis and treatment of diabetes (1).

"We wanted to exploit our recent discovery that a novel chemical tool, the polymer styrene maleic acid (SMA), can 'biopsy' human cells, extracting proteins without causing cell death," explains Andrew Smith, a researcher from the School of Biomedical Sciences at the University of Leeds. "This project will build on our previous findings with SMA by using it as a tool to investigate diabetic vascular disease development

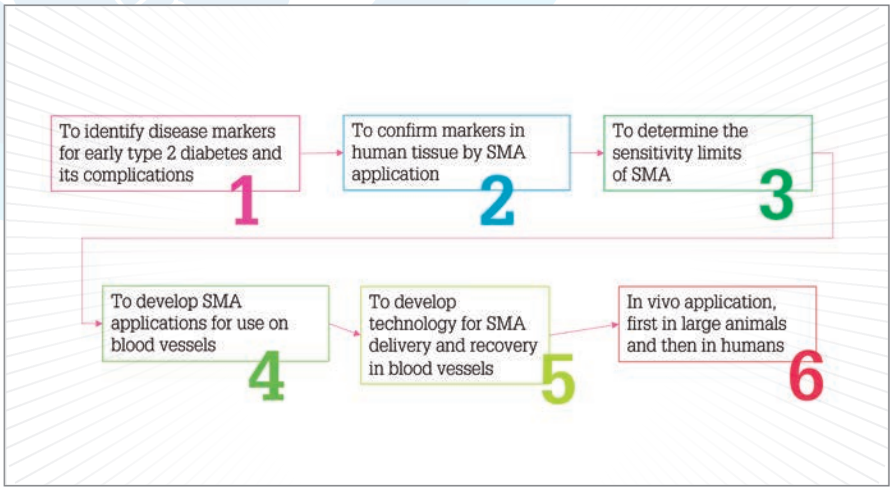


Figure 1. The research team's six goals for SMA.

and identify markers linked to specific aspects of this disease."

SMA isolates proteins from cell membranes in tiny, disc-like nanoparticles due to its structure, which cuts through the membrane to release the disc and maintain its stability. "We found that we were able to identify proteins from membranes and elsewhere in the cells in our collected material," says Smith.

The research group now plans to exploit their finding that SMA can nondestructively sample proteins from cells and intact tissues. To that end, they have a series of six goals.

But what happens if proteins that signal disease progression are identified? "Detecting a biomarker of change in cells due to the pre-diabetes state will give solid evidence of the need for intervention," explains Smith. "Early diagnosis of type 2 diabetes is linked to significant risk reduction, with scope for further reduction if treatments can be directed by evidence obtained from the site of disease damage." To that end, the researchers will not only identify biomarkers of disease development in patients with established diabetes, but also search for markers of higher risk of disease complications.

In My View

In this opinion section, experts from across the world share a single strongly-held view or key idea.

Submissions are welcome. Articles should be short, focused, personal and passionate, and may deal with any aspect of analytical science. They can be up to 600 words in length and written in the first person.

Contact the editors at charlotte.barker @texerepublishing.com

When Technology Bites Back

What can we do about plastic pollution – as citizens and as analytical scientists?

By Heather A. Leslie, Department of Environment and Health, Faculty of Science, Vrije Universiteit Amsterdam, the Netherlands.

Plastic pollution exists in our oceans, our food chains, and our bodies – nobody wants it, and yet it is building every day. Eliminating plastic pollution is hardly rocket science, but it requires courage and political action reaching the very apex of the world's power structures.

Like many of the pressing problems the world faces, plastic pollution is a symptom of other issues. All too often, a perceived solution creates yet another problem because there are feedback loops that we are unaware of. Things are often not as they appear on first examination, which will come as no surprise to analytical chemists.

A world free of plastic pollution will require large shifts not only in how we design, produce and consume products, but also in the world's underlying financial and economic infrastructure. What's more, these shifts need to be global. No environmental problem in history has been solved without strong regulation. However, simply complying with the current array of regulations is not enough, because pollution is still increasing in spite of these regulations. We can see some early micro-sized attempts at regulation of single-use plastics in Europe, and a proposed phase-out of intentionally added plastic particles in down-the-drain products and such. But if we proceed at a pace of regulating 10 disposable plastic articles at a time, the entire process may take millennia.

What are the other solutions being propagated today? I have a potentially unpopular opinion: end-of-pipe solutions do not change the system that creates the mess. Sometimes they even support that system and distract us from what we should be doing upstream – cleaner production and more deep-rooted changes in our society. The end-of-pipe idea of large-scale cleanups is popular and at first it seems like a great idea, but I prefer methods that do not wait until plastic has already become pollution. The oceans contain 1.3 billion cubic kilometers of seawater. How could we ever keep that volume clean without destroying it in the process? Clean-up operations also carry huge costs and there is minimal return on investment. These are all problems that are avoided when the focus shifts towards prevention.

Awareness campaigns regularly label us as consumers who need to change our behavior, but that limits our action to choosing between the products that companies market to us. As citizens we have a much wider repertoire of ways to change the world; for example, supporting civil rights organizations and independent journalism, petitioning, protesting, striking, and direct action. History is full of examples of people coming together to change the world, one small act of courage at a time.

Plastic pollution is created in a complex landscape of capital, power and global economics. As analytical scientists, we have a job to do here. We can develop methods to make the invisible visible and fill in the information gaps that facilitated the bad decisions of the past and their negative consequences. Knowledge is power, and sharing knowledge is even more powerful. To increase our knowledge in a relevant way, analytical scientists like me are currently facing the challenge of measuring exposure to sub-micron plastic particles "in the wild," meaning real fragments of plastic materials in real environmental matrices – or in our bodies. Exposure to these very fine plastic particulates may be a serious problem because they are a toxicologically relevant fraction. If threshold levels of fine plastic particles reach tissues and organs, they can potentially cause chronic inflammation, which is a prelude to a variety of chronic diseases.

We are now able to more quickly scan plastic materials for toxic additives with advanced techniques (such as the direct probe atmospheric pressure photoionization/atmospheric pressure chemical ionization high-resolution MS used at our laboratory). These techniques help reveal the amount of toxic chemicals from plastics in circulation in our living environment. Such information from the analytical sciences provides an important input for debates on whether or not public health and the environment are adequately protected from or, conversely, seriously threatened by plastic pollution; in my view, an honest government should always act to remove any serious threats. We need both hazard data and exposure data for risk assessment (risk = hazard × exposure), but we simply aren't able to adequately analyze exposure to very fine plastic particles at present. Without that information, others will create their own narratives, with or without data. The stakes are high, and many of us are working hard on analytics and quality control to get answers to the people who need them.

Those analytical chemists studying plastic pollution and wanting to offer powerful input into the plastics debate must think hard about the research questions they ask, carefully considering which new measurements really matter (and which do not). What new knowledge can be generated that might significantly update our understanding and shape a better future? It's not easy to see what others have not seen, and get out of the deep comfortable groove of our own discipline or research contract terms of reference. Working across disciplines helps keep us sharp – I like it when someone challenges my assumptions and I like to challenge theirs too. Not only do you generate an intellectually stimulating conversation, but it helps us progress further and faster towards our goals. We will need the combined talents and passion of a multiplicity of voices and collaborators thinking together if we are to effectively tackle a problem as wicked as plastic pollution. In the face of today's moral and economic imperative to turn the plastic pollution tide, we analytical scientists must ask ourselves, what are we doing with what we know?

ANALYTE *at the* MUSEUM

Join us for a behind-the-scenes tour of the Netherlands Institute for Conservation, Art and Science, as we hear from a group of analytical chemists who are helping to preserve important cultural artifacts – from textiles fished from shipwrecks to 20th century oil paintings.

LACQUER *of Interest*

Using GC-MS to investigate degradation of Asian lacquer

By Jonas Veenhoven, Researcher, Royal Institute for Cultural Heritage, Brussels, Ghent University, Belgium and University of Amsterdam, the Netherlands.

I work within an interdisciplinary project called Profound study of Hydrous and Solvent Interactions in Cleaning Asian Lacquer (PHySICAL; http://physical.kikirpa.be). We use state-of-the-art analytical techniques to develop safe and effective cleaning methods for cultural artifacts coated with Asian lacquer. Asian lacquer, made from the sap of trees in the sumac or cashew family (Anacardiaceae), is a highly durable coating, used on all sorts of objects, weapons, armor and even architecture. When exposed to light, degradation products start to appear in the lacquer, making the surface highly water-sensitive. Cleaning the degraded lacquer with solvents can cause swelling when the cleaning agent is absorbed into the lacquer layer during cleaning. Leaching of organic compounds from the polymer matrix can also occur – a complex problem with unpredictable long-term effects.

I'm responsible for the chemical side of the research at the Belgian Royal Institute of Cultural Heritage (KIK-IRPA), the Separation Science Group at Ghent University and Conservation and Restoration of Cultural Heritage Program at University of Amsterdam. The other partner in the project is the Royal Museums of Art and History (RMAH) in Brussels. Asian lacquer and polychrome sculpture conservator Delphine Mesmaeker is in charge of the RMAH research – studying their lacquer collection, improving preventive conservation conditions and investigating the visible changes to the lacquer surfaces through cleaning.

Let's get PHySICAL

My group applies chromatographic techniques coupled to MS to:

- Analyze objects
- Carry out quality control of materials
- Analyze our polymerized mock-up samples
- Monitor the effects of artificial aging on mock-up samples
- Investigate aqueous and solvent extractions using immersion and dedicated surface extraction methods.

For the analysis of objects incorporating insoluble polymers, such as the Asian lacquers, we use pyrolysis coupled to GC-MS (Py-GC-MS). This allows us to identify material-specific markers after deconvolution of the compounds. The small sample size, reduced sample preparation time and dedicated mass spectral libraries developed for this technique have proved to be valuable for the analysis of cultural heritage materials. Nevertheless, quantification is difficult, although peak area ratios can be used to semi-quantify material contributions. In addition, separation and identification using Py-GC-MS is complex because the numerous components that are formed through pyrolysis result in many coeluting peaks, which are not necessarily material-specific.

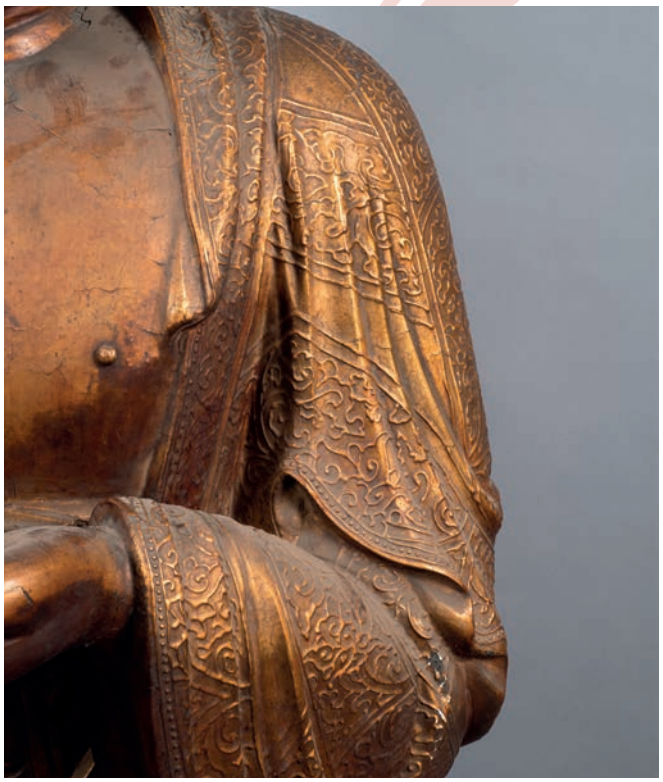
Right now, we are carrying out lacquer immersion experiments, assessing leaching of aged lacquer following exposure to solvents using conventional GC-MS. For this work we omit pyrolysis, to avoid overcomplicating interpretation and make sure the pyrolyzed fragments don't fall below the limits of detection. By working in splitless mode and using dedicated derivatization protocols in combination with MS we can achieve the required sensitivity and selectivity. Analyzing the chemistry of leaching helps us to understand ongoing/accelerated degradation phenomena caused by solvents and ultimately predict the effect of cleaning on ancient lacquer.

