FEBRUARY 2013 # 02

the Analytical Scientist

The Science of Art

How Analytical Chemists Help Understand and Preserve our Cultural Heritage.

Webinar

Virtual Events

Tips & Tricks for HPLC/UHPLC Method Development with Core-Shell Technology

Getting Ultimate Performance, Productivity, & Cost Savings from Your LC System

Register Free at:
link.theanalyticalscientist.com/core-shell

Event Overview:

This webinar will present a brief overview of the benefits of core-shell technology for UHPLC, HPLC, and PREP LC separations and provide practical advice to chromatographers who are developing new methods with core-shell columns or converting existing fully porous methods over to core-shell technology.

Key Learning Objectives:

- Review the fundamental factors that must be considered for thorough, logical LC method development
- Column selection including media type (silica, hybrid, core-shell) and stationary phase (C18 vs. phenyl, etc.)
- Mobile phase selection including effects of pH, organic solvents, and gradient programming
- How to implement core-shell technology into existing methods to achieve significant performance, productivity, and cost benefits

Who Should Attend:

- Lab Directors
- Analytical and Preparative Chromatographers
- LC Technology Enthusiasts

Speaker
Dr. Jeff Layne,
UHPLC/HPLC *Product Manager*

Moderator
Richard Gallagher

Date
14/03/13 - 8.00am PCT,
11:00am EST, 16.00pm GMT

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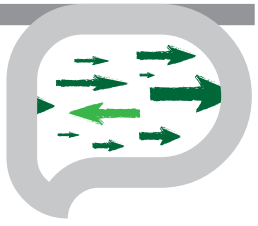
Online this Month

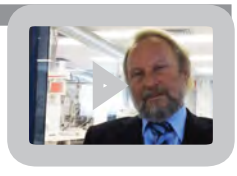
Talking Point



Sign up at The Analytical Scientist website to take part in lively online discussions each month.

This month's Talking Points:
Is free and open source hardware a threat or an opportunity?
www.theanalyticalscientist.com/issues/0213/104.
uBiome – crowd-sourced "citizen" science or an assault on the gullible? You decide:
www.theanalyticalscientist.com/issues/0213/207.

Video



Pat Sandra recalls his involvement in some high-profile analytical cases, including a Formula 1 dispute involving Michael Schumacher.
Go to www.theanalyticalscientist.com/issues/0213/602.

Poster

Sign up for free at theanalyticalscientist.com and make a (considered) comment on any article. The 20 best comments will earn their originator a piece of history: a large poster (A2) of our inaugural cover. Very rock & roll.

App

Our new app allows you to flick and swipe your way through the contents of The Analytical Scientist, and download the whole issue to read offline. It offers a rich and engaging multimedia experience to boot. If you've got an iPad or iPad mini, you'll love the The Analytical Scientist app.
link.theanalyticalscientist.com/app

Event

What do you look for in a successful scientific meeting? Jeff D. Chapman and James P. Landers, co-chairs of MSB 2013, question the status quo in "Overhauling Analytical Symposia", read it on the app or online: www.theanalyticalscientist.com/issues/0213/305.
The 29th International Symposium on MicroScale Bioseparations takes place at the University of Virginia, March 10 -14, 2013. (www.msb2013.net).

Twitter

Follow or be followed. The Analytical Scientist has started tweeting: @tAnaSci #theanalyticalscientist.
Quick recommendation: #overlyhonestmethods
(see page 14).

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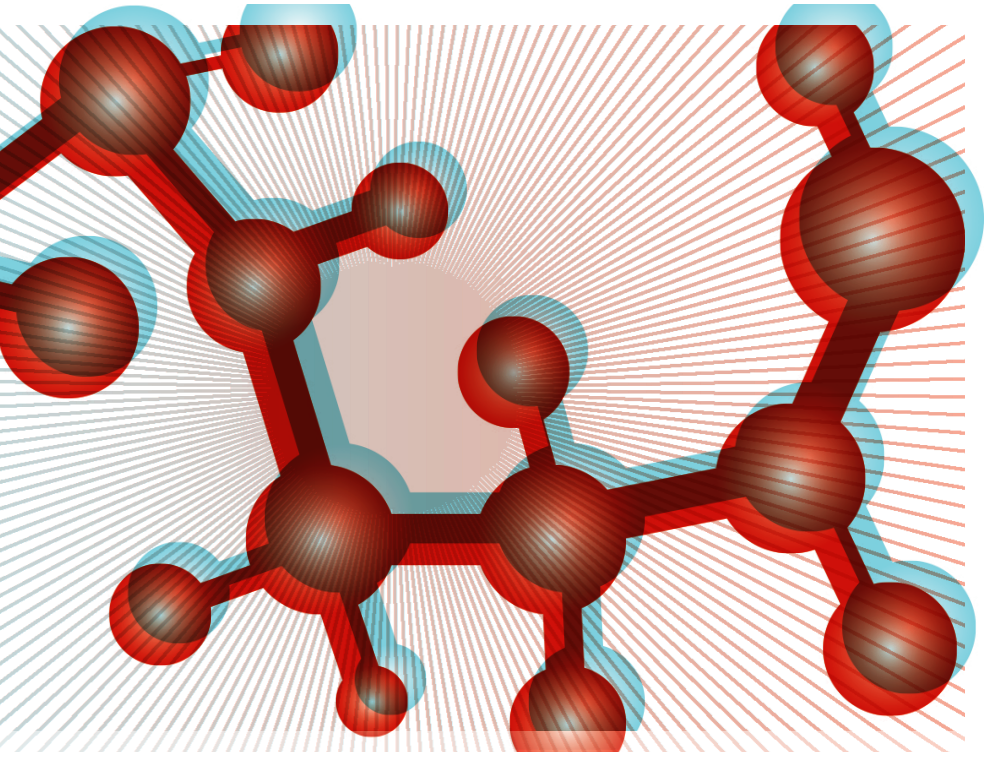

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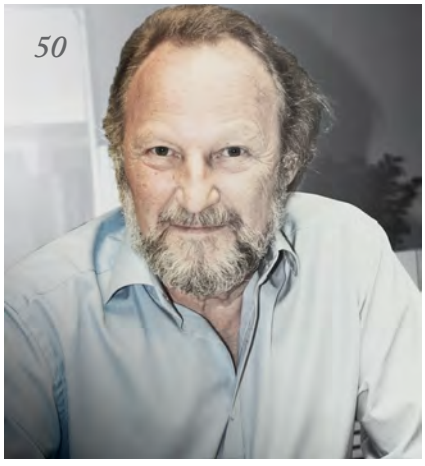

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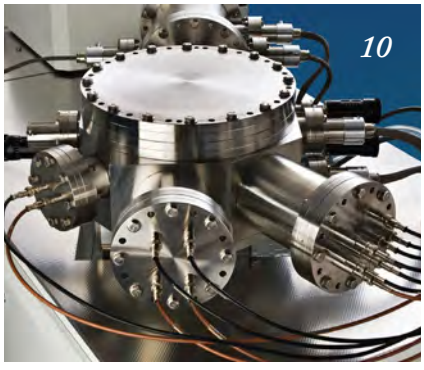

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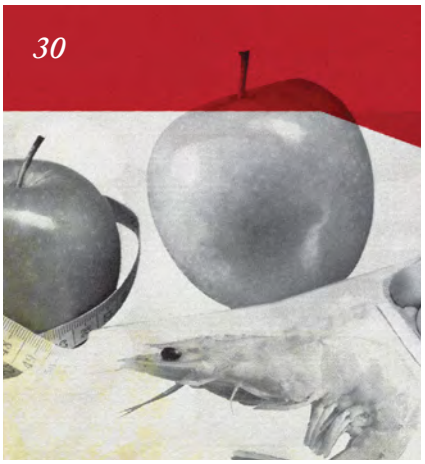
On The Cover

Upper half of the right panel of the Moreel triptych (Groeninge Museum,Bruges, Hans Memling, 1484), showing Barbara van Vlaederberghe van Hertvelde and eleven of her daughters.

Upfront

In My View



Features

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Sitting Down With

the Analytical Scientist

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A New Age Dawns

Open source hardware offers exciting prospects but demands a fresh way of thinking.

Very occasionally, one encounters an idea that truly offers a glimpse of the future. Joshua Pearce's enthusiastic account (page 16) of the application of open source hardware to analytical science is one such insight. The approach combines the sharing of design information with 3D printing, or additive manufacturing, which is the process of making solid objects from a digital model. Pearce's description of his experimentation to date and of the transformative potential of open source hardware in the long term presages a new age for our field.

The two elements of open source hardware are linked but separate. One is personal manufacturing – the capacity to affordably 'print' solid structures from polymers or metal, which opens doors for hands-on, innovation-minded scientists who want to create bespoke equipment. It will also impact the equipment vendors that most of us will continue to rely upon. Imagine a future where you could purchase and download schematics from your vendor's support page and print out new parts yourself. This reduces their manufacturing costs, your downtime and everyone's environmental impact. The phrase "warranty void" does spring to mind, however…

Of course, the impact of personal manufacturing isn't limited to analytical science – it has essentially transformed how we consume music and video, and will likely revamp many other aspects of our lives. There are risks though. Just as media digitalization has created a pirating tsunami, releasing intellectual property in such a way requires a fresh, collaborative way of thinking.

Which brings me to the second aspect – development of new hardware.

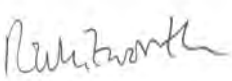
Open source development has always been an inherent feature of academic research, though under a different guise – 'the literature'. And recent projects such as ProteoWizard show the tangible benefits of open source software development to the analytical sciences. The cooperative development and design of hardware on a similar scale has only been made possible by recent advances in 3D printing. As that technology improves, the virtuous cycle of innovating, sharing, improving, and re-sharing will pave the way to faster advancement of technology.

How the substantial scientific talent and financial savvy that vendors possess will play into this process remains to be seen. I predict that the smartest companies will find ways to embrace the movement. And certainly in the near term, there is nothing to fear; reliability and performance, not cost, are top of the priority list in most cases.

We at The Analytical Scientist will follow progress in open source hardware development and take soundings on its commercial impact.

If you have supportive or sceptical views on the subject, or experiences with personal manufacture and open source development, positive or negative, we'd love to hear them. Join the debate at theanalyticalscientist.com/issues/0213/104.

Rich Whitworth
Editor



Rebecca Stacey

When Rebecca Stacey ditched her plans to study biochemistry and opted for Archaeological Sciences instead, she was told that she was mad to enter into such a specialist field with such limited employment prospects. Fast forward 20 years and it is clear that the impulsive decision paid off. "After completing my PhD on chemical characterization of ancient food residues, I joined the British Museum when it was expanding its facilities for organic analysis," Rebecca explains. "I am now responsible for the chromatography and mass spectrometry facilities there. My research applies the tools of analytical chemistry to interrogate the Museum's worldwide collections, seeking to understand the past use of materials and how best to ensure their preservation for the future." *See page 30.*

Lauren Jackson

Lauren Jackson is Acting Chief of the Food Chemistry and Nutrition Team at FDA/CFSAN located in Bedford Park, IL, USA. Lauren received her B.S. in Food Science from Cornell University, and her M.S. and PhD, both in Food Science, from the University of Wisconsin. Her expertise is in the area of processing and its affects on chemical contaminants and bioactive food components. Lauren is a member of ACS, IFT, IAFP and AOAC and serves as a scientific editor for the Journal of Food Science. "I'm currently working on several projects aimed at developing best practices for detecting and controlling food allergens." *See page 36.*

Don Richards

Don Richards received a PhD in Chemistry from the University of Keele in 1985 before holding several management positions in the mass spectrometry market. A 17-year career at Pfizer helped Don become an expert in the structure elucidation of a diverse range of small organic molecules: process intermediates, process impurities, degradants, metabolites, natural products. Don now holds a global role at Bruker as Director of Integrated Characterisation Solutions. *See page 44.*

Elizabeth N. Treher

Elizabeth Treher is the founder of several entrepreneurial organizations and was an invited member of the first U.S. delegation to China for Education and Training. Trained as a radiochemist, she led multinational chemistry projects in industry, government, and academia, and the startup of a corporate university serving 22,000 global employees. A graduate of Washington University in St. Louis with an M.A. and Ph.D. in nuclear and radiochemistry, Liz also attended Northwestern University and was a NSF Postdoctoral Fellow. She has more than 85 publications and patents. Wiley & Sons published her most recent book for technical managers. *See page 40.*

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Upfront

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

We welcome information on interesting collaborations, C-level appointments or research that has really caught your eye, in a good or bad way. Email rich.whitworth@texerepublishing.com.

CSI: Geographical Jigsaw

Can isotope analysis uncover enough pieces to build a better picture in a truly cold murder case?

The body of a young woman who had been murdered was recovered from under the I-75 Lake Panasoffkee bridge in Florida back in 1971. Lack of evidence meant that the victim was unidentified; she became known simply as 'Little Miss Lake Panasofkee'. Her body was exhumed for further investigation in 1986, and has been kept at the University of Florida (UF) ever since.

In spring 2012, the detective working on the case, Darren Norris, and Erin Kimmerle, a forensic anthropologist at the University of Southern Florida, contacted George Dimitrov Kamenov (UF) for some serious analytical support. Kamenov's research uses Sr, Pb, O and C isotope analysis to decipher ancient human migration patterns. Could the techniques geo-reference their unsolved case? "In ancient times, people likely consumed local food and water, so their teeth and bones tend to record the local environment signal. Today, our food, and in some cases even water, comes from different places. That's a big problem," says Kamenov.

The Analytical Scientist spoke with George Kamenov to find out more.

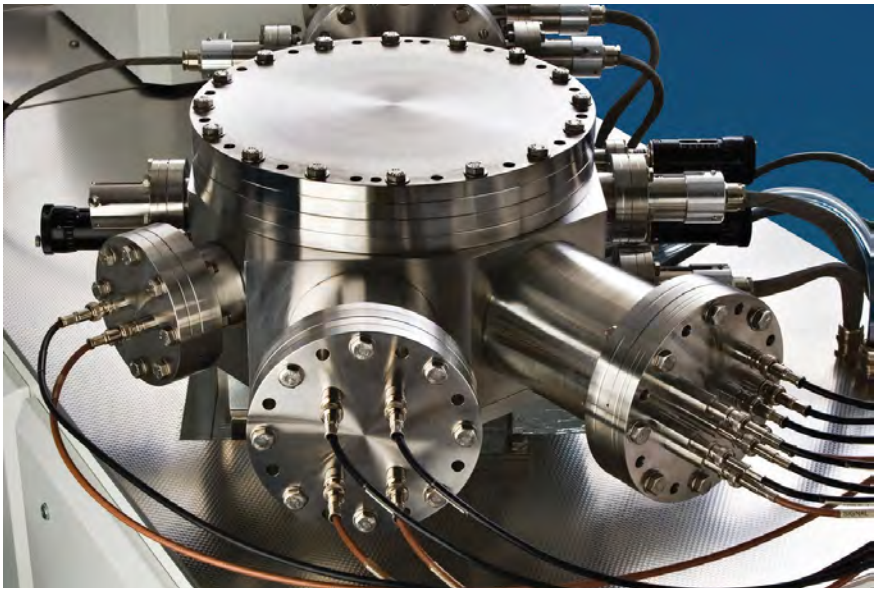
Does our peripatetic lifestyle present insurmountable problem?

The 'archaeological' approach does not work particularly well in modern cases but some modern activities, such as putting lead into gasoline, leave small clues. Everybody's teeth contain some Pb from leaded gasoline; while the Pb additive has been banned, it remains in the soil and because the USA and Europe used lead from different ore deposits, their distinct Pb isotopes have inadvertently created an environmental marker. I measured Pb isotopes in the victim's teeth and bones and the data

Image of the Nobel Prize medal courtesy of ®© The Nobel Foundation

100 Years of Recognition

A century of Nobel Prizes in analytical science chart the progress of the field and the origins of modern analytical instrumentation. Key: *P = Physics, C = Chemistry, Ph/M = Physiology or Medicine*



Multi-collector of the Nu Plasma II ICP-MS used in the research. Image courtesy of Nu Instruments.

was representative of a European Pb signal – the first indication that she was probably a foreigner. No wonder Florida locals failed to identified her…

What analyses did you perform and why?

Sr, Pb, C, N, and O isotope analysis. Each of these isotope groups provides different information, so the combinatorial data offered the best chance of success.

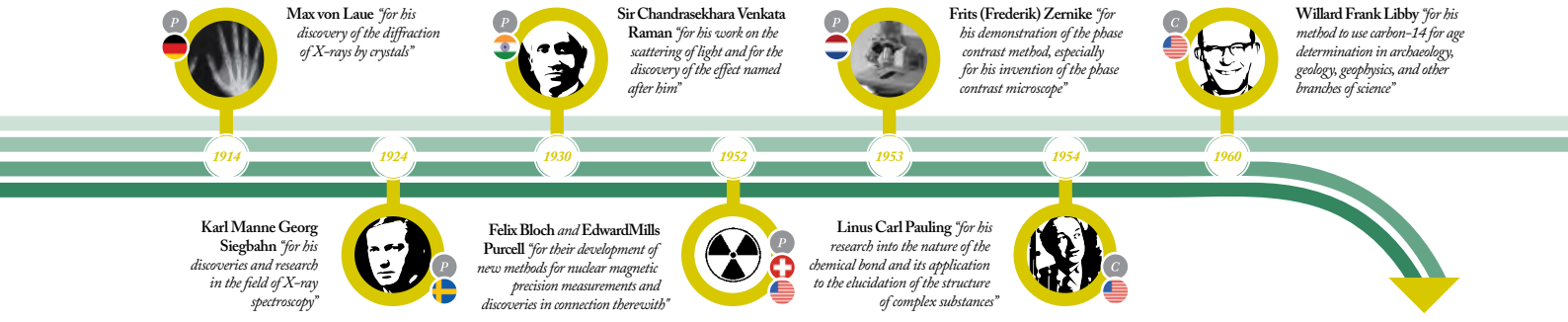
I asked my colleague Jason Curtis to measure C and N isotopes in her hair. C isotopes showed a shift towards heavier δ13C in the latest hair growth (closest to the roots) compared to lighter δ13C at the hair tips. This is indicative of a shift from a wheat-based to a corn-based diet in the last few months of her life. Corn is more commonly consumed in the USA than in Europe.

