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HUMANITY IN SCIENCE AWARD

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2015 Winners
Andreas Seidel-Morgenstern (left)
and Peter H. Seeberger (right),

Who will be the winner in 2016?

Nominations for the 2016 Humanity in Science Award are now open

Analytical science has the power to change human lives for the better, but rarely receives the same fanfare as other scientific disciplines. The Humanity in Science Award was launched to recognize and reward a recent breakthrough in analytical science that has truly made the world a better place.

The 2016 award will be presented on May 10 in Munich, Germany.

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- *Opportunity to tour Phenomenex headquarters in Torrance, California*

Nominations close on November 27, 2015 - *Good luck!*

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On The Cover

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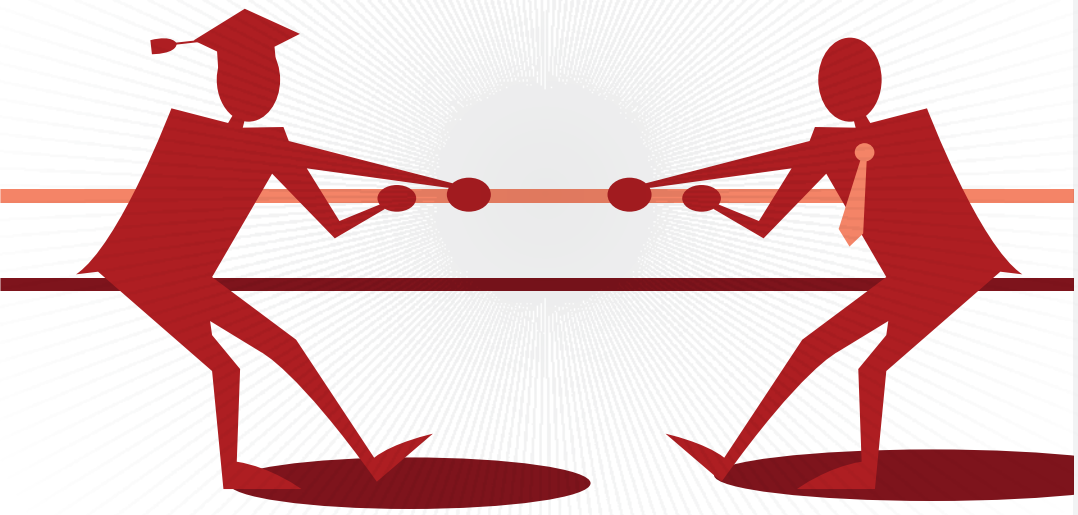

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We ♥ Pluto

And it appears Pluto loves us back – its "two-tone heart" has enchanted scientists and the general public alike. But what's that got to do with analytical science?

After a journey of over three billion miles, New Horizons has successfully completed its flyby of Pluto (1) – a feat akin to "a golfer in New York hitting a hole-in-one in Los Angeles," according to project manager Glen Fountain (2). And though I disagree with likening the accomplishment to a truly impossible task (that would be a truly gargantuan swing), I do appreciate just how thrilled everyone involved in the project must feel.

Avid readers of The Analytical Scientist will know that I'm somewhat hooked on our exploration of space. But it's not just because of my childhood (OK – and adulthood) love of science fiction. I am more fascinated by the deep collaborative effort required; to gain any (useful) knowledge from such bold attempts to reach beyond our own planet, we need the total diligence and focus of many scientific disciplines – including analytical scientists.

New Horizons' scientific payload was developed to answer some relatively simple questions about Pluto, for example, "What is its atmosphere made of, and how does it behave?" (3). To name but a few of the instruments employed, there is Ralph (visible and infrared imager/spectrometer), Alice (UV imaging spectrometer) and PEPSSI (Pluto Energetic Particle Spectrometer Science Investigation) – all of which demanded a great deal of effort behind the headline-grabbing scenes (for one such story, see page 14). Alan Stern, New Horizons Principal Investigator, shared a little news on that front: "We've discovered that the putative polar cap on Pluto's north pole is just that. We now have compositional spectroscopy that shows methane ice and nitrogen ice there."

But let's not forget even simpler, almost childlike, questions. How big is it? Well, bigger than we thought. Measurement of its mass was relatively straightforward (for astrophysicists), but accurately predicting size was evidently harder. Indeed, the latest data requires a rethink of the ice-to-rock ratio of a less-dense Pluto (or suggests that it has been hollowed out by aliens seeking refuge.)

And so to my first point: accurate measurements shape our world – and beyond. Whether we are investigating planetary bodies or metabolomic profiles of single cells, the measurements we deem to be acceptable form the basis of knowledge or decisions. My second point: as Barry Karger notes on page 48, there are plenty of questions left to solve. And accurately answering even the simplest ones is not always as straightforward as it first appears.