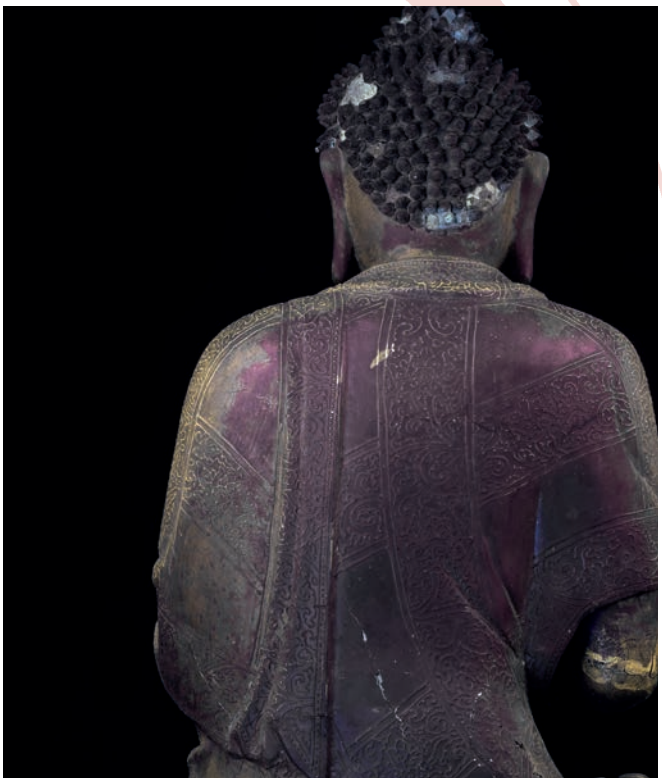
Back on display

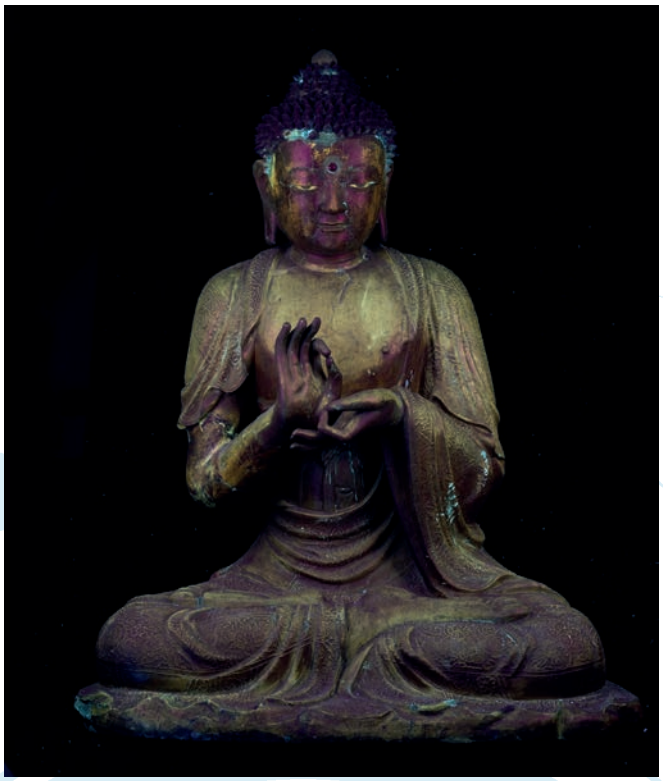
A thorough knowledge of possible solvent interactions with the lacquer surface will have a major impact on conservation of these objects. Because knowledge of the cleaning process is currently very limited, cleaning is often postponed, and objects put in storage rather than displayed in the museum. Not only does this remove them from public view but long-term storage could also lead to unwanted effects such as dust deposits. With a better understanding of solvent–lacquer interactions, we can propose cleaning methods that are not harmful to the object, so that they can be displayed once more.

Plans for the project include the continuation of the immersion extractions after artificial aging of the mock-up samples and development of surface analysis techniques in combination with stir-bar sorbtive extraction. These techniques are being developed at Ghent University and, in combination with thermal desorption GC-MS, allow us to reach ppt and even ppq level sensitivities, lowering the limits of detection of GC-MS by up to three orders of magnitude. The use of direct extraction of solutes from leachable surfaces has thus far been limited to some life sciences applications (such as skin sampling) and this will be the first time it is applied for the analysis of historical objects in general and for Asian lacquer in particular. LC-MS and other separation techniques will also be evaluated and, if needed, we will make use of high-resolution MS using LC-Time of Flight MS (LC-ToFMS) or Orbitrap to elucidate structures and form hypotheses about reaction mechanisms. Both GC-MS and LC-MS analysis techniques will be optimized for the analysis of Asian lacquers and compounds extracted from the damaged surface.

A statue depicting Buddha (17th-18th century) from the RMAH collection.







TRUE *Colors*

Speeding up the aging process to help reconstruct the colors of the past

By Maarten van Bommel, Professor of Conservation Science, University of Amsterdam, the Netherlands.

Preserving our cultural heritage has great societal impact. Millions visit museums and historical collections every year and derive enjoyment, inspiration and education from the objects they see there. My role is to help provide the context that makes these cultural artifacts so fascinating, and preserve them for future generations. I work both at the faculty of humanities, where we teach conservators, and at the faculty of science, within the analytical chemistry group. This ensures the integration of art and science, which is key in the preservation of cultural heritage.

Right now, I have two main lines of research, closely interconnected. One is the investigation of organic colorants used in textiles, furniture, paintings and drawings. I have studied objects from 3,500-year-old archaeological textiles to 20th century art. By understanding which organic colorants were used in an object and how they have changed over time, including degradation mechanisms, we can develop preservation strategies and even reconstruct the original appearance of the object.

Tools of the trade

Analytical science forms the basis of all chemical research carried out in the field of cultural heritage, and developing better analytical methods is critical to allow us to extract more information without damaging the objects we aim to preserve.

The main technique used for organic colorants analysis is chromatography, predominantly (ultra) high-performance LC ([U]HPLC). For organic colorants, photo diode array (PDA) is the detection technique of choice (1). For those components that cannot be identified based on retention time and PDA spectra, we are increasingly turning to MS. In particular, the sensitivity and high resolution of the Orbitrap MS offers new possibilities.

The chemical variety of organic colorants is huge and, to improve separation power, comprehensive 2D-LC techniques are being introduced. We use ion-exchange chromatography in the first dimension to separate dyes based on charge, followed by a second separation using ion-pair reversed-phase chromatography and detection by both PDA and quadrupole TOF-MS (QToFMS). This allows hundreds of colorants to be separated in one run (2).

Inorganic materials (used as fixation agents) and can also alter the color of the object. Scanning electron microscopy coupled to energy dispersive X-ray spectroscopy (SEM-EDX) is used to identify the inorganic composition.

Light touch

Analytical results are just the start of the research. Even with chromatographic information about the composition, is often difficult to know the exact color, since that is also dependent on how the colorant was applied. Therefore, we study historical sources for recipes, which we recreate in the lab. We then apply artificial aging to our "mock-ups"; for example, by exposing them to an intense light source to stimulate fading. The faded material can be analyzed for degradation products, and the fading rate can be used to determine future behavior. However, the color of an object often comes from a mixture of colorants and it is impossible to tell which degradation products originate from which parent molecule. To help solve this puzzle, we recently partnered with several organizations to initiate the Toolbox for studying the Chemistry of Light-induced Degradation (TooCOLD) project.

In the TooCOLD project, we are developing a light-degradation cell coupled on-line to chromatographic techniques and MS. We will first separate complex mixtures of dyes and guide each individual dye to an exposure cell, then the dye will be trapped and exposed to light, before the degradation products, also a mixture, will be separated in a second chromatographic system, followed by high-resolution MS. In this way, we can study the degradation pathway of individual components, which can be related to historical objects by analyzing samples or faded reconstructions. The main advantage of the TooCOLD system is the speed – normal degradation studies can take weeks or even months, but we expect to do this in a day. The toolbox can be applied in other fields as well – we are collaborating with Unilever to examine food sustainability and with water companies who wish to use the light treatment to purify water. We are working with a company to develop a commercially available product based on this technique.

Understanding the use and behavior of colorants is very useful but won't allow us to accurately reconstruct the appearance of the original object. Therefore, we developed a technique using colored light to mimic the original appearance, with the color of each section determined based on chemical analysis and reconstruction research (3). Pictured on the right-hand page is a small table designed by Piet Kramer, which was partly illuminated for a museum display, creating such a realistic impression that we received complaints from museum visitors who thought we had painted the object!

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Clockwise from top left: A. Bongen, Commode, 1766, oak, purple heart, holly, tulipwood, Photograph by Jaap Boonstra; The same commode illuminated with colored light to visualize its original appearance, Photograph by Federica van Adrichem; Possible handwarmer, with an internal cardan-mechanism. Gilded silver, possibly German, 17th century. Photograph by Restaura; Piet Kramer, Nightstand, 1933–1936. Half is illuminated with white light (left) and half with colored light (right), Photograph from the Cultural Heritage Agency of the Netherlands.

Paint IT BACK

From colors to proteins: modern technologies and ambient MS for cultural heritage objects

By Alina Astefanei, Research Scientist, Cultural Heritage Agency of the Netherlands, and Assistant Professor, Analytical Chemistry Group, HIMS, University of Amsterdam, the Netherlands.

As an analytical scientist, I believe that what the field needs most are modern and dedicated methodologies to tackle highly complex and severely degraded samples, and that is the main focus for my work.

My postdoc, with Garry Corthals at the University of Amsterdam, used a new ambient MS technique called surface acoustic wave nebulization-MS (SAWN-MS) for the first time in the field of cultural heritage. SAWN-MS allows much smaller samples and simplified sample treatment procedures, plus results within a minute. I applied the new technique first in the identification of organic colorants in wool samples, followed by fatty acids profiling in oil paint swatches that show different degrees of water sensitivity. In collaboration with the Rijksmuseum, Amsterdam, I also studied the effect of different cleaning procedures on oil paints.

Here at the Cultural Heritage Agency of the Netherlands in Amsterdam my role is to adapt and improve existing MS-based technologies and enable their implementation in the cultural heritage field. We need techniques that are gentle enough to preserve the fragile chemistry within the sample, yet powerful enough to characterize their complex system. Without this, further research on conservation treatments remains impossible, impeding our ability to protect cultural artifacts.

Modern tools and modernist art

The team in our Amsterdam laboratory relies on this type of technology to answer questions posed by conservators from different museums on the composition and degradation state of different historical materials. A recent example was three paintings by Marc Chagall from the collection of Stedelijk museum Amsterdam (Self-portrait with Seven Fingers; The Fiddler and The Pregnant Woman/ Maternity). We analyzed microsamples using a combination of different techniques to gain information on the organic materials used by the artist. Specifically, we used LC-PDA-HRMS to identify organic pigments from different regions of interest on the paintings – information that contributes to a better understanding of the objects and helps conservators make decisions.

My own work involves developing methodologies to identify organic colorants and understand their degradation mechanisms in textiles and paint swatches. One very interesting project involves the study of the organic pigments used in different artists' colors and commercial paints from the late 19th and beginning of the 20th century.

Another project involves identifying the proteinaceous materials used in cultural heritage objects. For this, we are working on adapting the extraction and digestion strategies used in modern proteomics to different types of historical materials. Due to the very small amount of proteinaceous material, the extreme complexity and high levels of degradation, samples from artworks are very different to those typically encountered by proteomics labs.

The techniques traditionally used in field of cultural heritage for the identification of organic materials (such as GC-MS, pyrolysis GC-MS, HPLC-PDA, direct temperature time-resolved MS) involve time-consuming preparation steps, chemical derivatization, high temperatures, high ionization energies and long analysis times with poor sensitivity for small samples. Moreover, traditional extraction methods may lead to chemical modification through hydrolyzation and esterification, and could even cause the breakdown of the compounds of interest. One big problem, especially for small molecules, is source-induced fragmentation, which can cause confusion about whether the detected fragments are due to degradation of the object or the analytical technique itself. To avoid source-induced fragmentation and reduce ion suppression as much as possible, we need to minimize stress on the sample.