We concluded that Little Miss Lake Panasoffkee was born and grew up in Europe and probably came to the USA several months before her death. To be more specific about where in Europe, we measured Sr and O isotopes in her teeth and bone. O isotopes showed relatively heavier δ18O values, which points to a southern Europe origin – close to a major water basin, perhaps the Mediterranean Sea. Sr isotopes showed a variable, somewhat bi-modal distribution that could represent a dietary change between early childhood and adolescence, or migration. On the other hand, such bimodal distribution is often seen in regions with complex geology, such carbonate rocks and old metamorphic rocks. Part of Greece, south of Athens, has such complex geology. When I compared the teeth sample Pb isotopes to published Pb isotopes for this part of Greece, there was a good match.

Where did that lead?

We considered the proximity of Tarpon Springs, the largest "Greek" town in the USA, to the place where the victim was found, and decided that Greek heritage was a likely scenario. The detective decided to publicize the case in Greek publications – hopefully some new information will emerge. *RW*

More online:
George Kamaenov describes the instrumentation used, the challenges and limitations of the approach, and his views on future applications of advanced mass spec techniques in forensic analysis.
Go to theanalyticalscientist.com/issues/0213/201.



Illicit Italy

Angelo Cecinato has been measuring psychotropic substances in the air of Italy's major cities. Here, he describes the background, methodology and implications of his study

How did you get started?

"The first measurement was a pure curiosity. No-one had reported these compounds in the atmosphere previously. Discovering cocaine in the air of Rome led me to investigate other substances in different cities and situations. I thought it might provide information about lifestyle in terms of drug consumption and perhaps identify any health significance."

Who funds the work?

"The Italian Department for Anti-Drug Policy support the work. They had interest on two levels: the actual concentration levels of illicit drugs in Italian cities, and whether this information could be used as a quantitative indicator of drug consumption."

What was your approach?

"Common and simple methodologies that could be easily applied by air pollution control authorities everywhere. Cost efficiency, equipment availability and ease of data comparison were at the forefront of my mind. We took measurements for an entire year in Italy's four largest cities as well as four medium sized cities."

What did you find?

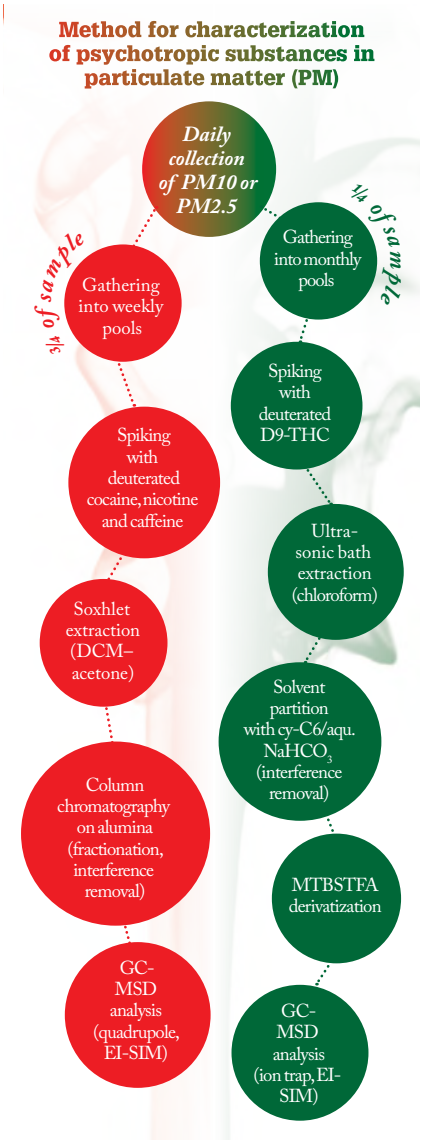
"We got reproducible results on drug concentrations. But providing conclusive answers to the second aspect is more difficult. The results provide some qualitative indicators about drug consumption in different cities and regions. But the main confounding factor is how environmental conditions, such as climate or reactivity of the atmosphere, and social factors, like population density, modify the results.

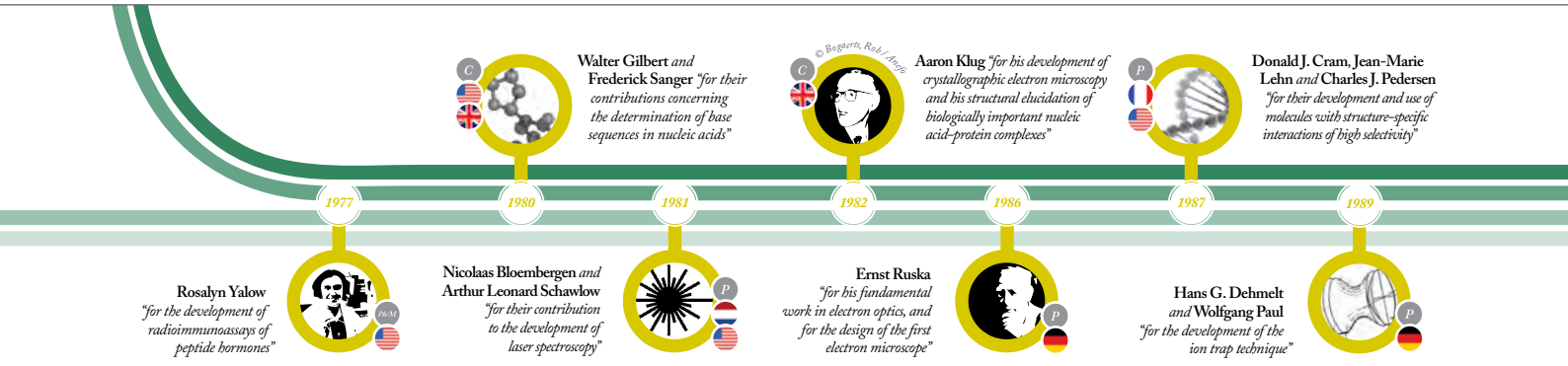
Normalizing for population density, Florence and Bologna have the highest levels of cannabinoids in the air, which fits well with estimates that these two cities have higher consumption of cannabinoids due to higher student populations…"

Are other countries showing an interest?

"I have taken measurements in Brazil, Chile and Mexico. Cocaine concentrations there are much higher than in Italy." *RW*

Angelo Cecinato, Institute of Atmospheric Pollution Research, National Research Council, Italy.



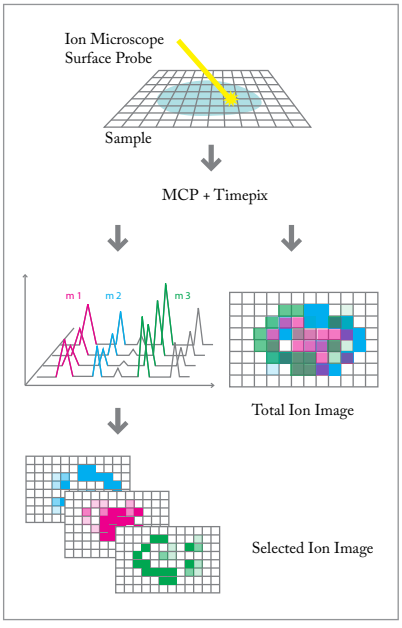


Camera Focus

How mass spectrometric imaging of complex surfaces, such as animal tissue, is being expanded with a position- and time-sensitive pixelated detector

By Julia H. Jungmann and Ron M. A. Heeren

In high-throughput time-of-flight mass spectrometric imaging (TOF-MSI), the pressure is on the detection system: it must measure the impact position and time of the entire ion load from an ionization event in a single measurement frame. Now, using an innovative electron and ion imaging camera, this can be achieved. The approach combines a chevron microchannel plate (MCP) stack with an active pixel detector chip. Ion mass microscopy is a molecular imaging technique that delivers analyte identity and spatial localization with very high throughput at sub-micron pixel sizes. A large-area desorption/ionization beam illuminates the sample surface; ion optics magnify the molecular images and retain the spatial information; and the molecular ion distributions are mapped on a position-sensitive detector.

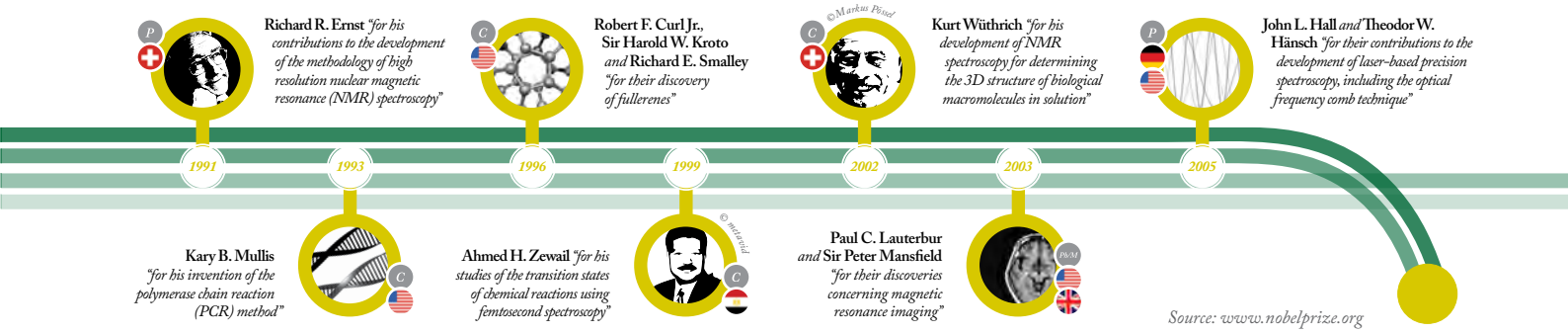


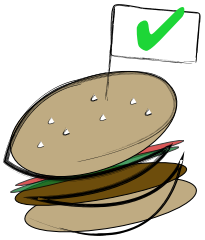
The new detection system is based on application-specific integrated circuits (ASIC) developed by the Medipix collaboration hosted by CERN, Geneva, Switzerland. The Timepix chips comprise tens of thousands of pixels each with a pitch of 55 µm, all of which function as individual units for parallel detection. Importantly, the Timepix chips provide spatial event information (via the pixel address) as well as time-of-flight, particle energy and event counting at the pixel level.

The new camera has been successfully tested on benchmark systems (protein and lipid standards) and with biologically relevant macromolecular tissue samples (rat brain and testes). TOF-MSI systems offer several unique capabilities afforded by the combination of high signal-to-noise ratios, multiplexed detection of events by a highly parallel detection system, high sensitivity, dynamic range, large mass range and simultaneous detection of position- and time-information by a single detector. All of which means higher throughput for faster analysis, the ability to detect small quantities of analytes, and better spatial resolution, revealing unprecedented detail.

As TOF-MSI continues to mature, applications in diagnostics, medical imaging, fundamental atomic and molecular physics, and even space science are likely to grow.

Julia H. Jungmann and Ron M. A. Heeren are members of the Biomolecular Imaging Mass Spectrometry group of the FOM-Institute AMOLF, Amsterdam, The Netherlands. For more information, visit www.amolf.nl/medipix.





Food Safety Net(work)

Waters Corporation and the Food and Environment Research Agency (Fera) launch second International Food Safety Training Laboratory (IFSTL)

"When we buy our food, we place our trust in others – from farm to fork… or net to knife," said Lord de Mauley, Parliamentary Under Secretary of State, Department for Environment, Food and Rural Affairs, UK at the opening of the Fera IFSTL in York in January.

Fera IFSTL will provide hands-on laboratory-based training in analytical techniques for food safety. Its goal is to enable food-producing countries around the world to implement their own solutions and gain access to the opportunities offered by trade with Europe.

Lord de Mauley acknowledged our reliance on food analysis, but also made light reference to a recent, ongoing UK meat scandal: "While the challenges of meeting regulatory standards are huge, the consequences of getting it wrong are very scary indeed. Yet – despite the occasional hiccup, like horse burgers – we buy what we eat without question. And we eat it without fear."

This is the second in a network of IFSTL facilities orchestrated by Waters Corporation. The first was opened at the University of Maryland back in September 2011 in collaboration with the US FDA, and with future IFSTLs planned for Asia, the aim of the whole network is to provide comprehensive training in food analysis to increase knowledge and facilitate global best practices.

Given the increasing complexity of global food supply chains, moves to harmonize analytical food safety should be welcomed with open arms according to the UK's 'Global Food Security Champion', Tim Belton of Leeds University. In his keynote speech, Belton backed an "international effort" and, in addition to resource scarcity, defined food security as a four-fold challenge: safety, authenticity, origin and quality – all of which place added emphasis on accurate analytical methods. Brian Smith, VP of MS Business Operations, Waters, added to the big picture: "In the UK, China, India and in the US, government budgets have not increased to keep pace with the growth of food imports […] No single organization, program or government can ensure the safety of the world's food supply on its own. The challenge is just too big […] It requires public–private partnerships." Waters, in addition to assisting in construction of both the facility and training programs, also supplied analytical systems, including an Acquity UPLC-MS/MS system.

Fera Chief Executive Adrian Belton said, "We welcome this opportunity to be able to pass on our expertise in food analytical testing [...] underpinned by over 30 years scientific experience in the area."

Upcoming courses include 'Illegal Dyes in Foods' and 'Drug Residues in Aquaculture'. Importantly, the IFSTL network adopts a "train the trainer" approach to further extend the reach and impact of the facilities with a single objective in mind: safer food for everyone. *RW*

For more information on UK courses: www.fera.defra.gov.uk/ifstl
More on the vision: goo.gl/iiUfq
More on food security: www.foodsecurity.ac.uk

Overly Honest Analysis

Analytical scientists have become caught up in a new meme on Twitter recently. For those not following #overlyhonestmethods, here are some of the best

"GC traces include an anomalous peak, but that's likely because a postdoc has been using a hot plate in lab to fry bacon"

"The Eppendorf tubes were 'shaken like a polaroid picture' until that part of the song ended."

"Since the mass spec was in use, I assumed that my product had been formed and proceeded to try to purify it."

"The HPLC method was optimized to hide the impurity peak under the main product peak in order to meet >98% purity spec."

"We keep that novelty magnet on the side of the mass spec because if we remove it nothing works. No idea why."

"HPLC-MS analysis was not performed because nobody knows how to make the expensive new instrument work."

"The constant mass peak on ms/ms is attributed to volatiles present while the institute's hallways were being painted."

"HPLC methodology cannot be replicated because the 30 year old pump broke and parts don't exist. Sample looks right anyway."

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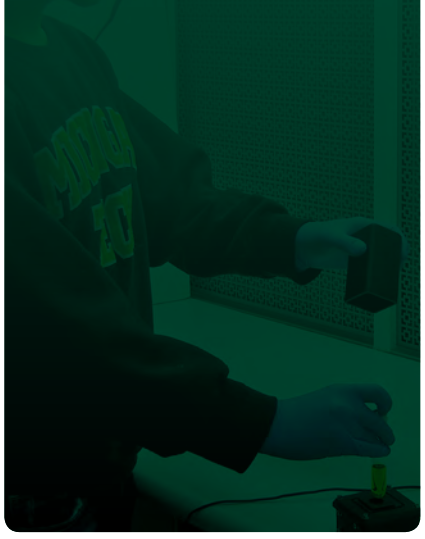
In My View

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, written in the first person.

Contact the editors at edit@theanalyticalscientist.com



Share, and We All Grow Richer

Free and open-source scientific hardware has the potential to liberate collective intelligence and cut costs

By Joshua M. Pearce, Departments of Materials Science & Engineering, and Electrical & Computer Engineering, Michigan Technological University, USA.

"The miracle is this: the more we share, the more we have." Star Trek's Leonard Nimoy summarizes beautifully here a concept that is already well known by real scientists. We are all accustomed to benefiting from the literature, where our past and present colleagues openly share both their genius and more modest good ideas. Academic scientists, who as researchers and teachers dedicate their lives to information sharing, even have a well-established gift culture solidified in the tenure process. You get tenure based on how much you have given away (the more valuable the better), not how much you hoard. This scientific sharing, until very recently, tended to be focused on what could be published in academic articles; that is to say, ideas. No more. The process of development that has succeeded with ideas (and software) is now being applied to hardware, providing an unprecedented opportunity to radically reduce the cost of analytical science.

Free and open-source software (FOSS), first widely demonstrated with the incredible success of Linux, is becoming the dominant method of software development simply because it is superior. It is superior because you have more people working and collaborating to solve problems. Collectively, we are all smarter than any individual. But, why stop at software? The open and collaborative principles of FOSS are easily transferred to scientific hardware designs with digital manufacturing (1). Thus, free and open-source hardware (FOSH) is hardware whose design is made publicly available for anyone to study, modify, distribute, make, and even sell the design or hardware based on that design.

> *"We are all accustomed to benefiting from the literature, where colleagues openly share both their genius and more modest good ideas."*

Currently, one of the most successful enabling open-source hardware projects is the Arduino electronic prototyping platform (www.arduino.cc). The $20–$50 Arduino is a powerful, yet easy-to-learn microcontroller that can be used to run useful scientific apparatus while slashing their costs. Projects include the pHduino (pH meter), Spectruino (UV/VIS/IR spectrometer), Xoscillo (oscilloscope), Arduino Geiger (radiation detector), and OpenPCR (DNA analysis). However, Arduino's most impressive evolution-enabling technological application brings us back to Star Trek, specifically, the "replicator"

"The process of development that has succeeded with ideas is now being applied to hardware, providing an unprecedented opportunity to radically reduce the cost of analytical science."

capable of creating objects from digital designs. By virtually eliminating material scarcity, replicator technology plays an important role in the moneyless human economy within the fictional Star Trek universe. The closest we have got to this technology in the real world is open-source self-replicating 3D printing.