Rich Whitworth
Editor

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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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Jurassic World... with Real Science

Laser-stimulated fluorescence shines a light on the hunt for dinosaurs

A recent paper in PLOS One about using laser-stimulated fluorescence (LSF) to find fossils couldn't have been better timed given the success of the recent movie reboot, Jurassic World. The research group demonstrated that the technique can be used to more effectively find and analyze dinosaur fossils – and provide greater detail in the process (for example, soft tissue information), which is invisible using more traditional methods, such as ultraviolet light (1).

"It's been known for some time that some fossils, but not all, fluoresce under UV light," says Thomas Kaye, a research associate at Burke Museum of Natural History and Culture in Seattle. "It's also known that ants often pick up microscopic fossils and take them to their anthill. So if you shine a UV light on an anthill at night, you can pick out the glowing specimens."

Compared with UV, LSF provides an order of magnitude improvement in the signal-to-noise ratio. After reading about the advances made through the use of LSF in biology, Kaye wondered if it would stimulate the fluorescence in dinosaur bones. And it did. "Since then, we've progressed the technique to develop a kind of automatic sorting machine. The system feeds gravel from the anthill through a small opening and we shine a laser on that opening. When something comes through that is brighter than normal, it gets separated," says Kaye.

But using LSF as a fossil sorter is only the tip of the iceberg. As lasers have become cheaper, Kaye and his collaborators have started using blue lasers, which produce greater fluorescence than the green lasers the group had been using before. "We could use a blue laser to identify some previously unknown specimens because it can fluoresce fossils where the bones are buried beneath the matrix," says Kaye (see Figure 2).

After travelling to China, one of Kaye's students from the University of Kansas was able to fluoresce a Chinese feathered dinosaur at a museum. To her amazement, the feet, which were just bones to the visible eye, showed the foot pad and scales when fluoresced. "We were stunned! When you look at something that looks like a piece of sand and a few bones, you wouldn't think this level of geochemical preservation was there. The fluorescence sorts out one geochemical fingerprint from another at a very minute level – so differences between the scale and the skin of the foot show up as color differences and illuminate the original soft tissue that used to be there. Some of the things we saw were like looking at an x ray of a chicken," says Kaye. "This could alter the paleontology field since experts may have been chipping away at soft tissue

Figure 1. Proof-of-concept prototype automated micro-fossil picker. The feeder bowl guides matrix under the laser; the video camera detects size and brightness; fluorescing fossils are selected for further investigation using a puff of compressed air.

information that they didn't know was there."

Now, the researchers are working on a second paper that will showcase in more depth what can come of using LSF on dinosaur fossils. The group also hopes to create a portable system that can use hyperspectral imaging. Kaye explains, "This would allow us to put together a spectroscopy for each of the minerals that we find are fluorescing differently. In an ideal scenario, we would create a data cube; each layer in the cube would represent a particular wavelength and if you stack the cube vertically it would create a low-resolution spectrum. From the spectrum, we could determine more about the minerals and what they are doing, and how this detail came to be preserved."

"In China, they have quarries where hundreds of people are toiling every day to split shale and search for fossils. They will split open a mountain of shale to find one feathered dinosaur fossil. One of the things we'd like to attempt is to bring a portable system into the field at night and to shine the laser on the quarry wall. Even if there is just the edge of a bone sticking out of the wall it should light up. We could scan an entire wall and see where the lights line up, which would be an indicator of where to dig."

And if you're wondering what Kaye thinks of the Jurassic World film – he still hasn't seen it. "I'm out in the field, so I'm miles from a cinema. But I'm sure people will be eaten, which is always good in dinosaur movies..." *SS*

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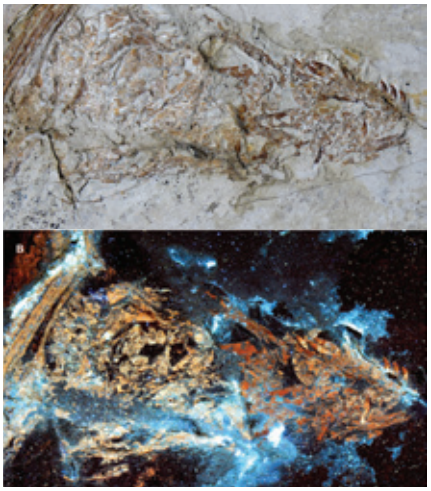

Figure 2. The skull of a Microraptor specimen was first examined under white light conditions (A). There appears to be nothing unusual about the specimen. Subsequent LSF imaging (B) reveals dramatic differences in fluorescence between the proximal and distal portions of the skull – is it a composite specimen?

Biosensing Gets Smart

Australian researchers harness the power of smartphone biosensing – without the need for specialized components

Many have attempted to couple ingenious technology with smartphones to create portable analytical or diagnostic platforms. But because such innovations rely on specialized add-ons, researchers from Macquarie University in Australia wanted to take a novel approach for their fluorescence based biosensor.