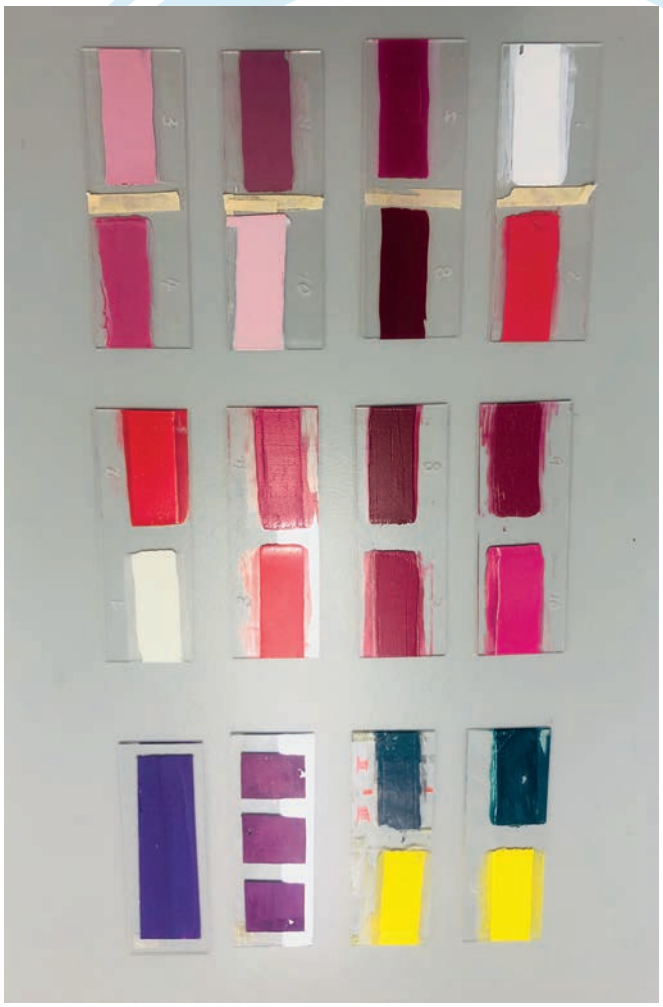
Do no harm

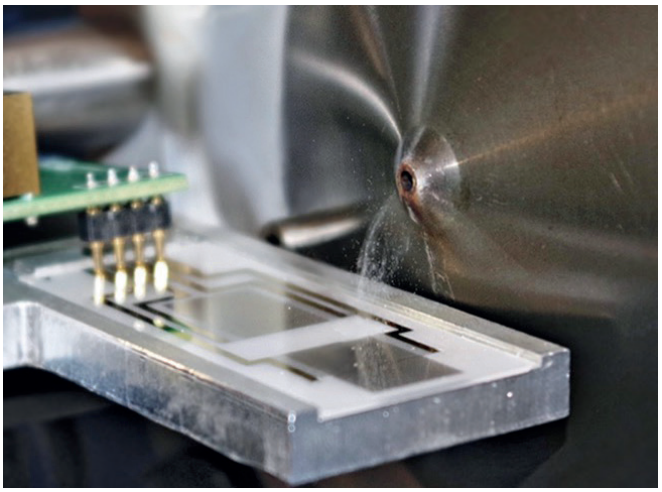
It's clear that for analysis of historical samples we need modern minimally invasive methodologies that provide detailed and reliable information. This is highlighted in Article 10 of the Venice Charter for the Conservation and Restoration of Monuments and Sites (the internationally recognized framework for the conservation and restoration of historic buildings): "Where traditional techniques prove inadequate, the consolidation of a monument can be achieved by the use of any modern technique for conservation and construction, the efficacy of which has been shown by scientific data and proved by experience."

Excellent progress is being made in several areas; for example, the introduction of ambient MS techniques, which eliminate the need for chromatographic separation and minimize harsh and time-consuming sample preparation steps. These techniques are minimally invasive, incredibly fast and require extremely low samples sizes.

The SAWN device is a straightforward portable device, in which a small chip containing a piezoelectric substrate is placed directly in front of the mass spectrometer without the need for a nebulization gas or the use of electrodes and voltages for the ionization. The SAWN creates plumes of droplets with ionized molecules that are further identified by the mass spectrometer. When applying this technology for cultural heritage materials, we noticed a significant reduction

Clockwise from left: Paint swatches from the RCE reference collection; SAWN power source and android controller; SAWN-MS.





in samples needed for analysis, which is critical in art analysis.

Another example of an ambient MS technique introduced in the field of cultural heritage is direct analysis in real time MS (DART-MS). Alba Alvarez-Martin (Smithsonian Museum, Washington DC, USA) was the first to use an enclosed solid-phase microextraction DART-MS interface to identify specific volatile organic compounds that are hazardous to museum objects. She has also used this setup to identify the breakdown products and effects of mixed inorganic pigments on eosin degradation in oil paints.

Mix it up

Considering the complexity and often severe degradation state of cultural heritage objects, we should not rely on one analytical platform or one technology, but explore and combine multiple techniques and analytical strategies that give complementary information. Innovative techniques suitable for the analysis of complex samples and fragile molecules in both liquid and solid form are becoming available and progress is being made in speeding up and simplifying the entire analytical workflow. However, one unmet need is smart, automated data analysis tools for faster data interpretation and I hope to see advances in the is arena in the near future.

A final thought: my work focuses on translating technological advances in other fields to cultural artifacts, but it's also true that the knowledge and insight gained by studying complex materials within the cultural heritage field are valuable for scientific progress elsewhere. Many of the processes studied – including degradation mechanisms of organic colorants, lipids and fatty acids oxidation, polymerization processes, protein analysis and molecular interactions – are of fundamental interest for environmental and food research, polymer science and biochemistry

From THE DEEP

Precious metals from a 17th century shipwreck yield their secrets to XRF and SEM

By Inke Joosten, Conservation Scientist, Cultural Heritage Laboratory, Ministry of Education, Culture and Science, Amsterdam, the Netherlands.

My main expertise lies in the study of archaeological metal and textiles. Currently, I am working together with researchers Janneke van der Stok (Metals, Inc), Tonny Beentjes and Maarten van Bommel (University of Amsterdam) to examine precious metals after excavation (the AMOR project). We selected several historically valuable gilded objects from a 17th century shipwreck, BZN17, which sunk near Texel, the Netherlands. One of the objects, a gilded brass oval powder box with an image of Venus and Cupid (pictured) is of special interest because we believe it may still have its original beeswax coating. In historic collections these type of objects have been polished and cleaned over and over again to make them shine, removing all original coatings. This box, buried for centuries underwater, may still preserve this important information on its original appearance. Our wider aim is to establish a practical and optimized research and conservation strategy for marine precious metals, to preserve this important surface information. Based on the analytical results, we plan to develop a flowchart and workshops for archaeologists and conservators to aid decision-making after excavation of precious metal.

One of the difficulties in studying these objects is the heterogeneity of the material and the fact that the objects contain layers. For instance, if we want to analyze the composition of the powder box with X-ray fluorescence (XRF), several layers of material obscure the inside, whether intentionally added (such as gilding) or corrosion products. Another problem is that an archaeological object may have been subjected to a conservation treatment that has removed relevant information on manufacture, use and burial conditions.

We prefer to study cultural heritage objects in a noninvasive manner, extracting as much information as possible from the object without taking samples, or using the smallest samples possible. For the AMOR project we used X-rays to study the construction of different objects, followed by careful analysis with XRF. Where sampling was possible, samples were embedded in epoxy and polished to study them with optical microscopy and SEM-EDX. SEM-EDX is my favorite instrument since it allows you to examine materials in high detail and analyze the chemical composition at the same time. Corrosion products give spectacular images! Corrosion products also hold a lot of information about the making of the object and the burial conditions it has been subjected to for all those years. Organic materials like our suspected beeswax coatings can be analyzed by GC-MS. Collaborations with the Technical University of Delft and the University of Amsterdam are providing us with access to promising new techniques like neutron and micro-CT imaging.

"One of the difficulties in studying these objects is the heterogeneity of the material and the fact that the objects contain layers."

I am also involved in the development of an "Irradiation Passport for Art". In the desire to extract as much information as possible from cultural heritage objects, we are increasingly exposing them to ionizing radiation. Modern analytical techniques use interactions with photons, electrons and ions to identify the materials in the object. But those interactions could induce visible or invisible alterations, the long-term effects of which are not fully known. Exposure to radiation is cumulative, which means that previous exposure may change the sensitivity of objects or research samples. Therefore, we believe art objects and research samples in the field of cultural heritage need an irradiation passport, recording the location, total exposure and circumstances of radiation exposure to date.

Oval powder box with image of Venus and Cupid - gilded brass.

MODERN ART

Meets Modern Analysis

Developing a toolbox to meet the unique conservation challenges of 20th century art

By Klaas Jan van den Berg, senior conservation scientist, Cultural Heritage Agency and Professor of Conservation Science (Painted Art), University of Amsterdam, the Netherlands.

My background is in organic and analytical chemistry but I have been involved in art research since 1995. In the last ten years, my research has focused on the chemistry and optical properties of paint surfaces and the impact of conservation measures on 20th century oil paintings. These paintings are distinctly different from the paintings of previous centuries and present a range of challenging conservation problems – in particular, the presence of new materials such as synthetic organic pigments and metal soaps. Plus, the paintings are often unvarnished, making the surface vulnerable to degradation as a result of the interaction with light, noxious gases and particulate dirt. Challenges for conservators of the artworks include the formation of vulnerable surface "skins" of medium and exudates on paint surfaces, efflorescence, unpredictable water and solvent sensitivity, and even paint dripping, which can occur for several years after paintings are completed.

The big picture

To understand these phenomena, my group collaborates with colleagues from museum laboratories and collections such as Tate, the Courtauld Institute of Art, The Getty Conservation Institute, Stedelijk Museum Amsterdam and the Universities of Pisa and Amsterdam.

One of our most fruitful areas of study has been exploring the archives of art materials supplier Royal Talens – a rich source of paint compositions over the years, information on historical materials suppliers, production philosophy and development. We also carry out studies on the degradation of oil paints and conservation research into alternative surface cleaning methodology. To analyze oil paints, a range of analytical techniques are used, including light microscopy, XRF, SEM-EDX, Raman, Fourier-transform infrared spectroscopy (FTIR), direct temperature-resolved MS, GC-MS and flow injection analysis, and LC- electrospray ionization MS (LC-ESIMS).

All white?

An interesting recent project studied the degradation of oil paints containing titanium white pigments. These pigments were introduced in the first half of the 20th century as an alternative for zinc white and (especially) the toxic lead white. The early titanium white pigments used by artists such as Pablo Picasso and Piet Mondrian were mostly produced from the mineral anatase. This pigment may absorb UV radiation, producing radicals that break down the paint binder, leading to chalking of the paint surface, compromising the appearance of the painting and leading to loss of original material. Nowadays, artists pigments are derived from another titanium oxide mineral, rutile, and are coated with thin layers of alumina and/or silica to block the detrimental effect of radicals on paint. In addition, museums often routinely block out the most damaging UV radiation. Nevertheless, especially for early titanium white-containing paintings, monitoring the paintings for degradation may prove useful.

PhD student Birgit van Driel investigated numerous aspects of titanium dioxide pigment and presented a number of analytical approaches and techniques that detect the degradation of titanium white paint before the damage becomes visible. This approach may be used as an early warning system by museums to see if additional lighting measures should be taken (1).

Scrub up

Soiling of paint surfaces with particulate dirt is inevitable and most paintings will need to be cleaned once in a while. For this, conservators generally use water and aqueous solvents with cotton swabs (Figure 1). While this works well for older paintings, modern oil paints are often sensitive to water and other solvents, creating a real challenge for conservators (Figure 2). We wanted to find the root cause of the problem, so we carried out a series of studies investigating the chemical reactions involved. We found that, in some cases, sensitivity is caused by the formation of water-soluble salts following a reaction with atmospheric pollutants (2,3) and more recently we discovered that degradation of the binding medium itself may also play a crucial role. As oil paint dries, the binder, which often consists of linseed oil, will polymerize thanks to its double or triple unsaturated fatty acids; however, there are competing oxidation reactions that form diacid moieties. Hydrolysis of these triglyceride molecules may also undermine the stability of the paint but this effect may be counteracted with the formation of metal soaps (4,5) (Figure 3). In collaboration with our colleagues from the Tate Gallery and the University of Pisa, we have been able to find, through analysis with direct infusion and LC-ESIMS, a firm analytical correlation between high concentrations of free oxidized degradation products and

Figure 1. Surface cleaning the surface with moist cotton swabs.
Photo credit: Louise Wijnberg.

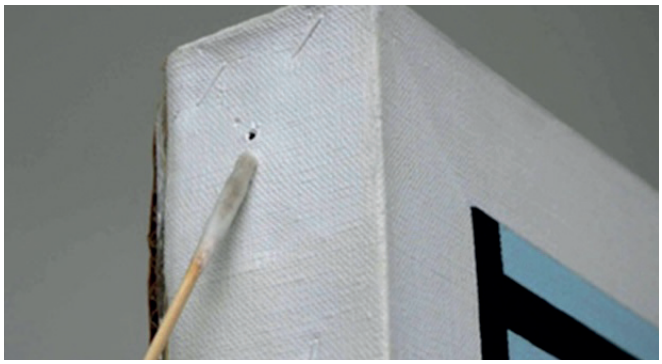


Figure 2. Karel Appel (1921-2006), Les Animaux, 1961.
Collection: Cultural Heritage Agency of the Netherlands.
This painting is sensitive to water in red, blue and black paint areas.