Using an Arduino as the brain, open-source 3D printers capable of additive layer manufacturing using a number of materials, such as polymers, ceramics and metals, have already been developed and are quickly proliferating. The most popular of these 3D printers is the RepRap, named because it is a self-replicating rapid prototyping machine (http://reprap.org). Currently, the RepRap, which can be made for about $500, can fabricate approximately 50% of its own parts.

FOSH has the transformative potential to dramatically reduce experimental research costs. It is less expensive to design and print research tools than to buy them, particularly if someone else has started the designs for you. A number of scientific equipment designs are flourishing in Thingiverse (www.thingiverse.com), a free and open repository for digital designs of real physical objects. These designs are becoming increasingly more sophisticated, starting with single component prints such as the DremelFuge chuck (a printable rotor for centrifuging standard microcentrifuge tubes) to the housing for an open-source chemical oxygen demand (COD) analyzer. The most aggressive savings can come from coupling Arduino controls to RepRaps to make research-grade open-source scientific hardware, which can save labs many times what they might pay for commercial versions of the same tools.

Your analytical group may already design some of its own customized equipment. By taking the extra step of sharing these designs with the open-source community, you will not only help other researchers reduce laboratory costs, but also benefit directly when the international open-source community 'hacks' your equipment to improve it and re-shares their results. We all win. Even Spock might smile.

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The Fight Against Doping in Sport

Three ways that the analytical scientist could – and should – play a more active role

By Klaas Faber and Joan Ferré. Klaas Faber is founder of Chemometry Consultancy (www.chemometry.com), and Joan Ferré is an associate professor at the Department of Analytical and Organic Chemistry, Universitat Rovira i Virgili, Spain

Concerns about stimulant use in sports were published in the New York Times as early as in 1895, but it was not until the Sydney Games of 2000 that the athletes' oath included a pledge against the use of doping. The clean sport ideal has been slow to mature!

Since doping was only gradually deemed to be unacceptable, it took many years before significant measures were taken. The intuitively appealing approach was to look for scientific evidence by testing body fluids such as urine and blood. Testing duly started out in equestrian sport in 1910, and was immediately challenged in court. Among human sports, the focus of this article, testing was first introduced for cycling in the 1960s.

Current anti-doping regulation formally defines the analytical method to be reliable; it can not be challenged in court. In absence of procedural errors that might invalidate the test results, alleged offenders face pre-determined standard sanctions, typically a one-to-two-year ban from all sports for a first offence, and a lifetime ban for a second;

prizes, titles and records stained by doping are usually returned.

The Remit of the Analytical Scientist

Given these harsh consequences, the analytical scientist must deliver proof in rigorous compliance with international standards. The actual role is a purely technical one.

Here we ask whether the role of the analytical scientist should be strictly confined to technicalities, that is, to formally assure that false-positives rarely occur. We think not. Instead, we propose an expanded role for the analytical scientist that includes views on: (i) the reasons for carrying out the analysis and (ii) the objectives of the process. The analytical scientist should engage in discussion with the client, in this case an anti-doping organization or a sports union.

We identify three aspects of the current anti-doping system where analytical scientists could play a more active role.

The False-Negative Problem

It's hardly a secret that doping tests invite evasion by meticulously organized counter-measures. As an illustration, recall that Lance Armstrong was recently stripped of his seven Tour de France victories, but mainly as a result of admissions of guilt by others: Armstrong was tested hundreds of times and, in the words of the International Cycling Union (UCI), he "was able to beat the system."

It's telling that the World Anti-Doping Agency (WADA) has created a working group to examine 'The ineffectiveness of the fight against doping in sport'. The analytical scientist has the ethical task of providing the client with realistic information about the inherent limitations of testing.

The Inconsistent Banned Substance List

Many substances that meet the criteria of doping are nevertheless allowed by WADA. One example is pain medication.

During major soccer and handball tournaments, up to 50 percent of players use pain medication.

Hans Geyer, deputy director of the Cologne laboratory, noted in a recent interview: "It's well known that Andreas Erm who won a bronze medal in the 50km walk in the 2003 world athletic championship in Paris received pain killers several times during the walk – can you tell me this is not performance enhancing?"

Such legal doping makes clean sport an unattainable ideal: by allowing pain medication, WADA unintentionally

High-Impact Liquid Chromatography

The development of analytical techniques requires a healthy balance between technology push and market pull. Here, the co-chair of HPLC2013 describes the three themes of the meeting that will capture this dynamic and provide a strategic agenda for the development of LC.

By Peter Schoenmakers, chair of HPLC2013 and a professor at the Faculty of Science, van't Hoff Institute for Molecular Sciences, University of Amsterdam, The Netherlands.

Arguably, the field of LC has advanced through the years thanks to a sustained technology push from within its own ranks. The transition from high-performance to ultra-(high-) performance LC, the development of new types of columns (porous-surface particles, monoliths), the emergence of micro- and nanofluidic systems and the advent of comprehensive two-dimensional liquid chromatography amply demonstrate the point. At HPLC2013, technology push is represented by the "HYPERformance LC" theme. The speakers in this parallel line of the program have been affectionately classified as "hardcore liquid chromatographers" or "HPLC nerds."

Thanks to the successful development of the technique, LC helps answer a myriad of questions in science and society. In return, demands from many different application areas should help LC move forward. One of the areas that has benefited greatly from demands from outside the community is the combination of LC with mass spectrometry (LC-MS), which is the second major theme of HPLC2013. LC-MS proved quite difficult in the previous century, but it was eventually developed successfully to meet great needs in life science, food science and environmental science. MS in itself is experiencing a significant technology push towards higher resolution, greater sensitivity and better multi-stage (MS^n) possibilities.

The third theme of HPLC2013, High-Impact LC, embodies the

"The analytical scientist has the ethical task of providing the client with realistic information about the inherent limitations of testing."

nurtures a culture of pills. We encourage analytical scientists to follow the example of Hans Geyer and voice concerns about the banned list.

Artificial False-Positives

In some countries, recreational drugs such as cannabis are responsible for half of the doping convictions. Unlike steroids or EPO, for example, the use of these substances is expressly allowed outside competition, though not during competition, owing to their short-lived effect. However, one could be positive days or even weeks after allowed use, producing an unavoidable minute trace during competition. Bizarrely, this counts as doping.

Specifying suitable thresholds on the banned list, as is done for alcohol, could markedly reduce the number of questionable convictions and allow a focus on 'real' doping. Introducing these thresholds is not far-fetched; they are common-place in assessment of traffic violations. We encourage analytical scientists to place thresholds for recreational drugs and the like on their client's agenda.

Analytical scientists could play a more active role in improving the fight against doping. We conjecture that it would make their work more gratifying as well as more effective.

market-pull mechanism. Our ambition is to outline a strategic agenda for the development of LC in the next decade.

"Our ambition is to outline a strategic agenda for the development of LC in the next decade."

For this purpose, leading scientists from seven fields (environmental, food, forensic, metabolomics, pharmaceutical, polymers, proteomics) will identify needs in their respective domains that may be met with the aid of LC. These challenges will provide a fresh perspective to the HPLC community. Each „challenger" is followed by an LC expert who is active within the same domain. These "responders" will summarize what is already possible with LC. The framework is completed by five submitted oral presentations on specific aspects of, for example, sample preparation, analysis, detection, and interpretation within the application domain. After the seven lectures, the moderator of the session will lead a discussion to draw conclusions and formulate specific targets for the HPLC community.

One potential weakness of the approach is that application domains other than the seven highlighted areas will be underexposed. These include important questions from life science, such as the study of nucleic molecules, lipidomics and glycomics. The growing biotechnology and biopharmaceutical industries also demand attention from liquid chromatographers. In part, these

will be addressed within other areas (for example, biopharmaceuticals within pharmaceuticals, lipids within metabolomics). And, by dividing the applications into small-molecule LC-MS and large-molecule LC-MS, few analytes can escape our comprehensive coverage.

Liquid chromatography still offers fantastic opportunities for separating complex non-volatile mixtures. And this will long be the case if we can ensure that HPLC remains relevant and contributes significantly to the efficiency of scientific research and industrial development and, ultimately, to safer, healthier and more enjoyable lives for all.

Results from the seven sessions will contribute to a first draft of a strategic agenda that will be briefly presented in the final plenary session of the meeting and published with the symposium proceedings. Eventually, the agenda may serve as a framework for the program of future HPLC meetings.

These High-Impact LC sessions will help all of us in the field. Challengers and responders will wrestle with major unmet needs of the market, and catalyse insights from every delegate into the analytical mission of the next decade. Let the games begin!

HPLC2013, the 39th International Symposium on High-Performance-Liquid-Phase Separations and Related Techniques, takes place in Amsterdam, June 16-20. www. hplc2013.org

Google: The Omnicompetitor

The Internet appears to satisfy our need for information and communication. But its proliferation has damaged businesses that, arguably, connect people and ideas in an even more indispensable way.

By Paul Petersen, Director at Federatie van Technologiebranches, based in Leusden, The Netherlands.

The origins of the Internet are attributed to several scientific and academic communities who all had one thing in common: the need to share concepts and research more easily. It is little known that the UK's National Measurement Institute (NPL) was one of the earliest contributors: in the late 1960s, NPL computer scientist Donald Davies invented a way to transmit long messages. His term, 'packet-switching', is still used today. The goal of Davies and other pioneers was to increase the speed of data transmission; the concept of the World Wide Web came later. The sharing of scientific knowledge provided the motivation for the inception of the Internet. It took off in the 1980s, with cultural and commercial use burgeoning throughout the 1990s. But it was at the turn of the new millennium, with the meteoric rise of social media, online shopping, and web-giant Google, that the Internet really started to shape our lives. A new world order was created, redirecting the way we research, share, connect, consume and work. But at what cost?

Back in the middle of the 20th century, the cooperative now known as the Federatie van Technologiebranches was founded to organize 'HET Instrument' in the Netherlands. Set up as a trade fair for equipment suppliers, it began with 60 exhibitors and several thousand visitors, and provided an opportunity for people to network and exchange information. By the 1980s and early 90s, its popularity had risen to encompass 40,000 square meters of exhibition space and nearly 70,000 visitors. But, since the mid-90s onwards, exhibitor and visitor numbers have been in decline. I believe that this is in no small part due to the Internet.

The Internet (and its almost permanent connection to modern smart phones) provides extraordinary access to information, in an environment where Google could be considered The Institute. It dominates the search market, despite advances from major competitors. The name itself is a play on the word "googol" (10^{100}) and represents the company's self-stated mission "to organize a seemingly infinite amount of information on the web".

Google can find information and even suggest the best contacts. In this sense, it is a modern-day alternative, even a direct competitor, to events like HET. It is also a rival for every magazine, newspaper and all other physical forms of communication. The Internet's colossal stockpile of information – coupled with Google's alleged ability to determine its true relevance – represents massive competition.

I contend, however, that information is not knowledge.

If you 'google' Google, you find that its objective is to be the "perfect

"Google-ing really can't replace a friend's recommendation, a colleague's introduction or even a hand shake. It may well be the repository of the world's information, but without experts assessing, analyzing and filtering, it has serious limitations."

search engine". Given its ubiquitous nature and the added value of social media, is Google a giant, web-based customer relationship management system? I think not. What it lacks is the human touch that provides depth and meaning to simple information. Google-ing really can't replace a friend's recommendation, a colleague's introduction or even a hand shake. It may well be the repository of the world's information, but without experts assessing, analyzing and filtering, it has serious limitations.

Part of the NPL's historical and modern vision could equally describe the challenges facing the analytical sciences in the near future: "To deliver social and economic impact through world-class measurement science, innovative applied research and knowledge services". The process of sharing original knowledge through real social interaction between industry and academia should not – must not – be lost. It provides much-needed navigation beacons in an ever-shifting, ever-growing sea of online information. We, the technology community, must continue to use the Internet to our advantage, whilst ensuring that "the good old ways" are not lost forever.

For a slideshow illustrating the analysis of cultural artifacts, go to theanalyticalscientist.com/issues/0213/401

The Science of Art

How analytical chemistry contributes to understanding and preserving our cultural heritage.

By Marco Leona

Behind the scenes at many museums, scientists provide essential support to archaeologists, art historians and conservators. Their work may or may not be immediately visible to museum visitors, but it is fair to say that no decision on authenticity, provenance, conservation, or even lighting and environmental conditions is made in a modern museum without scientific support. And analytical chemistry is at the foundation of scientific research in cultural heritage.

Recent initiatives devoted to advances in the field, including a workshop at the US National Science Foundation (1), a Gordon Research Conference (2) and a full issue of Accounts of Chemical Research (3), highlight the importance of materials analysis and structural characterization in the study of works of art and in their preservation.

Traditionally, the main techniques employed in museum laboratories have been polarized light microscopy (PLM), X-ray diffraction (XRD) and fluorescence (XRF), scanning electron microscopy and microanalysis, Fourier transform infrared microspectrometry (FTIR) and gas chromatography–mass spectrometry (GC-MS). In the last decade, Raman microscopy has become a common tool thanks to its ability to non-destructively characterize pigments, minerals, and a variety of polymers. A striking trend of recent years is the rise of portable instrumentation, mostly for XRF but also for FTIR and Raman. Handheld XRF analyzers with performance similar to much larger instruments are now being used not only by scientists, but also by conservators.

One notable emerging trend is the application of proteomics techniques, such as matrix-assisted laser desorption/ionization (MALDI), LC-MS, and high throughput capillary electrophoresis techniques for the study of protein-based materials, such as egg-protein binding media in paintings, collagen in parchments, and silk and wool in textiles. Another trend is the development of immunoassays for the spatially-resolved identification of protein on cross-sections from paintings, a task complicated by changes in the proteins structure introduced by aging and by degradation catalyzed by pigments.

The potential of spectral mapping techniques has been illustrated in the examination of documents, prints, drawings and paintings, and will probably become commonplace as commercial instrumentation is developed. John Delaney's work (see page 24) at the National Gallery of Art in Washington, DC, is a key example of what can be done with hyperspectral imaging in the visible and near IR ranges. The extension of this approach to the mid-IR range is a logical progression of this technique.

One of the most exciting recent developments in the field is progress in fast XRF mapping instrumentation. The work of Koen Janssens in Antwerp and Joris Dik in Delft (see page 26) illustrates the utility of macroscopic elemental mapping in the study of paintings. Originally performed at synchrotrons, this type of analysis is soon going to be possible using commercial instrumentation, potentially extending to every museum the ability to identify changes in paint composition and detect images hidden under the present surface of a painting.

While imaging techniques are increasingly important in the field, microanalysis remains a key component of investigations into works of art. Surface-enhanced Raman scattering (SERS), the huge enhancement of Raman scattering experienced by molecules adsorbed on appropriate plasmonic substrates such as silver nanoparticles, has found one of its main areas of application in the identification of natural and synthetic compounds used as pigments and dyes in works of art. I have applied the technique to well over one hundred objects, ranging in dates from 2000 BC to the present (see page 28).

Cultural heritage material is invariably heterogeneous and complex. In the case of archaeological findings, analysis is further complicated by aging and changes due to burial. Rebecca Stacey at the British Museum (see page 30) successfully used a multianalytical approach, combining Raman, XRF, and GCMS techniques to identify the content of a Roman medicine container. In this case, however, chemical analysis was only the first of many steps. To better understand the function of the substances identified, Stacey and her coworker went back to the laboratory, combining the analytical results with the study of contemporary accounts, to reproduce some of the pharmaceuticals.

Scientific research in the field of cultural heritage encompasses a large number of disciplines. It deals with the material and structural characterization of works of art and archaeological objects, the study of their changes over time, including aging, restoration and degradation, and the development of new treatment methods and materials. Analytical chemistry, however, remains the foundational science in the field: the questions that art professionals and the public want scientists to answer most often are 'what is it?' and 'how did it get there?'.

Marco Leona is the David H. Koch Scientist in Charge at the Department of Scientific Research, The Metropolitan Museum of Art, New York, USA.

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Casting Light on Renaissance Illuminations

Spatial information derived from macroscopic maps provides important clues about an artist's working methods and helps guide conservation choices.

By John Delaney, Paola Ricciardi, Michelle Facini, Marcello Picollo, Jason Zeibel, Suzanne Lomax, and Murray Loew

The Question:

Can the pigments and paint binders used in illuminated manuscripts be mapped in situ?

The Object:

An illumination from a choir book commissioned by the Camaldolese monks of Santa Maria degli Angeli in Florence at the end of the fourteenth century. This commission includes some of the most beautifully illuminated volumes of the early Italian Renaissance. Contributing significantly to the production of these books was Lorenzo Monaco, known as one of the greatest panel painters of the time, and an accomplished illuminator of manuscripts. The illumination studied and discussed here (see figure) represents a bearded prophet with his hands raised in prayer, within a blue and green initial E decorated with filigree ornaments, blue and yellow circular 'gems', red-glazed gilt diamonds, and colorful foliage. The background is gold leaf.

The Challenge:

- Manuscript illuminations are extremely sensitive to physical handling, to environmental changes and to light.
- The collection of even a small sample would mar the miniature's appearance, ruling out analytical chemical methods such as HPLC and GC-MS.
- While site-specific in situ analytical tools, including X-ray fluorescence and Raman spectroscopy, do not require a sample, there is growing interest in obtaining chemical information over an entire art object.

The Solution: Reflectance imaging spectroscopy

Visible and near infrared (NIR) reflectance imaging spectroscopy is the collection of contiguous calibrated spectral images to provide the reflectance spectrum for each pixel of the scene. The method utilizes information from both electronic transitions in the visible and near infrared, as well as vibrational features from various organic and inorganic chemical groups, namely hydroxyl, carbonate, methylenic and amide groups. It was developed to remotely map and identify minerals and vegetation but applications have ranged from the study of planets to process modeling in the pharmaceutical industry.

