OCTOBER 2013 # 09

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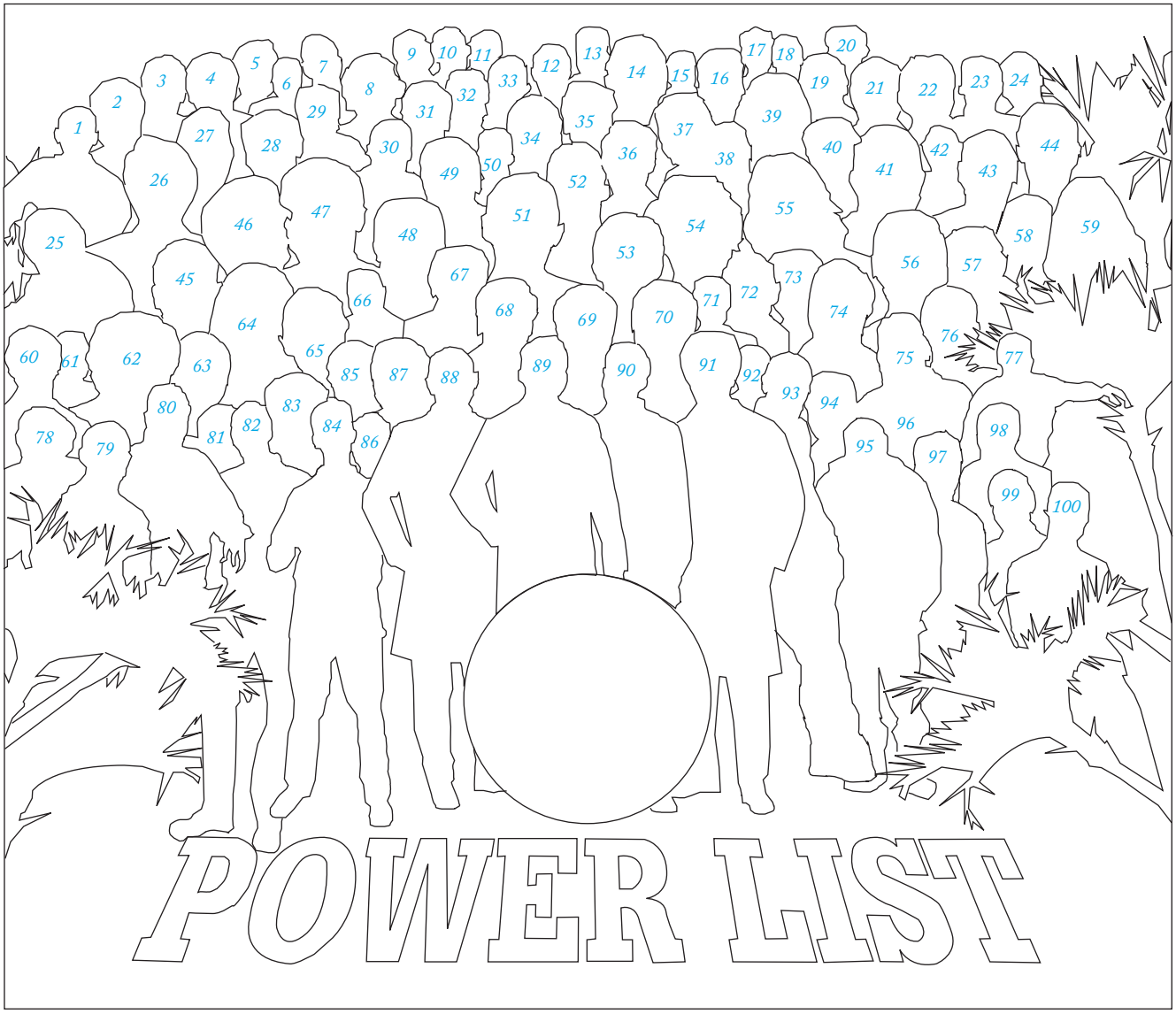

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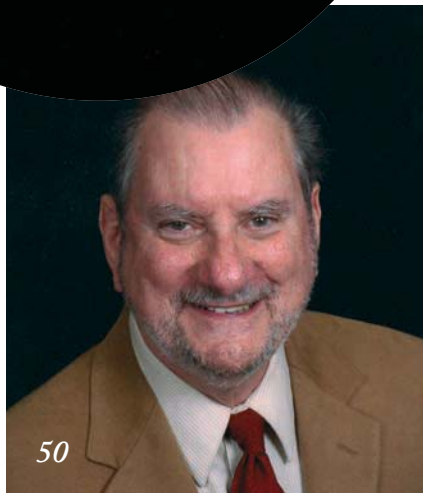

On The Cover

Power List pastiche of Sir Peter Blake's "Sgt. Pepper's Lonely Hearts Club Band" album cover (1967).

Upfront

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Sitting Down With

the **Analytical Scientist**

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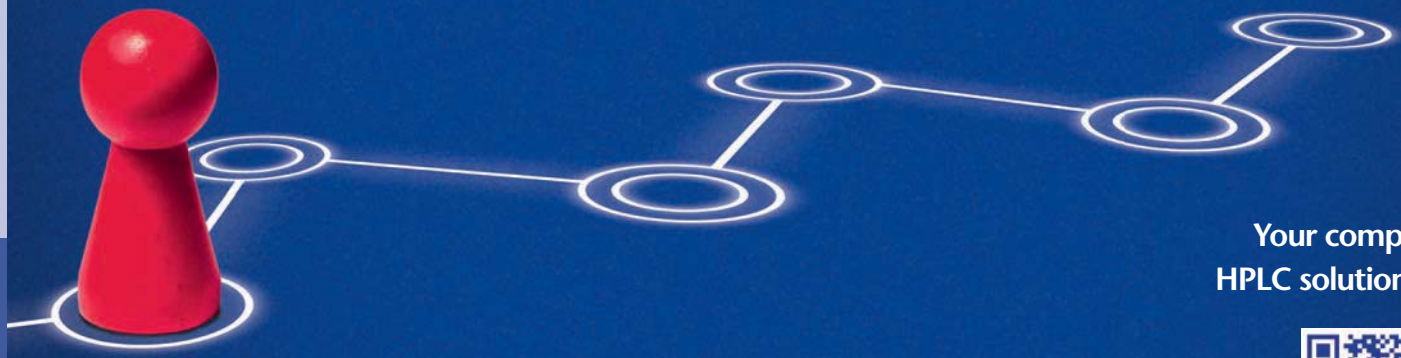

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The Top Ten Reasons For Doing the Power List

Why we've added to the craze of "a list for everything".

After some (quite heated) debate, we have developed and now humbly present The Analytical Scientist Power List 2013 – our catalog of the 100 most influential people in the field – on page 23.

Why generate a Top 100? Because, quite simply, you are a fascinating bunch, doing interesting and useful work that serves society – and you are doing it without much ado, humbug or pretention. The Power List is a contribution to the third part of our mission to record, scrutinize and celebrate analytical science, and applauds some of the self-effacing giants of the field.

To develop the list we requested nominations from our readers and then organized a jury to select the Top 100. Our editorial team represented one-fifth of the jury; the others were well-respected scientists who prefer to remain anonymous and were modest enough not to vote for themselves.

Let's be clear – we don't pretend that this list is definitive: it's subjective and may have shocking omissions (do let us know). We'll use any discussion, dissention and disagreement as fuel for 2014 list.

Lastly, in the spirit of list-mania, here are our Top 10 reasons for doing the Power List:

10. Survival. "We like lists because we don't want to die" - Umberto Eco (http://tas.txp.to/0913-lists)
9. Trendiness. Lists are pervasive, especially in this Internet age. Why resist?
8. Sophistication. The Power List lends the list craze an intellectual leg-up (not that the bar is set very high by "the highest-earning celebrities" and "worst movies of all time").
7. Devilment. The idea of taking a complex subject and reducing it to a tabloidesque list of characters fulfills a need for mischief.
6. Habit. Readers gravitate toward almost any list (so they say); magazines publish lists for that very reason.
5. Kinship. A list of like-minded souls reminds us that we're not alone.
4. Variety. From paper-based diagnostics to high-pressure mass spectrometry, the diversity of the field is amazing.
3. Serendipity. Lists act as a great source of information that you didn't even know you were looking for.
2. Imitation. If it's good enough for the Smithsonian, it's good enough for analytical science (www.aaa.si.edu/exhibitions/lists)
1. Celebration! The list includes contributions to many fields of science and practical improvements to the lot of humankind. We should all be proud of that.

Frank van Geel
Scientific Director

Jayne De Vos & Peter Gorst-Allman

"Watching countless episodes of Quincy on television directed my career aspirations towards becoming a forensic scientist," says Jayne De Vos, who started out in serology in the late 1980s before an interest in drug analysis, toxicology, and arson chemistry grabbed hold. A career shift took Jayne from qualitative chemistry to accurate measurement (metrology). Her interest in separation science and environmental monitoring led to a collaboration in 2008 with Peter Gorst-Allman and Jean-Fransçois Focant (University Liége, Belgium), which provided the platform to establish and develop dioxin capability for South Africa. But Jayne is still a forensic analyst at heart.

"Environmental analysis has always been a passion for me," says Peter Gorst-Allman. After early work on the contamination of food and feedstuff by mycotoxins (using primarily NMR spectroscopy), Peter has been in the field of chromatography and mass spectrometry for over 30 years. The last 13 years have been spent with LECO Africa where he is the Director of Separation Science Applications for Africa and Asia Pacific. "Collaborating with Jayne on developing alternative methods for POPs analysis in South Africa has resulted in some of the most personally satisfying work I have done."

Read about the collaboration on page 44.

Joan LLuis-Vives Corrons

The professor of medicine and head of the haematology laboratory department of the Hospital Clinic i Provincial (University of Barcelona) since 1976, Joan LLuis-Vives Corrons has been influential in haematology research, education and diagnosis. "My main focus has been on the development of new procedures for the diagnosis of anaemias and haematological malignancies (acute and chronic leukaemias and lymphomas) as well as in the standardization and quality assessment of haematology laboratory practice".

Joan requests your input on anaemia diagnosis on page 18.

Peter Kootstra

Laboratories can no longer have secrets with Peter Kootstra on the case. After more than 25 years working for the government, Peter, who has a background in medical and analytical chemistry, is now a consultant on analytical chemistry and quality assurance. He is co-owner of Lab-QAcademy, a provider of training courses and workshops on the quality assurance in laboratories. Peter believes that, by following a practical approach, the quality of laboratories can be improved: "If analyst know why rules are necessary, quality will be improved," he says.

Read more of his views on page 17.

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Upfront

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

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

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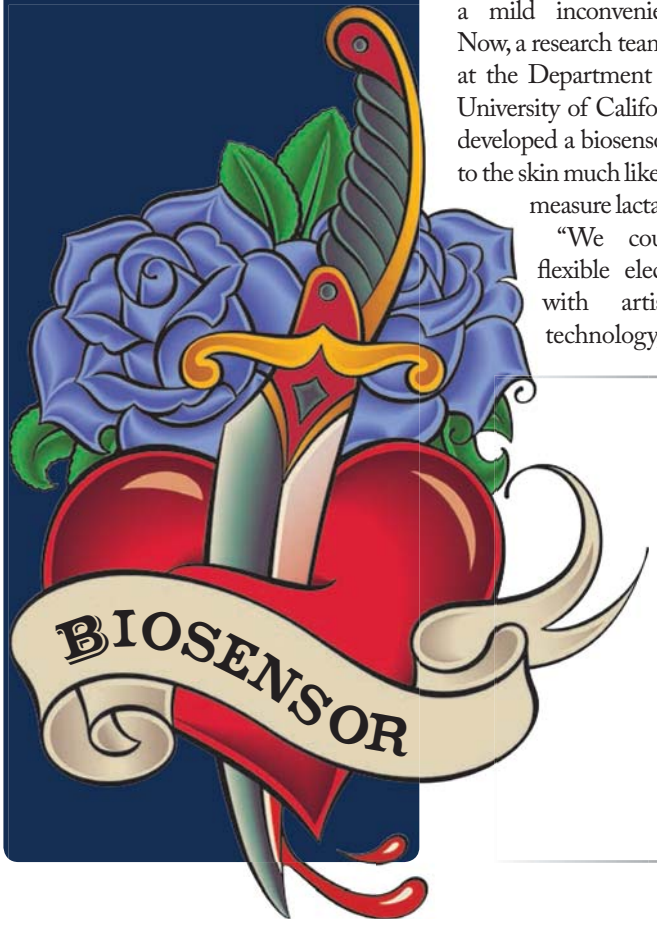

Analytical Tattoo

Non-invasive lactate monitoring adds function to form for athletes on the edge

The lactate threshold (the work rate beyond which blood lactate concentration increases exponentially) is a better predictor of performance than maximal aerobic capacity and a better indicator of exercise intensity than heart rate (1) so its measurement is of significant clinical importance in monitoring extreme athletes – or military personnel being put through their paces. But measuring lactate levels usually requires a small blood sample – more than a mild inconvenience mid-marathon. Now, a research team led by Joseph Wang at the Department of Nanoengineering, University of California San Diego, have developed a biosensor that can be applied to the skin much like a temporary tattoo to measure lactate levels in sweat (2).

"We couple our printable flexible electrochemical sensors with artistic tattoo-transfer technology, and use it for continuous monitoring for fitness, healthcare and military applications," says Wang, who also features on The Power List (see page 30).

The sensor comprises of three screen-printed electrodes, one of which is coated with lactate oxidase to provide chemical selectivity. The conversion of lactate into pyruvate releases two electrons – a wired device monitors the resulting current.

The metabolite biosensing tattoo readily flexes with movement and was able to accurately measure lactate levels in ten exercising volunteers. "Such electrochemical devices are low cost, low power, and portable – and hence highly attractive for such on-body operations," Wang concludes. To prove the point, start-up company Electrozyme (www.electrozyme.com) is currently seeking funding to further develop and commercialize the technology. *RW*

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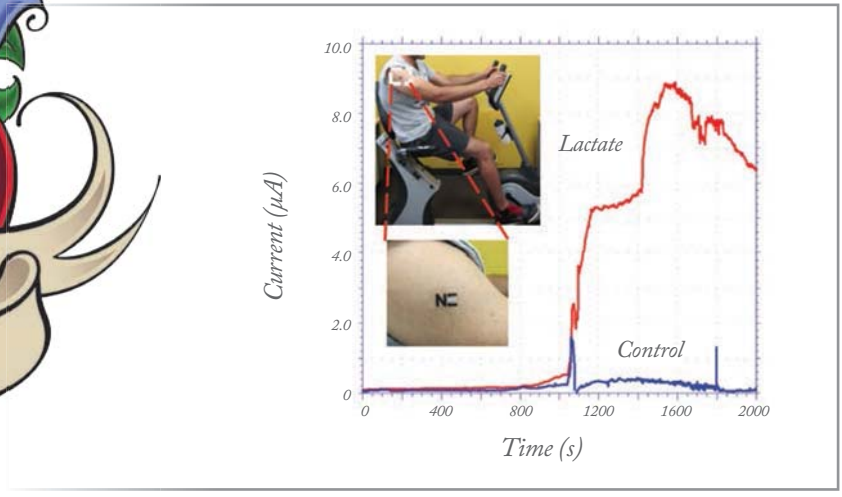
1. *J. Wenzhao Jia et al., "Electrochemical Tattoo Biosensors for Real-Time Noninvasive Lactate Monitoring in Human Perspiration", Anal. Chem., 85, 14, (2013).*
2. *M. L. Goodwin, "Blood Lactate Measurements and Analysis during Exercise: A Guide for Clinicians", J. Diabetes Sci. Technol., 1 (4), 558–569 (2007).*



Lipstick on Your Collar?

The non-destructive nature of Raman spectroscopy is a boon to forensic evidence continuity

A practical advantage of Raman spectroscopy was recently provided by researchers from the University of Kent, UK, in the forensic analysis of lipstick (1). They were able to differentiate samples found on cigarette ends and tissues without the need to remove the items from evidence bags, thus reducing the risk of "compromised continuity". Professor Michael Went of the University's School of Physical Sciences fills in the details.

Why lipstick?

"There is a general principle in forensic science that every contact leaves a trace, so we became interested in the transfer of cosmetic evidence between individuals and between individuals and objects. We had previously looked at Raman spectroscopy for the trace detection of drugs, so we began exploring its use in the analysis of foundation powders, skin creams and eyeliners, but have made the most progress with lipsticks."

Is this a forensic first?

"While Raman spectroscopy has been used before for lipstick analysis, we have arguably demonstrated its potential in forensically important situations."

How does it work?

"The experiments were conducted with a Horiba LabRAM-HR Raman spectrometer using three different lasers operating at wavelengths of 473, 633, and 784 nm. The lipstick data was pretreated to reduce noise and remove the baseline, and then principal component analysis was applied to reduce the dimensionality. The data were subsequently used to construct a simple k-nearest neighbours (kNN) classifier. Our analysis was implemented in MATLAB R2012a using the Statistics Toolbox."