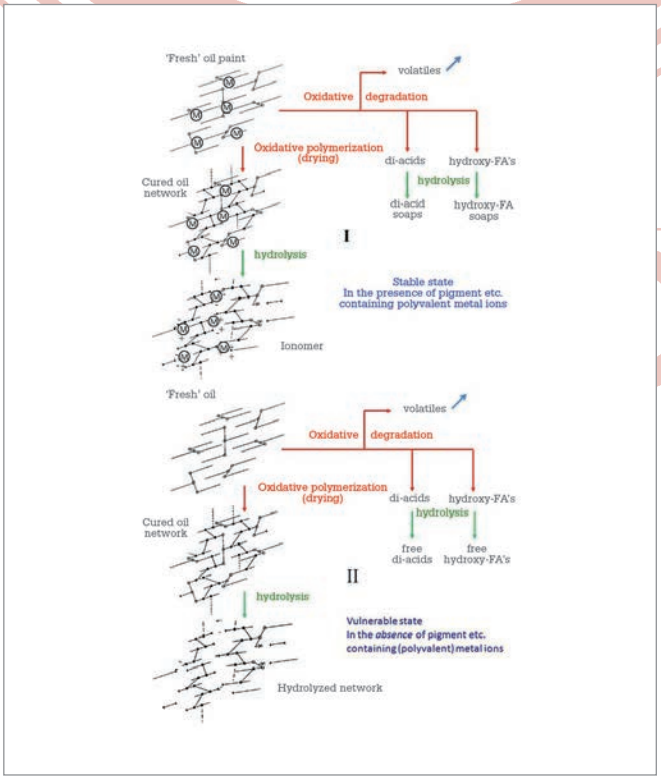


Figure 3. The competition between oxidative degradation and oxidative polymerization in oil paint, and hydrolysis, leading to a solvent-vulnerable paint in the absence of polyvalent metal ions (II). Reproduced with permission from (5).

water sensitivity, whereas the more stable paints show high degrees of polymerization and/or metal soap formation (6).

It's satisfying to know that we are helping to optimize the storage, presentation and guardianship of works of art that are of immense cultural value in our society. By understanding what materials have been used for paintings, and the changes that have occurred as a result of aging and the conditions of storage and display, we can predict (and avoid) changes in the future. In addition to the cultural value, paintings also represent economic value, reflected in the extravagant prices paid for paintings at auction. As a result, forgeries are ubiquitous, even in renowned museum collections, and this is another area where our knowledge of historical painting practice can be put to practical use!

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New Tools FOR OLD MASTERS

Conserving precious paintings for the art lovers of the future.

By Katrien Keune, Head of the Science Department, Rijksmuseum and Associate Professor, Van 't Hoff Institute for Molecular Science (HIMS), University of Amsterdam, the Netherlands.

The science department at the Rijksmuseum encompasses a large group of scientists with different specialisms. We conduct research on our collection in close collaboration with conservators, curators and (technical) art historians, with the aim of better understanding, managing and presenting the collection. At HIMS, we study fundamental chemical processes in paints. Dividing my time between the two roles means that I can function as a bridge (or translator) between the art and academic fields.

Fading beauty

We work with conservators to solve the diverse problems they face in conserving and restoring traditional paintings. It is extremely important that research on paintings is carried out before a conservation treatment starts to be able to select the most suitable conservation treatment to preserve and present the painting.

I specialize in aging and degradation studies of pigments and oil paintings at the microscopic and molecular level, especially the interaction between pigment and binding medium. An example of a degradation phenomenon we investigate in detail is the formation of metal soaps in oil paintings, the result of a reaction between the lead or zinc pigment and the oil binder. This phenomenon was first observed in 1997 during the restoration of Rembrandt's "Anatomy lesson of dr. Nicolaes Tulp" (Mauritshuis, The Hague) and since then has been widely investigated in traditional and modern paintings.

The impact of pigment degradation is clearly visible in the fading of the yellow orpiment paint in "Still Life with Flowers and a Watch" by Abraham Mignon (ca. 1660–1679) (pictured). The yellow and orange arsenic sulfide pigments in the Rosa rubiginosa have degraded after exposure to light, resulting in loss of the flower leaves. We are studying the pathways of the degradation, migration processes of the degradation products and the conditions under which new complexes are formed in the paint.

The future is bright

On a daily basis in my lab, I use mainly imaging-attenuated total reflection (ATR)-FTIR, SEM-EDX, py-GC-MS and Raman. However, I frequently make use of synchrotron facilities to study low-concentration materials at high resolution. The paint samples we investigate are around 300×100×100 microns in size. Within these samples we study pigment, binders and degradation materials at sub-micron to nanoscale. Synchrotron techniques we have used include XANES, EXAS, SAXS, micro-X-ray diffraction (XRD), CT-XRD, photoluminescence microscopy, micro-XRF and STXM.

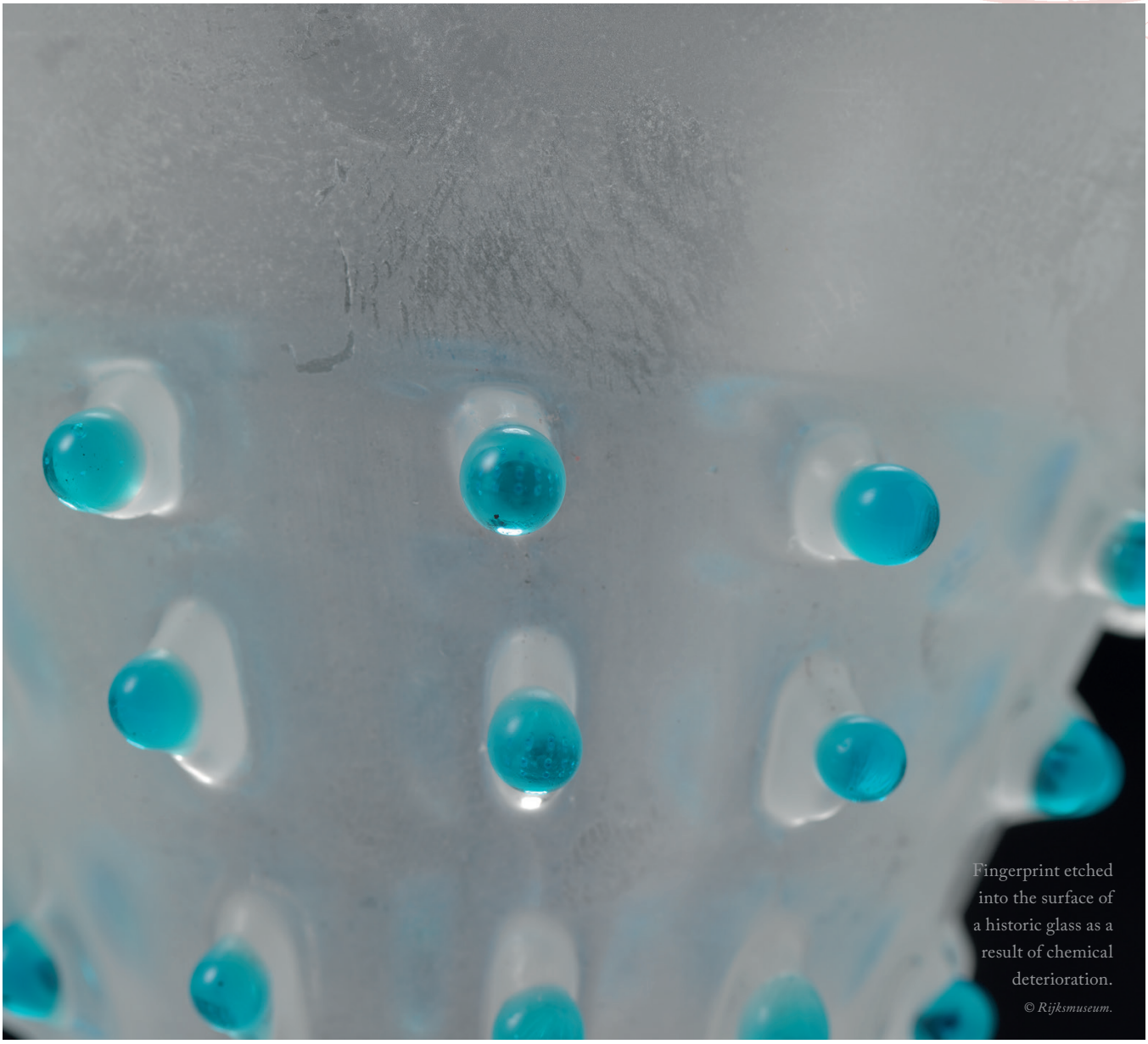
"I frequently make use of synchrotron facilities to study low-concentration materials at high resolution."

We recently used XRD microtomography (XRD-CT) to investigate a tiny paint sample taken from "Homer" by Rembrandt (housed in the Mauritshuis collection) at the Diamond Light Source synchrotron facility in the UK. The painting has suffered from reactions between lead pigments and SO2 pollution in the atmosphere. With advanced data treatment we could establish and localize various newly formed lead–sulfur species within the paint layers.

I'm excited by the rapid development of non-invasive imaging technique, such as the macroscale-X-ray powder diffraction (XRPD) developed by the University of Antwerp, which allows us to image the distribution of a specific mineral pigment in a painting. For example, we can visualize the copper distribution in a painting with macro-XRF, then use the new macro-XRPD technique to identify whether it is the blue azurite (Cu3(CO3)2(OH)2) or the green malachite (Cu2CO3(OH)2) pigment.

In the future, I see conservation scientists and conservators using an "imaging toolbox" holding a large variety of non-invasive imaging techniques to map the chemical, optical, structural and physical characteristics of paintings. Parallel to these developments is the fast growth of data fusion, data analyses and data visualization tools, which are key to deal with large data sets and extract useful information from them.

"Still Life with Flowers and a Watch" by Abraham Mignon (ca. 1660-79), Rijksmuseum, Amsterdam, The Netherlands.



Fingerprint etched into the surface of a historic glass as a result of chemical deterioration.
© Rijksmuseum.

In the CLEAR

Ion chromatography can predict invisible deterioration of glass objects

By Guus Verhaar, Postdoctoral researcher, Rijksmuseum, Amsterdam, the Netherlands, University of Texas, Dallas, USA, and Corning Museum of Glass, New York, USA.

Dealing with the chemical deterioration of glass in museum collections is a serious challenge for conservators and curators. It has been estimated that up to 30 percent of all glass objects in museums may be of unstable composition, but the associated visual changes cannot always be observed. Conservators asked me if it would be possible to identify unstable glass objects, before the irreversible changes occur.

In my research I therefore aim to identify unstable glass at an early stage using analytical techniques, before the damage is done.

The project I am currently working on is a collaboration between three partners: the Rijksmuseum, the Corning Museum of Glass and the University of Texas at Dallas.

The deterioration patterns observed in historic glass are associated with an ion-exchange process that occurs when the glass comes into contact with water. This includes atmospheric water, so relative humidity is a crucial parameter for unstable glass storage. During the deterioration process, cations leach out of the glass network and are replaced by hydrogen ions. The leached ions can subsequently react with atmospheric molecules and form new compounds on the surface of the glass. We use ion chromatography (IC) to quantify the ions present on the surface of the glass and use that data to predict glass stability and develop guidelines for storage climate.

To allow IC, the ions need to be sampled from the glass surface and brought into solution. The sampling method needed to be straightforward, to enable investigations of large glass collections, so we used a simple swabbing protocol to remove the ions from the surface of the glass. During the development and validation of the protocol – using dummy samples with inert surfaces – we obtained highly reproducible results. However, reproducibility dipped significantly once the technique was applied to real deteriorated glass surfaces. We are currently carrying out experiments to better understand whether this is a result of flaws in the analytical protocol, or if it is an intrinsic phenomenon related to the level of deterioration products on the glass itself.

Although the reproducibility of the protocol could be improved, we obtained exciting results when studying museum collections. Using IC, we were clearly able to discriminate between unstable and stable glass in museum collections, even though no clear signs of deterioration could be observed – our analytical data made the invisible visible.

The next step is to establish conclusively whether the presence of ions on glass surfaces is a direct result of glass deterioration. In collaboration with the National Institute of Chemistry in Slovenia, we have used laser ablation-inductively coupled plasma-MS for quantification of changes in the glass composition and in a later stage we will use SIMS to measure the extent of cation leaching to improve our understanding of the chemical decay of glass in museum collections

Ultimately, the goal of our research is to support the curatorial community in making evidence-based decisions about the conservation of glass objects in museum collections and prioritizing (often costly) conservation treatments. As the work continues, the collaboration between scientist, conservators, curators and collection managers is crucial. I often find that colleagues who don't have an analytical background find it difficult to translate scientific analysis into daily practice. Because my project started with a practical question from a conservator, I always try to provide practical implications of the research.