The Application:

The sensitivity of manuscript illuminations requires the optimization of hyperspectral camera systems operating from 400 to 2500 nm with a few nm sampling to conduct such studies. This is achieved by using high-sensitivity and low-noise visible and infrared focal planes that were originally developed for scientific and military applications.

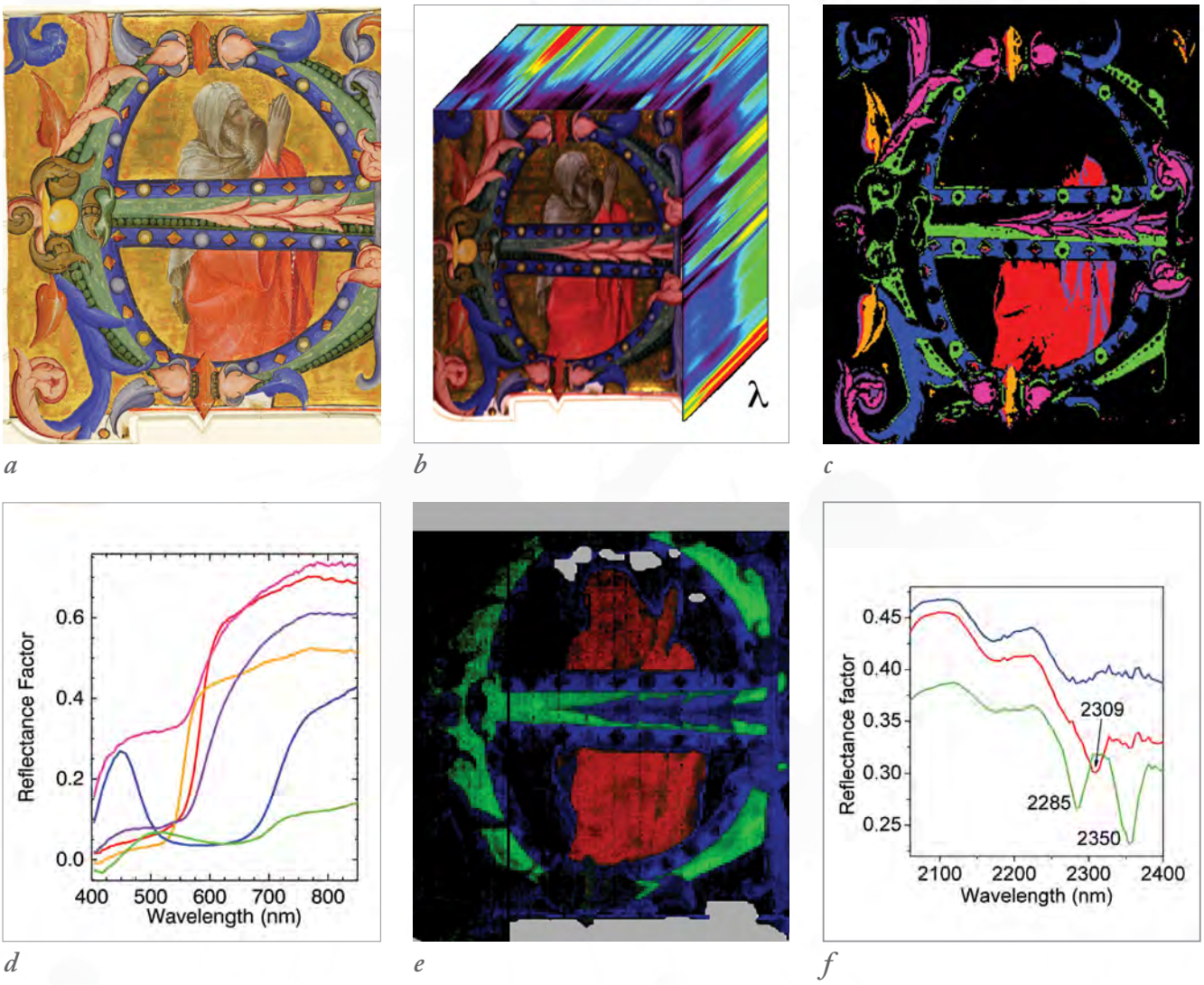
Once the image cubes (see figure) whose third dimension is spectral, are collected and calibrated, the hundreds of images are processed via an algorithm developed for clustering and setting apart the basis set of reflectance spectra which describe the art work. This method relies on both principal component analysis and convex geometry. The resulting spectral 'endmember' can be mapped using one of several algorithms including the 'spectral angle mapper', which identifies all the pixels in the cube whose spectra match that of the reference endmenber to within a fixed tolerance value.

Identification of the artist's material is then done in two ways: comparison with reflectance spectral databases, and by noting characteristic vibrational features such as position and slope of electronic transitions.

The Findings:

The analysis of the hyperspectral Vis-NIR cube and other analytical data revealed that the mineral azurite was used for the green portion of the initial, while blue areas were painted using two grades of ultramarine blue. The orange leaves were painted with red lead and the pink leaves with an insect-derived red dye. The spectral data also showed that the red robe of the Prophet was painted using vermilion and glazed with the red dye.

Analysis of the NIR cube also allowed a new insight into Monaco's painting technique, specifically the use of a fat-containing paint binder (likely egg yolk) only for certain compositional elements of this manuscript leaf



a *b* *c*

d *e* *f*

Visible and NIR reflectance imaging spectroscopy of (a) Lorenzo Moanco's Praying Prophet (1410/1413, Rosenwald Collection, National Gallery of Art, DC). (b) Visible and NIR Reflectance Image cube. (c) Image map showing the spatial distribution of primary pigments identified from the reflectance spectra (d) obtained from analyzing the visible/NIR image cube (400 to 850 nm), for example, Ultramarine (blue), Vermilion (red), Red Lead (orange), Red dyes (purple, maroon), azurite with yellow pigment (green). (e) Map of the reflectance spectra (f) of the egg yolk binder used to paint the Praying Prophet (red in map) and of azurite used in the green initial (green in map).

– the figure of the prophet, but not the decorated initial. The use of any fat-containing binder for manuscript illumination is surprising in itself since egg white and gum Arabic (based on proteins and polysaccharides) are historically considered to be the binders preferred by illuminators.

This shows how the use of reflectance imaging spectroscopy in the visible and NIR opens the opportunity for conservation scientists, conservators and art historians to explore further the painting techniques of Lorenzo Monaco and of other illuminators.

John Delaney is Senior Imaging Scientist at the Scientific Research Dept., National Gallery of Art, Washington, DC, USA.

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Deconvoluting the Creative Process

Elemental distribution distinguishes different phases of a work of art by Hans Memling and sheds light on the interaction between the artist and his patrons.

By Geert Van Der Snickt, Matthias Alfeld, Anne Van Oosterwijk, Till-Holger Borchert, Koen Janssens and Joris Dik

The Question:

Did the Moreel triptych initially look like it does today? If not, what was changed? And what does it tell us about the creative process that led to this masterpiece of medieval art?

The Object:

This altarpiece was painted for the Moreel family. William Moreel, Seigneur of Oost Cleyhem, was one of the wealthiest and most politically active men in Bruges. He was married to Barbara van Vlaederberghe van Hertvelde and they had eighteen children. They ordered this altarpiece for their funerary chapel in the Church of St. Jacques in Bruges, founded in 1484. The lower frame of the wings and the center panel bear the same date.

On the interior wings, the parents are represented with 16 of their children. On the left, William Moreel is shown with his five sons behind him and flanked by his name patron saint, William of Aquitaine. On the right panel, Mrs Moreel and her daughters kneel next to St. Barbara. Of the eleven daughters depicted, the oldest wears the habit of a Dominican nun.

X-ray radiographs of the side panels, recorded several decades ago, suggested that changes were made to the representation and position of the minor characters in both wings. The objective was to visualize more clearly any pentimenti to better understand the evolution of the triptych.

The Challenge:

To see through the upper layers of paint to lower layers that are now visible and offer information about the original painting.

The Solution: Macroscopic X-ray fluorescence (MA-XRF) imaging

X-ray fluorescence is a non-destructive method of element analysis. Materials are irradiated with high energetic radiation ionizing atoms which, upon relaxation, emit X-radiation

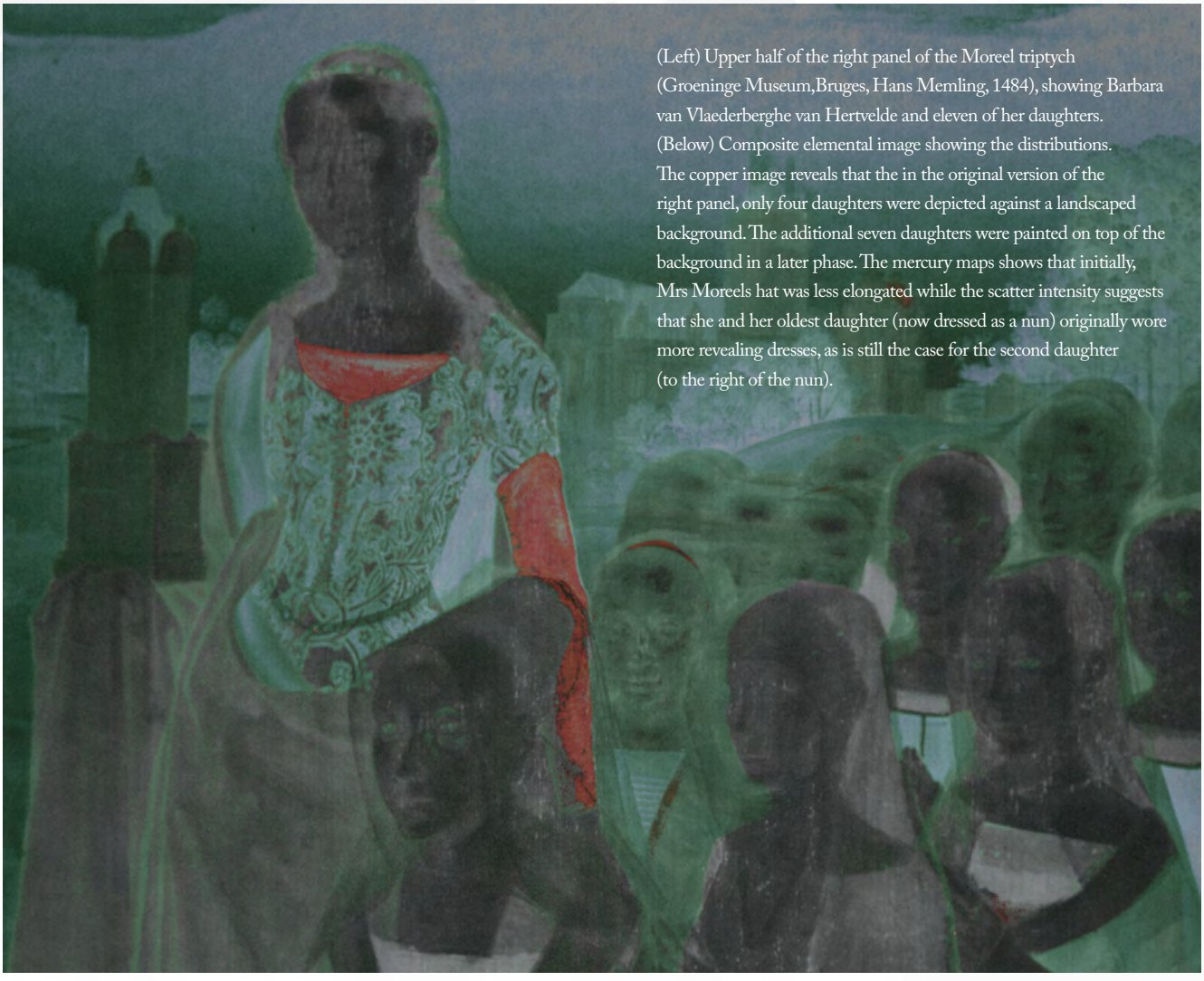
that is different for each atom. Using suitable solid state detectors, signals can be recorded for many chemical elements. A motorized assembly moves an X-ray tube and detectors in small steps over the surface of a painting, determining the local composition and generating element-specific distribution images of the painting.

The Application:

Radiation from fairly deep below the surface can be detected, revealing overpainted representations that are no longer visible to the naked eye. Most pigments are characterized by one or more characteristic chemical elements; many traditional pigments, such as malachite green and verdigris contain copper, vermillion red contains mercury, umber contains manganese and iron, etc. Combining elemental maps allows the construction of a (false) colour 'photo' of a buried paint layer.

The Findings:

Copper distribution (see figure, right) reveals that in the original version of the right panel only four daughters were depicted against a landscaped background, painted with one or more Cu-containing green pigments. Much more of the hill/lawn to the right of Mrs Moreel was originally visible; in the landscape, positions were left open for her portraits and four daughters. The faces of the additional seven daughters were painted later on top of the verdant background. The mercury map (red) reveals that Mrs Moreels' hat was originally less elongated. A different red (not containing mercury) was used to paint St. Barbara's skirt than the red parts of her left arm and bodice. Possibly the vermillion in these areas was added



(Left) Upper half of the right panel of the Moreel triptych (Groeninge Museum,Bruges, Hans Memling, 1484), showing Barbara van Vlaederberghe van Hertvelde and eleven of her daughters. (Below) Composite elemental image showing the distributions. The copper image reveals that the in the original version of the right panel, only four daughters were depicted against a landscaped background. The additional seven daughters were painted on top of the background in a later phase. The mercury maps shows that initially, Mrs Moreels hat was less elongated while the scatter intensity suggests that she and her oldest daughter (now dressed as a nun) originally wore more revealing dresses, as is still the case for the second daughter (to the right of the nun).

in a later restoration phase. Finally, the scatter intensity image (grey/white in the figure) suggests that Mrs Moreels and her oldest daughter (now wearing a nun's habit) originally wore more revealing dresses, as is still the case for the second daughter (to the right of the nun). Also in left panel of the triptych (not shown), changes were made to the positions of the male children behind William Moreel and the portrait of his fourth son inserted.

From this we can conclude that the process of creating this altarpiece went through at least two major stages. The relatively young Moreel family was represented in a balanced manner against a green landscape. In the second phase, incorporating the younger children, some of the balance of the representation was sacrificed by the artist. This also allowed a number of minor aspects of the painting (such as the dress of the eldest daughter) to be brought up-to-date.

This shows how MA-XRF allows art-historians and conservators to explore in greater depth and with unprecedented detail the creative process that led to paintings of this type.

Koen Janssens is professor of Analytical Chemistry at the University of Antwerp, Belgium. Geert Van der Snickt and Matthias Alfeld are researchers in his group. Anne Van Oosterwijk is scientific collaborator and Till-Holger Borchert is chief curator of the Groeninge museum, Bruges and Hohenberg Chair of Excellence in Art History at University of Memphis, US. Joris Dik is Antoni van Leeuwenhoek professor at Delft University of Technology, Netherlands.

The Stories That Colours Tell

Material identification studies using SERRS add to the knowledge of particular objects and the period in which they were produced.

By Marco Leona

The Question:

When were the dyes used by artists and craftsmen for pigments and painting introduced, what technology did this require, and what do these insights shed on the times?

The Objects:

1.A leather fragment of a quiver (see figure 1), found in an archaeological excavation led by the Metropolitan Museum in Egypt in 1911-1912. The fragment, which measures 11cm by 13cm, dates to the Middle Kingdom, ca. 2124-1981 BC, and was found in a tomb in Thebes, el-Khokha, Upper Egypt.

2. A small fragment from the purple robe of the Child in a French 12th century sculpture called Virgin and Child in Majesty. The sculpture (see figure 2), stands 79.5cm high and is from the Auvergne, France It was a gift of J. Pierpont Morgan in 1916.

The Challenge:

- To detect compounds that make up a very small percentage of the final product.
- To use minimally invasive techniques.

The Background:

For millennia, artists and craftsmen have used colored organic compounds to dye fabrics and to create pigments for use in painting. These dyes, such as madder dye, cochineal, logwood, and many others, were extracted from plants and insects. Quite naturally, the most successful dyes were those with the highest tinting strength. A clear advantage for a dyer, the need to purchase only small amounts of dye to tint several pounds of yarn is the bane of the analytical chemist: detecting compounds that make up a very small percentage of the final product.

To make things more difficult, the analysis of works of art should ideally be conducted with non-destructive techniques, and when sampling is necessary it should be limited to almost invisible amounts. In the case of dyes, non-invasive methods are of little help. UV-Vis reflectance spectra lack sufficient specificity, there is no X-ray fluorescence elemental signature characteristic of each dye, and most dyes are highly fluorescent under laser excitation, essentially hiding their Raman spectrum.

The Solution: Surface-enhanced resonance Raman scattering (SERRS)

SERRS is not affected by the above limitations. Natural and synthetic organic colorants are, in general, aromatic or heterocyclic compounds (or, in the case of the carotenoids, highly conjugated linear molecules), and when adsorbed on the surface of metallic nanoparticles they experience an enormous enhancement in Raman scattering.

Analysis of works of art has become one of the most significant applications of the technique, which is routinely applied to the identification of organic colorants at the Metropolitan Museum of Art. The high sensitivity of SERRS makes it possible to identify organic colorants in textiles, drawings, paintings, and other polychrome objects, from samples as small as 25 micrometers in diameter.

The Application:

Samples from art, as well as being microscopic, are invariably very complex. On top of that, the objects we routinely analyze are extremely old: aging and deterioration transform the target molecules and produce interfering species. Yet, SERRS has proven to be surprisingly immune to such interference.

Part of the success lies in the microanalytical protocol we developed after lengthy trials. We work at resonant excitation, using a monodisperse silver colloid produced by microwave-supported reduction of silver sulphate with glucose and sodium citrate, and we often employ a two-step measurement approach: analysis of the sample as-is, followed by recovery of the sample and a second analysis after a lossless non-extractive hydrolysis sample treatment. All work is performed with a Bruker Senterra Raman spectrometer, using 488nm laser excitation.