How reliable is the data?

"We achieved up to 98.7 percent correct classification over 30 spectra of 10 lipstick samples. Spectra from trace lipstick deposited on fibres were also analysed – with 100 percent correct classification."

Any surprises?

"We found that Raman spectroscopy could be used to obtain spectra of the lipstick smears deposited on a variety of surfaces – even through evidence bags, with little or no interference from the bag."

Any further forensic opportunities?

"We have certainly further demonstrated Raman spectroscopy's ability to non-destructively obtain highly discriminating data from microscopic samples without removal from transparent containers. We will continue to work on other forms of cosmetic evidence." *RW*

References

1. *F. Salahioglu, M. J. Went, and S. J. Gibson, "Application of Raman spectroscopy for the differentiation of lipstick traces", Analytical Methods, 5, 5392–5401 (2013).*

Onions Under E-Scrutiny

Italian researchers tackle the unlikely issue of red onion counterfeiting with an electronic-nose-based approach to flavor profiling.

The prevention of deceptive, fraudulent, or downright dangerous practices is a constant and major challenge facing the food industry. Now, a team from the Laboratory of Food Chemistry at the University of Reggio Calabria led by the (appropriately named) Mariateresa Russo has unveiled a new E-Nose system and data analysis approach that could strengthen the field's defensive armory (1). The product under analysis? Not red wine, for which Italy is rightly famed, but red onions.

"The Cipolla Rossa di Tropea [red onion of Tropea], produced in the Italian region of Calabria, has been recognized by the EU Protected Geographical Indication thanks to its unusually sweet aroma and low level of pungency – and hence its quality," explains Russo. Like many other goods covered by specific European protection, the cyanidin-rich bulbs prove too tempting to counterfeiters. "The implementation of simple, affordable, power efficient, reliable, and sensitive devices for real-time analysis is a current priority for food quality and authentication," Russo says. While some research groups are attempting to convert advances in microtechnology into viable miniaturized gas chromatographs and mass spectrometers, Russo and colleagues believe that nature offers a more affordable template: "the alternative is a biology-inspired approach where gas composition is recognized as an odor 'fingerprint' or 'pattern' rather than as a set of spectral features." A typical E-Nose system mimics the mammalian olfactory system with an array of partially specific artificial electrical 'receptors' – 12 metal oxide semiconductor sensors in this particular case – coupled with pattern recognition techniques to process the signals. "It doesn't decompose the aroma fraction of the matrix into its constitutive components," says Russo, "rather, it supplies a global evaluation of the aroma in an attempt to provide objectivity".

As with any system of this nature, it is perhaps the data analysis that provides the biggest challenge. The team used Discriminant Function Analysis (DFA) to convert the large amounts of information generated by the sensors. "DFA transforms data using linear discriminant functions (LDFs) in a similar manner to PCA. However, where PCA attempts to maximize all variances present in the data, DFA generates an LDF to maximize the distance between two given centroids within the data, taking the variances of the two groups into account," says Russo. "So, where PCA could be seen as part of an unsupervised classification system and is used to explore the data and to assess discrimination performance, DFA forms part of a supervised classification system – groups must be known a priori to perform DFA." In other words, DFA is used to categorize unknown samples into

one of several already known groups.

Russo's approach yielded an impressive 97.5 percent correct classification rate (CR) overall. "The discrimination is considered 'excellent' if the percentage of recognition is higher than 90%. The DFA of our onion samples showed a clear separation among the four onion groups assessed. Such a high recognition rate confirms our hypothesis based on results from classical analytical techniques, which demonstrated clear qualitative differences between the types of onions compared."

Whether the approach can be considered truly non-destructive, as the title of the paper suggests, is up for debate; the onion's edible parts were homogenised and filtered before the addition of 5 percent trichloroacetic acid to terminate allinase activity. It is not reported how good the red onion marmalade tasted after that… *RW*

Reference

1. M. Russo et al., "Non-destructive flavour evaluation of red onion (Allium cepa L.) Ecotypes: An electronic-nose-based approach", Food Chemistry 141, 896–899 (2013).

Bug ID by Mass Spec

FDA approval of a MALDI-TOF MS-based system for bacteria and yeast identification brings analytics to the clinic

The detection of microbes using matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) isn't new; Bruker's MALDI Biotyper has been on the market for some time. However, the Biotyper product page states that it is "For research use only. Not for use in diagnostic procedures!"

So the announcement from Biomérieux that they have US Food and Drug Administration (FDA) 510(k) de novo clearance for clinical use of the technology is big news. It could signal a mass adoption of MALDI-TOF MS, which can dramatically simplify and increase the speed of microorganism identification.

The Vitek MS connects Biomérieux's identification and antibiotic susceptibility testing platform (Vitek 2) to a MALDI-TOF MS, automatically combining the two sets of results to bring identification time down from hours to minutes.

To gain FDA clearance, 7,068 clinical isolates from several categories, including anaerobic bacteria, fastidious Gram-negative bacteria, and yeast, were analyzed and identified with 93.6 percent overall accuracy when compared with 16S Ribosomal RNA gene sequencing – the current gold standard.

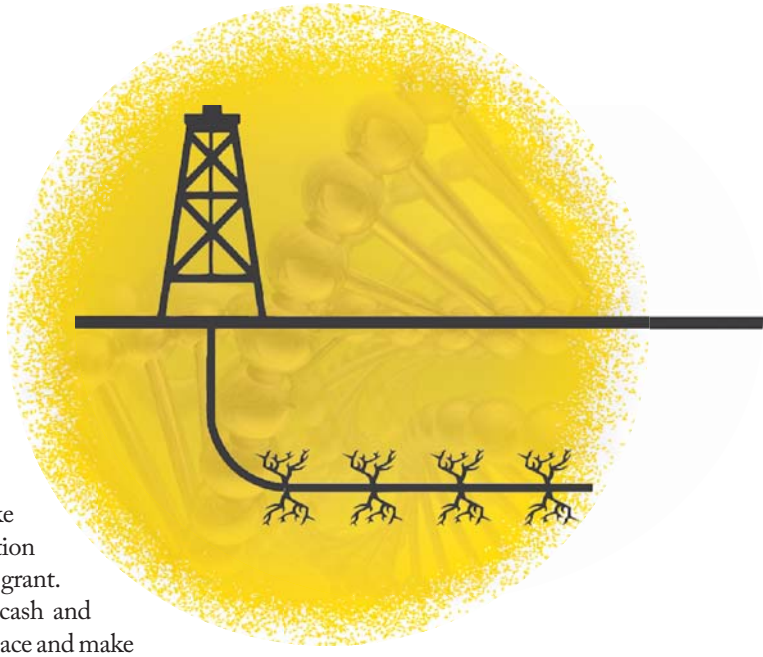
Researchers from the Washington University School of Medicine also rigorously tested the new system with a ten-year collection of clinical samples that were difficult to identify using traditional methods. According to Carey-Ann Burnham, Assistant Professor of Pathology and Immunology and Medical Director of Microbiology at Barnes Jewish Hospital, nearly all of the isolates were identified with high accuracy in a matter of moments.

No small wonder that the Cleveland Clinic, USA, has named the technique one of the Top Ten Breakthrough Medical Technologies of 2013. Which brings us nicely to The Analytical Scientist 2013 Innovation Awards… *RW*

To be published in our final issue of 2013, The Innovation Awards will celebrate the Top Ten innovations of the year. Nominations are now open – email the editor: rich.whitworth@texerepublishing.com. Please ensure you are signed up online for updates and more information: tas.txp.to/0913/subs

Tracking Fracking

Startup company BaseTrace applies DNA tracer technology to track contamination from hydraulic fracturing



Fracking is a hot-button issue. So, when they co-invented a technology to identify associated contamination problems, Justine Chow and Jake Rudolph saw an opportunity. They set up a company together, BaseTrace (www.basetrace.com), to commercialize it. Here, they answer our questions.

Could you describe how the system works?

Jake: "BaseTrace uses unique DNA sequences, designed around a proprietary oligonucleotide configuration, to confer a fingerprint to unique fluid sources – these could be in situ or in a tank in an industrial setting. We can test samples for the presence of that unique tracer to determine whether there's been connectivity where there shouldn't have been."

What's your background and why the interest in hydraulic fracturing?

Justine: "I studied biology at Harvard and came to Duke University for graduate school, where I began to learn more about hydraulic fracturing. In carrying out research for a nonprofit in Washington DC I realized that, regardless of which side people took on the arguments surrounding hydraulic fracturing, they were all looking for a tool to help objectively determine whether the process causes contamination.

Where did the inspiration behind BaseTrace come from?

Justine: "In part, from my background in biology. We have patent-pending DNA configurations that can act as tracers while remaining chemically and biologically inactive. We decided to enter the Duke Startup Challenge to see how far it would take us and won some money. We also secured a Duke Environmental Innovation and Entrepreneurship grant. That's what gave us the cash and courage to get some lab space and make our tracer technology a reality."

What technology choices did you make and why?

Jake: "Detection is performed using PCR, so you have to know what you're looking for to find it. It was an obvious choice, both for its versatility and for its wide availability; eventually, we'd like to be able to license out our detection capabilities, so that any lab with PCR capabilities is set up for our detection protocol, given our proprietary chemistry."

Were there any unexpected challenges in creating a robust system?

Jake: "Justifying the BaseTrace system has been both challenging and exciting because of the problem's cross-disciplinary nature – we've had to draw on expertise in hydrogeology, engineering, geography, and petroleum geology, as well microbiology, bioinformatics, and machine learning. This convergence creates a very exciting work environment, and allows us to bridge new gaps."

Did you face any opposition to the concept?

Justine: "No. The companies we've talked with see it as a way to prove their innocence. Right now companies are being pushed to disclose trade secret fracking fluid ingredient lists and formulas, but testing for potentially hundreds of different chemicals is hard on state and local regulators."

What are the main challenges from a business perspective?

Justine: Funding, to a certain extent. We haven't actively sought or obtained any funding from oil and gas companies, so this technology has been developed independently through local startup competition money and investments from friends and family.

Where do you see the company in five or ten year's time?

Justine: "Hopefully, we'll have expanded into different applications and possibly other countries, and the tracer will be present in most oil and gas wells, and certain underground storage tanks. Because our technology uses DNA, we're able to generate many trillions of different sequences, each of which can be assigned to an individual potential source of contamination or leakage."

Jake: "The beauty of the BaseTrace technology is its simplicity, but I'd love to see additional technological advancement of the tracer design for niche markets and perhaps more extreme environments." *RW*

What's that Smell?

A "nauseating odor" that alarmed citizens of Mangalore, India, apparently remains unidentified despite laboratory analysis.

Friday, 20 September, 2013, saw panic on the streets of Mangalore as a gas-like smell caused people to seek open space and safety, checking their own LPG canisters en route, according to several Indian news outlets (1, 2).

Within hours of initial reports and amongst a flood of further panicked calls to police and fire control rooms, Karnataka State Pollution Control Board (KSPCB) officials charged into the local area with a volatile organic compound meter to check levels, the mystery odor was described simply as a "smell" but quantified at 50 parts per million before dispersing.

Two days later, and the source of the "pungent smell" could still not be traced despite the KSPCB sending air samples for laboratory examination – the results allegedly did not show the presence of any chemical substance. A KSPCB spokesperson told The Times of India: "Samples were sent to Mangalore Refineries Petrochemicals Limited, but it was already diluted by the time it reached the lab" (3). Gas sample collection, it appears, is an art form, after all. *RW*

Does this smell like a cover up to you? Have you heard about other such analytical failures? Let us know by commenting: tas.txp.to/0913-smell

Sources

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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 and written in the first person.

Contact the editors at edit@texerepublishing.com

HPLC Down Under

Isn't it time for a change of scenery? Isn't it time for a different perspective? Isn't it time for a shake up? By limiting major symposia to the Northern Hemisphere, you're missing half the world's potential.

By Emily Hilder, Professor and ARC Future Fellow, University of Tasmania, Hobart, Australia.

The HPLC meeting series began in 1973 with annual meetings held alternately in Europe and North America. Although well established, it has been accused, in the past, of being old-fashioned or conservative – even unwilling to change. To some readers, HPLC2013-Hobart probably looks like "yet another one of those separation science meetings" – hard to distinguish from any number of similar symposia. As a regular participant of the HPLC meeting series since 2000 and, more importantly, co-chair of the Hobart meeting, I've been reflecting on what makes this one any different and what led to it being held in Tasmania – the first time the meeting will cross the equator into the Southern Hemisphere. Here, I answer those questions but also suggest that it bodes very well for a vibrant future for separation science right across the globe.

When faced with stiff competition, I believe that the ability to thrive stems from innovative thinking in the context of wisdom gained from previous successes – a delicate balance to strike with established meetings like the HPLC series. This is often reflected in the challenge of providing a forum for those long-established in the field while, at the same time, offering opportunities for young, up-and-coming scientists and those from non-traditional or developing regions. In fact, these are both issues that the HPLC meetings have actively tried to address over the past few years. The introduction of the Horvath Award from 2006, honoring the achievements of a young researcher (under 35), has not only created recognition but also highlighted the contributions that young scientists can make to the meetings. Moreover, such a commitment effectively mandates the inclusion of oral presentations from a younger crowd. The Hobart organizing committee has made the same promise to those at the beginning of their career with a truly inclusive program.

Since 2008, the HPLC Permanent Committee has included additional meetings in Asia. Now, Australasia is in the mix, with HPLC2013-Hobart providing the perfect example of the potential that new geography can bring. And the support of the international community is proven by the quality of the plenary and keynote speakers secured (many of whom appear on The Power List in this issue, see page 23). Such support is absolutely critical for the future growth of separation science in this region and, arguably, worldwide. It also differentiates this HPLC meeting from others. Why? Well, as an Australian, attending an international meeting usually requires over 24 hours of travel – and a generous travel budget that is prohibitive for many. The opportunity to hear from and interact with the best scientists in the field without such a travel burden is a huge advantage.

Conversely, we have endeavored to construct a program that also includes many speakers from the local region. For regulars of HPLC meetings, this

provides an exciting opportunity to listen to perspectives from a new, fresh-thinking crowd. For scientists within the region, it provides an opportunity to truly contribute to the direction of separation science from an international perspective. Given current growth within Asia and Australasia, these scientists will represent a big part of the field and its future, and I believe that we must engage more effectively with them.

The final question: why Hobart, Tasmania? As a native Tasmanian, I could simply say, why not?! Given its untouched wilderness, superb food and wine, and lashings of contemporary art, Tasmania has much to offer. But Hobart is also home to the Australian Centre for Research on Separation Science (ACROSS) at the University of Tasmania. How ACROSS has grown to a team of over 50 researchers in separation science is another story in itself, but is an example of what can happen when you think differently and aren't afraid to take risks. I feel the same excitement about HPLC2013-Hobart, but you should come and see for yourself.

The 40th International Symposium on High Performance Liquid Chromatography and Related Techniques (HPLC2013–Hobart) will take place at the Hotel Grand Chancellor, Hobart, Tasmania, Australia from 18–21 November 2013. For more information, visit: www.hplc2013–hobart.org ■

Pragmatic Red Tape

Documentation does not ensure effective, efficient or consistent performance. Paper is not a replacement for motivation, competence, and capable employees, working within well-designed processes. So, how do we guarantee quality from lab tests?

By Peter Kootstra, co-owner of Lab-Q Academy, Amsterdam, The Netherlands

To guarantee a 'standard' kilogram, meter, or any other SI unit, a network of metrological laboratories exists. The competence of this network means we generally trust 'the system'. Certainly, it would not be acceptable for the mass of a kilogram to vary – money is involved, afterall. Likewise, laboratory results play an important role in our society. Juries rely on forensic laboratories for evidence, we all have faith in food and environmental analyses, and we trust the findings of medical test results. But can these results always be trusted? Unfortunately, the answer is not clear-cut.

Our belief in pharmaceutical laboratories started to falter around 1970. Following cases of fraud in data submitted by toxicology labs to the US Food and Drug Administration (FDA), 1972 saw the introduction of Good Laboratory Practice (GLP) – the framework within which laboratory studies are planned, performed, monitored, recorded, reported, and archived. GLP makes everything traceable to original raw data and helps assure regulatory authorities that the data submitted are a true reflection of the results obtained during the study. GLP was one of the first quality management systems for laboratories.

In 1978, the US Environmental Protection Agency initiated a certification ▸

program for laboratories that analyze drinking water. Similar projects started in several other countries, which resulted in ISO/IEC 17025: General requirements for the competence of testing and calibration laboratories.

It was simple. The quality manager defined what 'quality' was and wrote procedures. Analysts were expected to read, understand, and act accordingly. But 'quality' is a relative term. Here's the International Organization for Standardization (ISO) definition: "The totality of features and characteristics of a product or service that bear on its ability to satisfy stated or implied needs". In other words, a product is deemed to be of good quality when it complies with the requirements specified by the client. When projected onto analytical work, quality can be defined as the delivery of reliable information within an agreed time span, under agreed conditions, at agreed costs, and with necessary aftercare – a long way, perhaps, from daily laboratory practice.