LIFE *Modeling*

Recreating the chemistry of paint degradation in the lab

By Joen Hermans, Scientist, University of Amsterdam and the Rijksmuseum, the Netherlands.

I am a postdoctoral researcher, splitting my time between the University of Amsterdam and the Rijksmuseum. I am trained as a chemist, and work on fundamental questions relating to oil paint degradation.

Model behavior

I do not often carry out analysis of real artworks. Instead, I design and create model systems that mimic the molecular structure or chemical reactivity of real aged oil paint, while still being suitable for a particular type of chemical analysis. In this way, it is possible to study in great detail how the materials in oil paint react with each other, and how fast these processes occur under certain conditions. Eventually, all this knowledge will be used to understand how current methods of oil paint conservation and restoration are associated with the risk of future degradation, and how we can minimize that risk.

Right now, it is very difficult to make a reasonable quantitative estimate of the risks involved with current practice for the conservation and restoration of paintings. How sensitive is a painting to changes in humidity or temperature, or how much impact does treatment with solvents have on the stability of a painting? While the extensive experience of conservators is a very good starting point, for better risk assessment we need to first understand the chemical and physical processes behind paint degradation. Secondly, we need to measure how the rate of paint degradation is affected by environmental conditions or restoration treatments.

We are still in the early stages of this research, unraveling the immensely complex set of chemical reactions and diffusion processes that occur in aged oil paint. However, we have already uncovered potential markers that can help determine how a painting is likely to change in the future. We are in constant discussion with the conservators of the Rijksmuseum and other museums around the world to test our ideas and share our findings. Together, we work to extend the lifetime of oil paintings for the benefit of future generations.

Imitating art

The model systems we design must strike the right balance of being tunable (so we have control over relevant parameters), while still yielding information that is useful for understanding real-world degradation. The formation of metal soaps in oil paint is a good example. If you mix a lead- or zinc-containing pigment with oil and let it age for a few months under humid conditions, metal soaps (complexes of metal ions and saturated fatty acids) will spontaneously form. However, if you want to understand what is really going on, you need to design systems in which you can break down the process into its constituent steps: the reaction between pigments and relevant functional groups of the oil, the formation of fatty acids in the oil, the reaction between fatty acids and the released metal ions to form metal soaps, and the crystallization of the metal soap end products.

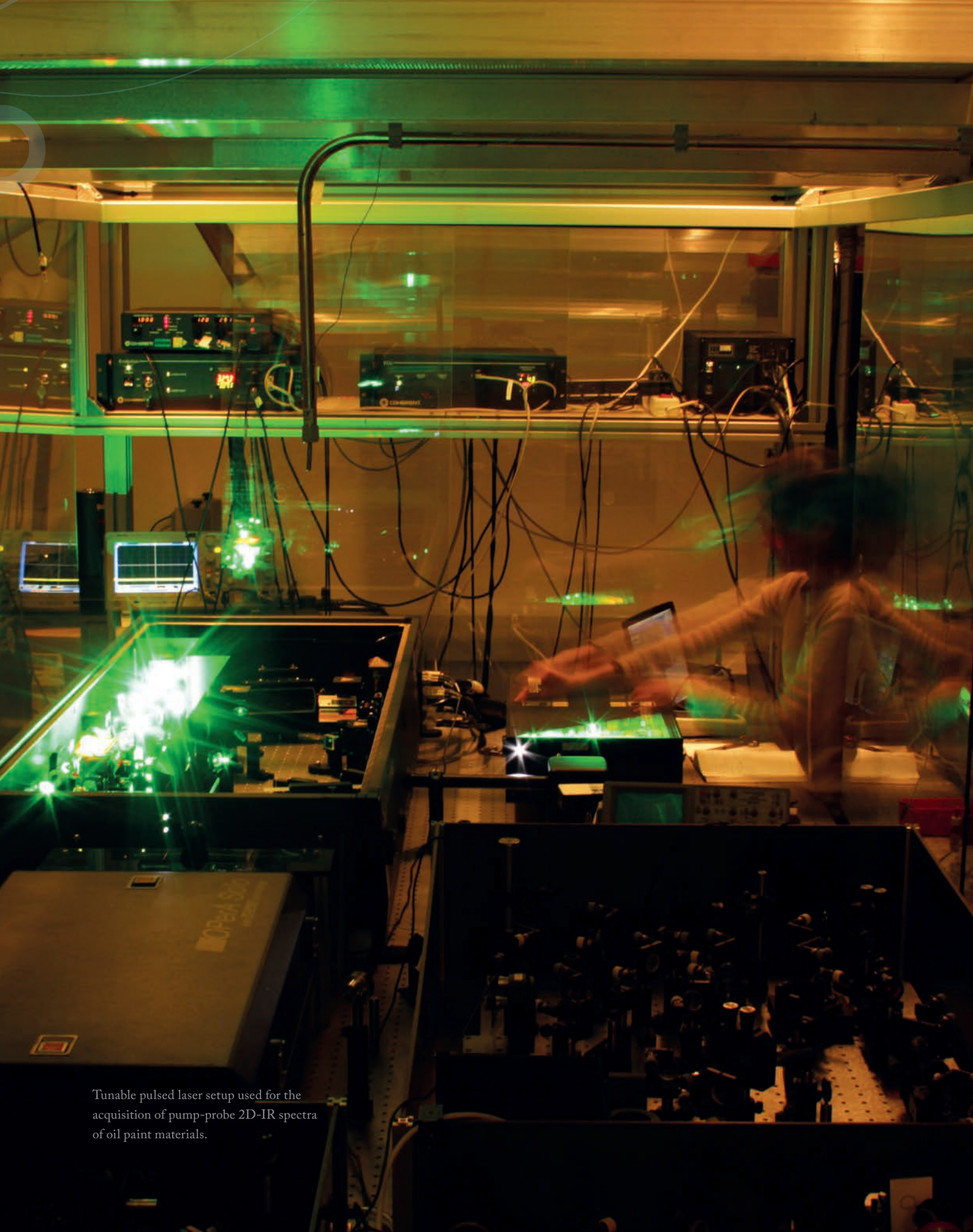
In real paintings these processes operate on vastly different timescales, so creative solutions are usually required to make them happen on a scale we can analyze. In addition, reactions in real paintings take place in an insoluble cross-linked polymer matrix, where most reactivity is diffusion-limited. To carry out analyses like infrared (IR) spectroscopy, MS or XRD, the relevant reactions sometimes need to be replicated in different environments to allow measurement.

Light at the museum

Our main workhorse is IR spectroscopy, in all its forms. With ATR-FTIR spectroscopy we can identify certain pigments and degradation products (like metal soaps) in oil paints or oil paint models, and follow the changes in chemical composition over time in situ while we expose samples to humidity, temperature or reactant solutions. We then apply custom-made spectral processing algorithms to the datasets to obtain concentration profiles, diffusion constants and rate constants. Recently, we have started applying the same approach to IR microscopy measurements, so we can follow diffusion of chemical species and their reactivity over time with micrometer spatial resolution. The main advantage of IR spectroscopy is that it is easy to use and relatively easy to interpret. We also make use of complementary techniques like XRD, DSC, SAXS, NMR, and even femtosecond pump-probe 2D-IR spectroscopy, to help us understand the molecular structure of our materials.

I see the field changing, with ever more data being collected on every painting during conservation treatment. On the horizon, we are seeing automated hyperspectral imaging systems being developed that can be used to identify pigments, and XRD-imaging systems that can be used to map crystalline phases with sub-millimeter spatial resolution in a painting.

As a consequence, major advances are needed in processing, correlating, matching and interpreting data. Machine learning algorithms and other forms of automation will be necessary, but it is crucial to keep thinking about the questions you really want to answer. What do we really need to know about a painting, and is that information worth the financial and time investment? How can we extract meaningful information out of a mountain of data? These questions are going to become more and more important in the coming years.



Tunable pulsed laser setup used for the acquisition of pump-probe 2D-IR spectra of oil paint materials.

MS: Access All Areas

In the May issue, we delved into the results of our survey on liquid chromatography trends and found several barriers to adoption of mass detection in routine analysis – in particular, the complexity, unplanned downtime and cost of ownership. The new Agilent InfinityLab LC/MSD iQ System was designed to help fill these gaps. We spoke to one man behind the machine – Shane Tichy, R&D LC/MS Single and Triple Quadrupole Manager, Agilent Technologies – to learn how the new system can push LC-MS into uncharted territory.

How did you find yourself in instrument design?

My career in mass spectrometry (MS) kicked off with a summer undergraduate research project, where I immediately fell in love with the instrumentation. I pursued a PhD at Purdue University in a group developing mass spectrometers for research purposes. I then took a position at Texas A&M University as a Research Scientist and was introduced to commercial MS technology for the very first time. After several years in academia, I moved to industry and I have been at Agilent for the past 12 years. Now, I'm responsible for leading an amazing team that conducts research and develops innovative systems – exactly what I dreamed of doing.

How long have you been working on the InfinityLab LC/MSD iQ System?

I have been the Program Manager since inception. You may be surprised to know that the technology was developed in a relatively short time frame – a little over a year. To get there that fast, we leveraged multiple innovative technologies from the Ultivo Triple Quad – but we also had to focus on ease-of-use, streamlined maintenance processes and optimized manufacturing. And that meant we essentially had to re-think the entire mechanical design and the layout. One reason for the rapid progress was our clear vision of what we wanted the LC/MSD iQ to be.

Why was it the right time to introduce such an instrument?

As confirmed by the survey, increasingly strict regulatory requirements mean that HPLC analyses often need more specific and selective detection than can currently be achieved with UV-Vis. Meanwhile, the technology all around us continues to become more integrated, easy to use, productive and self-aware – we wanted to bring all those qualities to LC-MS, to lower the learning curve and improve lab operations (overcoming some of the barriers identified in the survey – Figure 1).

Easier said than done – what were the challenges along the way?

Our biggest challenge was the need to rethink all the mechanical connections and the electronic architecture; we knew that we had to enhance the maintenance and serviceability by designing a modular system. Users don't want to unstack the LC components sitting on the mass spectrometer to do routine maintenance, so we developed a cable-free, centralized, interconnected board, which can be accessed from the side of the system.

Our goal was to get to a point where a user can walk up, put a sample in the autosampler, and, within a few taps of a touchscreen, be ready to run the analysis – and I'm pleased to say we've achieved that!

iQ in Action

If you missed the infinityLab LC/MSD iQ launch at ASMS, you can view our three-part in-the-lab demo series at *tas.txp.to/iQwebinar.*

Who do you expect will use this system?
We believe the LC/MSD iQ will appeal to users in a range of markets, including drug development, chemical synthesis, academia and food production. However, we believe that the system will be most quickly adopted by pharmaceutical laboratories working on reaction monitoring and in QA/QC settings.

Those working in pharma labs, who may have been happily relying on UV detection for the last 20 years, may not see the need to add MS into the mix – what would you say to them?
The big advantage of moving to mass detection is achieving more specific and more selective detection than is currently possible with UV. The InfinityLab LC/MSD iQ makes mass detection much more accessible to users who are new to MS. The launch of this systems points the way to a future where mass detection is no longer the exception for HPLC but is considered the standard analytical technique.

What feedback have you had from early users?
The early customer feedback has been very positive in terms of the analytical capabilities, the instrument health tracking and the simplicity and speed of the maintenance process. The LC/MSD iQ allows managers to predict and schedule maintenance in a way that optimizes their lab operation and minimizes downtime, which dovetails neatly with our overarching focus on greater efficiency in the lab (tas.txp.to/efficiency).

As the Project Manager, how did you feel about launching the product at ASMS 2019?
The team and I are extremely excited and honored that our system was launched at the most important MS event in the calendar. We believe that we have developed a very innovative product that is going to do well in the market because we are addressing real customer needs. The journey from inception to release can be a rollercoaster ride of emotions – from excitement to tearing your hair out and back again – but the feeling of launching something new onto the market is a real high! I never thought that I would have the opportunity to work on such cutting-edge products; I love it, and I'm already looking forward to the next challenge.

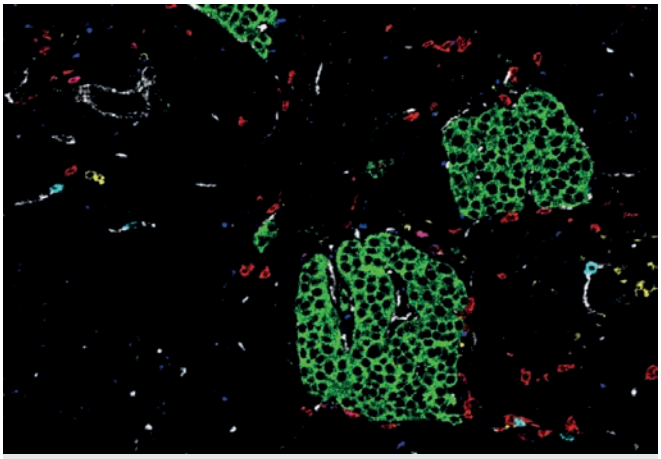
Shane Tichy is R&D LC/MS Single and Triple Quadrupole Manager, Agilent Technologies, Santa Clara, California, USA.