We have successfully demonstrated that the colloid we use is stable over long periods; that the sample treatment protocol enhances sensitivity over comparable approaches, and that the spectra obtained can be cross-referenced with digital spectral libraries using common software.

Fig 1 (below). Fragment of a quiver; Accession No. 28.3.5; Middle Kingdom, ca. 2124-1981 BC (H. 11cm; W. 13cm). MMA 1911-1912, Tomb MMA830, Thebes, el-Khokha, Upper Egypt; Rogers Fund, 1928.

Fig2 (above). Virgin and Child in Majesty; Accession No. 16.32.194; 1150-1200 CE; (H. 79.5cm; W. 31.7cm; D. 29.2cm).

Findings, Case 1:

Using SERRS we identified alizarin, a molecule obtained from the root of the madder plant (Rubia sp.), in a microscopic sample from the red tinted surface of the leather quiver. This is so far the oldest scientifically documented evidence for the use of natural dyes. Madder dye is one of the most stable red dyes and was commonly used from antiquity to the late 19th century, not only as a mordant dye for fabrics, but also as a pigment (properly a lake, a complex of the molecule with an inorganic cation such as aluminium, calcium, or tin).

The ancient Egyptians had mastered the art and science of extracting the dye from the root (the process requires alkali at low temperatures) and precipitating it as a pigment using alum under carefully controlled pH and temperature. This was 4,000 years ago. Older examples of such knowledge surely exist in other museums: with SERRS, we now have a way to find out how far dye chemistry goes back in time – with essentially no impact on the precious archaeological evidence.

Findings, Case 2:

The analysis of the purple robe of the Child showed that lac dye, a colorant extracted from an insect native of South East Asia had been used. This is the first evidence for this colorant in Europe: the fact that it reached southern France from India at the time of the crusades points to the extent and strength of global trade networks. These results – the foundation of our work on the analysis of art – can be translated to other fields, making SERRS more easily applicable in food and cosmetics studies, environmental analysis, and forensic science.

Marco Leona is the David H. Koch Scientist in Charge at the Department of Scientific Research, The Metropolitan Museum of Art, New York, USA.

Understanding Ancient Prescriptions

How the ingredients of Roman medicines can be determined using a multi-analytical approach.

By Rebecca Stacey

The Question

What can analysis of an ancient medicine container tell us about 1st century therapies?

The Object

A Roman multi-compartment bronze medicine container in the collection of the British Museum (BM Cat no. 1968,0626.37). The radiograph shows the individual sections, each of which contains well-preserved residues of the medicinal contents. Few medicine containers from the Roman period survive and this one is the only known example of this multi-compartment form with separate sections that stack together. This container comes from a set of Roman (1st century) surgical instruments in the British Museum collections.

The Challenge

Medicines typically comprise complex mixtures of organic and inorganic ingredients, a combination of active therapeutic substances with fillers and delivery substrates. Active ingredients are likely to be the most expensive (and potentially toxic) components and are therefore more likely be minor constituents. These ingredients are also more likely to be reactive substances vulnerable to loss in archaeological conditions and timescales. This is a frustration because these are key ingredients for inferring the intended past medicinal application. Interpretation of molecular data obtained from these types of sample is further complicated by the alterations that take place in archaeological materials as a result of degradation. Analysis of comparative reference materials and artificial degradation experiments are a routine part of research to characterize such material. In this case experimental simulation of ancient processing methods - the production of Punic wax from beeswax – made a crucial contribution to the interpretation.

The Approach

A multi-analytical approach was adopted to ensure maximum capture of compositional information from the sub-milligram samples available from the medicine residues.

After initial visual examination using optical microscopy, inorganic components were analyzed non-destructively by X-ray fluorescence and Raman spectroscopy. Analysis by gas chromatography - mass spectrometry (GC/MS) was carried out on solvent extracted and hydrolyzed sub-samples prepared both as trimethylsilyl (TMS) and methyl ester derivatives. The separate preparation methods enabled detection of wax, lipid, resin and carbohydrate constituents.

The detection of interesting wax compositions prompted experimental preparation of a beeswax derivative described by Pliny (1st century) as 'Punic wax' and a laboratory protocol was devised to mimic the ancient production method he documents:

'Punic wax is prepared in the following way. Yellow wax is exposed to the wind several times in the open, then it is heated in water taken from the open sea, to which soda has been added. Then they collect with spoons the 'flower', that is, all the whitest parts, and pour into a vessel containing a little cold water. Then it is boiled again by itself in sea water, after which they cool the vessel itself with water. When they have done this three times, they dry the wax in the open, by sunlight and by moonlight, on a mat of rushes'.

The Findings

Archaeological finds of ancient medicines are rare and so our understanding of medicinal treatments in antiquity relies heavily on the accounts of contemporary writers such as Dioscorides (1st century). The few examples of ancient medicine containers with surviving contents thus present an important opportunity to examine primary evidence for ingredients and formulations. The pool of data accumulating from these studies offers scope to investigate ingredients used in different kinds of treatment and to consider their properties and therapeutic value alongside the documentary accounts. It also provides an opportunity to improve our understanding of the preservation of medicinal materials in archaeological environments.

The residues in the different sections of the container all have compositions consistent with ointment preparations: compounds indicative of beeswax, fat/oil, conifer resin, plant gum and possibly pulverised herbs were identified, as well as lead and zinc compounds. The preparations almost

Roman multi-compartment medicine container in the collection of the British Museum (1968,0626.37). The radiograph shows the individual sections of container, each containing residues of the medicinal contents.

certainly contained further medicinally active constituents too volatile or labile to survive archaeologically, so the specific ailments that these ointments were intended to treat cannot be determined with any confidence. Nevertheless, the substances identified here were all considered to have therapeutic value according to the Classical sources. Celsus (1st century), for example, describes wax as discutient, emollient and, along with pine resin, as good for forming flesh and filling in ulcerations. Gums were used to arrest bleeding and agglutinate wounds and to relieve irritation, and fats were considered to be cleansing and emollient. The inorganic components lead and zinc were also valued medicinally: zinc oxide as an exedent, desiccant and extractive, for relief of irritation and as an ingredient in eye salves, and lead in various forms in external treatments. Pliny noted that Punic wax was good for use in medicines but this is the first time that the product has been identified in association with ancient medicinal residues.

The variable composition of the four residues in the multi-compartment container implies that each section contained a different treatment; this is perhaps to be expected given the form of the container, although it is interesting that all of the preparations are all ointment-like.

Rebecca J Stacey is Senior Scientist at the Department of Conservation and Scientific Research, The British Museum.

Further information

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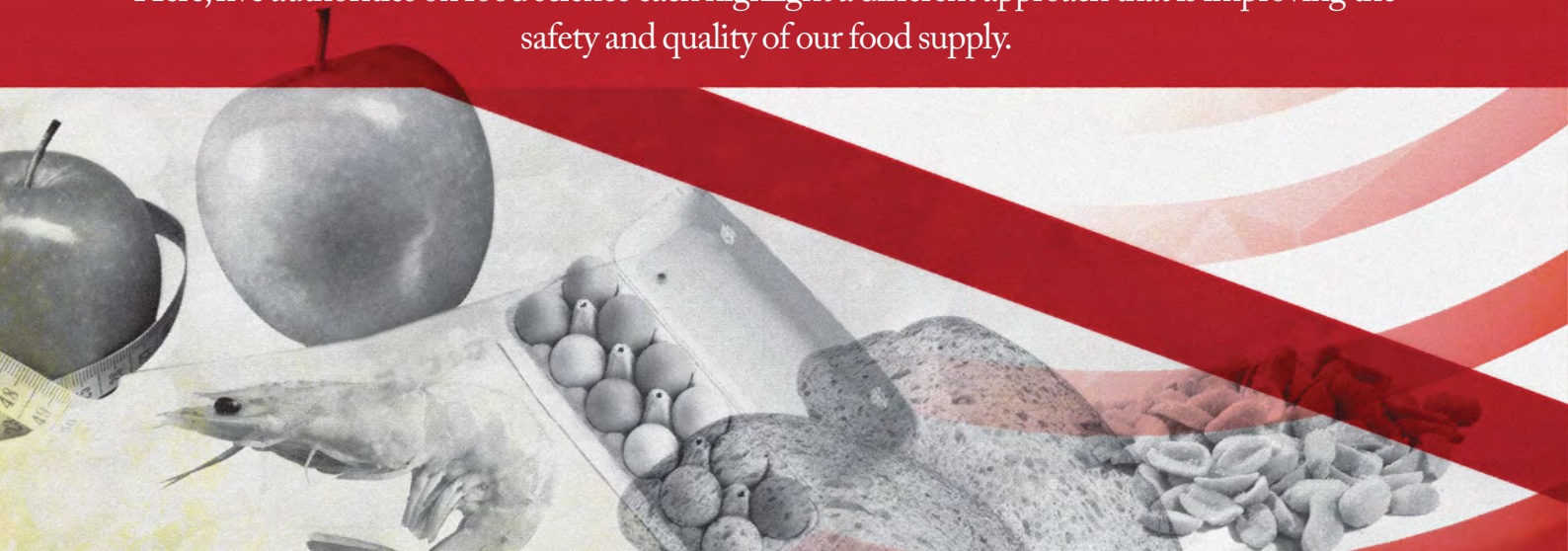
FIVE FRONTIERS IN FOOD ANALYSIS

The food sector grows ever-more complex. Global markets, our increasingly sophisticated palates, a food allergy epidemic, and the increasing focus on the link between diet and health are just some of the factors putting pressure on food analytics. But pressures also bring opportunities. Here, five authorities on food science each highlight a different approach that is improving the safety and quality of our food supply.



1

Non-Targeted Analysis

Recent advancements in analytical chemistry are beginning to highlight not only the potential of technology, but also the need to change how we monitor food in the future.

By Paul Brereton

We analytical chemists are not renowned for having exciting lives. Traditionally, we've been a reactive rather than proactive breed. Tell us what the analyte is and we will design a method that can measure it to the nearest mg, µg, ng, or even pg. We can provide you with a method that is accurate, precise and robust. We can analyze hundreds of your samples and tell you if that analyte is there, and in what quantity. And when you have another set of analytes, we go through the process again and produce further accurate and precise methods to identify and measure them.

Ask us what the problem is, or even if there is a problem, and we are less assured. The more forensic aspects may take us longer to solve; days, weeks, possibly months. One reason for this is that we haven't had a great set of tools available for looking for unexpected analytes. We usually have to rely on a series of experiments to elucidate the analyte and diagnose the problem.

A good example of where analytical chemists were found wanting was melamine contamination of baby food. Here, we didn't know what the problem was – or even that there was a problem – until it was too late. Melamine, a molecule of high nitrogen content, was used by fraudsters to enhance the apparent protein content of foods. The incident highlighted two key problems with the methodology used. First, protein was being measured using an indirect method that analysed the nitrogen content of the food and converted it to apparent protein content through a nitrogen factor. Second, there were no systems in place for measuring unexpected analytes in the sample. Not only was the real protein overestimated, more importantly there was a failure to detect the melamine adulterant – with tragic results.

"Put simply, what analytical chemists really want are rapid methods and systems that can detect and identify analytes that shouldn't be in the sample."

Put simply, what analytical chemists really want are rapid methods and systems that can detect and identify analytes that shouldn't be in the sample. But such information rich systems have not been available... until now.

It is an exciting time for analytical chemists and biochemists because of the step change in technology that is now available. The latest generation of mass spectrometers coupled with state of the art chemo-informatics provide some great tools for us to enhance our forensic capabilities. The next generation of high-resolution LC and GC mass spectrometers using "Time of Flight" technology provide excellent separating power and the ability to identify and quantify analytes in a non-targeted way. When combined with sophisticated chemometric outputs, these instruments have the potential to be used in a profiling mode, much like an infrared spectrometer. The difference being that the spectra are information rich, which allows for more rapid elucidation of the analyte.

At present, such technology is mainly confined to research institutes for discovery and characterisation work. The main stumbling block for greater uptake is the storage and interrogation of the huge data files generated. However, it is starting to be employed within food surveillance where, traditionally, considerable resources have been spent on ensuring that target analytes or multiple analytes are absent from samples. By measuring change in an intelligent way, we can quickly identify abnormal or contaminated samples and provide a much more efficient way of safeguarding and assuring the food supply. Whether undertaking large-scale food safety surveillance or assuring the quality of a globally produced food product, such systems allow us to be much more proactive. Instead of reacting to customer requests, we can now inform the customer of an issue before they are even aware it exists.

Paul Brereton is at The Food and Environment Research Agency, Sand Hutton, North Yorkshire, UK.

2

Foodomics

The integration and application of powerful post-genomic technologies is required for food scientists to meet their latest challenges. Here's how it can be done.

By Alejandro Cifuentes

The first demand in food science is to ensure food safety. Today's global movement of food and related raw materials presents researchers with a new challenge: the threat of worldwide contamination episodes. This is complicated by the fact that many food products contain multiple and processed ingredients shipped from all over the world to share common storage spaces and production lines. As a result, ensuring the safety, quality and traceability of food has never been more complicated or important than it is now. It requires the development of new, more advanced and more powerful analytical strategies.

Another general trend in modern food science is the connection between food and health. Indeed, food is fast being considered not only a source of energy but also an affordable way to prevent future illness. However, to scientifically understand and demonstrate the healthy effects of food and food ingredients, analytical strategies must overcome the challenges of food complexity. There is huge natural variability in foodstuffs, which contain a vast number of different nutrients and bioactive food compounds at a wide range of concentrations. The bioavailability and transformation of these compounds in the human gastrointestinal tract multiplies this complexity, even before consideration of the numerous targets with different affinities and specificities within the human body.

To meet these challenges, researchers in food science are moving from classical analytical methodologies to more advanced strategies, usually borrowing from well-established methods in medical, pharmacological and biotechnological research. In this context, Foodomics (1, 2) – a discipline that studies the food and nutrition domains through the application of advanced omics technologies to improve consumer's well-being, health, and confidence – offers a new approach to food science and nutrition considered unapproachable a few years ago. Foodomics incorporates multiple concepts and approaches, such as nutrigenomics, nutrigenetics, microbiomics, toxicogenomics, nutritranscriptomics, nutriproteomics, nutrimetabolomics.

"Another general trend in modern food science is the connection between food and health. Indeed, food is fast being considered not only a source of energy but also an affordable way to prevent future illness."

These powerful platforms to analyze gene expression, proteins and metabolites must be adequately integrated to extract maximum biological meaning. Examples of this come from our recent studies on the effect of dietary ingredients on the variation of expression of gene, protein and metabolite levels in colon cancer (3) and leukemia cell proliferation. In the latter case, we integrated results from transcriptome and metabolome variations (4). Differences between two leukemia cell lines in the induction of transcription of genes that encode phase II detoxifying and antioxidant genes, as well as in the metabolic profiles, suggest that some dietary polyphenols exert differential chemopreventive effects in leukemia cells of different phenotypes. Foodomics can also help to investigate and solve other crucial topics in food science and nutrition, such as:

- Establishing the global role and functions of the gut microbiome.
- The assessment of unintended effects on genetically modified crops and foods.
- Obtaining sound scientific evidence that supports or refutes the beneficial claims of functional foods and constituents.
- Establishing analytical methods to guarantee food safety, origin, traceability and quality, including:

- The discovery of biomarkers to detect unsafe products
- Understanding the stress adaptation responses of food-borne pathogens
- Early detection of food safety problems before they become global.

• Understanding the molecular basis of biological processes with agronomic and economic relevance, such as the interaction between crops and their pathogens, as well as physicochemical changes that take place during fruit ripening.

I fully expect Foodomics to lead food science and nutrition research into a new era.

Alejandro Cifuentes is full research professor at the Laboratory of Foodomics, Institute of Food Science Research (CIAL), CSIC, Madrid, Spain. a.cifuentes@csic.es

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3

Regulating Food Allergens

Current methods to detect food proteins that cause adverse immune response can, and are, being improved.

By Lauren S. Jackson

Food allergies represent an important health problem in industrialized nations, affecting an estimated 10-12 million people in the US alone (1). Some data indicate that the prevalence of food allergies appears to have risen in recent years, particularly in children (2-4). Preventative medical treatments are not available for individuals with food allergies, so strict avoidance of the allergy-causing food is currently the only means of avoiding a reaction – consumers must rely on accurate labeling of foods. However, allergenic proteins can be introduced into food due to labeling errors, improper handling of rework, cross-contact during and after processing, and incomplete cleaning of food processing equipment (5).