From an analyst's point of view, quality relates to the analysis of a given sample – and can mean finding an answer that meets their own expectations. If the result indicates that the product is out of specifications, the analyst is likely to reanalyze the sample until the result is within specifications. Surprised? A doping laboratory, which acts in compliance with the World Anti-Doping Agency (WADA) international standard, can be similarly flawed by confirmation bias (the tendency of people to favor information that confirms their hypotheses and reject that which does not) because "the objective of the confirmation assay is to accumulate additional information regarding an adverse finding".

Furthermore, the identification criteria described in technical documents leaves plenty of room for interpretation. Anyone who has worked with liquid chromatography-tandem mass spectrometry (LC-MS/MS) data analysis will be aware that it requires only trivial manipulation of the parameters to acquire the desired result, especially when a ratio is just outside the required limits.

Going back to the laboratory quality management system, remember that it was based on GLP – and the bureaucracy has become a kind of tradition. Often, nobody in the laboratory (except the quality manager) has bothered to read ISO/IEC 17025. It is the quality manager alone that translates the clauses into standard operating procedures (SOPs). The only feedback he or she receives is that it is too bureaucratic.

Have you asked your analysts what their SOPs would look like, if they were involved in their inception? How about providing flow charts rather than long procedures? Quality also means taking the time to think about the design of your processes and evaluating and improving current practice. Certainly, it takes more effort, but a well-designed and accessible system benefits one and all – including quality. ■

Rare Analytical Need

Anemia becomes much more serious in countries where rare hereditary forms can remain undiagnosed. A symposium aims to tackle the issue head on – and analytical science has its part to play.

By Joan-LLuis Vives Corrons, Head of the Red Cell Pathology Unit and ENERCA Project; Professor of Medicine (Hematology) at the University of Barcelona, Spain.

Anemia, defined as a decrease of hemoglobin (Hb) concentration in blood, is a common condition in humans. It has a wide variety of causes, both congenital and acquired, but it is always a manifestation of an underlying disease, not a disease in itself. Iron deficiency (in women and children) and chronic diseases (in adults and the elderly), are the most frequent causes of mild to moderate anemia in developed countries. Diagnosis of decreased Hb levels is relatively easy and inexpensive; all modern automated and semi-automated analyzers measure Hb concentration with great precision and accuracy.

However, another group of anemia sufferers occurs at a frequency of less than one in 2,000 in Europe. Up to 80 percent of these rare anemias (RA) are hereditary. Due to the low number of patients, a lack of professional experience, and social or cultural barriers, a large percentage of RAs remain undiagnosed. The clear need to mobilize resources will only be achieved through coordinated multi-centre and multi-disciplinary action. The European Commission (EC) is, therefore, co-financing the European Network for Rare and Congenital Anaemias (ENERCA). One activity is the 5th European Symposium on Rare Anaemias*, a forum on diagnosis and clinical management of RA, and a workshop to explore the types of tests that could provide correct diagnosis most quickly.

For RAs, the pivotal diagnostic tests are red blood cell (RBC) morphology examination and reticulocyte count. The latter allows differentiation between a central (bone marrow) or peripheral ⧫

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(hemolytic) origin of the anemia. Peripheral blood film examination and osmotic fragility tests (OFT) can sometimes confirm the diagnosis of hereditary spherocytosis, one of the inherent causes of rare anemias. When the OFT is negative, RBC enzyme assays are required for the diagnosis of a hereditary enzymopathy, with glucose-6-phosphate dehydrogenase (G6PD) or pyruvate kinase (PK) being the most common.

Hemoglobinopathies, which lead to moderate or severe anemia, are the most common genetic defects worldwide, with an estimated number of 269 million carriers. These hereditary conditions are the consequence of mutations that result in abnormal hemoglobin. Thalassaemias, on the other hand, result from decreased synthesis of normal globin chains. The two conditions can overlap. In Europe, certain populations of southern countries are particularly at risk of thalassaemia – the cause of so-called 'Mediterranean Anemia'. But increasing migration to Europe from African and Asian countries has drastically changed this scenario: sickle-cell disease (SCD) is becoming an important challenge for public health care. Diagnostic approaches for these disorders range from electrophoresis and high performance liquid chromatography (HPLC) for hemoglobin fractionation in beta thalassemia and structural haemoglobinopathies (sickle cell anaemia) to polymerase chain reaction (PCR) for alpha thalassemia and gene sequencing for the identification of specific mutations.

The two key discussion points at the symposium of greatest relevance for those in the analytical sciences are (a) preventive programs for SCD control, such as neonatal screening, and (b) new methodologies for diagnosis and genetic counseling, and genetic characterization in cases where laboratory 'blind spots' are caused by co-inheritance of hemoglobinopathies and other RBC genetic defects. The organizers would welcome your input!

**The 5th European Symposium on Rare Anaemias takes place 15–16 November, 2013, in Ferrara Italy. For more information, visit: www.enerca.org.* ■

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the Analytical Scientist Power List 2013

Who are the 100 most influential people in the analytical sciences? That's the question we posed to ourselves – and then to you – over two months ago, ahead of open nominations and a painstaking judging process. Here, without further ado, we celebrate the answer.

Yoshinobu Baba

Professor, Department of Advanced Medical Science, Graduate School of Medicine, Nagoya University, Japan

Research: Nanobiosicence and nanobiotechnology for genomics, proteomics, glycomics, systems biology, single molecule manipulation, and medical applications.

www.apchem.nagoya-u.ac.jp/III-2/baba-ken

Douglas A. Berthiaume

Chairman, President and Chief Executive Officer
Waters Corporation, Massachusetts, USA

Revenue: $1.64 billion (2010)
Employees: 5,700

www.waters.com

Marc N. Casper

President and Chief Executive Officer
Thermo Fisher Scientific, Massachusetts, USA

Revenue: $13 billion
Employees: 39,000

www.thermofisher.com

Andrew deMello

Professor of Biochemical Engineering
ETH Zurich, Switzerland; Imperial College London, UK

Highlight: "The development of microfluidic systems for high-throughput chemical and biological analysis. Further highlights include the first demonstrations of microfluidic combinatorial chemistry, chip-based nanoparticle synthesis, continuous flow PCR, the application of high-contract fluorescence lifetime imaging to microfluidic environments, and pioneering developments in droplet-based microfluidics."

Research: Microfluidics and nanoscale science.

www.demellogroup.ethz.ch

Monika Dittman

Principal Scientist, R&D
Agilent Technologies, Germany

Highlight: "The introduction of the HP Capillary-Electrophoresis System in 1992. This was the first instrument that I accompanied as an R&D scientist from the early investigation stage to manufacturing release. The technology was extremely exiting at the time and we were very proud when the instrument finally sold to customers."

Allen J. Bard

Professor and Director, Center for Electrochemistry, University of Texas, USA

Highlight: "Development of the scanning electrochemical microscope."

Research: Application of electrochemical methods to the study of chemical problems, including investigations in electro-organic chemistry, photoelectrochemistry, electrogenerated chemiluminescence, and electroanalytical chemistry. *bard.cm.utexas.edu*

Lutgarde Buydens

Professor and Head, Analytical Chemistry/ Chemometrics, Radboud University Nijmegen, The Netherlands

Research: Chemometrical techniques for optimization of molecular structures with respect to (bio) chemical activity and for the processing/interpretation of (medical) multivariate images. *www.ru.nl/science/analyticalchemistry*

Yi Chen

Professor and Laboratory Director, Institute of Chemistry. Chinese Academy of Sciences, Beijing, China

Gary Christian

Emeritus Professor of Chemistry, Department of Chemistry, University of Washington, USA

Research: Flow and sequential injection analysis and related techniques.

Gert Desmet

Professor and Head, Department of Chemical Engineering, Vrije Universiteit Brussel, Belgium

Research: Miniaturization of separation methods and modeling of flow effects in chromatographic systems.

vubchemicalengineering.be

Norman Dovichi

Grace-Rupley Professor of Chemistry and Biochemistry, University of Notre Dame, Indiana, USA

Highlight: "Ultrasensitive laser-induced fluorescence has driven a wide swath of research in the biological and physical sciences. Most notably, ultrasensitive fluorescence detection enabled both capillary array and next-generation DNA sequencers. This technology also laid the foundation for single molecule detection and imaging."

Attila Felinger

Professor, Department of Analytical and Environmental Chemistry
University of Pécs, Hungary

Highlight: "We were able to extend and apply the microscopic theory of chromatography to model the details of the chromatographic process at the molecular level. With that tool a large number of phenomena, including the adsorption on heterogeneous surfaces or the size exclusion process, are now described."

Research: Characterization of the retention mechanism, thermodynamics and kinetics of adsorption-desorption in HPLC, multivariate chemometrics.

Scott E. Fraser

Director, Biological Imaging Center
Caltech, California, USA

Research: Patterning of cell lineages, cell migrations and axonal connections during vertebrate embryogenesis. *bioimaging.caltech.edu*

Christian Griesinger

Group Leader, NMR-Based Structural Biology; Director and Scientific Member Max Planck Institute for Biophysical Chemistry, Göttingen, Germany

Highlight: "It has always been a dream of mine to use NMR spectroscopy for the clarification of absolute configuration of molecules in organic chemistry. With the usage of residual dipolar coupling enhanced NMR spectroscopy, this is in reach." *www.nmr.mpibpc.mpg.de*

Detlef Günther

Head, Department of Chemistry and Applied Biosciences; Group Leader: Trace Element and Micro Analysis, ETH Zurich, Switzerland

Research: Ion molecule and plasma induced gas phase reactions, laser-induced ablation processes, plasma formation, ultra trace multi-element analysis, nano-depth layer ablation. chemistry, chip-based nanoparticle synthesis, continuous flow PCR, the application of high-contract fluorescence lifetime imaging to microfluidic environments and pioneering developments in droplet-based microfluidics.

William Hancock

Faculty Fellow, Bradstreet Chair in Bioanalytical Chemistry, Northeastern University, Massachusetts, USA (Editor-in-Chief, Journal of Proteome Research.)

Research: Glycoproteomics and glycans associated with cancer and infectious disease. *www.northeastern.edu/barnett/research/hancockgroup.html*

Catherine Fenselau

Professor, Chemistry and Biochemistry
Unviversity of Maryland, USA

Highlight: "Being a thought leader and an experimental contributor to the extension of mass spectrometry to the analysis of biological molecules, including polar molecules, such as phospholipids and glucuronides, and biopolymers, such as DNA adducts, carbohydrates, and protein complexes."
www2.chem.umd.edu/groups/fenselau

John Justin Gooding

Scientia Professor; Co-Director of The Australian Centre for NanoMedicine, University of New South Wales, Australia

Highlight: "We developed sophisticated surface chemistries that allow biosensors to operate in complex biological fluids, which has enabled us to make antibody-based electrochemical biosensors and photonics crystal cell chips to monitor the response of live immune cells to pathogenic stimuli." *tas.txp.to/901-Gooding*

Davy Guillarme

Senior lecturer, School of Pharmaceutical Sciences, University of Geneva, Switzerland

Highlight: "During the last few years, I have worked actively in the field of liquid chromatography. I have tried to demonstrate the potential of state-of-the-art instruments and columns (high temperature UHPLC, core-shell, SFC), for fast and/or high resolution analysis of small molecules and large biomolecules." *(see page 38)*

Paul Haddad

Distinguished Professor, Chemistry; Director of the Australian Centre for Research on Separation Science (ACROSS), and Director of the Pfizer Analytical Research Centre, University of Tasmania, Australia

Highlight: "The most satisfying achievement of my research career has been the privilege to collaborate with, mentor and support the careers of PhD students and postdoctoral researchers of extraordinarily high caliber and dedication. It has been their accomplishments that have given me the greatest professional reward." *www.utas.edu.au/across*

Albert Heck

Head, Biomolecular Mass Spectrometry and Proteomics Group, Utrecht University, The Netherlands

Research: Development of mass spectrometric methods applicable to the structural characterization of biomolecular systems, in relation to their biological function. *bioms.chem.uu.nl*

Gary Hieftje

Distinguished Professor; Robert and Marjorie Mann Chair in Chemistry; and Group Leader, Laboratory for Spectrochemistry, Indiana University, USA

Highlight: "The 65 PhD students who have graduated from our laboratory."

Research: Investigation of basic mechanisms in atomic emission, absorption, fluorescence and mass spectrometric analysis, and the development of instrumentation and techniques for atomic methods of analysis. *www.indiana.edu/~gmhlab*

Michal Holcapek

Professor, Analytical Chemistry, Faculty of Chemical Technology, University of Pardubice, Czech Republic

Research: Mass spectrometry and its coupling with HPLC, specializing in structural analysis of organic, bioorganic and organometallic compounds, mainly lipidomics, metabolomics, drug metabolite identification. *holcapek.upce.cz*

Pavel Jandera

Professor, Analytical Chemistry, Faculty of Chemical Technology, University of Pardubice, Czech Republic

Highlight: "Development of unified theory of gradient elution in reversed-phase, organic normal-phase and HILIC systems, later extended to two-dimensional LCxLC techniques. Elaboration of new approaches for characterization of particulate and monolithic stationary phases; prediction and optimization of HPLC separations."

Gui-bin Jiang

Director, State Key Laboratory of Environmental Chemistry and Ecotoxicology, Chinese Academy of Sciences, Beijing, China

Research: Analytical development and environmental characterization of persistent organic pollutants (POPs), and the speciation of organometallic compounds.

english.rcees.cas.cn/au/bi

Frank Laukien

Chairman, President and Chief Executive Officer. Bruker Corporation

Revenue: $1.79 billion (2012)

Employees: >6,000

www.bruker.com

Emily Hilder

Professor and ARC Future Fellow, School of Chemistry, University of Tasmania, Australia

Highlight: "The most satisfying achievement of my career to date has been to develop new materials through fundamental research that have since been applied in commercial products."

Research: Synthesis of novel polymeric monolithic materials as selective adsorbents for sample preparation/pretreatment, chromatographic stationary phases and other applications in analytical chemistry. Development of miniaturised analytical systems, particularly for applications in clinical diagnostics and remote monitoring. *(see page 16)*

Gerald Hopfgartner

Full Professor, Analytical Pharmaceutical Chemistry, Life Sciences Mass Spectrometry, University of Geneva, University of Lausanne, Switzerland

Highlight: "To apply mass spectrometry for life sciences research from elements to macromolecules."

Research: Bioanalysis, metabolism, miniaturization of sample preparation, multi-component analysis, rationalization of fragmentation mechanisms for metabolites ID. *www.unige.ch/sciences/pharm/lsmv*

Klavs F. Jensen

Warren K. Lewis Professor of Chemical Engineering and Department Head, Massachusetts Institute of Technology, USA.

Highlight: Having worked with and educated a large number of hard working and bright graduate students and postdocs.

Research: Microsystems for chemical and biological applications, materials synthesis and processing multiscale simulation of reactive processes.

web.mit.edu/jensenlab

Michael Lämmerhofer

Professor, Pharmaceutical Analysis and Bioanalysis, University of Tuebingen, Germany

Hian Kee Lee

Professor, Department of Chemistry National University of Singapore, Singapore

Highlight: "I have been fortunate to have been able to train so many students in miniaturized sample preparation and extraction. More importantly, that I have learnt more from them than they have gained from our interactions in my laboratory has really been my greatest satisfaction."

Milton Lee

H. Tracy Hall Professor of Chemistry, Department of Chemistry and Biochemistry. Brigham Young University, Utah, USA

Highlight: "Learning of the ongoing activities of my ninety-plus talented former graduates and postdoctoral researchers who not only performed spectacular research while in my laboratories, but have assumed or are assuming responsible positions around the world, making significant contributions in a variety of ways."

Susan Lunte

Director Ralph N. Adams Institute for Bioanalytical Chemistry; Director COBRE Center Molecular Analysis of Disease Pathways, The University of Kansas, USA

Highlight: "Mentoring students and postdocs in bioanalytical chemistry through the development of separation-based methods for the determination of peptides, drugs and neurotransmitters in biological fluids, single cells and freely roaming animals." *sluntegroup.ku.edu*

Brendan MacLean

Lead Developer, MacCoss Lab University of Washington, USA

Career: Managed development of Skyline; one of the key programmers responsible for the Computational Proteomics Analysis System (CPAS); significant contribution to the development of X!Tandem and the Trans Proteomic Pipeline; and created the LabKey Enterprise Pipeline.

brendanx-uw1.gs.washington.edu

Ron Majors

Senior Scientist
Agilent Technologies, Delaware, USA

Highlight: "I was one of the early workers in HPLC, especially in column technology. I packed the first high performance columns and studied early bonded phases. I have been an editor for LCGC for over 30 years."