"We wanted to create a biosensing device that could test biological samples for levels of trypsin and collagenase – clinically relevant biomarkers found in high concentration in many human diseases including arthritis, cystic fibrosis, acute pancreatitis and other clinical diseases," says Ewa Goldys, a professor at the university and deputy director of the Australian Research Council Centre of Excellence in Nanoscale Biophotonics. "However, it was important that our device had a minimal number of commonly available components. The device needed to be able to be built anywhere in a truly cost effective fashion. A specialized add-on creates additional expense and logistics issues."

And so Goldys and her colleagues developed a device that uses readily available components – a tablet, a polarizer, a smartphone (camera) and a box that provides dark readout conditions – to perform fluorescence based tests (1). "The assay in a well plate is placed on the tablet screen, which acts as an excitation source. A polarizer on top of the well plate separates excitation light from assay fluorescence emission, enabling readout with a smartphone camera," explains Goldys. "It can be used anywhere – at the bed-side, in doctors clinics and surgeries, and in remote locations that are far away from expensively equipped laboratories."

Goldys is passionate about the future relationship between smartphones and analytical science. "Seventy percent of a standard laptop's capability is now available in our phones and it's an exciting time as researchers realize that consumer electronics have the capacity to be reconfigured for a variety of purposes," she says.

"The wider application of diagnostic tools will help people get health related advice far more quickly than was previously the case, which is critically important for many diseases, especially those that need to be diagnosed rapidly." *SS*

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Catalyze This (or That)

A simple yet innovative catalytic reactor – the Polyarc – aims to give GC-FID a fresh lease of life

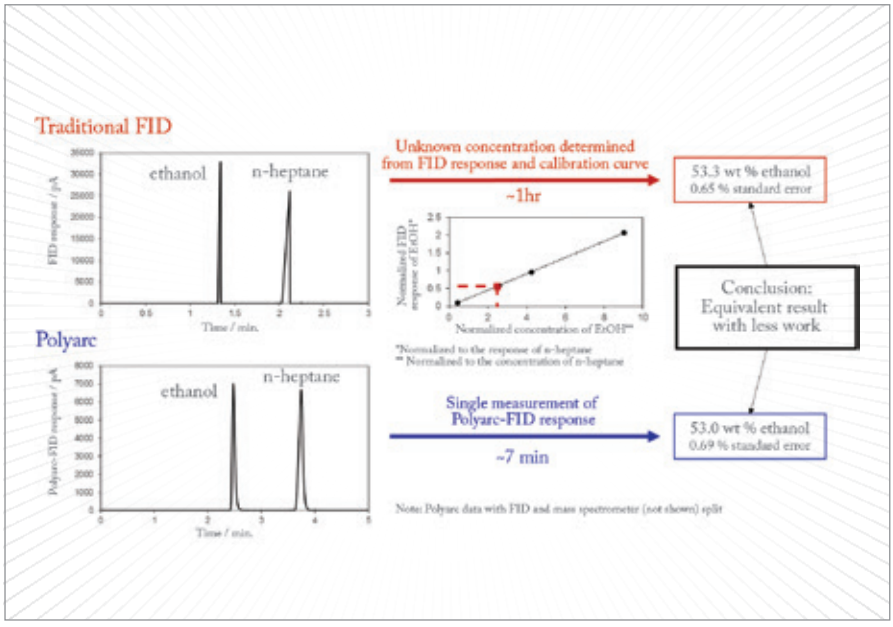

Figure 1. Comparison of the work required for the equivalent determination of the concentration of ethanol in a mixture using (top) an FID and a response calibration, and (bottom) the Polyarc with a single measurement.

Who?

Brad Cleveland and I (Andrew Jones) founded Activated Research Company (ARC) in July 2014. I had just finished my PhD in Chemical Engineering focusing on catalysis at the University of California, Berkeley. Brad brought 13 years of experience as CEO of Proto Labs. We wanted to create a company that improved lives using catalysis; we believe our first product really embodies this spirit. Kimberly Herzog, also a chemical engineer, soon joined us to lead commercialization of the product. We all share the same roots: the University of Minnesota, Twin Cities.

What?

The Polyarc is a small catalytic reactor, born out of Paul Dauenhauer's research lab at the University of Minnesota, that converts gaseous carbon-compounds into methane. When integrated after column separations in gas chromatography (GC) systems, flame ionization detection (FID) of the resulting methane leads to a higher and equivalent sensitivity on a per carbon basis (see Figure 1). We have finished beta testing trials with very positive results and feedback, and are finishing up a more extensive pilot testing of the product at a number of universities and global corporations.

Why?