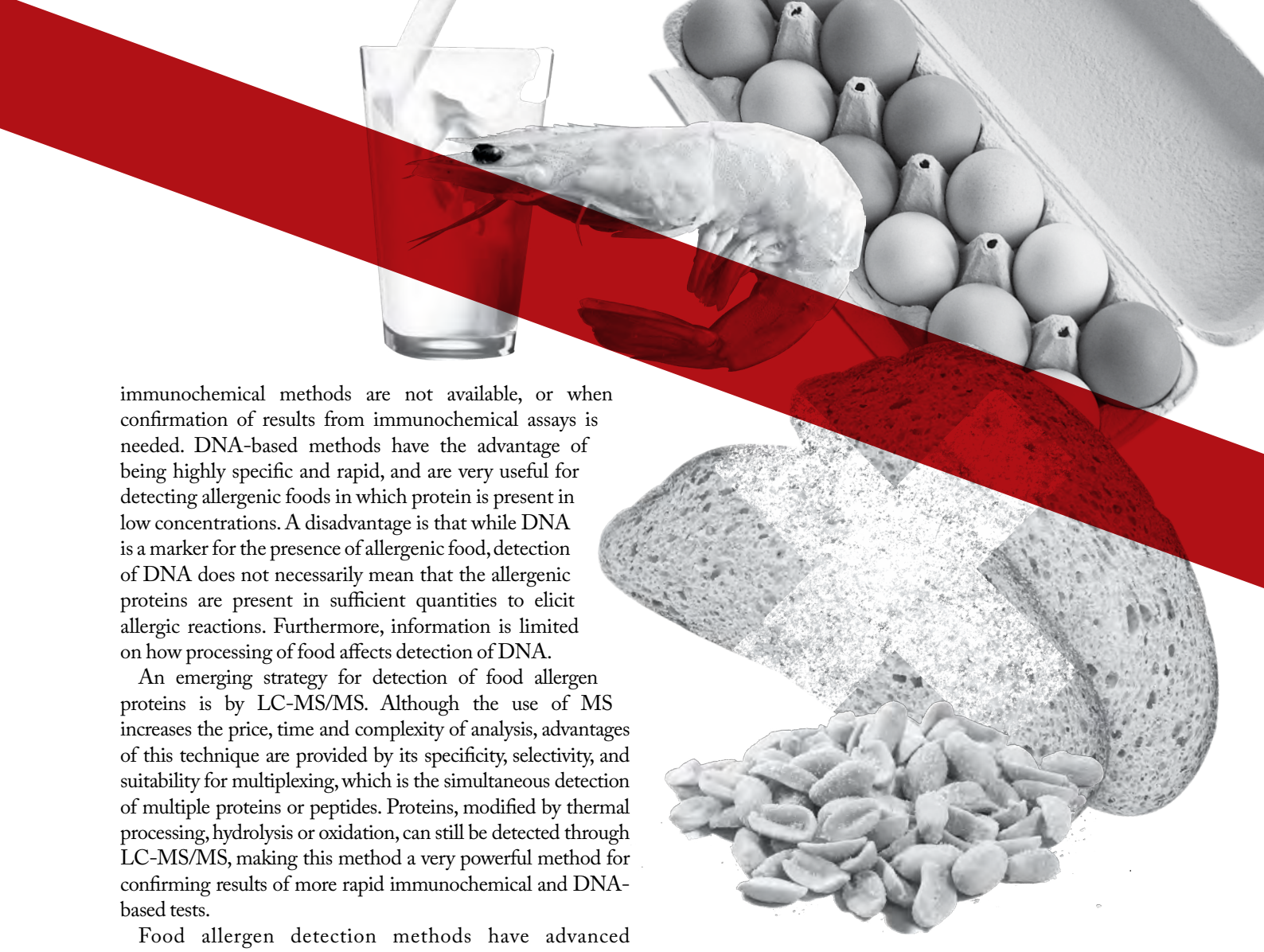
Legislation has been implemented to protect the food-allergic consumer. In the US, the Food Allergen Labeling and Consumer Protection Act (FALCPA) of 2004 requires food labels to clearly state if a food product or ingredient is, or contains, one or more of the eight major allergenic foods, namely milk, peanut, egg, tree nut, soy, wheat, crustacean shellfish and fish. More recent legislation in the US goes even further to protect those individuals with food allergies. The 'Proposed Rule for Preventative Controls for Human Food' issued under the Food Safety Modernization Act (FSMA) proposes that food manufacturing facilities have a written safety plan that requires the identification of preventative controls for food allergens, and establishment of monitoring and verification procedures to ensure that the preventative controls are correctly implemented (6). Analytical methods to detect and quantify the presence of allergens in foods, ingredients and in the food processing environment are essential for establishing and supporting preventative control procedures for the industry, and for development of compliance and enforcement activities for regulatory agencies.

Analytical methods currently used for the detection of potential allergens in foods target either the allergen itself or markers that indicate the presence of the offending food, such as specific proteins, peptides and DNA fragments. However, the ability to detect and quantify these markers is affected by the composition of the food and the manner in which the food has been processed. There are situations where allergens may be present in concentrations that are capable of eliciting allergic reactions, yet are not detectable by established analytical methods because of food matrix components that affect the extraction and detection of analytes (7). In addition, some analytes, particularly proteins, are susceptible to chemical and thermal modifications that occur during food processing, rendering them undetectable with established methods.

"Food allergen detection methods have advanced dramatically in the past ten years, resulting in new strategies, such as LC-MS/MS, and improvements in traditional analyses, for example, immunochemical analysis."

The most commonly used method for detecting and quantifying allergenic or marker proteins are immunochemical in nature, and include enzyme-linked immunosorbent assays (ELISA) and dipsticks or lateral flow devices (LFD). These systems are able to detect and/or quantify most of the eight major allergenic foods and typically have detection limits in the low µg/g (ppm) range. While ELISA assays and dipsticks are generally considered to be accurate, reliable, simple to operate and rapid, they do have drawbacks. Since immunochemical detection is achieved through binding of target protein(s) with antibodies, any changes in the binding properties (immunoreactivity) of the target proteins will influence assay results. Hydrolysis, thermal denaturation, and exposure to oxidizing chemicals, for example, some sanitizers, can change the immunoreactivity and solubility of proteins, and render them undetectable by immunochemical techniques.

DNA-based detection methods are currently used to detect the presence of allergenic foods or ingredients when



immunochemical methods are not available, or when confirmation of results from immunochemical assays is needed. DNA-based methods have the advantage of being highly specific and rapid, and are very useful for detecting allergenic foods in which protein is present in low concentrations. A disadvantage is that while DNA is a marker for the presence of allergenic food, detection of DNA does not necessarily mean that the allergenic proteins are present in sufficient quantities to elicit allergic reactions. Furthermore, information is limited on how processing of food affects detection of DNA.

An emerging strategy for detection of food allergen proteins is by LC-MS/MS. Although the use of MS increases the price, time and complexity of analysis, advantages of this technique are provided by its specificity, selectivity, and suitability for multiplexing, which is the simultaneous detection of multiple proteins or peptides. Proteins, modified by thermal processing, hydrolysis or oxidation, can still be detected through LC-MS/MS, making this method a very powerful method for confirming results of more rapid immunochemical and DNA-based tests.

Food allergen detection methods have advanced dramatically in the past ten years, resulting in new strategies, such as LC-MS/MS, and improvements in traditional analyses, for example, immunochemical analysis. Despite these advances, there are several obstacles that limit the effectiveness of allergen detection methods. Such challenges include the need to characterize how components of the food matrix influence extraction/detection of allergens. There is also a critical need to identify how allergens change during food manufacture to enable selection of the stable allergen marker molecules that survive food processing. Finally, further research is needed to develop appropriate food reference materials that could be used to calibrate allergen detection methods. Overcoming these research challenges will ultimately result in development of more reliable and accurate allergen detection methods that could be used to better protect the food-allergic consumer and for compliance purposes by regulatory agencies.

Lauren S. Jackson is at the Division of Food Processing Science & Technology, Institute for Food Safety and Health, Food and Drug Administration, Bedford Park, IL, USA.

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4

Electronic Senses

Can miniaturization and microfluidic advances take 'taste' and 'smell' to the next level?

By Michele Suman

In food analysis, arrays of gas sensors are termed "E-Noses" while arrays of liquid sensors are referred to as "E-Tongues". The first scientific literature on these systems appeared in the 1980s but it has only been in the last decade, due to the food industry's progressive interest in rapid at- and on-line analysis of product quality and safety, that special attention has been given to emerging technologies in electronic senses.

Taste in humans can be classified into five basic categories: sweet, sour, salty, bitter and umami (borrowed from the Japanese and translated as "pleasant savory"). Unlike taste, smell cannot be easily classified into various groups. Humans can distinguish around 10,000 chemicals, with olfactory receptors being stimulated by different combinations of a limited number of primary odors.

E-Noses and E-Tongues, as their names suggest, are inspired by the neurophysiology of smell and taste and attempt to mimic the abilities of their human counterparts. These technologies automate the evaluation of samples with complex composition and are able to recognize specific properties and characteristics. In animals, sensory information is processed by the neural system. Likewise, data collected through selective sensor arrays must be analyzed by pattern recognition tools that employ various mathematical and statistical processing techniques. Such systems can provide quantitative results and, in some cases, are even able to detect differences that a human sensory panel cannot distinguish.

E-Nose instruments typically exploit four main sensor types: conducting polymers (CP), metal oxide semiconducting (MOS), metal oxide semiconducting field-effect transistors (MOSFET), and oscillating sensors, such as quartz crystal microbalances (QCM). E-Tongue instruments generally use the following analytical solutions: mass sensors, which are miniaturized solid-state devices that exploit the piezoelectric effect; potentiometric methods, for example, ion-selective electrodes; and voltammetric or optical sensors, in which an indicator molecule changes its optical properties when exposed to a target analyte. Hybrid E-Tongues, based on a combination of potentiometry, voltammetry and conductimetry, offer great potential and are the subject of an increasing number of papers.

Concrete applications of the discriminating power exhibited by E-Noses can be found in the analysis of meat flavors, volatile organic compounds (VOCs) formed during post-harvest ripening of fruits, ham product evolution during storage, packaging off-flavors, olive oil defects and the identification of geographical origin of foodstuffs. In the last 10 years, for example, Barilla has been successfully implementing MOS-based E-Noses in different quality control labs to recognize residual solvents and to continuously monitor the various plastic food-packaging materials adopted within bakery production sites. At Barilla, E-Noses are, in fact, used as the first appraiser of packaging quality, which limits the number of gas chromatographic confirmatory analyses required solely to the samples that are marked as uncertain or bad by the MOS instrument.

E-Tongues can be used to monitor and discriminate among mineral water, coffee and soft drink samples. Reported applications of E-Tongues in food analysis cover process monitoring, foodstuff recognition/characterization, evaluation of 'freshness', quality control and authenticity assessments.

Challenges that remain with both E-Nose and E-Tongue technologies are the needs to improve sampling procedures (by reducing clean-up or extraction before analysis, for example) and to reduce carry-over/environmental noise (for instance, in the form of moisture contamination), which affect sensor drift and sensitivity.

It is realistic to imagine that within the next few years, thanks to significant advances in microfluidics and electronics, that E-Nose and E-Tongue technology will evolve both in terms of robustness and reduction in the current need to optimize each application – a process that requires significant investment of time and resources. Miniaturization will further extend flexibility. Beyond food, E-Sense technology may find applications in other industries, for instance in environmental analysis to detect water contamination or illicit drugs; in clinical diagnostics to monitor saliva, sweat or urine; and in agriculture to detect fungal contamination in feed. There is great potential in these applications, in spite of the fact that the term 'E-Tongue' doesn't conjure up a wonderful image in some instances.

Michele Suman is food chemistry & safety research manager in the Research, Development and Quality Department at Barilla, Parma, Italy.

5

Emerging Contaminants

A toxicological point of view can help close off concerns about bioaccumulating compounds, and other natural and man-made contaminants.

By Alberto Mantovani

An emerging contaminant can be a newly recognized entity or a known compound that presents new characteristics or risks. In either case, new analytical approaches may be required to guarantee consumer safety. For example, arsenic speciation is now necessary to discriminate between organic compounds, for example, arsenobetaine in fish, and inorganic arsenic, which is of far greater concern. And organotins, which show significant immune and endocrine toxicity, need to be differentiated from the background tin in foods.

From a food analysis standpoint, emerging contaminants include compounds that are not yet fully integrated into routine monitoring, yet are able to bioaccumulate. Brominated flame retardants and perfluorinated compounds are two such examples.

Bioaccumulating compounds mainly enter the food chain in commodities of animal origin: they are deposited and metabolized in different tissues and in different animal species. Such information informs detection strategies, but bioaccumulation is not always straightforward; for example, perfluorinated compounds are unusual in that their accumulation is unrelated to lipophylicity.

A further complication is that multiple related contaminating compounds can be present in the same food commodity. Take the endocrine-active polybrominate diphenyl ethers (PBDEs) as an example. These comprise over 200 congeners that might be present in fatty foods. As with PCBs, only the most representative 'marker' PBDE congeners are monitored in food and animal feeds. It is equally important to identify compounds or congeners that may be grouped together because of a common mode of action as is the case for dioxin-like compounds, which can be monitored as a group according to their additive mechanism of toxicity, which is interaction with aryl-hydrocarbon receptors. A mechanism-based grouping could also be applied to clusters of the main non-dioxin-like PCB congeners. The most representative PBDEs seem to have analogous toxicological targets, albeit with different potency, so there is potential for additive toxicity and for a more comprehensive test.

On a positive note, I believe that there is great scope for the development of in vitro methods, such as the use of cell lines and biosensors, that target relevant biological activities in foods. Examples include antioxidant potential and steroid receptor transactivation. These tools could contribute to a 'whole food' assessment, incorporating the effects of foreign and natural substances present in the food. From a practical point of view, in vitro methods would aid efficient risk management along food chains, acting as a first-tier screen ahead of targeted chemical analyses. Multi-parameter platforms that provide time-effective responses would be of great value. One can imagine batteries of multiple biosensors targeting different parameters and placed at critical points of the production chain. I envisage that studies on the predictive value, robustness and cost-benefits of in vitro methods for food chain analysis will take off.

"I believe that there is great scope for the development of in vitro methods, such as the use of cell lines and biosensors, that target relevant biological activities in foods."

In conclusion, we are witnessing the development of food analysis integrated with toxicological input. Monitoring emerging contaminants, exposure assessment and trend monitoring is of paramount importance.

Alberto Mantovani works at the Food and Veterinary Toxicology Unit, Department of Food Safety and Veterinary Public Health, Istituto Superiore di Sanità, Italy.

Profession

Leadership
Talent Development
Career Planning

Confronting Conflict

Conflict is a natural and healthy element of communication. Here are constructive strategies to handle it in a positive and supportive way.

By Elizabeth N. Treher

Do you leave work with a knot in the pit of your stomach, worrying about interpersonal conflict between staff members in your lab? Do you get caught between staff members and flounder, not sure whether to intervene or ignore the situation? Do you tend to see the positive side of conflict or does the mere thought of tackling a problem make you want to call in sick?

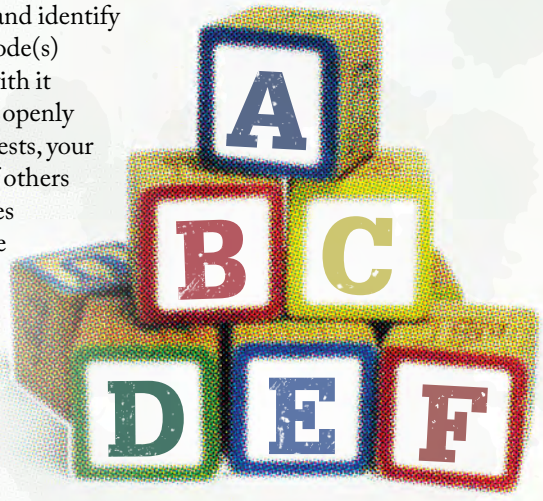
Conflict can arise from many sources in organizations. You may face 'internal conflict' between responsibilities of your work and family, or other personal demands. As a manager, you may experience 'interpersonal conflict' between two of your staff, or 'hierarchical conflict' between you and a staff member. You may struggle to manage an individual who was formerly a peer and close friend. There may be 'organizational conflict' between departments or companies.

As long as conflict is not resolved, organizations and those who work in them will feel the impact. Thomas Crum (1) teaches that by replacing reflexive, unconscious "I win - you lose" reactions to conflict with conscious "you and I" approaches, we can capitalize on conflict to achieve goals and objectives.

Most of us have one or two preferred ways of dealing with conflict that we rely on too heavily (see The Five Approaches to Managing Conflict). There are many questionnaires to help you assess your conflict management style, such as the Thomas Kilmann Conflict Inventory (2). The terms used in the assessments vary, but the styles are generally consistent with the five-mode conflict resolution model developed by Robert Blake and Jane Mouton (3). It shows conflict styles based on assertiveness and cooperativeness. Moving from low to high on the cooperativeness and assertiveness scales leads to an increasingly collaborative mode of conflict resolution.

Conflict resolution A, B, Cs:

Analyze the conflict and identify the best resolution mode(s)
Be prepared to deal with it
Confront the conflict openly
Determine your interests, your position, and those of others
Expand on alternatives
Facilitate an exchange of information



Improving Conflict Resolution Skills

In conflict situations, understandings, feelings, perceptions and assumptions all come into play. Perspectives differ and assumptions interfere. As hard as it may be when you are sure you are in the right, you will benefit if you listen and try to understand the concerns of others. Peter Drucker put it perfectly when he said, "The most important thing in communication is hearing what isn't said."

Ideally, conflicts should be managed face-to-face, to use as many

communication "channels" as possible. Communication is enhanced when we use multiple senses. This means that leaving a voice mail message or sending an email or text message are typically not as effective as face-to-face communication, where there is opportunity for questions and feedback. To guide your approach, see 'Quick Six to Resolving Conflict', page 42.

Remember, conflict is a state and conflict resolution is a process. Making assumptions about another's perspectives does not lead to resolving conflict and may make it worse. Managers can easily provoke defensive communication simply by making comments based on their own assumptions. For example, when you provide feedback to an employee, which of the following comments is least likely to create conflict?

1. a. You were disruptive during our meeting today.
   b. You interrupted Alison and Jim several times during the meeting.
2. a. Your lab work was sloppy and careless, so we have to redo all the tests.
   b. By omitting the second step, you didn't follow the SOP, so we have to redo all the tests.

Answer 'b' is the approach least likely to create conflict in both cases, but what is the real difference between the two statements in each example? Answer 'a' is an interpretation of events – your conclusion, not an observation. Answer 'b' provides specific observations that are also available to others.

In the first example, the employee may feel he or she was being helpful by interrupting to share information that Alison and Jim may have needed but did not have. An accusation of being disruptive may well cause an unpleasant emotional response – and unnecessary conflict; it will not help to resolve the issue of concern. And by using terms like "sloppy and

The Five Approaches to Managing Conflict

Thinking about your own approach to managing conflict, do you typically:

1. Tend to ignore the signs of conflict, hoping the issues will resolve themselves over time.
2. Allow others to 'win' in conflict situations, so you can avoid confrontation.
3. Stand strong, perhaps forcing others to back down, until you get your way.
4. Try to identify the issues and work toward a solution where everyone involved gives a little.
5. Take the time to work with others to solve the conflict together, even finding solutions not considered initially.