Alan G. Marshall

Robert O. Lawton Professor, Chemistry & Biochemistry; Director, Ion Cyclotron Resonance Program, Florida State University, USA

Highlight: "I am the co-inventor and leading innovator in Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR-MS). I am now pioneering mass-based structural analysis of biomacromolecules and complex chemical mixtures."

www.magnet.fsu.edu/usershub/scientificdivisions/icr

Charles M. Lieber

Mark Hyman Professor of Chemistry, Department of Chemistry and Chemical Biology, Harvard University, Massachusetts, USA

Highlight: "Making groundbreaking advances in the synthesis, characterization and assembly of semiconductor nanowires, and pioneering their applications in nanomedicine through the creation of nanoelectronic biosensors and cell interfaces that blur the distinction between digital electronics and living systems."

Research: Nanoscale science and technology, using novel synthesized building blocks to push scientific boundaries in diverse areas from biology/medicine to energy and computing.

cmliris.harvard.edu

Mike MacCoss

Associate Professor, Genome Sciences; Group Leader, MacCoss Lab, University of Washington, USA

Research: Development of stable isotope and mass spectrometry based approaches to improve understanding of biology on a molecular, cellular, and whole organism level. *maccosslab.org*

Fasha Mahjoor

Founder, President, and Chief Executive Officer, Phenomenex, California, USA

Revenue: not listed

Employees: >700

www.phenomenex.com

Matthias Mann

Director, Department of Proteomics and Signal Transduction, Max Planck Institute of Biochemistry, Munich, Germany

Research: Developing and applying methods of mass spectrometry-based proteomics in a variety of biological areas.

www.biochem.mpg.de/en/rd/mann

Hans H. Maurer

Full professor, Toxicology and Pharmacology; Head, Department of Experimental & Clinical Toxicology, Saarland University, Homburg/Saar, Germany

Highlight: "My most satisfying achievement is to have established mass spectrometry in clinical and forensic toxicology documented by numerous papers, review articles, and handbooks/libraries of reference GC-MS and LC-MS spectra. This led to various major scientific awards and the honorary doctorate of the University of Ghent in Belgium 2007."

David McCalley

Professor, Bioanalytical Science
University of the West of England, Bristol, UK
Highlight: "While I have been fortunate in receiving research funding from industry (particularly pharmaceutical companies), I was very pleased to receive UK Research Council funding for an (ongoing) study of hydrophilic interaction liquid chromatography in 2012, against strong competition from projects in the traditional areas of organic, inorganic and physical chemistry."
Research: Fundamental mechanisms and applications of HPLC and GC especially in biomedical and pharmaceutical science.
www.indiana.edu/~gmhlab

Luigi Mondello

Full Professor, Analytical Chemistry,
School of Pharmacy,
University of Messina, Italy
Research: Development of analytical methods for the characterization of complex samples.
www.sepsci.unime.it

Akira Nakamoto

President and Chief Executive Officer
Shimadzu, Kyoto, Japan
Net sales: ¥264 billion ($2.67 billion, 2012)
Employees: 10,395
www.shimadzu.com

Milos Novotny

Distinguished Professor Emeritus, Lilly Chemistry Alumni Chair, Department of Chemistry, Indiana University Bloomington, USA
Research: Improving resolution of complex biological mixtures and identification of the separated compounds through techniques such as electrospray mass spectrometry (MS) and matrix-assisted laser desorption/ionization MS. *www.indiana.edu/~novweb*

Jeanne E. Pemberton

Professor, Chemistry,
The University of Arizona, USA
Research: Chemistry at interfaces in electrochemistry and electrochemical devices, chromatography, organized molecular assemblies, and environmental systems. *www.chem.arizona.edu/faculty_profile/pemb*

Chad Mirkin

Director, International Institute for Nanotechnology; George B. Rathmann Professor, Chemistry; Professor, Chemical and Biological Engineering, Biomedical Engineering, Materials Science & Engineering, and Medicine.
Northwestern University, Illinois, USA
Research: Developing strategic and surface nano-optical methods for controlling the architecture of molecules and materials on a 1-100 nm scale.
sites.weinberg.northwestern.edu/mirkin-group

Royce W. Murray

Kenan Professor, Chemistry
The University of North Carolina, USA
Research: Electrochemistry, molecular design, sensors.
www.chem.unc.edu/people/faculty/murray

Michel Nielen

Project Manager, Professor, Special chair on Analytical Chemistry, RIKILT Wageningen UR (University & Research centre), The Netherlands
Research: Bioactivity-related detection and identification technologies for chemical contaminants in the food chain, ultimately leading to the identification of emerging unknown bioactive contaminants.

Ulrich Panne

President, BAM Federal Institute for Materials Research and Testing; Professor, Instrumental Analytical Chemistry, Humboldt University of Berlin, Germany
Highlight: "The establishment of the graduate School of Analytical Sciences, SALSA, in Berlin Adlershof, for a renaissance and renewal of analytical sciences. The vision that SALSA will be the place where students and scholars discover analytical sciences to answer their key scientific questions."
Research: Analytical chemistry with focus on spectro-chemical analysis.

Colin Poole

Professor, Department of Chemistry
Wayne State University, Michigan, USA
Highlight: My contributions to the development of the solvation parameter model for method development in chromatography and as a tool for the estimation of environmental distribution and fate of industrial compounds."
Research: Design of novel stationary phases; design and construction of small devices to be added to existing equipment to enhance analytical utility. *www.chem.wayne.edu/faculty/poole*

Michael Quilliam

Principal Research Officer, Measurement Science and Standards, National Research Council, Nova Scotia, Canada

Highlight: "The reduction of shellfish poisoning incidents worldwide and improved international trade following the development of an improved approach to the monitoring of shellfish toxins, based on LC-MS and certified reference materials."

Marja-Liisa Riekkola

Professor, Analytical Chemistry; Head, Laboratory of Analytical Chemistry, University of Helsinki, Finland

Highlight: "The applicability of fused silica capillaries coated with human biomaterials in CEC. Moreover, the development of a special sample valve for in-situ aerosol MS measurements is another innovation also useful in other instrumental techniques." *www.helsinki.fi/kemia/analyyttinen*

Gerard Rozing

Research fellow (retired: September, 2012) Agilent Technologies, Germany

Highlight: "Being part of a culture shift – viewing academic researchers not as demanding customers (high discounts, special requirements and many complaints!) but as partners in the development of new analytical technology, and as a pool of excellent young scientists with potential as future employees and customers." *rozing.com*

Claudio Soto

Professor of Neurology; Director, Mitchell Center for Alzheimer's Disease and Related Brain Disorders, University of Texas Medical School at Houston, USA

Highlight: "The invention and development of Protein Misfolding Cyclic Amplification (PMCA) technology. This technology was first published in a Nature article in 2001 and is today widely considered as a major breakthrough in science and technology. PMCA enabled for the first time the ability to cyclically amplify the folding and biochemical properties of a protein in a manner conceptually analogous to the amplification of DNA by PCR."

William P. (Bill) Sullivan

President and Chief Executive Officer Agilent Technologies, California, USA

Revenue: $6.9 billion

Employees: 20,500

www.agilent.com

Mike Ramsey

Minnie N. Goldby Distinguished Professor, Chemistry; Professor, Biomedical Engineering; Professor, Genome Sciences, University of North Carolina at Chapel Hill, USA

Highlight: "I am most proud of the teams of outstanding scientists that I have been fortunate enough to assemble over my career. These teams have made seminal contributions to the development of microfabricated devices for chemical and biochemical analysis, particularly in the areas of microfluidics, nanofluidics, and high-pressure mass spectrometry (HPMS)."

Peter Roepstorff

Professor, Protein Chemistry University of Southern Denmark, Denmark

Highlight: "In 1982, I saw a signal from my protein flying in a mass spectrometer at the Tandem accelerator Laboratory at the Uppsala University in Sweden. This fulfilled a 15-year-old dream of mine and opened up the world of proteomics."

Research: Development of methodology for mass spectrometric protein analysis with focus on post translational modifications including protein oxidation as a function of aging; the use of mass spectrometric protein analysis in the biotechnological and pharmaceutical industry.

Wilhelm Schänzer

Head, Institute for Biochemistry, German Sport University Cologne, Germany

www.dopinginfo.de

Richard Stadler

Group Expert, Chemical Food Safety at Nestlé Quality Assurance Centres, Nestec Ltd, Vevey, Switzerland

Ulrich Tallarek

Full Professor, Analytical Chemistry Philipps-Universität Marburg, Germany

Highlight: "My recent personal research highlight was to elucidate the formation and properties of the water-rich layer at the mesoporous silica surface. Now, we have a molecular-level picture of the conditions under which analytes partition from the acetonitrile-rich mobile phase into the retentive water-rich layer in hydrophilic interaction liquid chromatography."

Koichi Tanaka

General Manager, Mass Spectrometry Research Laboratory, Shimadzu Corporation, Kyoto, Japan

Highlight: Nobel Prize in Chemistry (2002) "for the development of soft desorption ionisation methods for mass spectrometric analyses of biological macromolecules".

Dianping Tang

Full Professor, Analytical Chemistry Fuzhou University, Fujian, China

Highlight: "I received the Alexander von Humboldt Fellowship in 2008, and worked at Technische Universitat München, Germany, from 2008 to 2009. I am currently a member of the editorial board of "Advanced Material Letters" and "The Open Systems Biology Journal". Up to now, more than 100 publications under my authorship appeared in reviewed international scientific journals."

Research: Nano-electrochemical biosensor design and application in clinical immunology, food and environmental immunological analysis.

Jean-Luc Veuthey

Vice-rector; Professor, School of Pharmaceutical Sciences, University of Geneva, Switzerland

Research: Developing pharmaceutical separation by liquid chromatography, as well as by capillary electrophoresis, coupled with various detectors.

www.unige.ch/sciences/pharm/fanal/lcap

David Walt

Robinson Professor of Chemistry; Professor, Howard Hughes Medical Institute, Tufts University, Massachusetts, USA

Highlight: "Successfully commercializing technologies that were discovered in my laboratory. These technologies are enabling researchers to make new discoveries, protecting and enhancing the food supply, and saving lives by changing the way people are diagnosed and health care is administered. Obviously, this is a team effort by many talented individuals."

ase.tufts.edu/chemistry/walt

Mark Wightman

W.R. Kenan, Jr. Professor of Chemistry; Director of Undergraduate Studies, The University of North Carolina at Chapel Hill, USA

Research: Ultramicroelectrodes, electrochemistry, neurochemistry.

www.chem.unc.edu/people/faculty/wightman/group

Nobuo Tanaka

Technical Advisor, GL Sciences, Inc. (Professor Emeritus, Kyoto Institute of Technology)

Highlight: "Gaining an understanding of the solute-stationary phase interactions in reversed-phase HPLC systems leading to the proposals for a column characterization method and preparation of monolithic silica columns."

Albert van der Berg

Professor, Nanotechnology and Lab-on-a-Chip systems; Chair, BIOS Lab-on-a-Chip Group, University of Twente, Enschede, The Netherlands

Highlight: Fabrication and characterization of FlowFET, a microdevice to control fluid flows by field-effect influence of the electrical double layer in a thin-walled microchannel. The same field-effect principle was recently applied to generate highly charged microdroplets that directly convert hydraulic energy in electrical energy.

Research: Microanalysis systems and nanosensors, nanofluidics and single cells and tissues on chips. Applications in personalized health care, drug development and development of sustainable (nano)technologies.

www.utwente.nl/ewi/bios

Tuan Vo-Dinh

PR. Eugene and Susie E. Goodson Distinguished Professor; Professor, Chemistry; Director, The Fitzpatrick Institute for photonics, Duke University, North Carolina, USA

Research: Bio/nanophotonics, plasmonics, laser-excited luminescence spectroscopy, room temperature phosphorimetry, synchronous luminescence spectroscopy, SERS, nanosensors, biosensors and biochips.

www.vodinh.pratt.duke.edu

Joseph Wang

Distinguished Professor; Vice Chair, Nanoengineering . University of California San Diego (UCSD), USA

Highlight: "Making pioneering contributions to the development of electrochemical biosensors, nanoscale bioelectroanalysis, modified electrodes, wearable sensing devices, and synthetic nanomachines." *joewang.ucsd.edu* *(see page 10)*

Ian Wilson

Professor, Drug Metabolism and Molecular Toxicology, Department of Surgery and Cancer, Imperial College London, UK

Highlight: "The achievement that has given me the most, long-term, satisfaction is to have helped train some 30 postgraduate students in the art of research up to the point where they were able, with increasing confidence, to make their own contributions to their respective fields of scientific endeavor."

Nicholas Winograd

Evan Pugh Professor of Chemistry
Penn State University, Pennsylvania, USA

Highlight: "The development of MS imaging at the submicron level using cluster ion beams is a satisfying achievement for me. It now appears that we will have the spatial resolution and the chemical specificity to learn something about fundamental biochemical pathways at the level of a single biological cell."
Research: Molecular imaging of biomaterials - single cells, surface chemistry studies with ion beams and lasers, chemical imaging with cluster ion beams and lasers. *winograd.psu.edu*

Kurt Wüthrich

Professor of Biophysics, ETH Zürich, Zürich, Switzerland; Cecil H. and Ida M. Green Professor of Structural Biology, Scripps Research Institute, California, USA

Highlight: "The first protein structure determination in solution."
Nobel prize in Chemistry: "for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution"
Research: Molecular structural biology, protein science, and structural genomics. *www.scripps.edu/wuthrich*

Takeshi Yasumoto

Academic Advisor, Japan Food Research Laboratories (Inc. Foundation); Distinguished Research Fellow, National Research Institute of Fisheries Science, Fisheries Research Agency; Professor emeritus, Tohoku University, Japan

Presentation: tv.campusdomar.es/en/video/1853

Richard Zare

Marguerite Blake Wilbur Professor in Natural Science. Stanford University, California, USA
Research: cell imprinting, reaction dynamics, mass spectroscopy, nanoparticles.
www.stanford.edu/group/Zarelab

Hanfa Zou

Professor; Vice Director of Biotechnology Division, Dalian Institute of Chemical Physics Chinese Academy of Sciences, Dalian, China
Research: Stationary phases for liquid chromatography, capillary electrochromatography and chiral separation; Novel matrices for analysis of low-mass compounds by MALDI-TOF MS; screening and analysis of bioactive compounds in TCMs by biochromatography; hphenated technology of 2D-HPLC with MS/MS detection.

Mary Wirth

W. Brooks Fortune Distinguished Professor, Department of Chemistry
Purdue University, Indiana, USA

Research: Developing new materials for protein separations in characterization of protein drug heterogeneity, top-down proteomics, and trace protein biomarkers discovery for screening of early aggressive cancer. *tas.txp.to/0913-Wirth*

Guowang Xu

Director of Metabonomics Research Center; Deputy director of CAS Key Laboratory of Separation Science for Analytical Chemistry, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, China.

Highlight: "I have published more than 300 peer-reviewed papers, co-written four books, and hold 20 Chinese patents."
Research: "My main research field is in the method development of chromatography and mass spectrometry and their applications in metabolomics, especially for disease biomarker discovery, traditional Chinese medicines and food safety." *www.402.dicp.ac.cn*

Ed Yeung

Distinguished Professor, Liberal Arts and Sciences, Iowa State University, USA

Highlight: "Developing sensitive imaging techniques for tracking the behaviors of single biological cells and single molecules in real time. I elucidated biological processes, including neuronal signaling, enzymatic activity, gene expression, and endocytosis."
Research: Identification, development, evaluation, and application of new measurement concepts through an in-depth understanding of the associated fundamental chemical and physical principles.

Yukui Zhang

President, Chinese Chromatography Society; Professor, Applied Chemistry, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, China

Research: Biological analysis by modern analytical methods (multidimensional separation techniques); genetic engineering projects, including cell expression, separation and purification of human kallikrein; and establishment of display library of cDNA of liver cancer cell.