The product improves GC-FID analysis in three main ways:

i. Calibrations of FID response factors for individual components are no longer required because methane is the only gas created, eliminating the need for expensive standards and also saving time.
ii. CO, CO_2, formic acid, formaldehyde – and many other compounds – that have little-to-no response in a typical FID are all converted into methane, allowing their detection with an equivalent per carbon sensitivity.
iii. Integration of peaks from unknown compounds gives the carbon content of those compounds, allowing users to close their carbon balance, estimate carbon fractions, or determine purity without knowledge of the exact structure or molecular weight.

How?

The reactor is a two-step catalytic process. Carbon-containing molecules are first combusted on a metal catalytic surface into CO_2 and the resulting CO_2 is subsequently reduced to form CH_4. We have spent the last year developing the technology to optimize the internal reactor design and catalytic support, mitigate any impact on separation performance, and ensure long-life and complete conversion of a wide variety of carbon compounds. We have done extensive testing and have yet to find a molecule that doesn't work with the Polyarc, which can be seamlessly integrating into existing GC-FID systems.

Next?

ARC is dedicated to doing everything we can to ensure this product makes our customers' lives easier and improves their GC-FID analytics. We are very excited for our full product release, which will happen once our pilot program is wrapped up. We have also scaled our operations to meet what we expect will be a very large demand. We can't discuss any future products at this time, but we can tell you they will be equally compelling and, of course, involve catalysis.

Winning Wines Under Scrutiny

Chemical profiles link production methods with characteristic flavors

Pinot noir wines all start off with Pinot noir grapes, and yet there is great variation in color and taste. To find out why, a team of analytical scientists from the University of Helsinki embarked upon research (that was in no way enjoyable) to analyze the chemical profiles of eight Pinot noir wines from across the world. They were able to determine some of the finer processing points, such as which sugars had been added and whether sulfur dioxide was added to prevent the wine from oxidizing.

Heli Sirén, a researcher from the university's department of chemistry, believes that if more information was included on the label, such as sugar content and organic acid content, it might also provide a clue as to how the wine would taste. For instance, the team found that biodynamically produced grapes fermented without sulfur dioxide and micro-oxygenation treated grapes gave the lowest organics contents – and it is the content of organic acids that can give wine a characteristic taste.

"I'm very interested in winemaking processes and in this study I wanted to look at what's happening at a molecular level," says Sirén. "It is commonly known that the flavors and colors of wine are influenced by aging and sunlight, but we also wanted to look at winemaking processes and whether producers use artificial improvements."

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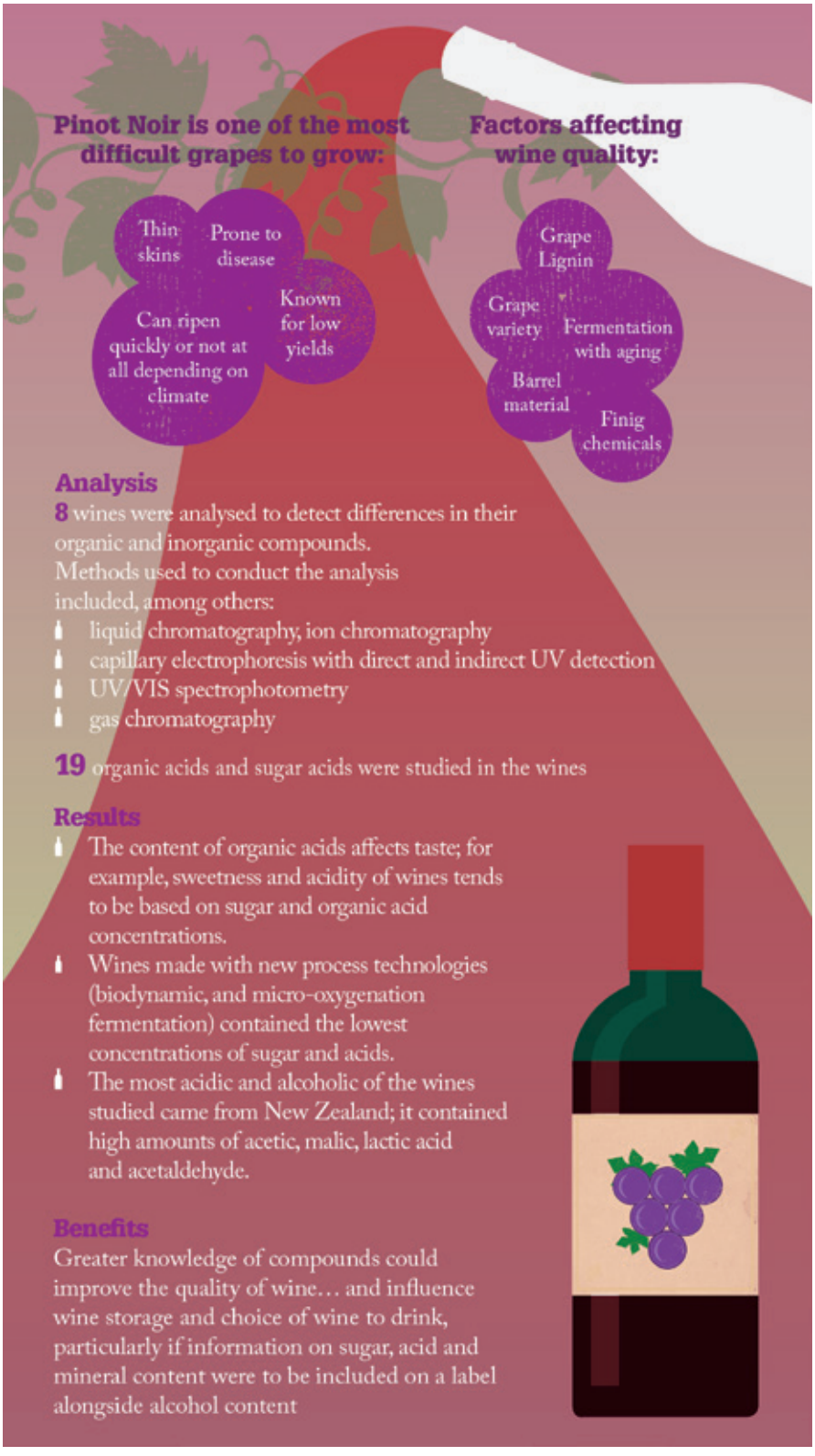