OUR RESEARCH *In Images*

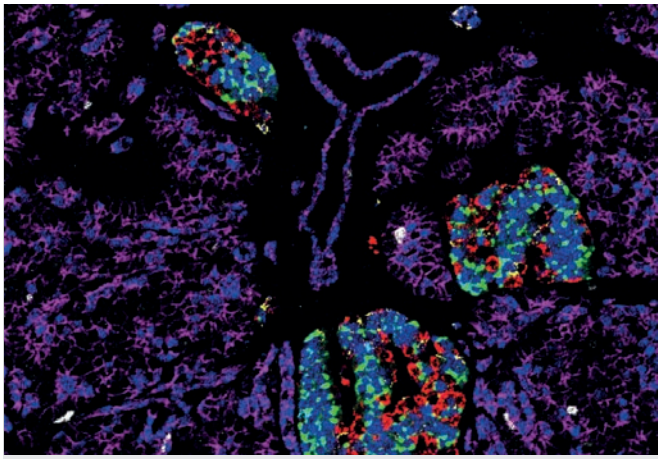
They say a picture is worth a thousand words and these three leading proponents of MS imaging would certainly agree. We asked each group to choose a selection of powerful images to tell the story of their work.

ALL EYES ON PRECISION MEDICINE

Bernd Bodenmiller and his colleagues at the University of Zurich explain how highly multiplexed imaging can facilitate precision medicine – from diagnosis to treatment.



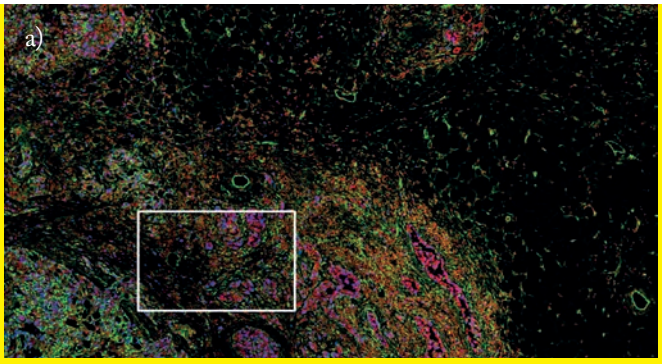
Synaptophysin (pancreatic islets)
CD8 (cytotoxic T)
CD4 (helper T)
Myeloperoxidase (neutrophils)
CD68 (macrophages)
CD45RA (naïve)
CD31 (blood vessels)

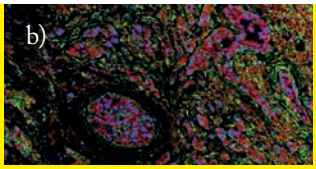


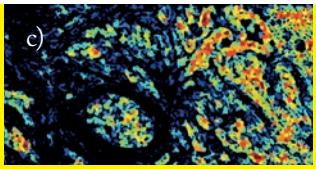
Insulin (β cells)
Pdx1 (transcr. factor)
Glucagon (α cells)
Ki-67 (cycling cells)
Somatostatin (δ cells)
Pancreatic polypeptide (γ cells)
E-cadherin (epithelial cells)

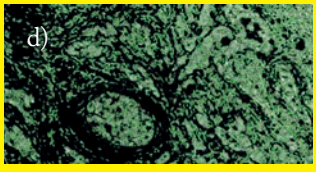
Exploring diseased tissue

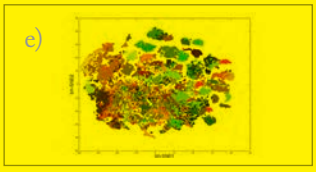
Imaging mass cytometry can visualize the different immune cell populations that infiltrate pancreatic islets and attack insulin-producing beta cells in type 1 diabetes (Left), while simultaneously profiling pancreatic endocrine and exocrine cells (Right). This deep phenotyping reveals new insights into the interactions between immune and beta cells during disease progression (1). *Credit: Nicolas Damond*





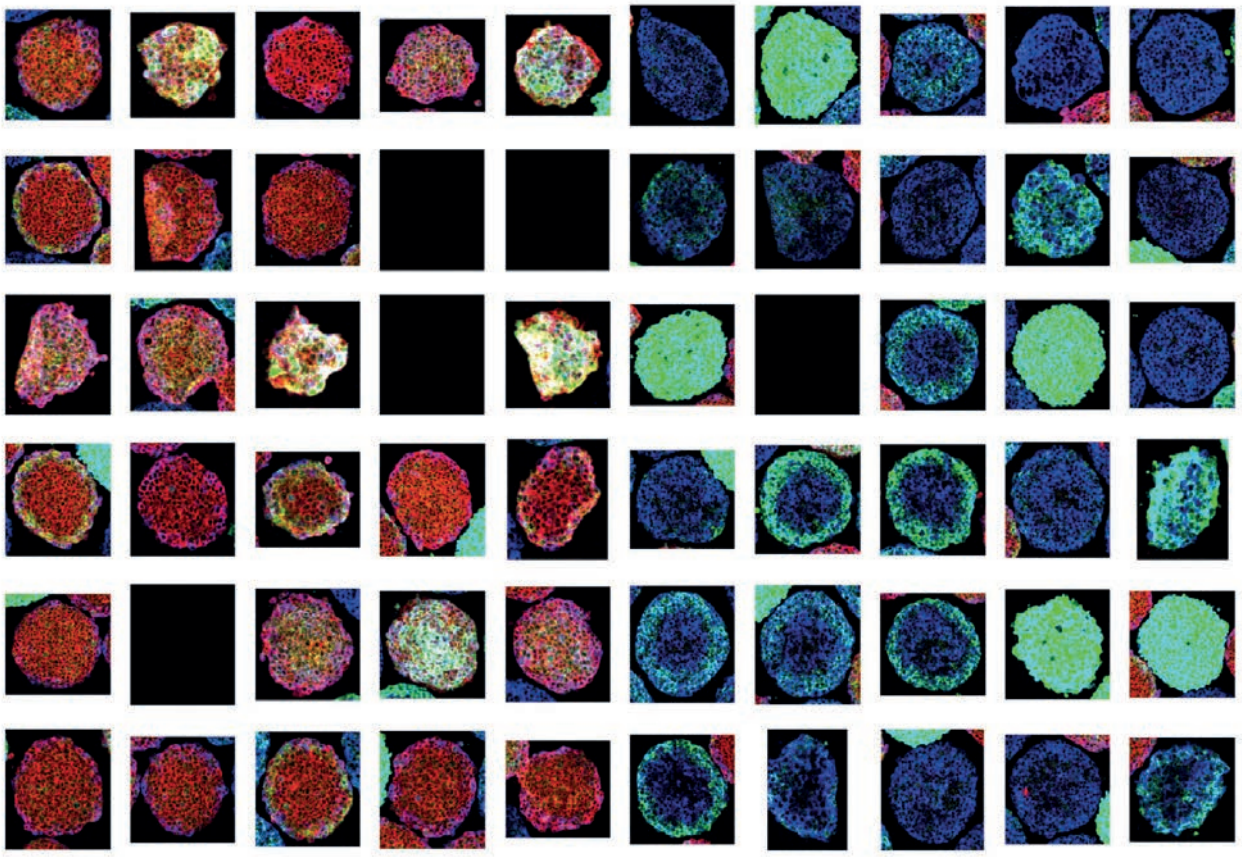






Identifying relevant features

Once the tissue has been analyzed, it's time to identify the features that are relevant to the disease in question. Here, imaging mass cytometry data from breast cancer tissue (a,b) has been segmented, defining the area that corresponds to individual cells (c). Then, the antibody signals are quantified and the spatial features of the cell are identified, including their shape and arrangement. The resulting information can be visualized as a heat map on the original image (d) or in a variety of single cell plots (e). *Credit: Hartland Jackson*



Drug testing for precision medicine

The final stage of precision medicine is to tailor the treatment to the patient's own genetic and epigenetic makeup. Here, individual 3D spheroids were used to assess the impact of different drugs. 3D spheroids grown from two cell lines are visualized using imaging mass cytometry. The colors indicate the presence of three antibody markers; red for E-Cadherin, blue for pS6, and green for pERK. This multidimensional perturbation data reveals detailed mechanistic insight into the complex responses of the microtissues to the drugs.

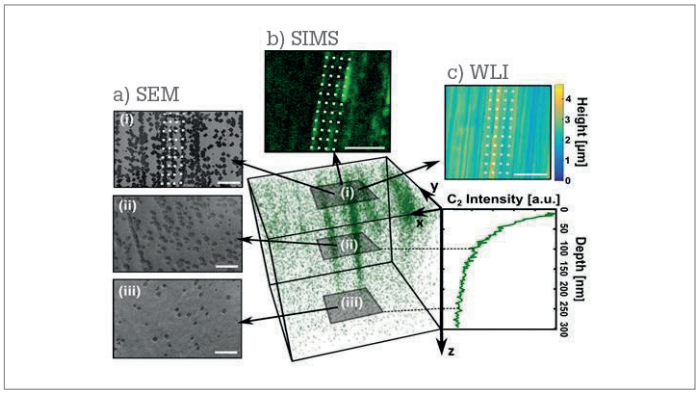
Credit: Vito Zanotelli

Reference

1. *N Damond et al., "A map of human type 1 diabetes progression by imaging mass cytometry", Cell Metab, 29, 755–768 (2019). DOI: 10.1016/j.cmet.2018.11.014.*

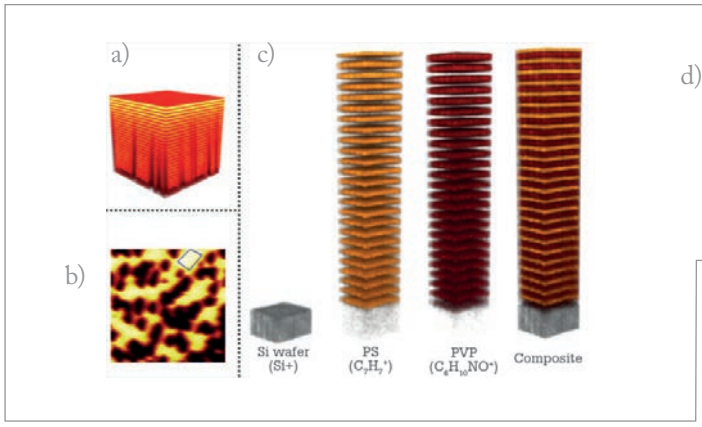
IMAGING INNOVATION

Scientists from the UK's National Centre of Excellence in Mass Spectrometry Imaging (NiCE-MSI) showcase the potential for MSI in a wide range of fields.



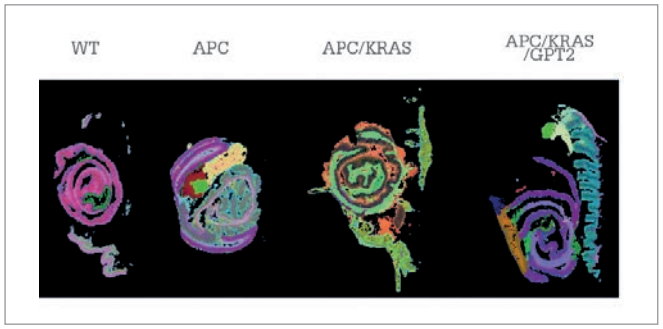
Graphene graphics

By measuring carbon impurities in Cu foils before graphene growth with time-of-flight secondary ion MS (ToF-SIMS) and correlating this with graphene nucleation density (GND) after graphene growth, we can track how carbon distribution within the untreated Cu foil impacts GND. Here, the surface ToF-SIMS maps of C_2 ion signal (green) from the Cu foil surface show how graphene nucleates along a preferred direction. This corresponds to areas of high carbon concentration located along rolling striations of the Cu foil (1).



Picturing polymers

SIMS can image novel devices and biological tissue in both 2D and 3D, at an elemental and molecular level. Images a–c show 3D ToF-SIMS imaging of polymer multilayer films using argon cluster sputter depth profiling (2), while d – a 3D molecular image of a novel reference material – shows how the "delta" layers – less than 2 nm thick – are sandwiched between layers of another organic molecule (3). The depth resolution of this technique is a remarkable 5 nm.