The five questions above each link to a specific approach to conflict. They are:

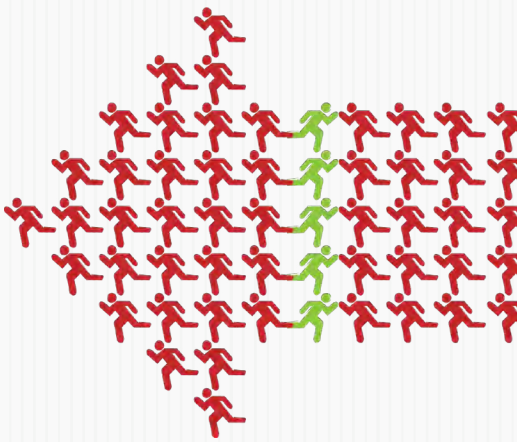
1.Avoid
Avoiding is useful when you have other more important issues or someone else is better able to handle the conflict. In those cases, it makes sense to withdraw. In some conflict resolution publications, avoiding is suggested as a good response to buy time for cooling off. Research since has shown that many people never follow up after they cool down, and the conflict is not resolved. If you take time to calm down, don't forget that you haven't resolved the conflict.

2.Accommodate or Smooth
Accommodating can be useful when you want an employee to learn from his/her mistake. It is a style where you stand back or pretend there are no issues and can be a way to support your employees.

3.Compete
Situations needing fast, decisive actions call for a competing style where you push for your own way and control the situation. Emergencies, for example, generally call for quick thinking and action.

4.Compromise
With a compromise, both parties settle for less. Compromises are appropriate if you need a solution where time does not permit or warrant collaboration. It can also provide a temporary solution to buy time to further explore the conflict and collaborate.

5.Collaborate or Integrate
Collaboration takes the most time, and the goal is a win-win. It is useful when you need everyone involved fully committed to the solution, and the situation warrants spending enough time to achieve an integrated solution fully agreeable to all. Studies show that the integrating or collaborating style is clearly related to positive outcomes in the widest range of situations.



Quick Six to Resolving Conflict

1. Focus your attention.
   - Look for key points and underlying goals or principles.
   - Avoid evaluating or judging; keep an open mind.
   - Prove you are listening with non-verbal signs.
   - Listen between the lines; pay attention to voice inflection, rate of speech, and non-verbal cues.
   - Take notes to capture key words and ideas, and refer to them.

2. Avoid Assumptions
   - Summarize to check for understanding.
   - Ask questions to clarify/amplify.

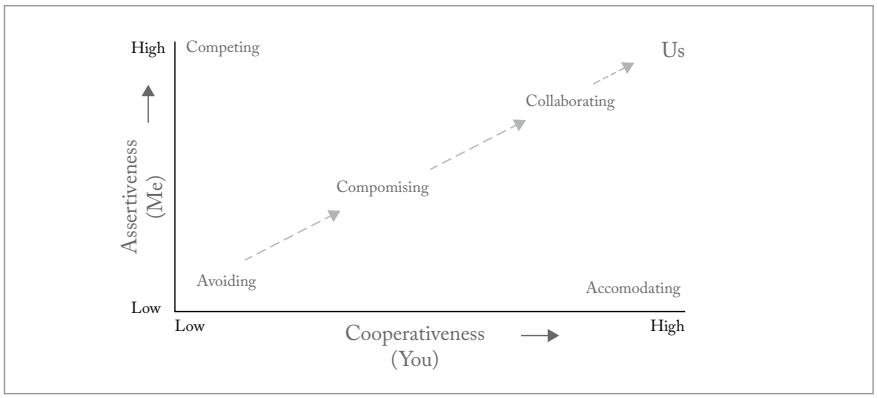
3. Separate the people from the problem. Focus on "what" not "you."

4. Focus on interests, not positions. Interests are the unspoken driving force behind demands and positions. Identifying interests opens the way for resolving conflict. Ask questions to challenge your assumptions; be willing to listen to understand other's concerns and interests.

5. Explore options for mutual benefit. In thinking about positions (yours and others), look for underlying interests. Which are most important?

6. Identify an overarching principle or standard to help shift conflict to a broader perspective. Examples include, "It's better to settle this between ourselves than go to our manager" and "Accuracy has the highest priority".

(3-6 from the book "Getting to Yes" (7))



Five Modes of Resolving Conflicts

careless," you escalate the situation and perhaps set yourself up to have to deal with a disgruntled employee. It certainly won't help foster a teachable moment.

To improve your skills, first take the time to jot down the feedback you plan to provide. Ask yourself, "How do I know this happened?" or "What behaviors did I see or hear?". Sharing observations, rather than conclusions, goes a long way towards preventing defensiveness and avoiding unneeded conflict.

Other attitudes that lead to defensive reactions include attempts to evaluate, control, or manipulate, and appearing cold, aloof, or superior. The greatest barrier to effective communication has been described as the tendency to judge, evaluate, and approve or disapprove what another person is saying, therefore misunderstanding or not really hearing (4).

Managing conflict requires the ability to bridge vocabulary differences, respect new frames of reference, listen to the perspectives of those from other disciplines or specialties, and go outside your area of expertise – tasks that many individuals find difficult. If someone is angry, find out what he or she wants you to do.

Effective conflict management is an important skill in managing a team (5, 6). Yet, few of us actively examine our own approaches to conflict. Accept the need, and make the effort to broaden your reactions and approaches to dealing with conflict.

Liz Treher is CEO and founder of The Learning Key in Washington Crossing, Pennsylvania, USA. Join her on March 19 at Pittcon 2013 at Short Course #141 to learn more about conflict resolution and discuss your own challenges.

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2. *T. Kilmann, The Thomas Kilmann Conflict Inventory, CPP, Inc.*
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6. *R. Peterson and K. J. Behfar, "The dynamic relationship between performance feedback, trust, and conflict in groups: A longitudinal study", Organizational Behavior and Human Decision Processes, 92,102–112 (2003).*
7. *Fisher, R. & Ury, W., Getting to Yes, Negotiating Agreement Without Giving In. Houghton Mifflin Company, 1981.*

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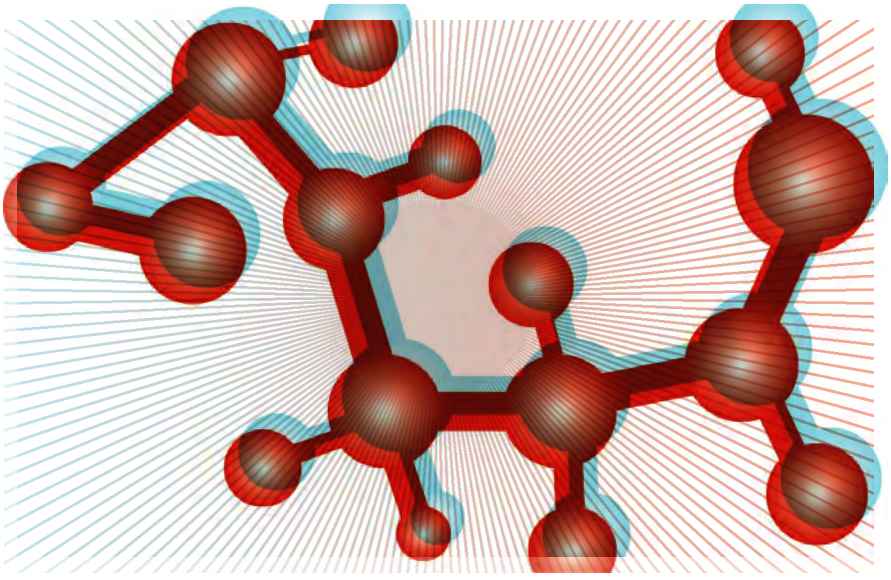
Overcoming Chemical Prejudice

A Pfizer structure elucidation scientist teams up with Bruker's software programmers to go 3D.

By Don Richards



The Problem

The number of potential formulae for unknown impurities can be huge. How can this list be intelligently reduced without relying on assumptions based on what we think is known?

Background

In my role at Pfizer, I worked in a team responsible for the structure elucidation of unknown impurities in pharmaceuticals using LC-MS and NMR, which usually presented themselves as small peaks in HPLC. Accurate mass measurements allow formulae to be predicted but the list of possibilities is often long, so there is a need to decide which possibilities to consider first. There is a great temptation to use chemical knowledge, such as the formula of the main component or its synthetic route to reduce this list, which is referred to as using chemical intelligence. A less polite description is chemical prejudice.

A good example springs to mind. The task was to identify a small impurity in an intravenous solution of an antifungal drug. Amongst the list of formulae predicted by accurate mass measurement was a formula containing a large number of oxygen atoms—many more than were in the formula of the drug. The MS/MS spectra of the drug and the impurity indicated that the impurity was drug related. The formula containing many oxygen atoms was abandoned, and I was unable to solve the structure.

Some months later, when others had toiled to isolate sufficient material for NMR, the impurity was found to be a sugar derivative of the drug molecule. The formula containing the large number of oxygen atoms was the correct one.

I decided there must be a more objective way of deciding on which formula from a long list of possibilities is the correct one rather than relying on chemical prejudice. Whether my need for more objective decision making was driven by ever-increasing demands for efficiency and productivity or the avoidance of professional embarrassment, I would not like to say.

The use of MS/MS seemed a good place to start since we were able to acquire data with the same high mass accuracy as for the parent ion. The correct formula for each fragment must be a subset of the correct formula for the parent ion. I tried to apply this logic to eliminate parent ion formulae that were inconsistent with the possibilities for all fragment ions. Even with this level of effort the list remained stubbornly long. For example, a parent ion with 10 possible formulae made up of five fragment ions (each with 10 possible formulae) requires 500 comparisons to be made. It was clear that this strategy was

likely to reduce efficiency or productivity if applied routinely.

Greater mass accuracy would of course shorten the list of formulae. I calculated that a mass accuracy of 0.03 milliDaltons (30 microDaltons!) would be required to produce only one formula for reserpine (m/z = 609). This was and still is far beyond the capability of the instruments available. Matching the theoretical isotope pattern of the possible formulae with the observed pattern was another possible approach. This proved to be trivial when chlorine or bromine were present but, for C, H, N, O, F and even S combinations, the fits were very poor

During the 2004 ASMS conference in Nashville, I bumped into Bruker's Ian Sanders, who wanted to introduce the new MicroTof. Ian proudly told me about its excellent isotopic fidelity. The isotope patterns in the spectra were indistinguishable from the theoretical simulations; using the isotope fit on this instrument for the parent ion would clearly be an advantage in reducing my stubborn lists of formulae. I decided to do a blind test on some typical drug samples to assess the MicroTof and was very impressed with the results.

Certainly, the MS/MS and isotope approaches were both able to reduce the lists of possible formulae, but they were mutually exclusive. Our QStar Pulsar had excellent MS and MS/MS measurement capabilities, but it had poor isotopic fidelity. While the MicroTof had excellent isotopic fidelity but was not capable of MS/MS measurements. Therefore, neither of these parallel approaches was able to deliver what we really needed. But what if they could be combined?

The Solution

In the tender process for a new mass spectrometer, we had placed high mass accuracy in MS and MS/MS and high isotopic fidelity at the top of our 'most wanted' list. Our need for mass accuracy was easily understood, but what the vendor applications chemists thought of my apparent obsession with measuring isotope ratios, I do not know.

I had previously explained to Ian my idea to combine accurate mass measurements, isotope pattern and fragment information into what I was now calling the Molecular Formula Machine.

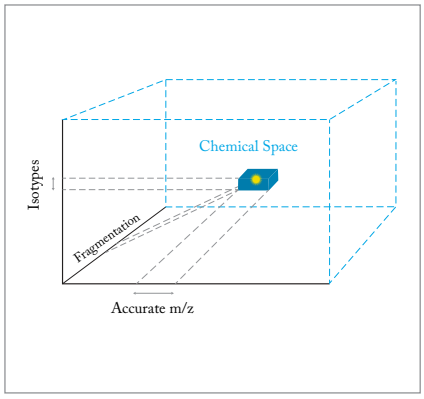


Fig 1: The correct formula resides in a 3D chemical space along with many other incorrect formulae. The space can be investigated by accurate mass measurement, which slices through in one dimension creating a band of possibilities. If we then investigate using isotope measurements, we slice again but through a second dimension. Using fragmentation to slice through the third dimension, we can create a cube containing the correct formula and very few other possibilities.

At the Bruker MicroTof Q evaluation, Ian introduced me to Ilmari Krebs, a software programmer but perhaps more importantly a very able analytical chemist. He immediately understood what I wanted to do and said with typical modesty that he may be able to help. Within a short time he had produced a rudimentary program using excel spreadsheets.

Then disaster struck: our funding for the new instrument was withdrawn because of a more urgent need elsewhere. Fortunately, Ian could see the value in the 3D approach to formula determination and was able to provide a MicroTof to allow the work to continue. This was the beginning of a formal and very fruitful collaboration with Bruker.

The MicroTof did not allow MS/MS measurements and the use of 'In source CID' can be misleading—ions of lower m/z than the parent ion originating in the source are more likely to be the result of ion-molecule reactions than CID, so their use in unknown structure elucidation is a very risky business. To ensure that we only considered 'In source CID' ions equivalent to true MS/MS ions, we used our QStar to determine the true MS/MS spectra. This meant repeating everything on the QStar to select ions for the MS/MS dimension. Though it was an onerous task it proved to be a very fortunate one. The program had to be written to allow selection of the MS/MS peaks that must be explained in the correct formula. This would later prove to be invaluable as it allowed us to process the data for low intensity ions with larger m/z measurement errors and whose isotope patterns may be incomplete or distorted as a result of low s/n, but to use only the most intense peaks to eliminate incorrect formulae. Had the MicroTof–Q been available to us immediately, we may not have implemented this feature to prevent smaller, less well-measured peaks to influence the result without eliminating them altogether by applying a data threshold. Smaller peaks can be very important in determining the structure of the molecule at a later stage.

Our budget for the new instrument purchase was restored the following year. On a visit to Bruker to discuss the Molecular Formula Machine, Ian showed me an instrument so new that it didn't even have a name. And it was clear that it would have superior resolution

and mass accuracy performance – an "Enhanced MicroTof-Q". I placed an order and was the first customer to take delivery of the Maxis.

Beyond the Solution

The Molecular Formula Machine became known as Smartformula3D. The combination of the new Maxis and software meant that our lists were often reduced to a single correct formula. Fragment ion formulae were provided as bi-products, which gave us a flying start with structure elucidation. It became so successful and reliable that when one of my NMR colleagues was given a formula to work with she would ask if it was from Smartformula3D and treat the formula with healthy suspicion if it was not. The only downside to this success was that my colleagues would walk past the QStar to form a queue at the Maxis. While I had great affection for the Qstar, I had been promoted to Head of Structure Elucidation and could not justify keeping it for my own infrequent visits to the lab. It was donated to the University of Sheffield—another cloud with a silver lining, I hope.

My colleague Richard Joyce provided a beautiful illustration of our success when he was asked to determine the structure of a small HPLC peak arising from the synthesis of a relatively small molecule using a rhodium catalyst. Accurate mass measurement suggested only one possible formula: $C_{11}H_{27}N_4O_5^+$, but Smartformula3D gave no result. Had it failed? The mass error on the one proposed formula was larger than we would expect from the Maxis, so I suggested that he try allowing for the presence of sulphur and fluorine. Smartformula3D was again unable to produce a result. He then tried phosphorus and Smartformula3D produced a single formula: $C_{11}H_{27}N_4O_5^+$, with a very small accurate mass error. Very quickly, Richard was able to elucidate the structure of the impurity (see Figure 2).

Where did the phosphorus come from? When reporting the structure to the chemist, the reply came: "Oh, that will be the catalyst!" (see figure 3).

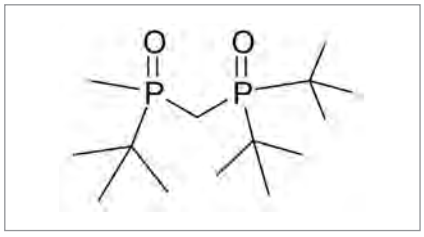


Fig 2: Impurity

I think I can claim success with this solution. There has certainly been an increase in efficiency and productivity, as well as considerably less potential for professional embarrassment…

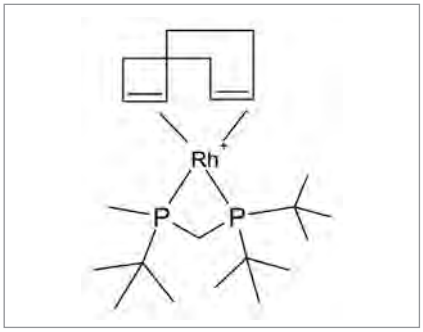


Fig 3: Catalyst

Today, the flagship of the Structure Elucidation Team at Pfizer is an LC-NMR-MS system incorporating a 600MHz Cryo-cooled NMR and a MicroTof-Q2. Rosalind Richards has perfected the use of Smartformula3D in fully deuterated conditions. And the structural information yield is truly phenomenal. But that's another story.

Don Richards is Director of Integrated Characterisation Solutions at Bruker. www.bruker.com

2003

Definition of problem, example of failure to predict correct formula.

2004

September
ASMS Nashville; Ian Sander introduces me to MicroTof and Sigma fit of isotopes.
October
Samples sent for evaluation.

2005

January
Molecular Formula Machine (MFM) concept born.

2006

March
Instrument evaluation, meet Ilmari Krebs, loss of funding, loan of MicroTof. Formal collaboration with Bruker begins.

2007

May
Enhanced MicroTofQ ordered.
September
MFM presented at BMSS Annual Meeting.
November
MFM embedded into data analysis and named.

2008

September
Maxis/ Smartformula3D (SF3D) presentation at BMSS concluded project.