Pluto: the New Red (Dwarf) Planet

Fingerprinting ice with FTIR spectroscopy ahead of New Horizons flyby of Pluto

The New Horizons spacecraft has just successfully conducted its first flyby of Pluto – and there are jubilant scenes in Mission Control as we write this on July 14, 2015. After a nine-year journey of more than three billion miles, expectations are certainly high – and, so far, those expectations are being spectacularly met. Surprise number one: Pluto is bigger than we thought. Surprise number two (breaking news): Pluto is red, just like Mars.

But the flyby itself shouldn't take all the credit. To help the New Horizons science team interpret the incoming spectra, analytical scientists from Northern Arizona University's (NAU) ice lab have been growing and analyzing ice samples that simulate Pluto's surface. The group hopes to understand how composition, temperature, and ice phase affect the absorption coefficient spectra of CH_4 and N_2 ice mixtures – the dominant species on the surface of Pluto. Stephen Tegler, professor and chair of NAU's Physics and Astronomy Department and overseer of the ice lab, tells us more about the work.

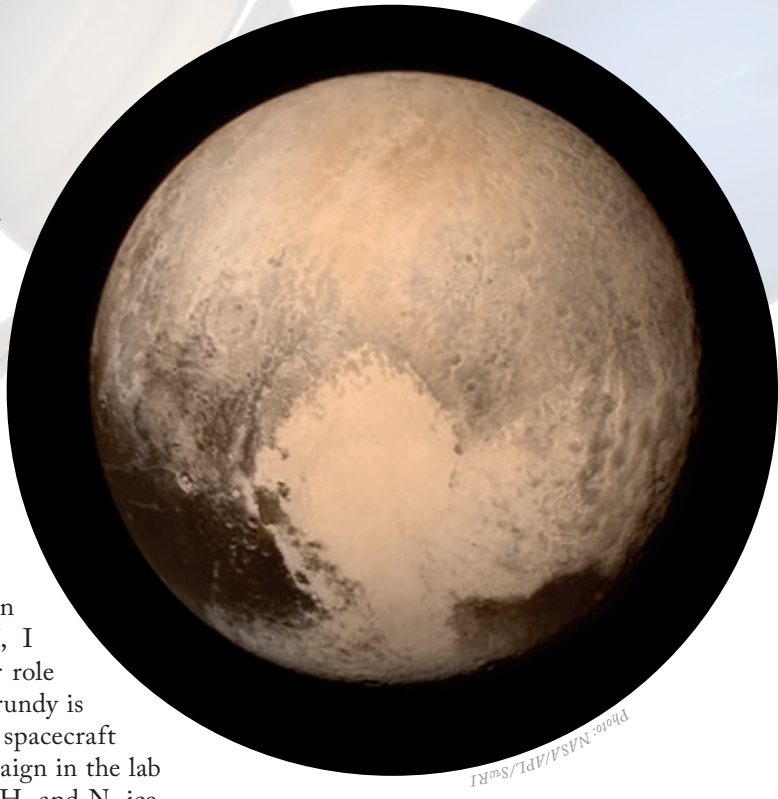

Photo: NASA/APL/SwRI

How did you get involved with the ice lab and NASA?

My first professional contact with NASA was as a graduate student. My PhD thesis concerned measuring the abundance of NH3 in comet Halley.