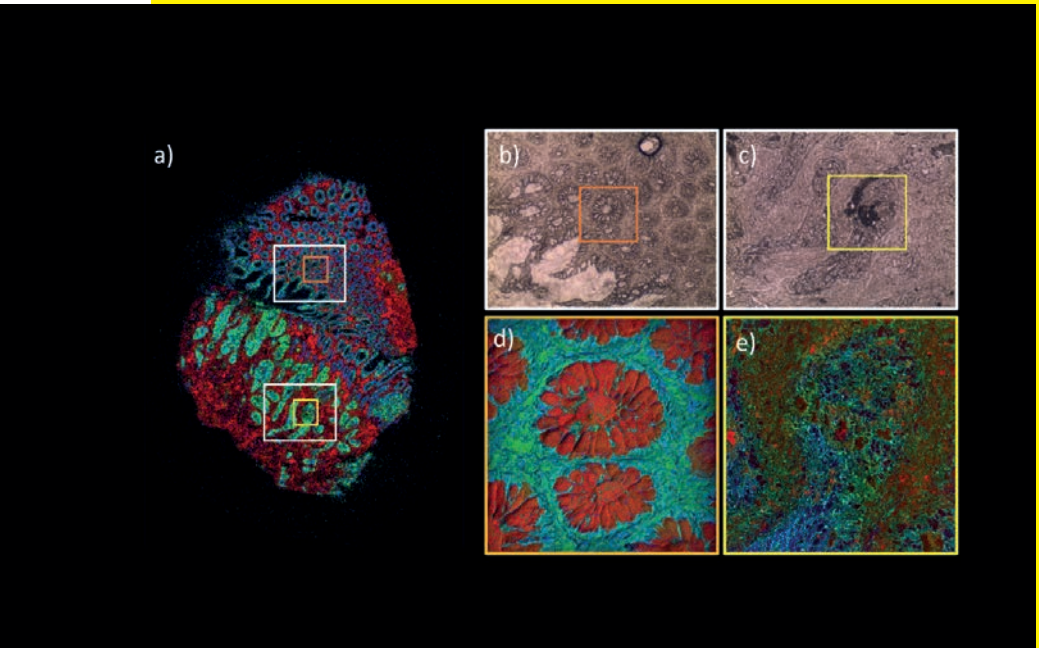


Credit: Rory T. Steven, Andrew Campbell, Alex Dexter, Spencer Thomas, Kenneth N. Robinson, Alan M. Race, Rasmus Havelund, Ian S. Gilmore, Owen Sansom, Zoltan Takats, Josephine Bunch (as part of the CRUK funded Rosetta consortium)

Spot the difference

MS imaging (MSI) is a powerful tool for relating molecular phenotype to tissue structure. Here, matrix assisted laser desorption ionization (MALDI) MSI was applied to "swiss roll" prepared colon samples with genetic modifications and deletions to APC, KRAS, and GPT2 genes. A machine-learning algorithm – T-distributed stochastic neighbor embedding – allowed us to visualize and interpret these highly dimensional, complex data. Here, similar colors reflect the level of similarly in the molecular composition of tissues, highlighting how different the APC/KRAS model is compared to the wild-type (WT) and other models.

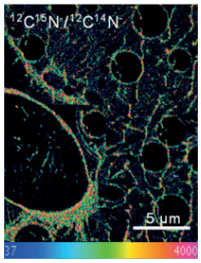
The National Centre of Excellence in Mass Spectrometry Imaging (NiCE-MSI) at the National Physical Laboratory and the Rosetta consortium includes collaborators at Imperial College London, AstraZeneca, Barts Cancer Institute and the University of Cambridge. The Rosetta consortium is using MSI methods to study cancer models from The Francis Crick Institute, The Institute for Cancer Research, and the CRUK Beatson Institute.



Keeping it complementary

In MSI, there isn't a one-size-fits-all instrument; instead, the complementary characteristics of several instruments are often required to build the most complete picture of tissue structure. In this image, MALDI MSI was first used to analyze the tissue from a human colon biopsy (a), before secondary ion MS (SIMS) was applied to further investigate regions of interest (b,c,d,e). This multimodal approach ensures that there is both reliable detection of certain molecular classes and accurate analysis of the fine structure at high spatial resolution.

Credit: Rory T. Steven, Andrew Campbell, Alex Dexter, Spencer Thomas, Kenneth N. Robinson, Alan M. Race, Rasmus Havelund, Ian S. Gilmore, Owen Sansom, Zoltan Takats, Josephine Bunch (as part of the CRUK funded Rosetta consortium)



NanoSIMS rainbow

This image conveys the mechanism of an antimicrobial peptide on a lipid bilayer, revealing that the peptide is concentrated at the pore boundary. This is made possible with the help of a NanoSIMS 50L instrument that has a spatial resolution of less than 50 nm. The rainbow scale ranges from blue, representing the antimicrobial peptide's natural abundance ratio of 0.37 percent, to red, which represents an abundance of over 100 times the natural ratio (4).

References

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3. *AG Shard et al., "Argon cluster ion beams for organic depth profiling: results from a VAMAS interlaboratory study", Anal Chem, 84, 7865–7873 (2012). DOI: 10.1021/ac301567t.*
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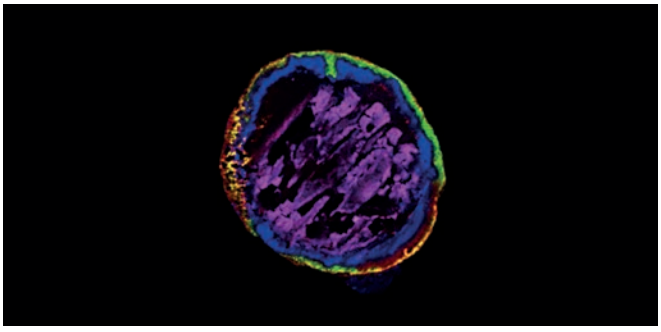
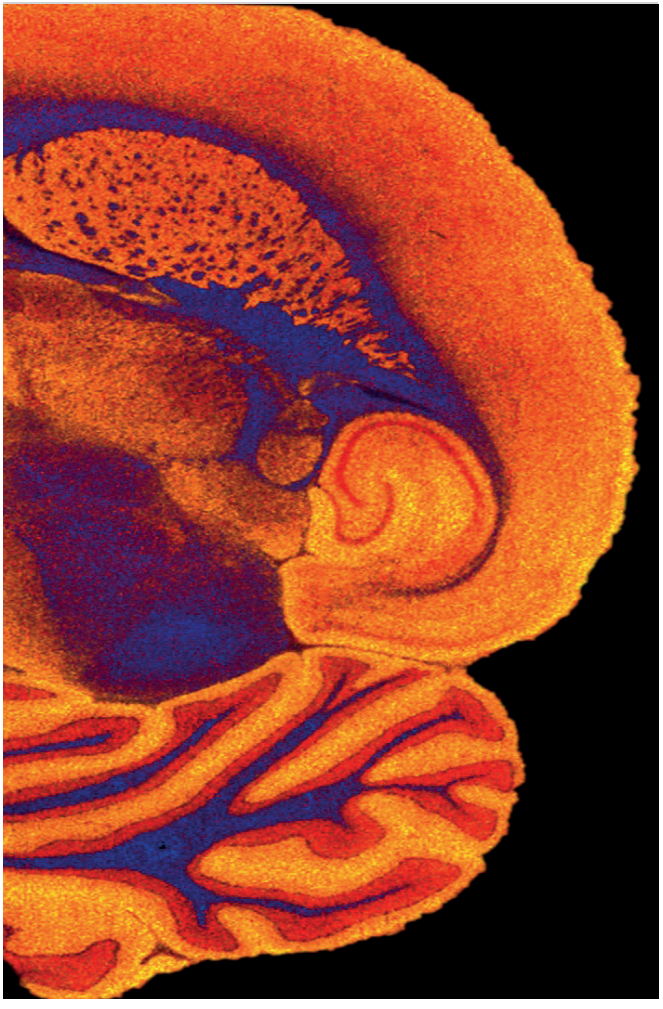
BODY OF EVIDENCE

Maastricht MultiModal Molecular Imaging Institute scientists explain how the power of advanced imaging is delivering a wealth of new data for biomedical researchers.



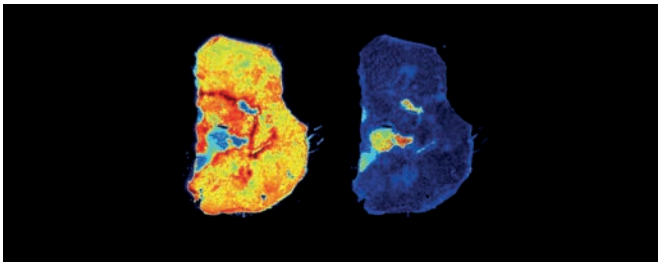
Eye on the future

MS imaging (MSI) allows us to analyze the spatial distribution of molecules in biological tissues. Produced by metabolomic MSI, this striking view of a mouse eye was measured with the rapifleX matrix-assisted laser desorption/ionization (MALDI) Tissuetyper from Bruker at a spatial resolution of 15 µm. The iris and pupil are visible on the left of the image, and the different retinal layers are can be seen in the bottom right. *Credit: Saleh Khalil*



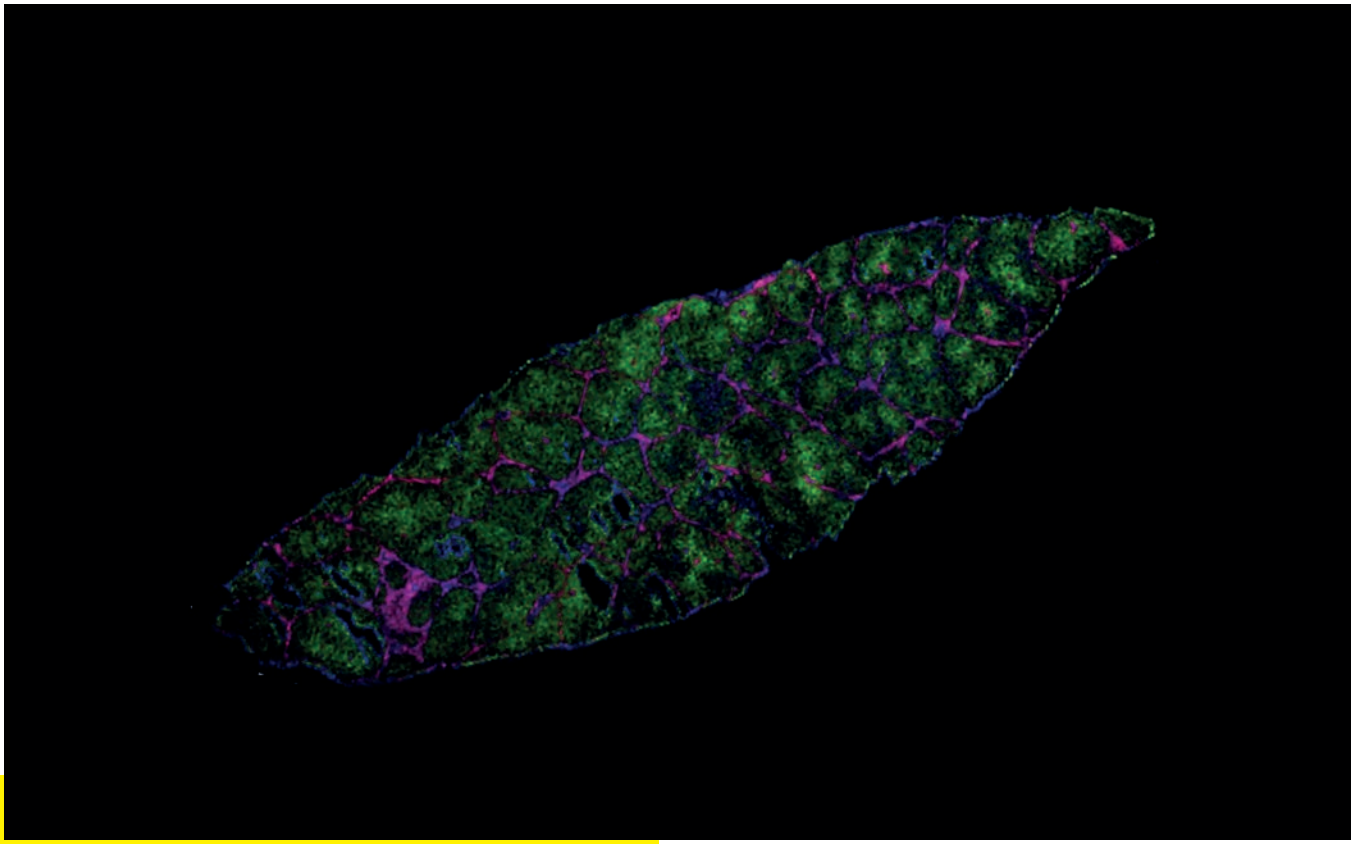
uMALDI on the brain

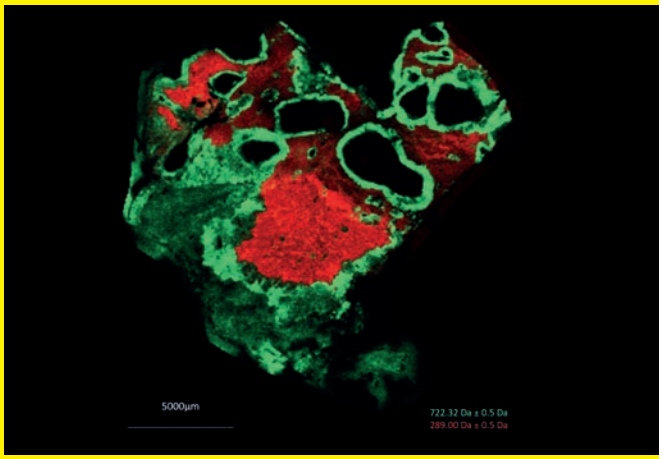
In this MALDI-TOF image of a rat brain section, the distribution of three different lipids displays its fine structural details. The section was imaged using a Synapt G2-Si coupled to an innovative new source called uMALDI, which allows a lateral spatial resolution down to 15 µm. Using new WREnS software from Waters, the image was captured in continuous raster mode at a speed of 20 pixels per second (2). *Credit: Florian Barré*