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Fred Regnier

Founder, Perfinity Biosciences; John H. Law Distinguished Professor of Chemistry Purdue University, Indiana, USA

Research: Targeted glycoproteomics
Snapshot: "Among the many Purdue faculty who have used their research to make a direct impact on our quality of life, Fred Regnier is a renowned pioneer […] His research on chromatography is directly responsible for the development of many life-saving biopharmaceuticals. The entire world has benefited from his vision and expertise." - Martin C. Jischke, 10th President of Purdue University (2006).
Perfinity.com

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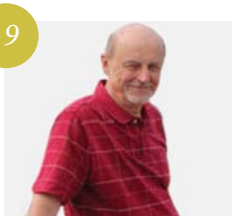

Frank Svec

Senior Scientist; Facility director at the Molecular Foundry Lawrence Berkeley National Laboratory, California, USA

Highlight: "Invention of polymer-based monolithic columns and development of monolithic materials that inspire other people, leading to a number of follow ups focused on new chemistries, approaches, and applications."
Main motivation: "I have always been trying to break new ground. I am opposed to following the old paradigms and seek ways to come up with new ones. I like face-to-face discussions with people from around the world that often lead to friendships and interesting ideas."
Future aspiration: "I would like to stay in the "business" of research for the foreseeable future and attract young people to follow in my foot steps."
svec.lbl.gov
Sitting Down With... theanalyticalscientist.com/issues/0413/601

18

Jack Kirkland

Vice-President, Research and Development Advanced Materials Technology (AMT), Delaware, USA

Highlight: "Since 1966, I have had an interest in the unique properties of superficially porous particles for HPLC columns. The strongly positive scientific and commercial response to the introduction of unique sub-3 µm Halo fused-core (core-shell) particles by AMT in 2006 has been quite satisfying as it verified my continued interest in this technology."
Main motivation: "I have always been interested in solving problems and developing new technology. The intellectual challenge of this has been stimulating. Some positive scientific results have been sufficiently gratifying so as to lead to additional efforts on projects for new technology that would assist scientists."
Future aspiration: "My intention is to continue to develop new technology largely in separation science. Of particular interest are better approaches for analytical separations in the biosciences. This difficult area presents unique challenges, but technology gains would have an important impact on health and environmental issues."
www.advanced-materials-tech.com

17

Andreas Manz

Professor, Microfluidics for the Life Sciences, Mechatronics Department; Head of research, Korea Institute of Science and Technology (KIST), Saarland University, Saarbrücken, Germany.

Snapshot: "Andreas Manz is one of the pioneers in microchip technology used for chemical applications. He was involved in the development of high speed analyzers based on CE, LC and flow injection. These analyzers are based on the microfabrication know-how originally developed for microelectronics.

"He developed a novel concept for Miniaturized Total Analysis Systems (µ-TAS), which involves sampling, sample pretreatment, separation, and detection performed in an integrated microsystem, with a chemical parameter (for example, the concentration of a compound) that is periodically transformed into an electronic or an optical signal. Such a system is in fact a hybrid, which offers the advantages of a sophisticated analysis system within the size of a chemical sensor."
(Source: Freiburg Institute for Advanced Studies; tas.txp.to/0913-Manz)
www.kist-europe.com

16

Daniel Armstrong

Robert A. Welch Professor of Chemistry & Biochemistry, University of Texas at Arlington, USA

Highlight: "Developing many of the earliest chiral phases for HPLC and GC ranks high. Our chiral HPLC work provided much of the impetus for the FDA to pass new drug development guidelines – and that changed the pharmaceutical industry worldwide. Our GC columns have been sent on space missions to comets, Mars and Venus."
Main motivation: "My main motivation has always been to do, develop and/or explain things that are new, interesting and potentially useful – and to teach others to do likewise. This is the enjoyable and most gratifying part of research. Another aspect is the chance to solve problems and the mysteries of nature."
Future aspiration: "My goal is to continue to innovate and be as useful and productive as possible with the time I have – and to have as good a time as possible doing so!"
tas.txp.to/0913-Armstrong

15

Barry Karger

Director, Barnett Institute of Chemical and Biological Analysis and James L. Waters Chair in Analytical Chemistry, Northeastern University, Massachusetts, USA

Highlight: "Scientifically, my most satisfying achievement was the development of linear polyacrylamide matrices used in sequencing 40 percent of the genome in the Human Genome Project by capillary electrophoresis. I get great satisfaction from the success of the close to 200 students, post docs and staff who've worked in my lab."
Main motivation: "I find science exciting and I am interested in not only analytical chemistry but the problems it must address. I try to integrate various technologies into separations and detection, especially LC- and CE-MS. I try to understand what's important in the areas where we apply our technology, for example, biotechnology or clinical research."
Future aspiration: "I have been a professor for a very long time. I am the founding director of the Barnett Institute of Chemical and Biological Analysis, which just celebrated its 40th year. My goal is to see that it flourishes for many years into the future."
www.northeastern.edu/barnett/research/kargergroup.html

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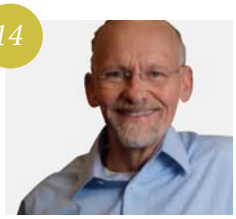


Richard Smith

Battelle Fellow, Chief Scientist, Biological Sciences Division Pacific Northwest National Laboratory, Washington, USA

Highlight: "The greatest satisfaction has been derived from my efforts to develop improved capabilities based upon various combinations of high performance separations with high resolution mass spectrometry, and the broad impacts these techniques are having upon our abilities to characterize the constituents (e.g. proteomes and metabolomes) of biological systems."
Main motivation: "My primary motivation has been the need to better characterize biological systems, and provide the information needed to understand how they operate. I have long believed that approaches based on separations and mass spectrometry would be ideally suited for this purpose, and this has guided many of my efforts."
Future aspiration: "I am interested in exploring completely new paradigms in which the gas phase ions can be manipulated in complex ways and in a lossless fashion, and using such approaches for greatly increasing the measurement throughput and sensitivity possible, for the characterization of biological systems."
Sitting Down With... theanalyticalscientist.com/issues/0713/601

13

Robert Kennedy

Hobart H. Willard Professor of Chemistry; Professor, Pharmacology, University of Michigan, USA

Highlight: "Although most of our work has been in chemical separations, our development of an electrode to measure insulin secretion at single cells was a surprising success that led to many discoveries about insulin regulation. A close second is the r ealization of the potential for rapid separation in many areas of chemical analysis."
Main motivation: "I have always been fascinated by biology. I am motivated by the excitement generated from harnessing the power of new chemical instrumentation to answer both curiosity and disease-centered questions in biological systems."
Future aspiration: "In the next 10 years, I hope that we can prove the potential of droplet microfluidics for drug discovery, make our in vivo neurochemical analysis methods routine so that they can be used to study the regulation of neurotransmitters, and improve metabolomics to discover underlying causes of diabetes."
kennedygroup.lsa.umich.edu

12

James W. Jorgenson

W. R. Kenan, Jr. Professor of Chemistry, University of North Carolina at Chapel Hill, USA

Highlight: "The development of capillary zone electrophoresis. This work offered an unexpected and unique alternative to liquid chromatography for the separation of substances of all kinds. CE ended up bringing together a remarkable group of highly creative people from a wide variety of scientific disciplines, all trying to make use of this apparently simple separation method."
Main motivation: "I enjoy working together with bright and talented young students in an effort to try to make sense of how chemical separations work and how they can be improved. It's a delight to watch a student work hard for many years and finally see them achieve success in what they set out to do."
Future aspiration: "To better understand the causes of peak broadening in chromatographic columns, to use that knowledge to design and prepare columns that can achieve even more remarkable separations, and to have plenty of fun in the process."
jjorg.web.unc.edu

11

Janusz Pawliszyn

Professor; Canada Research Chair, Department of Chemistry, University of Waterloo, Ontario, Canada

Highlight: "Inventions which were accepted by the scientific community: Solid Phase Microextraction (SPME), Capillary Isoelectric Focusing with Column Imaging Detection (CIEF/WCID) and Needle Trap (NT)."
Main motivation: "My group is actively pursuing solvent-free, "green" approaches that can integrate both sampling and sample preparation steps. This effort will lead to high throughput laboratory determination, as well as convenient on-site and in-vivo analysis."
Future aspiration: "The long-term objective of our efforts is to move analytical chemistry 'on-site' – where the sample is located – to facilitate low cost, rapid and accurate measurement and monitoring."
uwaterloo.ca/pawliszyn-group

10

Georges Guiochon

Distinguished Professor, Analytical Chemistry, Department of Chemistry The University of Tennessee, Knoxville, USA

Snapshot: "In 1984, I decided to come to the US. There were too many smart people in LC and GC, so I decided to go into something that no-one else was doing seriously – preparative chromatography. Chemical engineers had no idea about the subtleties of the stationary phase, for instance, and analysts had no ideas about chemical engineering. I didn't have much idea either but I knew enough to marry them together.

"Computers were starting to play a bigger role and I was able to solve numerically the mass balance equation for mass transfer in chromatography. I published a lot of papers and made my reputation with that [...] Now I'm doing supercritical fluid chromatography."

Main motivation: "Understanding phenomena, solving problems, and training people."
www.chem.utk.edu/Faculty/guiochon
Sitting Down With... theanalyticalscientist.com/issues/0613/601

9

Wolfgang Lindner

Professor Emeritus, Analytical Chemistry, University of Vienna, Austria

Highlight: "My most rewarding intellectual achievement relates to a deeper understanding in molecular recognition phenomena in separation sciences, which is the basis for "selectivity" in chromatography, electrophoresis, etc. In this context, the development of highly dedicated stereoselective chiral selectors and chiral stationary phases (CSPs), which eventually got commercialized, are highlights."
Main motivation: "My main scientific motivation has always been driven by the curiosity and the desire to discover correlations. I was very fortunate to share this passion with excellent co-workers and students with whom I had the pleasure of cooperating. Chemistry was already my dream when I was at high school."
Future aspiration: "My aspiration was and still is to combine several aspects: (i) to dedicate all efforts to basic research, (ii) to translate the gained knowledge to the development of novel products and methodologies useful for the public, (iii) to work as a teacher and to stimulate young people to find fascination in science – academia and industry." *www.univie.ac.at/rg_lindner*

8

Alexander Makarov

Director of Research, Life Science Mass Spectrometry, Thermo Fisher Scientific, Bremen, Germany

Highlight: "I am known for being the inventor of the Orbitrap mass analyzer, which allowed the introduction of high-resolution, high mass accuracy MS into thousands of laboratories around the world. Orbitrap-based instruments have revolutionized proteomic research and enabled significant progress in screening, toxicology and forensic analysis."
Main motivation: "The desire to make the very high performance of large, difficult-to-use mass spectrometers available to all analytical labs – not only high-end research but also routine labs. This could only be achieved by using different physical principles – and that resulted in the novel ion optics of the Orbitrap analyzer."
Future aspirations: "I want to make MS as extensively used as optical spectrometry and apply it to as wide variety of analyses as possible. My dream is to have an Orbitrap-based MS in every major hospital and clinic to enable more reliable, more sensitive and faster disease diagnostics."

7

Peter Schoenmakers

Education Director COAST; Editor, Journal of Chromatography A; Professor, Analytical Chemistry/ Forensic Science, University of Amsterdam, The Netherlands

Highlight: "One single (non-scientific) achievement is the creation of COAST – the national collaboration on analytical sciences in The Netherlands, which has more than sixty partners already. It has taken more than ten years, but our field is starting to get the recognition it deserves. Hopefully, it sets an example for other countries or regions."
Main motivation: "My motivation is definitely the bigger picture of analytical chemistry and a longer time scale (which is why details sometimes suffer and I may be less adept at celebrating moments). Consciously or unconsciously, I try to fit everything in my own picture. It may bring a bit of coherence to my work – or a bit of bias."
Future aspiration: "In my group we finally have a somewhat coherent program on (multi-dimensional) liquid chromatography, with a nice bunch of students and post-docs. I am counting on some great results in the next two or three years. Specifically, let's see if we can move from time to space."
Sitting Down With... theanalyticalscientist.com/issues/0513/601

6

R. Graham Cooks

Henry B. Hass Distinguished Professor, Analytical Chemistry Purdue University, Indiana, USA

Snapshot: "The subject for which I am being recognized has been decades in the making and many labs and individuals have contributed. I feel fortunate to have been part of this long-running campaign and to have experienced mass spectrometry when it was more a game with expensive toys and lots of promise than a real science.

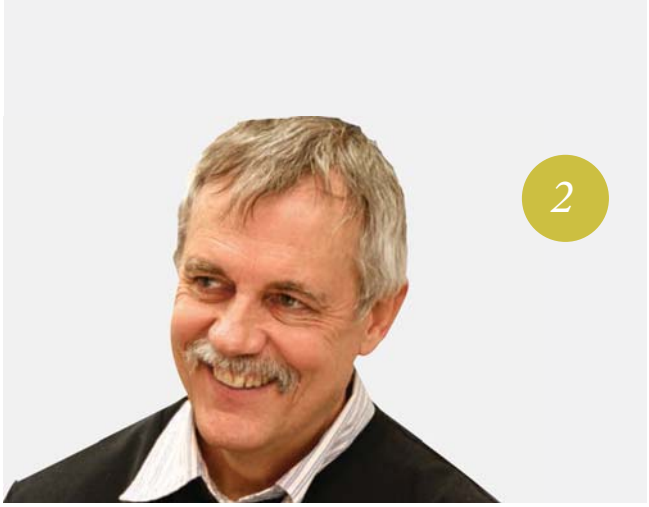
"All my work goes back to simplifying the process of complex mixture analysis – this includes the MS/MS experiments on plant material and biofluids that we did in the mid-1970s and the recent ambient ionization experiments and the attempts to do on-site measurements by mass spectrometry. The latter requires a miniature mass spectrometer."
(Source: theanalyticalscientist.com/issues/0713/mass-spec-approval)
aston.chem.purdue.edu

5

Pat Sandra

Emeritus Professor, Organic Chemistry, Ghent University; Founder and President Research Institute for Chromatography, Kortrijk, Belgium

Highlight: "The foundation of the Research Institute for Chromatography (RIC). Through the activities of RIC, I got in touch with the real analytical needs of the industry and we could help in providing solutions that are economically relevant. Moreover, it allowed me to keep my best PhD students around me, which resulted in high scientific output in a non-academic environment."
Main motivation: "My main motivation was linked to the high impact of our field on developments within different disciplines. No other field is so broad that the same instrumental development could be applied to solve different challenges – for example, the application of GCxGC to unravel the complexity of a synthetic kerosene, to elucidate pesticide residues in food, or to detect biomarkers of chronic kidney diseases in biological fluids."
Future aspiration: "My aspirations are two-fold: improving my knowledge and knowhow in fields related to life sciences and contributing to the education (knowledge and knowhow) of neophytes in separation sciences and mass spectrometry."
www.richrom.com
Sitting Down With... theanalyticalscientist.com/issues/0213/601



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4

Jonathan Sweedler

Editor-in-Chief, Analytical Chemistry; James R. Eiszner Family Chair in Chemistry, University of Illinois at Urbana-Champaign, USA

Highlight: "My highlight is the graduate and postdoctoral students that I have mentored who have gone on to successful careers in education and research."
Main motivation: "I am passionate about mentoring and training students to become successful scientists, about developing new tools that can make unique measurements from complex samples, and in using these new tools to understand how our brain works. Being an analytical chemist and a university professor is a great career!"
Future aspiration: "I am enjoying my new challenge of being editor of Analytical Chemistry. I want to ensure the journal stays the preeminent journal in its field and serves the analytical community's needs as our field and scientific publishing evolves."
www.scs.illinois.edu/sweedler

3

George Whitesides

Woodford L. and Ann A. Flowers University Professor, Department of Chemistry and Chemical Biology, Harvard University, Massachusetts, USA

What do you consider to be your biggest impacts on the field?
"In science: methods that are *simple*: self-assembled monolayers, micro-contact printing, microfluidics, paper diagnostics, cells-in-gels-in-paper, soft robotics/actuators."
What keeps you excited about your work and at the leading edge?
"*Starting* new areas. Working with graduate students/postdocs."
What are you hopes for your research projects over the next few years? "That they are useful/stimulating to others."
How do you anticipate the area of analytical science developing over the next five/ten years? "More emphasis on problems that require systems approaches, and integration of information of a number of different sorts." *gmwgroup.harvard.edu*

Ruedi Aebersold

Professor, Institute of Molecular Systems Biology, Swiss Federal Institute of Technology (ETH), Zurich, Switzerland