Almost ten years ago, I began a program to obtain optical spectra of icy dwarf planets using the 6.5-meter MMT telescope on Mount Hopkins in Arizona. I needed laboratory data of ices to interpret the telescope data, so I began collaborating with two colleagues who were building the ice lab, William Grundy of Lowell Observatory and David Cornelison, then of NAU. When Cornelison left NAU, I began to take a bigger role in the ice lab. Since Grundy is on the New Horizons spacecraft team, we began a campaign in the lab to better understand CH_4 and N_2 ice. One purpose of the ice lab from the start was to maximize the scientific return of icy dwarf planet spectra taken with ground-based telescopes, as well as Pluto spectra returned by the New Horizons spacecraft.

How do you fingerprint the ice samples?

We collect optical and near-infrared spectra of ice samples with a Fourier transform infrared spectrometer (FTIR) and use the MATLAB programming language to remove instrumental and atmospheric signatures in the data. Our final products from the lab data are absorption coefficient spectra. We determine the effect of composition, temperature, and ice phase on the absorption coefficient spectra.

How difficult is it to translate findings here on Earth to an alien planet?

Our program requires the collection of astronomical spectra from a telescope or a spacecraft. The astronomical spectra must be processed to leave only the signature of the astronomical source. Laboratory data must be collected and processed as well to yield absorption coefficient spectra. Finally, we use a radiation transfer model, the Hapke model, to relate the laboratory absorption coefficient spectra to the astronomical spectra. The Hapke model takes into account the scattering of light in the surface of the icy dwarf. In summary, our program requires laboratory, telescope observing, radiation transfer modeling, and computer programming skills. So to answer the question – it's very difficult!

What have been the most surprising findings so far?

We were able to measure the CH_4 and N_2 abundances on Pluto and Eris using telescope observations and laboratory experiments and found the two bodies have similar CH_4 and N_2 abundances.

Are you excited about New Horizon's flyby of Pluto in July?

Yes, I can't wait to see the high-resolution images of Pluto and Charon's surface! The solar radiation field should destroy CH_4 ice on the surface of Pluto. So, there must be a source replenishing the CH_4. I hope New Horizons will help us understand the replenishing source.

By Royal Appointment

From analytical entrepreneur to Outward Bound Trustee, Fasha Mahjoor breaks the mold – again

In our very first issue, we "sat down with" Fasha Mahjoor, CEO of Phenomenex – he had just abseiled down The Shard. More recently, Phenomenex teamed up with The Analytical Scientist to launch the Humanity in Science Award. Fasha was strangely absent from the presentation ceremony in New Orleans – but he had a pretty good excuse...

Why did you miss the Humanity in Science Award event?
It was really quite unfortunate – I had been looking forward to meeting the two distinguished winners – however, I had another philanthropic obligation that same day; I needed to attend a board meeting for The Outward Bound Trust (OBT) in the UK – with the chairman, Prince Andrew, Duke of York. The OBT is very near and dear to my heart as it works primarily with disadvantaged young people with low aspirations from inner-city areas, helping them to see the great things they are capable of achieving in their lifetimes. I've personally witnessed the great impact of these programs.

Your appointment nicely matches your philanthropic views...
As a medical doctor, my father spent his entire life providing free and low cost medical care to underprivileged families, so the desire to 'give back' has been part of me from a very young age. As I built Phenomenex, I wanted to carry on this tradition by weaving a strong commitment to humanitarian work into our mission and global company culture. I believe it is the responsibility of all businesses to give back whenever and however they can, even in the smallest of ways – after all, every small act adds up to big change.

You shaved your hair recently for charity – what's the next?
Actually, I am excited to announce that I'll be leaping off three skyscrapers in London for the City Three Peaks challenge, raising money for OBT. Though I'm terrified of heights, I couldn't say no to this crazy fundraising adventure. I just hope I survive in one piece – and if not, thankfully the money needed will have already been raised!

Nomination for the 2016 Humanity in Science Award are now open: www.humanityinscience.com

We dig deeper into corporate social responsibility on page 40.

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
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Keep On Innovating

Are today's 'blue sky' instrumental techniques tomorrow's industry standard?

By Philip Marriott, 'ARC Discovery Outstanding Researcher', Deputy Director, Australia Centre for Research on Separation Science, School of Chemistry, Monash University, Victoria, Australia.

The research-driven imperative to conduct innovative and instrument-focused new research could be viewed as 'blue sky' and possibly remote from reality. But industry should keep an eye on such research – and ideally engage with its proponents. Why? Because it maintains and encourages real-world applications informed by best-practice studies. For instance, the pace of introduction of new mass spectrometry techniques probably significantly exceeds the speed with which new – and validated – standard methods of analysis can be written, at least initially. However, in time, they may become the new industry standard.

University research, for example, in instrument development typically must be 'discovery-focused', where grant success requires a significant discovery component to the research program. Application of a newly reported technique to a specific chemical problem might be noteworthy, but this alone does not constitute instrumental technique development. In my view, innovation is also necessary for its own sake.