Tailoring treatment

Diffuse large B-cell lymphoma is an aggressive disease – one third of patients are either resistant to initial therapy or relapse after treatment. With MALDI-MSI, we can differentiate between untreated and relapsed tumors via their lipid and metabolic profile, and reveal specific molecular signatures associated with intratumor heterogeneity. Here, you can see the heterogeneity within a treated tumor, showing both viable (left) and necrotic (right) tissue. The image was produced using an Orbitrap Elite hybrid ion trap mass spectrometer, at 30 µm spatial resolution (3).*Credit: Florian Barré and Britt Claes*





Typing tumors

MSI data can be used to investigate intratumor heterogeneity by segmenting histologically undistinguishable tumor areas into distinct subpopulations. This image shows the distribution of two lipid species in a human breast tumor section analyzed by MSI (tumor in red, healthy tissue in green). *Credit: Frédéric Dewez*

Mapping metabolites

MALD-MSI maps the spatial distribution of metabolites within liver tissue. The specific localization of certain biomolecules highlights histopathological structures, including the hepatic lobules in green, the connective tissue in pink, and the portal triad that consists of bile duct, vein, and artery – all in blue. *Credit: Klara Scupakova*

References

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3. *F Barré et al., "Specific lipid and metabolic profiles of R-CHOP-resistant diffuse large B-cell lymphoma elucidated by matrix-assisted laser desorption ionization mass spectrometry imaging and in vivo imaging", Anal Chem, 90, 14198–14206 (2018). DOI: 10.1021/acs.analchem.8b02910.*

Profession

Leadership
Talent Development
Career Planning

Industrial Revelations: Darlene Solomon, Agilent Technologies

Our series of interviews with industry scientists returns to shine our spotlight on Darlene Solomon, Agilent's research and technology guru.

Darlene Solomon took on her current role of Senior Vice President and Chief Technology Officer (CTO) at Agilent Technologies in 2006, having previously been the company's head of research. As CTO, she has a broad range of responsibilities, from leading Agilent's technology strategy to enabling external collaborations and partnerships. Darlene also serves on the board of directors at advanced materials manufacturer Materion Corporation, and is a member of multiple academic and government advisory boards, and has been recognized by awards including being elected to the National Academy of Engineering and receiving the Daniel J Epstein Engineering Management Award at the Viterbi Awards – "the academy awards of engineering". We spoke to Darlene to find out more about her work at the cutting-edge of technology.

What was your route into science?

Growing up, I was much more interested in math. I always enjoyed science, but applied to college as a math major – it wasn't until the end of the second year of my undergraduate degree at Stanford University that I decided to make the switch to chemistry. I just didn't see myself fitting into the career paths ahead of me in math. So, I took lots of biology, physics and chemistry courses the following year and found that understanding molecular activity, metabolism, and immunity at a chemical level was what intrigued me most.

At what stage did you move into analytical chemistry?

In my PhD I worked as a bio-inorganic chemist and spectroscopy formed a major component of my research, particularly electron paramagnetic resonance (EPR). I joined Hewlett-Packard Laboratories' medical products group in 1984 as a scientist working on a biosensors project for arterial blood gas monitoring, but when that project concluded I soon found that the lab's overall focus on electrical engineering approaches, such as ultrasound, was not the best fit for a biochemist. I moved to another research group within HP Labs focusing on analytical chemistry, which later became Agilent. After a couple of years in this analytical environment, I got the opportunity to try my hand at management – first as a project manager and then as a department manager. This department was soon rebranded the Chemical and Biological Systems Department as our focus expanded into genomics and biology – I was in my element!

What would you advise a student or early career scientist faced with a choice between industry and academia?

It really depends on the individual and their preferences – both paths provide great opportunities. The first thing to consider is where your motivation lies. For me, I knew during my studies that being a professor wasn't for me because the teaching aspect of the role didn't excite me, and while I was hugely passionate about science, there wasn't one specific area I felt compelled to pursue. Rather, I was attracted to many areas of research and the idea of developing technologies that make a real difference to customers, and ultimately to society.

"Many labs are embracing artificial intelligence to help generate and process the wealth of data needed for omics studies."

Another factor is if you are motivated by working closely with others – for a career in industry, I think it helps if you really thrive on teamwork.

What is your role at Agilent?

Agilent invests a significant percentage of its revenue into research and development, and I work alongside the CEO and executive staff to make sure we make the most of that investment. One of our main aims is to support innovation in the global technology community, which lends itself to further improving our own technologies and products. I also manage long-range technology development in our research labs, lead collaborations with faculty Principal Investigators and universities, and partner with start-up companies. Plus, I represent Agilent on various boards and review committees – including National Academies' Board on Chemical Sciences and Technology, UC Berkeley's College of Engineering Advisory Board, and Singapore National Research Foundation's Scientific Advisory Board – to keep the company connected to amazing academic, industrial and governmental leaders. Essentially, I'm constructing a virtual crystal ball to help guide the future direction of our research.

What collaborations are you excited about?

We have many exciting collaborations. Just recently we set up a new center of excellence with Imperial College London at their Molecular Sciences Research Hub. We have already identified opportunities to collaborate in areas such as precision medicine, cellular manufacturing and synthetic biology. The sense of possibility is thrilling – you never know just what will come of new projects like this. We're planning cross-organizational seminars and technology days with the university, which will bring our scientists together and open the door to further collaborations in future.

How has instrumentation changed in the time you've been in the field?

We have come to appreciate the complexity of biology, evidenced by the shift from being a largely qualitative to an increasingly quantitative science in the last decade or two. This movement and the rise of precision medicine has driven advances in bioanalytical instrumentation, including the development of new sequencing platforms and the expansion of long-standing techniques like MS to explore not just proteomics, but also glycomics, metabolomics and so on; many of these techniques are now tied to an automated analysis tool, which streamlines the process even further.

What do you see for the future of analytical instrumentation in your "virtual crystal ball"?

Many labs are embracing artificial intelligence to help generate and process the wealth of data needed for omics studies. I think this trend is going to evolve over time along with the tremendous capability of intuitive and easy-to-use software systems trained on data to simplify research endeavors. Essentially, what we will see are smarter instruments, with optimized workflows and more heavily interconnected laboratories that are enabled by the ability to leverage largescale data and rapidly advancing technologies like augmented reality – it's going to be a lot of fun. Regarding specific areas in which these tools will be used, I'm especially hopeful for immuno-oncology and gene and cell therapies.

What are the biggest challenges facing instrument manufacturers?

In the past it was all about instrument performance. Now, some of the focus has shifted to usability and providing actionable information, as our customers increasingly deal with large-scale, complex and heterogeneous datasets. Compared with 10 years ago, we now require much more knowledge of the specific application area to provide the required level of information. What's more, instruments must be easy to use and ideally failsafe, to improve overall productivity.

What motivates you?

It's exciting to see our products benefit customers and make a difference in the world. Day-to-day, however, I have two main drivers: doing things that have never been done before and contributing to the success of my incredibly talented teams and partners. I am faced with interesting and unique challenges on a daily basis and thrive on our being able to devise totally new ways to overcome them. That's what gets me out of bed in the morning…and what keeps me up late at night!

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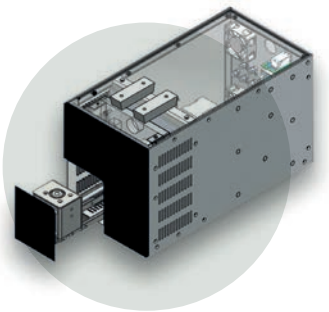

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On the Scent

Sitting Down With... Katelynn A. Perrault, Assistant Professor of Forensic Sciences and Chemistry, Chaminade University of Honolulu, Hawaii, USA.

What was your route into analytical science?

I was always interested in science, but I didn't want to study a subject for its own sake – I wanted to help people. I decided to take forensic science for my undergraduate degree and that's when I was introduced to analytical chemistry.

What is your current research focus?

I work on a variety of applications of odor analysis. Within forensic science, my primary focus is profiling the odor from decomposing remains. For example, we provide information to organizations who train human remains detection canines ("cadaver dogs"). The dogs are very good at their job but we still don't fully understand the science behind what they do. By better understanding the subtleties of the odor profiles that the dogs are reacting to, we can boost the value of the evidence (important in the courtroom) and provide useful information to handlers; this information can be used to choose the most appropriate samples for training the dogs, and how those samples should be stored to keep the odor profile consistent.

The analytical targets we develop could also be used to develop electronic odor analyzers. We're a long way from being able to replace dogs, but man-made detectors could be used to support their training, and might one day be able to support them in the field. Dogs, like people, cannot operate around the clock and complementary tools could be used to cover a larger area, faster.

What are the main tools you use?

First, we use a range of sorbent-based sampling tools. To analyze the sample, we typically use comprehensive 2D GC with both a quadrupole mass spectrometer and a flame ionization detector. Having two detectors operating at the same time allows us to do identification on one detector and quantification on the other. The samples we are analyzing have complex odors that require good resolution between peaks. I believe multidimensional chromatography will help answer some of the really big questions in odor analysis.

The use of odor analysis data in court has proved controversial….

I don't think we'll see odor profiles being used routinely in crime labs – at least not for the next five years or more. The best-known example is probably the trial of Casey Anthony. In that case, the prosecution tried to use odor analysis to prove that a body had been in the trunk of a vehicle. The expert witnesses in the case had conflicting opinions about the scientific value of that evidence, which has created a lot of skepticism about our field of study. It's important to point out that since that trial in 2011, we have a much better understanding of cadaveric odor profiles and a wealth of published literature behind us. When the case was tried, experts would have been testifying with only four or five published papers to refer to – now, they would have around 50. But there are important questions to answer before it becomes a routine tool in forensic science.

You seem to really enjoy the teaching aspect of your role – what makes a good teacher?

You have to try new things – I've never taught the same class in the same way. One thing I'm passionate about is teaching effective communication skills. As I tell my students: to be a successful scientist today, you need to be able to communicate. For example, if they appear in court as an expert witness, they will need to communicate complex ideas in a straightforward and confident manner.

Another way in which I do things a little differently is to bring research projects into the classroom. Rather than just a few undergraduates doing summer research projects, we involve the whole class. It's not a new idea, but it's been exciting to try it with advanced techniques, such GC×GC, which aren't usually taught until graduate level or above.

"You have to try new things – I've never taught the same class in the same way."

And what makes a good student?

In my experience, the students that excel are the ones who are able to identify their passion early on. If you find something that you're passionate about, it doesn't feel like work.

Is that how you feel about your work?

Absolutely. When I started my undergraduate degree, I envisaged working in a crime lab. But once I got to grad school and started teaching, I realized that if I became an academic I would probably never have two days the same for the rest of my life. And that's turned out to be true. I love it!

What are your plans as co-chair of the Multidimensional Chromatography Workshop?

My co-chair Pierre-Hugues Stefanuto and I are busy planning the 11th Workshop in January. I attended the event early in my career and the inspiring people I met there were a major factor in my decision to enter the field. I was delighted to take on the role of co-chair, which allows me to give other young scientists the same amazing experience I had. Registration is free and, as it's a smaller event, there's plenty of chance to network and get advice from experts in the field.

The 11th Multidimensional Chromatography Workshop will be held in Honolulu, Hawaii, on 5–7 January 2020. Find out more at www.multidimensionalchromatography.com

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