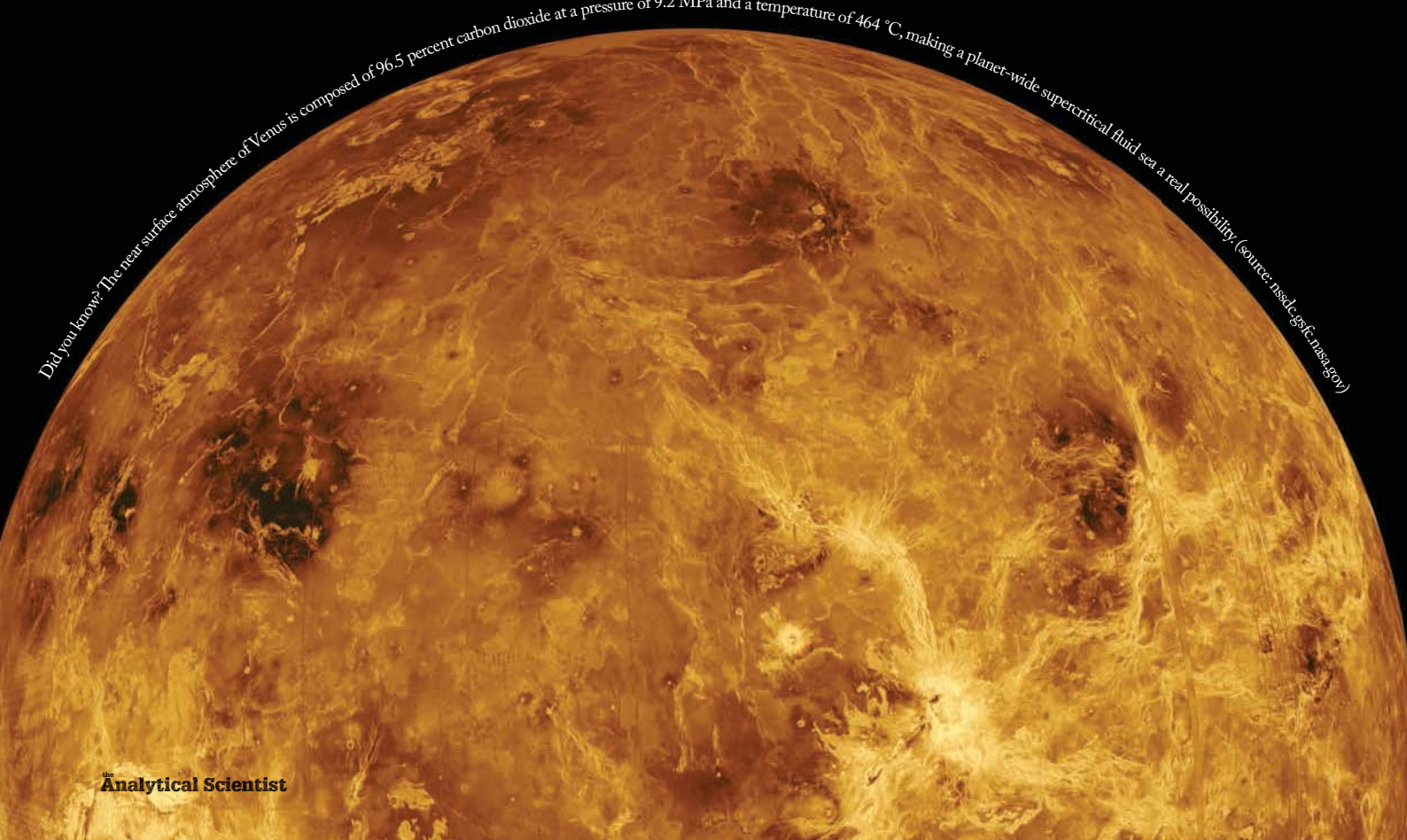
What do you consider to be your biggest impacts on the field? "The development of techniques to analyze the complexities of the proteome. ICAT (Isotope-Coded Affinity Tag) labeling is one of them. We then developed a whole range of computational tools to analyze MS data culminating in the open-source Trans-Proteomic Pipeline (TPP). More recently, we have contributed new analytical workflows for targeted proteomics to more precisely observe the quantitative behavior of sets of proteins across many samples."
The Power List's top two spots go to proteomics pioneers... "I think it's clear to everyone that the genome is only part of the picture in terms of how biological systems function. It's also clear that most of the cell's executive molecules are proteins. That's why there is enormous interest in being able to comprehensively and quantitatively analyze the proteome."
What keeps you excited about your work and at the leading edge?
"What's most exciting is that through technology development we generate the ability to see a completely new and different picture of what's going on in biological systems. There are very few research fields – or jobs – that enable you to see something for the very first time. We are in a privileged position."
Future aspirations? "I want to continue to make headway in understanding how the proteome relates to function. We are only at the beginning of this journey. We need to understand how multiple proteins cooperate and organize themselves in living cells – and how changes in this organization affects cell health."
Where do you see the field of proteomics in ten year's time?
"The goal will be to understand the dynamics of the proteome in time and space – an enormous task. I think MS will continue to play a substantial role, but single cell and imaging approaches will also be essential. We need to know how healthy and diseased cells differ mechanistically and how we can pharmacologically reset those cells in a diseased state. That will be the future of proteomics."
Further comments? "We have been very fortunate to lead research programmes with long-term perspectives and relatively good funding, which is essential for the development of breakthrough techniques. In the current climate, investment is in jeopardy because funders are pushing for immediate translation of results into the health sector, which is great... if you have something to translate. My hope is that some funding agencies will continue to support basic technology development, because, if successful, it can have an enormous impact by opening new avenues for scientific research."
www.imsb.ethz.ch/researchgroup/rudolfa

John Yates III
Professor, Department of Cell Biology,
The Scripps Research Institute, California, USA

Congratulations on topping The Power List!
"It's quite an honor. Surprising too, given that there are so many good analytical chemists out there."
What do you consider to be your biggest impacts on the field?
"There are two, and they are connected. One is the development of software methods to search tandem mass spectrometry data for sequence databases. That enabled the other, shotgun proteomics, which allows large-scale analysis of proteomes."
What keeps you excited about your work and at the leading edge?
"Besides fear of losing funding? It's the power of the technology that we and others have developed in quantitative proteomics to enable the study of all kinds of new things. As new questions come up in biology it often requires technology development to get a real insight, and that's made life fun over the last 20 years."
So is life science today first and foremost a technology-driven venture?
"In my view it always has been. Generating questions from biological research is of course important but when new technologies come around that can be applied to biology it can open up whole areas that hadn't previously been thought of."
Do the technologies get the credit that they deserve for this?
"No, not at all. Most of the high profile awards are given for biological and medical discoveries; very few go to people who develop technology. Maybe we need an Oscar's-type ceremony for technologists!"
fields.scripps.edu

Three Gurus of Supercritical Fluid Chromatography

Is the ongoing resistance to SFC a simple misunderstanding and the legacy of past disappointments? Here, Isabelle François, Davy Guillarme, and Eric Lesellier highlight the positive aspects of this underused technique and urge sceptics to re-evaluate the potential of modern SFC systems.



Isabelle François completed her PhD in 2009 in Pat Sandra's lab at the University of Ghent. Isabelle currently works at Waters, where she has recently become involved in the introduction and support of new technologies, using her expertise in ultra-high performance LC, SFC, comprehensive and heart-cutting two-dimensional fluid based chromatography (LC×(2)LC and SFC×LC) in combination with optical detectors and MS.

Davy Guillarme holds a PhD degree in analytical chemistry from the University of Lyon, France. He is now senior lecturer at the University of Geneva in Switzerland. Davy has authored over 80 journal articles related to pharmaceutical analysis and is editor of a recent book: UHPLC in life sciences (RSC, 2012). His expertise includes HPLC, UHPLC, HILIC, LC-MS, SFC, SFC-MS, analysis of proteins and monoclonal antibodies.

Eric Lesellier is Associate Professor at the University of Paris sud (Orsay), researching at the ICOA (Institut of Organic and Analytical Chemistry, Orléans). Eric tries to better understand the behavior of compounds being carried by sub/supercritical fluid through varied stationary phases. "Just like in Richard Fleicher's 'Fantastic voyage'," he says, "I would like to be reduced in size to introduce myself into the fluid entering the column, to discreetly observe the subtle interactions".

What are the main advantages offered by SFC?

Isabelle François: SFC can be used in a wide range of industries. In laboratories where organic synthesis is carried out, the medium used for synthesis is very often an apolar solvent, which can be easily injected into an SFC system. The pharmaceutical industry is significantly benefitting in this respect from this technology. Achiral SFC provides an alternative method to RPLC to search for additional impurities present in the sample, whereas enantiomers are separated by chiral SFC. Chiral separations are the niche application for SFC. SFC is even more advantageous when separations are scaled up to preparative mode. Compared with normal-phase liquid chromatography (NPLC), preparative SFC uses less solvent, produces less waste, and requires less time for fraction evaporation. The result is a greener, more cost-effective solution.

In the food industry, SFC can be used for the analysis of nutrients, vitamins, lipids and so on. In nutriceutical applications, it can aid in the search for interesting compounds, certainly when coupled with time-of-flight mass spectrometry.

In the petrochemical industry, applying a pressure gradient allows the density of the mobile phase to be increased, resulting in enhanced solvent strength, which allows the implementation of flame-ionization detection (FID).

Davy Guillarme: SFC becomes a good alternative to NPLC when large amounts of toxic and expensive solvent can be substituted by a mixture of supercritical carbon dioxide and a polar co-solvent, such as methanol. It is superior to RPLC and NPLC for chiral separations; here, SFC has a high success rate, particularly with polysaccharide stationary phases. At the preparative scale, SFC has some advantages over other chromatographic techniques, since the main mobile phase component evaporates easily, leaving only the analyte and a small volume of polar co-solvent.

Today, SFC is mostly used in the pharmaceutical industry for the purification of enantiomers. However, based on its kinetic performance and orthogonal interaction mechanism compared to RPLC, I believe it will become more and more widely used, even for the analysis of achiral substances in pharmaceutical, food, and environmental fields.

Eric Lesellier: It is almost impossible to write an exhaustive list of the benefits of SFC systems. All of the classical separation problems are handled, with the exception of water-soluble compounds. It handles interactions through mobile/stationary phase couplings, it allows coupling of columns for higher theoretical plate number, and it provides the natural concentration of the mobile phase for fraction collection. Of all the benefits, I would highlight isomer separation. Such compounds differ only by subtle geometry, so their separation requires high efficiency and interaction specificity – requirements that are easily met by SFC.

What are the barriers to implementation of SFC?

Since the introduction of SFC in the 1960s, popularity has seen highs and lows. From a user perspective, I think that resistance is a legacy of past negative experience. Major issues have included a lack of robustness and repeatability (particularly detrimental for implementation into QA/QC environments), and low sensitivity when using UV detection. Instrument builders have addressed these problems in the latest SFC equipment, and will undoubtedly continue to develop the technology, if interest is maintained.

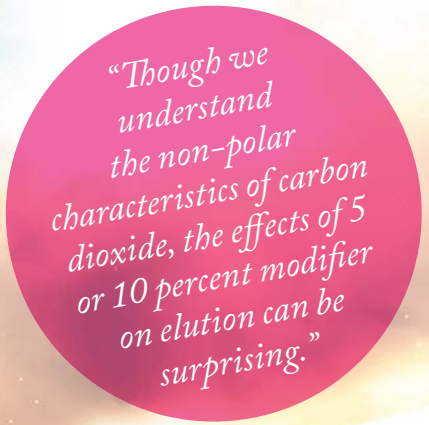
The limited understanding of the fundamental theory of SFC is one of the barriers against uptake. Certainly, when adopting SFC, interaction mechanisms are not always easily understood – a fact that is even more challenging in chiral SFC, where method development is performed by trial-and-error.

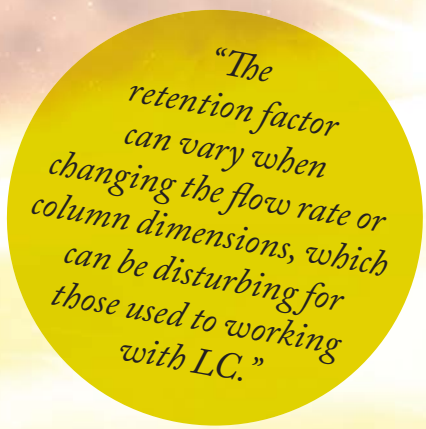
At the analytical scale, there are several 'historical' shortcomings of SFC. These issues, which really only apply to old-generation devices, include:

- Low UV detection sensitivity
- Low robustness and reliability
- Unacceptable quantitative performance (precision and accuracy) for rigorous method validation.

There is also a general lack of SFC education. This makes people reluctant to adopt it, even when the advantages are obvious. Recently, two important providers of chromatographic systems have entered the SFC market. Given the promotional capabilities of these providers, curiosity and knowledge about SFC will steadily grow.

Working with a compressible fluid raises theoretical questions. Compressibility also occurs in GC, but because of a lack of solute–mobile phase interactions, there are no serious consequences. In HPLC, liquids are generally considered to be uncompressible. However, in SFC, compressibility means that fluid properties can vary – firstly along the column and secondly when changing other parameters. Some of these can be surprising. Due in part to that compressibility, the retention factor can vary when changing the flow rate or column dimensions, which can be disturbing for those used to working with LC. It also promotes different method development practices, isopycnic or not, which lead to straightforward approaches in the first case – far from the reality of SFC practice, but more rigorous in a 'university sense' for studying specific theoretical points. Solubility in supercritical fluids – and the methods of measuring it – can also be challenging. Though we understand the non-polar characteristics of carbon dioxide, the effects of 5 or 10 percent modifier on elution can be surprising. Moreover, we are far from modeling (and understanding) the relationships between solubility in organic solvents and carbon dioxide/modifier mixtures.





What are the analytical challenges?

As identified earlier by Eric, density plays a crucial role in SFC – if it is not managed properly, solvent strength can differ between analyses, leading to shifting retention times. In SFC systems, pressure is maintained by the backpressure regulator (BPR), so excellent design is essential for maximal control. Changes in incoming carbon dioxide temperature also result in a shift in retention times, so repeatable cooling of the carbon dioxide pump heads is also crucial.

As with LC, good batch-to-batch column reproducibility is essential. Furthermore, when scaling up to preparative mode, the selectivity of the analytical sub-2µm or 5 µm particles and the preparative 5, 10 or 20 µm particles must be identical.

Injection volume flexibility was limited in older generations of SFC equipment, which indicates that designing the partial loop injector was a serious challenge – not surprising, if you consider the different states of the solvents used (injection solvent and mobile phase are under liquid and super (or sub) critical conditions, respectively) and the changes in pressure (aspiration of the sample is done in liquid mode, and when placing the loop off-line from the mobile phase flow, expansion occurs and carbon dioxide gas is present in the loop).

From a detection perspective, there are various options for MS hyphenation, but further development is always welcome. In UV detection, reduction of the noise level (linked to the difference in refractive indexes of the mobile phase constituents) needs to be optimized.

In the beginning, SFC was dedicated to the analysis of lipophilic compounds using capillary columns, supercritical carbon dioxide and FID detectors (similar to GC). It has always been a reference standard for analyzing apolar substances, such as lipids and lipo-soluble vitamins, but was less appropriate for polar compounds. Today, this has been corrected to a large extent since SFC is now performed in the presence of a polar co-solvent, using a packed column and UV detection (similar to LC). However, because a polar stationary phase is often used in SFC, polar substances may not easily elute from the column without significant amounts of co-solvent.

Another challenge for SFC is the analysis of substances in biological matrices, which is clearly of prime importance for clinical, forensic, and toxicological applications. So far, only a limited number of such applications have been demonstrated.

The utopia? Separation of proteins and highly polar compounds. However, capillary electrophoresis for protein, and hydrophilic interaction chromatography (HILIC) for very polar compound separation already do these jobs rather well.

From a practical point of view, the real challenge for SFC is method development; firstly, because of the many parameters acting on retention and separation, and secondly, because the stationary phase choice is huge, covering all those used in RPLC, NPLC, and HILIC. For RPLC, it is rather easy: choose a C18 phase, 35°C, 1 ml/min and then perform two or four water/methanol or water/acetonitrile gradients, at two pH values, at which point, dedicated software can calculate the optimal point. But in SFC, choosing the stationary phase (from pure silica to bonded C18), the modifier (from methanol to hexane), the modifier percentage (from 3 to 50 percent), the temperature (from 10 to 60°C), and the backpressure (from 8 to 40 MPa), in a system where flow rate, particle diameter and column dimensions act on fluid density – and therefore, retention – can get very complicated and daunting.

"In SFC systems, pressure is maintained by the backpressure regulator (BPR), so excellent design is essential for maximal control."

Any other potential pitfalls?

Instrument manufacturers have made huge investments in countering the main pitfalls. And development has not only been devoted to instrumentation but also to column technology, for example, the introduction of typical SFC stationary phases in sub-2 µm particles.

The future will bring a focus on overall system performance (in terms of individual parts and their integration), and on pushing pressure and flow rate boundaries to fully exploit the features of using a supercritical fluid as the mobile phase (low viscosity and low resistance to mass transfer). Accessibility and flexibility must also be improved, both in terms of hardware and software.

The biggest pitfalls are related to understanding the interaction mechanism in SFC. Firstly, it is important to understand that retention in SFC is mostly driven by H-bond capability rather than hydrophobicity of the molecule. Secondly, the relationship between retention and lipophilicity is poor in SFC and can result in some surprising behavior. Interestingly, SFC's retention mechanism and the chemical nature of its stationary phases are similar to those employed in HILIC for polar compound analysis, but HILIC cannot be considered a green technology. Thirdly, the dissolution solvent must contain as low an amount of polar solvent (water or methanol) as possible, to maintain reasonable peak shape. Finally, in modern SFC, up to 30-40% MeOH can be added to the mobile phase. Under such conditions, the kinetic advantage of SFC (low viscosity) is no longer valid and performance becomes close to that of LC.

To echo Davy, a misunderstanding of the fundamental theory and retention/separation behavior is probably the biggest potential pitfall. For instance, the effect of temperature increase is dependent on other analytical conditions: when working with 5 percent modifier and a backpressure of 10 MPa, a rise in temperature increases retention, which is typical SFC behavior. On the other hand, at 10 percent modifier and a backpressure of 15 MPa, an increase in temperature decreases retention – typical LC behavior. The transition percentage (from SFC to LC behavior) is dependent on the nature of the modifier.