Look at the list of Nobel Prize winners. New instrumental approaches enable us to understand nature and can open up a completely new area of science. Would we deny Fenn the opportunity to develop electrospray ionization (ESI)? What about discoveries in sub-cellular processes or knowledge of the heavens that can only be revealed by the extraordinarily high resolving power of super-resolution spectroscopy and the Hubble telescope, respectively? There is always scope for new techniques that measure better, have increased resolution, lower detection limits, and increased molecular clarity or certainty. This is the essence of innovation. The fact that ESI has transformed the conduct of HPLC-MS is now a matter of historical record...

Using a standard method, it may be simply impossible to provide some measurements on conventional lab instruments at the required level of detection – or without an inordinate sample handling process that makes the task overly expensive. So what about a new technique that costs more but offers a 10-fold improvement in detection limits, simplifies sample preparation, and allows greater throughput? Suddenly, innovation is sounding rather appealing.

New techniques require time and research funds to develop. The research that we have been particularly engaged in – comprehensive two-dimensional gas chromatography (GC×GC) – is an example of this. The ability of GC×GC to provide greater resolution, improve detectability, and offer novel structured retentions is an example that challenged the paradigm of the day. Now, it has proven to be an incredibly powerful technique across a range of applications.

However, that's not to say that every analysis has to be performed with GC×GC! A toolbox containing sufficient tools for analyses from the most complex to the exceedingly simple allows the analyst to choose accordingly. Probably more importantly is that if a task can be conducted reliably using a simple approach – such as GC with a selective detector for pesticide

analysis – then it should not require the use of a more convoluted method.

There is a rider, however. We have shown in certain cases, such as pesticides analysis using GC×GC with specific detection (electron capture and nitrogen-phosphorus), that unexpected matrix impurity interferences often still arise. Notwithstanding the use of specific detection, higher resolution may still be advised – and GC×GC could provide the answer. Issues regarding the training needed within a GC×GC technical environment are relevant, but if the application demands it, this should not be considered an impediment.

Once, we approached a lab doing a particular regulatory analysis, offering to conduct a study using our new techniques. The response was: "We have all the techniques we require, and we are not planning further acquisitions – thanks, but no thanks". We approached the same lab some years later; they had since purchased both MS/MS and high-resolution MS. We asked again if they would be interested in conducting a study much as proposed earlier. The reply was again: "We have all the techniques we require…"

In another study, we did not need to convince our industry research partners to undertake a new multidimensional gas chromatography (MDGC) study – they had already exhausted their efforts and patience on classical extraction methods. Our new method allowed direct injection (and, therefore, high recovery), high resolution, specific chemical analysis at trace level – and it was fast. In other words, it delivered on many fronts. In yet another study with an industry association, we applied fast MDGC and GC×GC enantio-separation methods to natural oil authenticity. The association is now keen to base a new international standard on chiral analysis to protect the industry against adulteration.

In my view, industry and government analysts can be served very well by linking with university research groups in a win-win collaboration. Users can access and evaluate new methods reasonably readily, while providing the university with a much-needed industry-relevant application base against which to benchmark and assess their innovative methods. Eventually, a new industry standard method may result.

Digging into Biomarkers of Oxidative Stress

Hyphenated chromatography techniques enable the selection of representative biomarkers of oxidative stress – and help resolve the huge complexity of lipid oxidation products.

By Michael Lämmerhofer, Professor of Pharmaceutical (Bio)Analysis at the University of Tübingen, Germany.

Our bodies' cells are under constant threat from various toxic agents, including reactive oxygen species (ROS) formed by normal physiological processes. Fortunately, our antioxidant defense systems can inactivate them. However, under certain conditions, prooxidative/antioxidative homeostasis may get out of balance and excess ROS may be present in cells – a condition known as oxidative stress.

Oxidative stress is a prominent feature or a secondary effect in many acute and chronic diseases, the list of which is almost endless: atherosclerosis, asthma, chronic obstructive pulmonary disease (COPD), Alzheimer's, amyotrophic lateral sclerosis (ALS), multiple sclerosis, diabetes, rheumatoid arthritis and cancer... Notably, many of these diseases are age-related, but ROS reaction products increase during normal aging too. Notably, there is a lack of definitive evidence on the contribution and/or association of excessive ROS generation to/with age-related diseases, which is in no way helped by shortcomings in utilized/available biomarkers and deficiencies in analytical methods for accurate and reliable analysis.

There is no doubt that ROS can exert major damages to cellular components and biomolecules such as biological membranes, DNA, proteins and lipids. Oxidative protein modifications may induce loss of functional integrity, leading to inhibition of enzymatic and binding activity, susceptibility to aggregation and proteolysis, altered uptake by cells, and increased immunogenicity.