2009

January
Rosalind Richards develops method for the use of SF3D in fully deuterated conditions for LC-NMR-MS.

Extraction of 'Bath Salts' (Substituted Cathinones) from Human Urine using ISOLUTE® SLE+ Columns prior to GC-MS Analysis

Rhys Jones, Gavin Jones, Biotage, Cardiff, UK

This sample preparation method to extract and analyze 'Bath Salts' uses ISOLUTE SLE+, a Supported Liquid Extraction product, that offers an efficient alternative to traditional liquid–liquid extraction (LLE) for bioanalytical sample preparation, providing high analyte recoveries, no emulsion formation, and significantly reduced sample preparation time. Analyte recoveries achieved using this method ranged from 87–99% with RSDs below 10% for all analytes and linearity in the range of 5–250 ng/mL.

Introduction

'Bath salts' is the street name for a family of designer drugs chemically similar to cathinones that give the user similar effects to amphetamines. The abuse of these drugs is on the increase and regulation against their use and supply has now been implemented in the EU and North America.

Method

Column configuration: ISOLUTE SLE+ 1 mL Sample Volume column, part number 820-0140-C

Sample pre-treatment: Dilute urine 1:1 (v/v) with 150 mM ammonium hydroxide.

Sample loading: Load the pre-treated sample (1 mL total volume) onto the column and apply a pulse of vacuum (VacMaster 20 Sample Processing Manifold, 121-2016) or positive pressure (PRESSURE+ 48 Positive Pressure Manifold, PPM-48) to initiate flow. Allow the sample to adsorb for 5 minutes.

Analyte extraction: Apply MTBE (2 mL) and allow to flow under gravity for 5 minutes. Apply a further aliquot of MTBE (2 mL) and allow to flow under gravity for another 5 minutes. Apply vacuum or positive pressure to pull through any remaining extraction solvent, collecting into a glass culture tube containing 0.2 M hydrochloric acid (100 µL) to add stability during evaporation.

Post extraction: Evaporate the extract to dryness (ambient temperature). Add pentafluoropropionic acid anhydride (PFPA) (50 µL) and ethyl acetate (50 µL) for derivatization. Vortex for 20 seconds, transfer to a high recovery glass vial and cap with a non-split cap. Heat vial in a heating block (70 °C) for 20 minutes. Remove vial and allow to cool. Evaporate the mixture to dryness (ambient temperature). Reconstitute in dichloromethane:isopropanol (95:5, v/v) (100 µL). Cap with a non-split cap and vortex for 30 seconds.

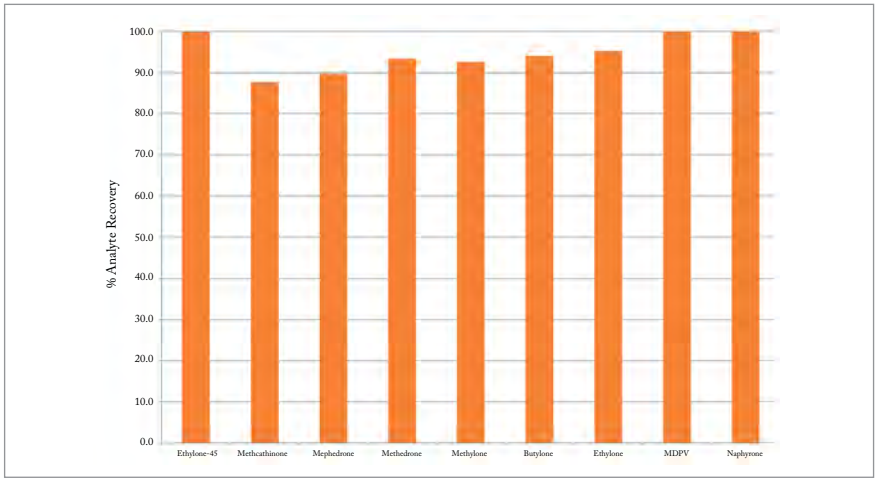


Fig 1: Typical analyte % recoveries for a range of extracted bath salts (n=7) using the ISOLUTE SLE+ protocol

Results

Extracted samples were quantified using an Agilent GCMS (7890A/5975) with an SGE capillary column (30mx0.25mmx0.25µm). Analyte recoveries achieved were 87-99% (n=7) with RSDs below 10% for all analytes and linearity in the range of 5-250 ng/mL with an r^2 coefficient of 0.99.

Analyte	LOQ (ng/mL)
Methcathinone	5
Mephedrone	10
Methedrone	5
Methylone	5
Butylone	10
Ethylone	10
MDPV	5
Naphyrone	10

Table 1: Limits of Quantitation for extracted bath salts using the ISOLUTE SLE+ protocol

Conclusion

This method shows that ISOLUTE SLE+ is well suited in efficient clean up and extraction of these new substituted cathinone drugs from urine, giving high analyte recoveries and low quantitation limits.

For more information, please see the full application note at: theanalyticalscientist.com/issues/0213/701

Saccharide and Polysaccharide Analysis

Polysaccharides are very important in nature, occurring in food (starches in rice, wheat etc.) and plants (cellulose). Some polysaccharides are also produced commercially e.g. Dextrans, which are manufactured through the fermentation of sugar solutions. These are higher molar mass polysaccharides.

Dextrans are used in clinical and technical applications, where molecular weight is critical in determining the properties of the final product. Accurate determination of the molecular weight distribution is vital.

Experimental Conditions:

Eluent:	$NaNO_3$ 0.1M
Columns:	PSS SUPREMA 5 µm 3 x 100Å (8 x 300 mm) + precolumn
Data acquisition:	PSS WinGPC UniChrom
Detectors:	SECcurity GPC 1200 RI
Flow-rate:	0.25 ml/min
Concentration:	4 g/l
Injection volume:	5 µl
Sample Fig 1:	Dextran T1, Glucose
Sample Fig 2:	Disaccharides

On the other hand, low molar mass saccharides are also very common in food, such as fruits, honey and sweets. Examples for low molar mass sugars are mono- (glucose, fructose), di- (lactose, isomaltose, trehalose) and trisaccharides (maltotriose, isomaltotriose). The separation and identification of low molar mass polysaccharides is a challenge as the compounds have the same chemical formula and only small differences in structure, e.g disaccharides maltose, isomaltose, gentiobiose cellobiose and trehalose $C_{12}H_{22}O_{11}$.

Results & Discussion

A high resolution and therefore a good separation on the column is necessary for precise analysis. This is particularly important when new analytical LC coupling methods like GPC/SEC-ESI-MS are used, as the MS detector requires the columns to have a much higher resolution power within an overall smaller column volume.

The new SUPREMA column, with a reduced particle size of 5µm, offers a significant improvement in performance compared to 10µm materials and provides outstanding additional resolution, especially in the low molecular weight area, which is a major consideration when analyzing oligomeric polysaccharides.

The analysis of dextran T1 shows the separation power when a combination of three SUPREMA 5µm 100Å columns is used. The oligomers in the low molecular weight are able to be resolved up to P10. A glucose separation is overlaid, as a reference.

The analysis of different disaccharides shows the ability to separate compounds with the same chemical formula and with only small differences in structure and hence size in solution.

PSS SUPREMA 5 µm columns can be used for numerous neutral and anionic aqueous applications in the molecular weight area between 100 Da to around 5 million Da. The columns are available in analytical (ID: 8mm) and micro (ID: 4.6mm) dimensions with different porosities. Linear or mixed columns are also available.

For more information, please see the full application note at: theanalyticalscientist.com/issues/0213/702

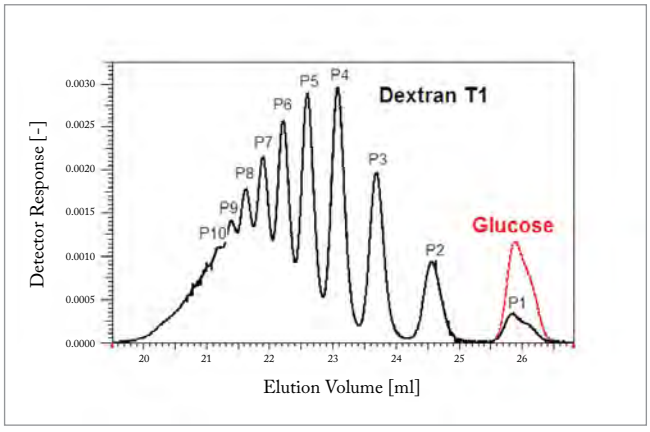


Fig 1: Overlay of elugrams of a glucose (red curve) with a low molar mass Dextran T1 (black curve)

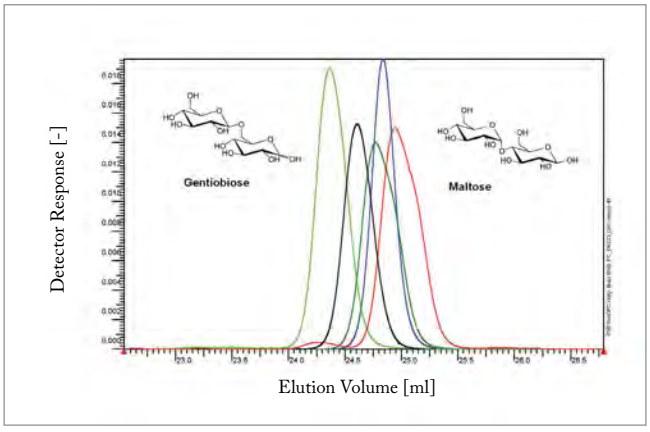


Fig 2: Overlay of elugrams of isomaltose (black), maltose (red), gentiobiose (green), cellobiose (dark green) and trehalose (blue).

Analysis of Synthetic Oligomers and Polymers

New roles and applications in the areas of science & technology are continuously being found for synthetic polymers. As the applications of synthetic polymers increase, there is a need for methods to accurately, precisely characterize these materials.

The utility of size exclusion chromatography (SEC or gel permeation chromatography, GPC) for synthesis monitoring and oligomeric analysis makes it an invaluable tool for characterizing synthetic polymeric material for use in medicine, as these materials require thorough characterization. The synthesis of two PEGylated synthetic polymers intended for use in medical applications was monitored and the oligomeric content was analyzed on an EcoSEC GPC System equipped with a column bank consisting of two 6.0 mm ID × 15 cm, 3 µm TSKgel® SuperH3000 columns.

The synthesis process was analyzed by comparing the SECchromatograms of the two PEGylated polymers with that of one of the starting materials. From this comparison it was concluded that starting material remained in one of the PEGylated samples, PEG-A, and was absent in the other PEGylated sample, PEG-B (Figure 1). The SEC chromatograms of the PEGylated polymers also provided indication of differences in the molar mass distribution between the two PEGylated samples. Additionally, based on the peak-average molar masses Mp the oligomeric content of the two PEGylated polymers were shown to differ, with PEG-A containing mainly oligomeric species and PEG-B containing both low- and high-molar mass species.

Isocyanates are both highly reactive and highly toxic low molar mass chemicals. One comon technique used to take advantage of isocyanate reactivity while eliminating safety concerns is to synthesize polyurethane prepolymers for use in subsequent polymerizations. The physical properties of the resultant polymer are influenced to a large degree by the size of the polyol chains in the prepolymer. Harder polymers are formed with larger polyol chains and softer polymers are formed with smaller polyol chains. The molar mass and molar mass averages of an isocyanate modified polyurethane prepolymer (IMPP) with residual dimethyl sulfoxide (DMSO) were measured with an EcoSEC GPC System with a refractive index detector using a column bank consisting of two TSKgel SuperH3000 columns and tetrahydrofuran (THF) as mobile phase.

The low dead volume of the EcoSEC GPC System combined with the use of semi-micro GPC columns allowed for an efficient separation and characterization of the prepolymer sample in less than hour. The molar mass averages and polydispersity index of the IMPP sample was determined using a polystyrene relative calibration curve. The chromatogram of the IMPP displayed twelve distinctive peaks. Peaks 1 through 5 were determined to be the urethane prepolymer component of the IMPP. The sample was analyzed at two different chromatographic flow rates, 0.3 and 0.6 mL/min. The flow rate of 0.6 mL/min (Figure 2) compared to that of 0.3 mL/min resulted in a decrease in analysis time from 45 minutes to 22 minutes.

References: Amandaa K. Brewer, Ph.D.

For more information, please see the full application note at: theanalyticalscientist.com/issues/0213/703

TOSOH

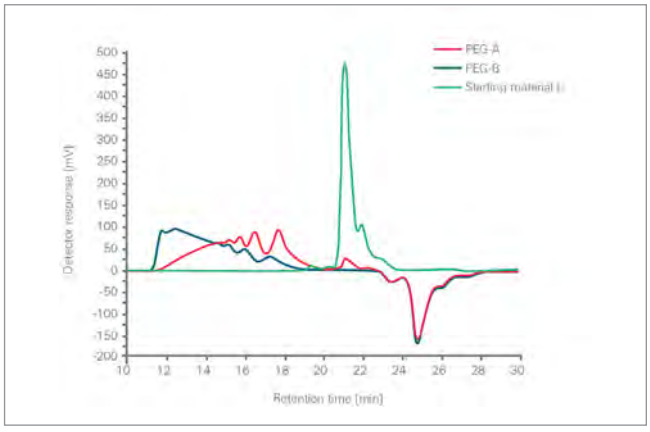


Fig 1: Synthesis monitoring of pegylated polymers. Elution profile of PEG-A (red), PEG-B (blue), and starting material c (green) monitored by ri detection at 0.3 Ml/min in THF at 35°c

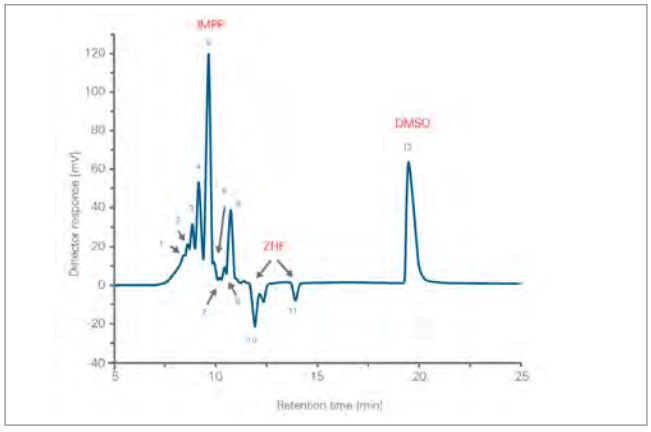


Fig 2: GPC elution profile of impp sample. Monitored by ri detection at 0.6 Ml/min in THF at 35 °c.

Connecting Separation Science

Sitting Down With **Pat Sandra,** Chairman of the Research Institute for Chromatography and Emeritus Professor of Organic Chemistry, University of Ghent

You coupled an academic career with running a commercial operation. What's more exciting to you, blue skies research or solving a practical industrial problem?

I have never been a scientist who has developed things that could not be applied. At RIC, we try to combine good science with business, but scientific quality is paramount and if you start there, the business works out fine. I approached my academic position in a very similar way – being very precise in selecting what to develop and implement, and tackling real practical problems.

Is this a way of focusing science and making it much more relevant?

Not really, I think you need both basic and applied research. But in analytical chemistry, the first task is to solve problems. You should only develop things if you need them or if you cannot provide a solution. I have a bit of a problem with some of the recent literature: there are too many publications on things that will never be applied, either because they are too complicated or because they are not using state-of-the-art instrumentation.

How did RIC come about? It was unusual for the 1980s.

Yes, at that time it was extremely unusual for university staff to have contact with industry – it was not appreciated. But analytical chemistry is partly about problems in industry and I decided to start the institute to handle more of those challenges. A special arrangement was made: the university allowed me to take two years sabbatical leave to start RIC. After that time, they offered me a 50% professor position, which was ideal.

One of the great advantages is that most of the staff are my ex-students. At least 10 of them work at RIC today, which illustrates the high level of our research. They are all happy to work on challenging problems and know that when we start on a project, we keep going until we find a solution.

"I have a bit of a problem with some of the recent literature: there are too many publications on things that will never be applied"

What niche did RIC carve out?

Initially, the company was intended to be a small consultancy, with no involvement in developing instruments, after-sales support and so on. But, on the request of industry, it became all of those things. We began developing methodologies that often combined instruments from different manufacturers. But if there was a problem for the customer, the companies would blame each other. So we took over full responsibility: we developed the method, provided the instrumentation and service, transferred know-how and followed up continuously to ensure that the data was always very good. This complete service became one of the success stories of the institute.

Looking at analytical science today, if you could change three things, what would they be, and why?

First, the new generation should try to understand better what they are doing. They don't know or remember the fundamentals, making it difficult for them to make good selections.

Second, companies are now so pushed into doing marketing that it sometimes seems more important to them than the science. That's a little bit shocking.

Third, there is a problem with software. You can't operate a system without spending a day with the software manual; each instrument and manufacturer have their own software, which is frustrating – it should be uniform across all the analytical techniques to make it easier. Thirty years ago, I could work with all the instruments immediately without any problem. It was all so logical. But now all the logic is in the software and not on the instrument. This connects back to the first problem: I see my students at the university spending much more time on the computer than on the instrument. In my day, it was completely the reverse.

What's really exciting to you in the field at the moment?

Despite what I said above, instrumentation today is extremely powerful; especially the hyphenation of chromatography and mass spectrometry. Chromatography is doing well, although we presently struggle with all the different columns and column formats in liquid chromatography. We only need a dozen of high quality columns like we have in GC. Once that issue is resolved, we will have all the tools: sensitivity and selectivity, good chromatography and excellent mass spectroscopy. In my opinion, the bottle-neck that needs attention is sample preparation. It's not easy. In all fields – food analysis, environmental analysis, pharmaceutical analysis, even in the life sciences – we should concentrate on good sample preparation, which if at all possible should be automated.

To hear about Pat Sandra's most memorable projects, and the highlight of his career, see the video at theanalyticalscientist.com/issues/0213/702

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