Confusion also arises from the (large) amount of mobile phase that is adsorbed onto the stationary phase in SFC, as it can induce unexpected retention and separation effects. In fact, SFC (as with NPLC in the past) is subject to many subtle phenomena that can be underestimated when switching from RPLC in which the acidic and hydrophobic properties of water are the main drivers of retention.

Do separation scientists need to change their attitude/focus/scope, if they want to stay in tune with developments in their field?

To dispel the negative connotations of the past, there needs to be a shift in mentality or a re-education. The advantages of SFC include:

- Much faster separations, with higher efficiency
- Faster column regeneration
- The ability to use smaller particles or longer columns
- Alternative, orthogonal approaches to standard RPLC and GC setups
- The green aspect, which is certainly a consideration at preparative scale

Despite the fact that many chromatographers have recognized the advantages of SFC, it has never really taken off. due to the historical lack of robustness, repeatability, and low sensitivity when using UV detection. Furthermore, the simple introduction of a new analytical instrument can be a little frightening for some…

Of course. It is always important for scientists to take the time to evaluate new analytical approaches. Those who were disappointed by SFC in the past because of its lack of robustness or sensitivity compared with RPLC should give it a second chance using state-of-the-art instrumentation. The potential of SFC is real – it has been employed for a wider range of compounds than RPLC (except therapeutic biomolecules, for which it is clearly unsuitable). In an analytical laboratory, having at ones disposal a ratio of five HPLC systems to one SFC instrument could be of interest.

On my thesis manuscript, 25 years ago, I used this quote:

"When I believe I understand something, I note the day, the hour, the longitude, the latitude. Then I take one step to the side and ask myself again what I have understood." – Yves Simon (translated).

Final words?

SFC has a lot to offer. I would highly recommend analytical laboratories to get in touch with an instrument vendor to discuss applications and take SFC for a test drive. Think not of SFC as a panacea for all your analytical challenges, but rather as an additional tool alongside your RPLC system – it might bring you solutions faster, more efficiently and in a more sustainable way: a win, win, win.

What about mass spectrometry? Just like RPLC, SFC can easily be coupled with MS with either electrospray ionization (ESI) or atmospheric-pressure chemical ionization (APCI) sources. In the past, when SFC was predominantly used for apolar compound analysis, APCI was used because it is a mass flow-dependent device and offers better sensitivity at high mobile phase flow rates. However, ESI has been adapted for a wider range of compounds and often provides better sensitivity than APCI, so providers have developed several SFC interfaces to simplify coupling. Using an appropriate interface, analyte precipitation during carbon dioxide decompression can be avoided, while sensitivity and robustness are drastically improved for routine use of SFC-ESI MS.

The pioneers who invented SFC and demonstrated its potential – Terry Berger, Larry Taylor, Pat Sandra, David Pinckston – should be thanked for giving us the opportunity to work today with such powerful separation science. Now, we have the responsibility to show how this versatile and unified chromatographic method can be used to separate terpene isomers, polymers, enantiomers, sunscreens, anti-oxidants, sugars, lipids, pigments, and so many other compounds.

SFC is what I have been involved in for the last 25 years – and I will fight with the last of my strength to give it the position it deserves!

For a longer discussion on system performance, method development and column dimensions, and more, please check out the online version of this article at: theanalyticalscientist.com/issues/0813/402.

Solutions

Real analytical problems
Collaborative expertise
Novel applications

Dioxin Analysis Access

Safe toxic waste disposal and its subsequent monitoring pose significant challenges. In the developing world, where access to qualified staff and adequate facilities are often lacking, creative solutions are required. This one is time-efficient, financially viable, and suitable for use in developing economies.

By Jayne de Vos and Peter Gorst-Allman

The Problem

The entrenchment of gas chromatography-high resolution mass spectrometry (GC-HRMS) as the tool of choice for quantitation of chlorinated dioxins and furans has left some countries without access to adequate analytical infrastructure. How can advances in instrumentation and technology be leveraged to the benefit of low-economy nations?

Background

The disposal of toxic waste is a matter of enormous concern globally. The problem is most acute in the developing world, where legislation is often in place but not adequately regulated or enforced, opening the door to unscrupulous operators. Despite the potential risks, many poor countries are driven to import toxic waste for disposal as a means of raising revenue. The result? Waste disposal that is at best careless and at worst criminally negligent. To exacerbate the problem, the facilities and instrumentation required for the extraction, sample clean-up and determination of persistent organic pollutants (POPs) is frequently not in place. Consequently, there is a lack of coordinated routine capability.

For twenty years now, the quantitation of chlorinated dioxins and furans has been governed internationally by US Environmental Protection Agency (EPA) Method 1613 or methods derived from it. This has led to the entrenchment of HRMS as the analytical option of choice. For quantitation at concentration levels under parts per billion (ppb), selected ion monitoring (SIM) is used.

In South Africa, there is no established facility capable of routine dioxin measurement using GC-HRMS. While GC-HRMS was the only available technique that could reach the low levels required by EPA 1613 at the time of its publication, the advancement of instrument technology over the last twenty years has given rise to alternative approaches. There is a clear need for methodology that offers simple implementation, fast turn-around, reliability at EPA Method 1613 levels, and cost effectiveness.

Notably, in the study below, GC-HRMS comparative analysis was performed overseas after threshold screening. A process that was not only extremely costly but also impractical, giving rise to delays that would be unacceptable in critical projects, for example, assessing bird population decline (1) or large-scale crocodile deaths in Kruger National Park (2).

The Solution

We chose to combine two screening techniques: the H4IIE-luc bioassay and comprehensive GC-time-of-flight MS (GC×GC-TOFMS). The former is fast, user-friendly and inexpensive; the latter is unique in its ability to detect all compounds in complex samples at the levels needed for priority pollutant determination in a single analysis, can

provide quantitative data, and is capable of reaching the levels stipulated in EPA Method 1613. Positive samples can also be sent for quantitative analysis using the reference GC-HRMS technique, which removes the costs associated in analyzing negative samples.

During quantitative method development, we compared the results of GC×GC-TOFMS with those obtained for the same sample set using GC-HRMS to confirm validity, making it the most comprehensive environmental screening and dioxin determination study to date in South Africa using GC×GC-TOFMS.

H4IIE-luc Bioassay

In this bioassay, dioxin-like chemicals bind the aryl-hydrocarbon receptor (AhR), initiating transcription of the reporter gene, luciferase. Luciferase activity, proportional to the amount of dioxin-like chemical present, is measured using a microplate-scanning luminometer. This provides information on the cumulative biological effects of the sample, and allows samples to be ranked according to their toxic potential. It is not compound specific, however, reacting with any chemical that can bind to the AhR receptor; it therefore provides no information on the concentration of individual compounds.

GC×GC-TOFMS

GC×GC-TOFMS perfectly complements the bioassay with the necessary selectivity (through the added peak capacity of GC×GC), and sensitivity (through the focusing effect of the modulator). The instrumentation is more affordable and more user friendly than GC-HRMS. And, because it is not a target molecule technique, GC×GC-TOFMS can provide a comprehensive snapshot of total sample toxic potential in one run (3). Furthermore, it meets the requirements of EPA 1613 by providing acceptable quantitation at the mandated levels of detection (4,5).

South African Soil and Sediment Analysis

Fresh soil and sediment samples were taken from diverse regions of South Africa to represent different land-uses and anthropogenic impacts. The samples were first analyzed for dioxins and furans by GC-HRMS and then by GC×GC-TOFMS. The excellent agreement between GC-HRMS and GC×GC-TOFMS for the total sample toxicity results (total toxic equivalents, TEQ) confirms the reliability of the new method (data available in online article).

The extraction and clean-up procedure for the H4IIE-luc bioassay and GC×GC-TOFMS samples is similar. Samples are air dried and homogenized. A 40 g portion is mixed with sodium sulfate before accelerated solvent extraction using dichloromethane and hexane. The extracts are treated with activated copper to remove sulfur, and cleaned by gel permeation chromatography (GPC) and acid digestion. The samples for GC×GC-TOFMS analysis are spiked at appropriate levels using the internal standards for the 17 toxic dioxin and furan congeners recommended by EPA 1613.

The bioassay detected dioxin-like activity in 22 percent of the sediment samples (BEQ20; n=96) and 58 percent of the soil samples (BEQ20; n=66). BEQ20 indicates a sample extract that gave a 20 percent response to the dioxin (TCDD) positive control.

All samples that tested positive and six samples that tested negative in the bioassay analysis were then analyzed by GC×GC-TOFMS for dioxins and furans. Of these, 23 percent of positive soil samples and 41 percent of positive sediment samples were found to be false positives (the bioassay is not dioxin/furan specific). In South Africa, polynuclear aromatic hydrocarbons (PAHs) are generally present at levels an order of magnitude higher than the dioxins/furans, and this is most likely the cause of the many false positive results.

A prime consideration in method development is the accurate determination of low concentrations of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD). Using the EPA-1613 standard calibration set (0.5 - 200 pg/µl), a calibration curve was constructed for the seventeen congeners. The 2,3,7,8-TCDD calibration curve obtained was linear (R^2 = 0.9996); and an average

The System

GC×GC-TOFMS: LECO Pegasus 4D (Agilent GC and autosampler, a secondary oven, and a dual stage modulator). Liquid nitrogen cooling was used for the cold jets; synthetic air for the hot jets. Primary and secondary columns were connected using a press-tight connector.
A GC multi-step temperature program was developed to facilitate separation and quantification of the maximum number of POPs that could be present in environmental samples in a single analysis, thus fully benefitting from the added selectivity of GC×GC and the full range mass spectra generated by TOFMS.
Tuning: The less conventional 414 ion was used in an attempt to improve the signal intensity in the higher mass range (3).
Software: All instrument functions and data processing were managed with LECO ChromaTOF software, including the manual review of all peak identifications and integrations. Searches were performed using a dioxin/ furan user library compiled from the 17 toxic dioxin and furans congener standards.

response factor of 1.06 was obtained. The quantitation capability was further investigated using the low-level standard (0.5 pg/µl) to calculate a signal/noise (S/N) ratio for the ion of mass to charge ratio (m/z) 322 for 2,3,7,8-TCDD. The resulting S/N of 20 is well above that set by EPA Method 1613 (>10).

To confirm the limit of detection (LOD) in soils, two 10 g confirmed blank soil samples were spiked with native dioxins at concentrations of 0.5 pg/µl and 200 pg/µl for 2,3,7,8-TCDD. After the addition of labeled material, extraction, clean-up (GPC) and concentration, it was possible to calculate LODs for 2,3,7,8-TCDD of 322 fg and 353 fg respectively. These calculations were made by determining the S/N for the ion of m/z 322 and extrapolating linearly to an S/N of 3:1. Results were consistent with the LOD determined from the lowest calibration standard, thus providing assurance that the method has the sensitivity necessary for low-level dioxin determination.

Beyond the Solution

We now have a combined method for the analysis of dioxins and furans in soil and sediment samples. It uses the H4IIE-luc bioassay as a preliminary screening tool, reducing the need for unnecessary instrumental analysis and driving down the cost per sample. Analysis of positive samples is conducted using GC×GC-TOFMS, which provides dioxin sensitivity at the required levels. In addition, since this is not a target compound technique it is capable of providing information on multiple compound classes present in the sample in one run, giving a comprehensive picture of sample toxic potential.

A lack of access to certain analytical resources means that South Africa is not always able to quickly assess and respond to POP emergencies, which could negatively affect human and environmental health, as well as trade and industry. South Africa is not alone. We hope we have emphasized a real need to develop local analytical capability that employs regionally relevant methods to generate internationally acceptable results. Our end result is a method that is time-efficient, financially viable, and suitable for use in developing economies where instrumental availability, skills and finances are often limited.

Please view the online version of this article for additional data table and figures: tas.txp.to/0913-dioxin

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High resolution separation of related compounds of Erythromycin using the new VWR-Hitachi ChromasterUltra Rs and LaChromUltra II C18 column with dimensions 250 x 3 (1.9 µm particle size)

Synthetic impurities as well as degradation products are becoming increasingly important in today's analytical laboratories. Over the past few years there have been steps made by The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) to produce a consensus guideline on the assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk. In this current M7 step 2 draft document lower thresholds of impurities are mentioned. It therefore appears that there will be a need in the near future for HPLC with improved sensitivity and resolution.

It is proposed that the ChromasterUltra Rs together with the LaChrom Ultra II high resolution column is able to fulfill some of these future needs. The ChromasterUltra Rs is equipped with Liquid Beat Technology (LBT), which is the automatic continual adjustment of the piston stroke using four independent pressure sensors in order to compensate for the change in compressibility of the solvent as the mobile phase composition and the back pressure changes over time. LBT, along with the new double cork mixing technology, allows exceptional baseline stability. The ChromasterUltra Rs DAD has an optional 65 mm capillary flow cell. These key features help to deliver the excellent sensitivity and resolution required for more stringent requirements of impurity and related compound testing.

Erythromycin is a widely prescribed antibiotic manufactured using either fungal fermentation or a highly complex chemical synthesis, owing to the presence of ten asymmetric carbon atoms. Therefore, there is an increased probability of structurally similar impurities being present in the final product. There are a number of publications of methods involving high end mass spectroscopy for the analysis of related substances, however, these methods are not suitable for the tight budgets of small and medium sized pharmaceutical companies.

Column temperature: 50 °C
Eluent: 20 mmol/L Phosphate Buffer/ CH3CN/CH3OH = 45/40/15 (pre-mixed)
Wavelength: 210 nm
Column Type: LaChromUltra II C18
Max Pressure: 1350 bar (Coupled columns)

Sample: Erythromaycin A: Wako pure chemicals
056-07361 DCH57893

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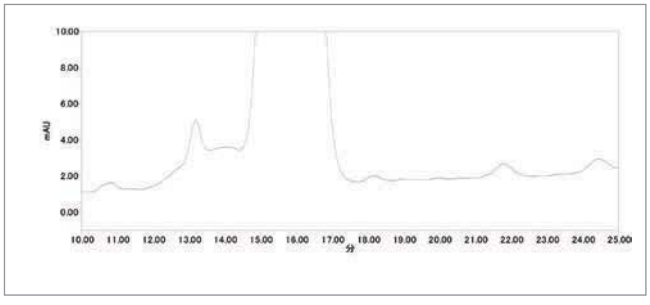


Figure 1: Zoom of main peak (Poor separation between main peak and suspect impurity peak) Flow rate: 1.000 mL/min. Inj. Vol.: 20 µL Column: 4.6 x 150 x 5µm

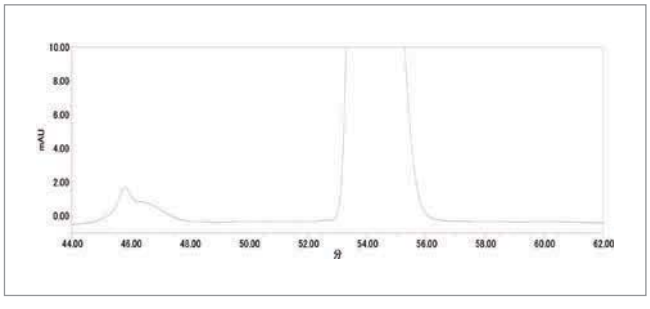


Figure 2: Flow rate: 0.50 mL/min. Inj. Vol.: 10 µL. Two columns coupled (3.0 mm x 250+250, 1.9 µm). Showing excellent separation of the suspected impurities.

For more information: chromatography@eu.vwr.com

Sophisticated antibody analysis by GPC/SEC

Monoclonal antibodies (mAB) are increasingly growing in importance for the diagnosis and therapy of various diseases, including cancer as well as autoimmune and inflammatory disorders. One essential parameter to define their quality is the content of aggregates (dimers, trimers and higher aggregates). These aggregates can be formed during processing and purification or are the result of long-term storage. Due to the aggregation antibodies lose their pharmaceutical efficacy and can facilitate an immune response.

Antibody fragments, which lack the Fc region, can be used for the treatment of diseases. Also, they can be the result of degradation of full length antibodies. Therefore, a GPC method that offers the opportunity to analyse antibodies and their aggregates as well as antibody fragments simultaneously with superior resolution is worthwhile, in addition to offering highly sensitive detection.

Experimental:

GPC/SEC analysis was performed on a PSS SECcurity GPC System, equipped with a PSS SECcurity SLD1000 light scattering detector, using the following conditions:

Columns:	PSS PROTEEMA, 5 µm, 2x300 Å (8x300 mm each) + precolumn
Solvent:	100 mM sodium phosphate pH 6.7 + 0.25 M NaCl
Flow-rate:	1.0 mL/min
Temperature:	25 °C
Detection:	Refractive index increment (RI), UV at λ=280 nm, PSS SLD1000 (RALS) at λ=488 nm
Calibration:	Light scattering
Injected mass:	60 to 80 µg
Data acquisition, Calibration and Evaluation:	PSS WinGPC UniChrom 8.1

Results

Figure 1 shows an overlay of elugrams obtained for a full length antibody and antibody fragments analysed on one set of columns.

All three detector signals for the analysis of a monoclonal antibody are shown in Figure 2. The light scattering signal shows improved sensitivity for high aggregates compared to the other signals.

Conclusion

The GPC/SEC method including UV, RI and RALS can be used for the simultaneous determination of aggregate content of monoclonal antibodies and antibody fragments. The column combination used covers the separation range for all three types but nonetheless provides a high resolution for the determination of the dimer content. Due to its molecular weight dependency, the PSS SLD1000 RALS detector offers high sensitivity for small quantities of high aggregates and also allows the determination of the absolute molecular weight of the antibodies.

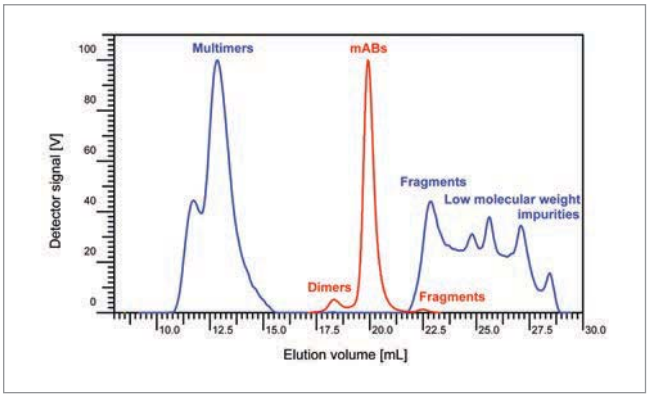


Fig 1. Separation range of the column combination. Red curve shows the UV signal of a full length antibody and its dimers plotted against the elution volume. The blue curve is the elugram of antibody fragments and their high level aggregates.

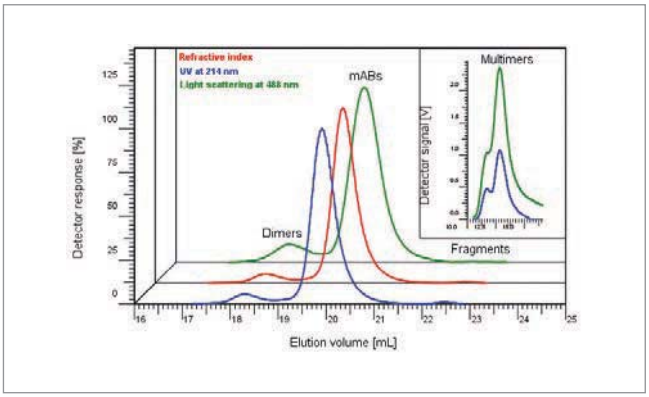


Fig 2. Sensitive analysis of antibody aggregates. The light scattering signal for the dimer is relatively high compared to that of the mABs due to molar mass dependency and provides improved sensitivity for the detection of high aggregates (inset).

Analysis of Synthetic Oligomers and Polymers

New roles and applications in the areas of science and technology are continuously being found for synthetic polymers. As the applications of synthetic polymers increase, there is a need for methods to accurately and precisely characterize these materials. Here, we summarize two GPC applications developed on the all-in-one EcoSEC® GPC System. The system was used to monitor the synthesis and to quantify the oligomeric content of two PEGylated synthetic polymers and to measure the molar mass of an isocyanate modified polyurethane prepolymer in less than one hour.

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 SEC chromatograms 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 common 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 1 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., Tosoh Bioscience LLC; A13I15A & A13I14A

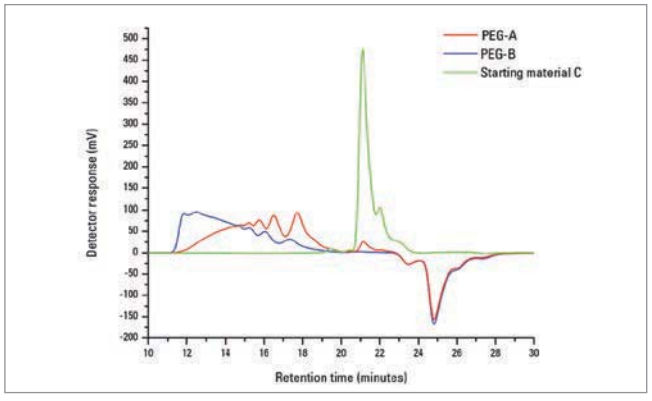


Figure 1: Synthesis monitoring of PEGylated polymers
Elution profile of PEG-A (red), PEG-B (blue), and starting material C (green) monitored by refractive Index detection at 0.3 mL/min in THF at 35°C

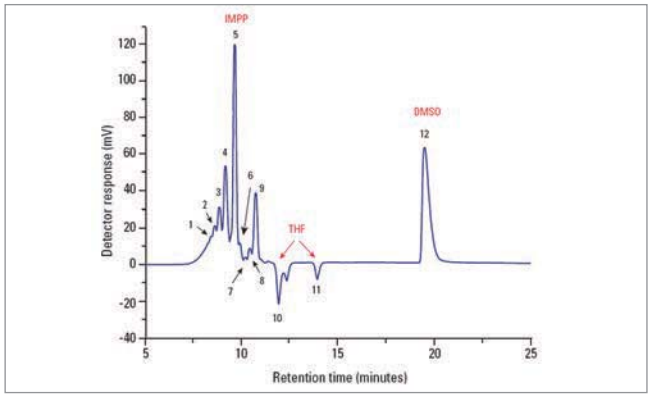
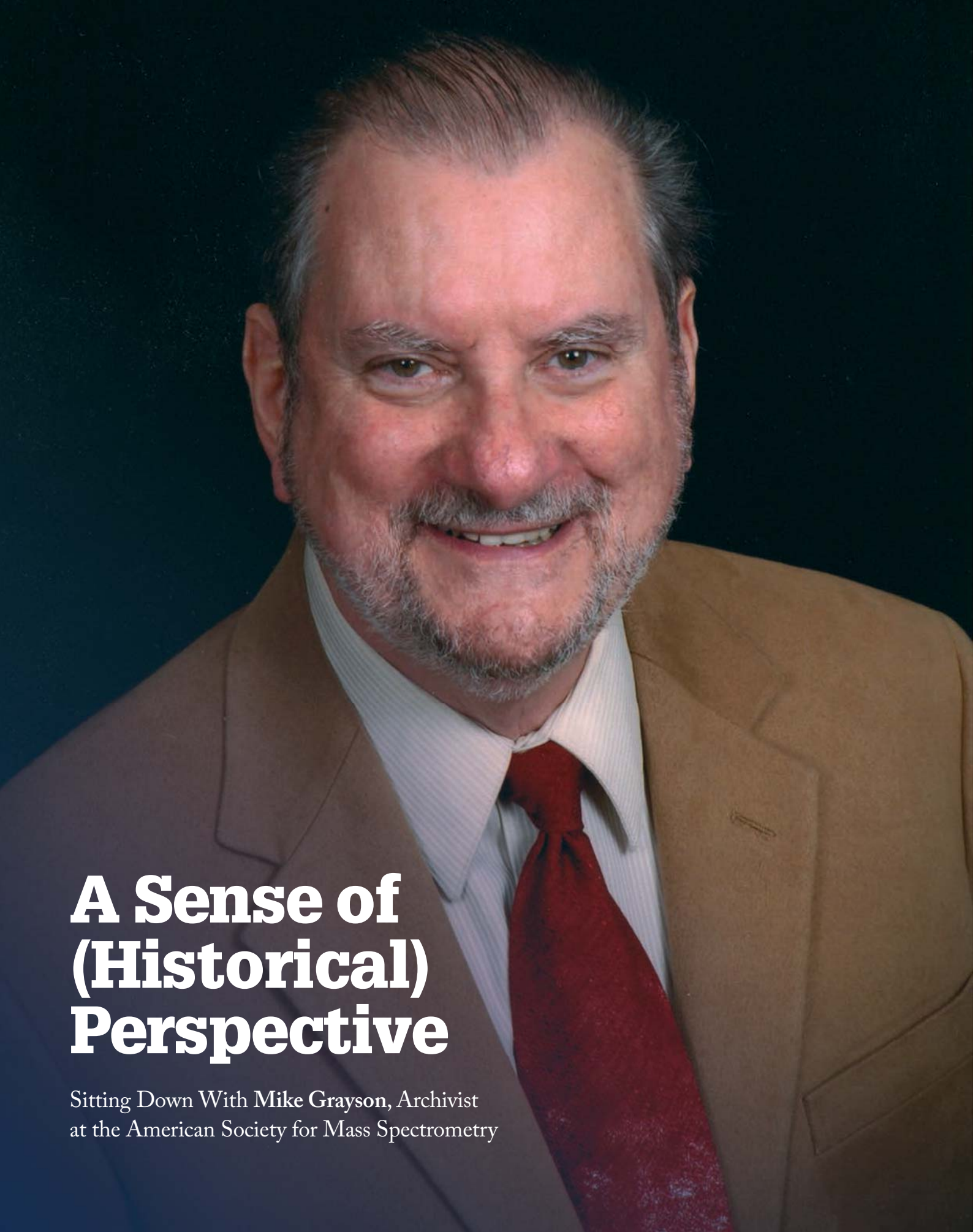


Figure 2: GPC elution profile of IMPP sample
Monitored by refractive index detection at 0.6 mL/min in THF at 35 °C.



A Sense of (Historical) Perspective

Sitting Down With **Mike Grayson**, Archivist at the American Society for Mass Spectrometry

What does a science archivist actually do?

The primary functions are to collect information that would otherwise be lost and to provide a repository for items that are of historical value. There is not a fixed set of criteria for what to archive; everything is judged on individual merit.

What are your functions as ASMS archivist?

There are several. I preserve the papers from ASMS Board meetings. Some of it can seem a bit mundane, for example, deliberations on whether posters should be allowed at the annual meeting, but it also provides a useful record to help determine when important events occurred and how they were perceived by the community. I also run an oral history project: these are in-depth interviews with two or three key contributors to mass spectroscopy every year. And I represent ASMS to the Chemical Heritage Foundation (CHF), where we have pursued the collection of mass spec instrumentation. But that can be a little rough because of the sheer size of the instruments, some of which take up an entire room.

Is there any way around this?

One idea is to record instrument history via video. Rather than collecting the instrument itself, this involves someone using the instrument and talking about its application and idiosyncrasies.

Are you also an historian of science?

I do not consider myself a historian as I lack the formal training, but it does really interest to me. Obviously, the interpretation (history) is more fun than cataloging (archiving). These days the opportunity to do historical research is there: you can dig quite deeply into the primary source literature using the Internet where twenty years ago you would have required access to a major, physical library.

I am drawn to controversies. Certain ideas have been dismissed out of hand as impossible, useless or meaningless, which, later on, have opened new vistas. Let me give two examples. The original study submitted by Frank Field and Burnaby Munson to JACS on chemical ionization got scathing reviews. They stuck with it and when it was eventually published it kick-started gas-phase ionization chemistry. I'd love to know who the reviewers were. Another is John Fenn's work on electrospray, which was rejected on a number of occasions before it became a powerful tool for the ionization of proteins. Both instances reflected the 'old boys club'. Field and Munson worked for a small oil company called Humble Oil; and Fenn, while he had a reputation in supersonic expansion nozzles, was an outsider in mass spec.

You enjoyed a long career in the lab, were you interested in history then?

No, it was a subsequent development. At the lab bench, I was focused on the research and day-to-day instrumentation, although the history interest group of ASMS did intrigue me. What really got me involved was the sense that some classical instruments should be preserved. Then, when I was involved in running a local mass spec discussion group we invited Al Neer from Minnesota to give a talk about his career and his research. That was when the oral history project got up and running – I wrote up a proposal to spend the weekend interviewing Neer. From then on, I had the bug.

Why should lab scientists take note of the history?

Apart from its intrinsic fascination, having a historical perspective can help you become a better scientist; it helps set the tone for the things that you publish.

As an example, 2013 is, I have argued, the centenary of mass spectrometry as an analytical tool. In 1913, J. J. Thomson published both his book, "Rays of Positive Electricity and their Application to Chemical Analysis," and his concept of the atom; and it was the year that an x-ray tube sufficiently powerful to x-ray something other than a human being was developed. These were essential developments that should be celebrated.

Should scientists make a personal archive of their work?

Yes, even if it is for no other reason than your own interest in retirement and your children and grandchildren's interest. A lot of it can be done by filing away daily work and notebooks. I have a miniature archive that captures contributions from my career. However, don't expect an archive to take it; they have limited space for Frank Field's papers but not for mine.

Which two historic figures would you most like to have had dinner with, and why?

J. J. Thomson would be one. He has not been adequately recognized for his contributions, although the mass spectrometry community now appreciates him. Before him, the concept of the atom was a philosophical one; after him, it was physically available for examination and experimentation, a paradigm shift for atoms and elements. I'd be fascinated by Thomson's reaction to how we do mass spectrometry today, would it be beyond what he could have imagined? The other would be Werner Heisenberg. I'd like to discuss his decision to use heavy water for fission reactions in the 1940's, specifically if he had non-scientific reasons for doing it. It's something I'm really curious about.

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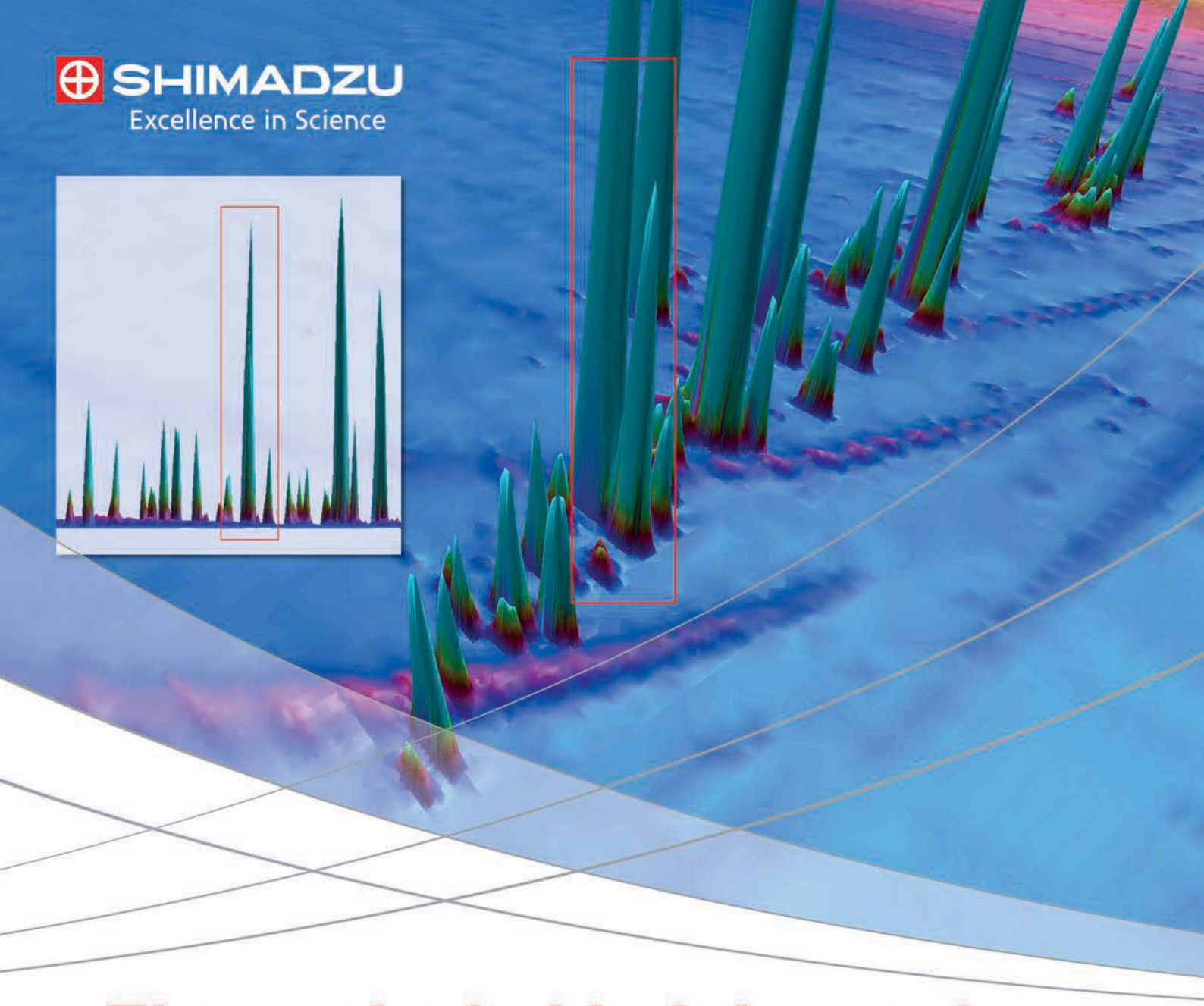

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