ROS may also oxidize membrane lipids and can impair membrane function due to altering fluidity and inactivating integrated membrane-receptors. In particular, polyunsaturated fatty acids (PUFA) are susceptible to attack by ROS, which may lead to enhanced levels of oxidized phospholipids (OxPLs) and exhibit pro-inflammatory and pro-atherogenic properties.

In short, lipid oxidation products are interesting because they are biomarkers of oxidative stress – and OxPLs (because of their roles in membrane function and distinct signaling cascades) are particularly important. Overall, the available information on bioactivity of various OxPLs is limited, and their utility as biomarkers is hindered three-fold by their structural complexity, the scarce availability of published analytical

methods, and the limited sensitivity of methods (we are looking for trace amounts in the presence of huge excesses of non-oxidized PLs). Which OxPLs should be part of a powerful biomarker panel? Only adequate analytical methods hold the key to answering that question.

It is not surprising that stereoisomer separations caught our attention. If, for example, ROS attack a PUFA with two double bonds, such as linoleic acid, a single preferential methylene position for preferential attack is available, which results in stabilization into two possible preferential constitutional isomers (regioisomers). Because a new stereogenic center is formed by oxidation, a racemic mixture is formed as there is no stereogenic preference for non-enzymatic oxidation. Therefore, a single compound is transformed into four isomers. If this happens, for example, on a PL with a single linoleic acid, the chirality of the sn2-position of the glycerophospholipid means that the enantiomers change into diastereomers (or epimers). Since RPLC can resolve diastereomers, up to four peaks could become visible in the RPLC chromatogram. If a PL with single arachidonic acid side chain has three methylene groups that are attacked by ROS, it gives six preferential positions for the formation of primary oxidation products, for example, hydroperoxide. Because of sn2 chirality, 12 diastereoomers are present! Moreover, primary oxidation products of PUFA are accompanied by further oxidative degradation (cyclization, side chain fragmentation, transformation to other functional groups), so the actual number of oxidation products isn't clear. You get the picture: there is an avalanche of possible OxPLs, and it is unclear which of them is bioactive and of practical relevance.

To nail down this structural complexity of PUFA oxidation to a specific example, consider isoprostanes, which are metabolites of free radical-catalyzed arachidonic acid peroxidation. Up to 64 distinct structures (four regioisomers each in 16 stereoisomeric forms) of four major structural classes (H_2-, F_2-, D_2-, E_2-isoprostanes) may be formed by this non-enzymatic arachidonic acid peroxidation process (note, minor isoprostanes and other follow up reaction products of H2-isoprostanes are not even considered). Among them, 8-iso-prostaglandin F2α has attracted particular attention due to its biological activity as a potent vasoconstrictor in lung and kidney tissue. A lack of research means that the biological activities of other isomers are unknown.

The enormous structural complexity may be the reason that simple structures such as malondialdehyde (MDA) and 4-hydroxynonenal (HNE) are often analyzed as biomarkers of oxidative stress instead of OxPLs. However, (various) OxPLs may be bioactive and interfere with signaling pathways downstream of membrane processes. Our goal is, therefore, to analyze the structural complexity in a more comprehensive way using selective chromatography hyphenated with high-resolution mass-spectrometry and selective MS/MS transitions that implement MS/MS^{all} with Sequential Windowed Acquisition of All Theoretical Fragment Ion Mass Spectra (SWATH) technology. Ion-mobility analyzers hyphenated with such LC-MS systems are further strategies to cope with the enormous diversity of structural isomerism and complexity. Nanoparticle-based sample preparation and enrichment platforms help us to reach adequate sensitivities, which was my presentation topic at HPLC 2015 in Geneva last month.

Overall, the project is very challenging but also absolutely fascinating – in my opinion, much more research is needed; it will certainly keep our group busy for quite a while.

Rewarding Lab Effectiveness and Efficiency

S-Lab – a new higher-education initiative in the UK – is using an awards scheme, an annual conference, and assessment tools and guidance to drive improvement in areas that are common to both analytical and research laboratories.

By Peter James, Director, S-Lab: Supporting World Class Science, Sheffield, UK.

Laboratories are expensive to build and operate – fact. Right? The 2015 S-Lab Awards and Conference (September 16 and 17, University of Leeds, UK) will provide evidence that they can be built and operated more effectively and efficiently, without sacrificing – in fact, often enhancing – science and staff well-being. And that goes for all laboratories, from analytical to research. We'll look at improving space utilization through designing for flexibility, and we'll cover the management of usage – as with the award-shortlisted OpenSpace software used by the Wellcome Trust Sanger Institute (Hixton, UK). In addition, we'll show how good tracking can greatly reduce costs and risks associated with chemicals and sub-optimal sample storage.

The program includes many conference

sessions and S-Lab workshops on items such as autoclaves, microscopes and ultra-low temperature freezers that will highlight the potential for improving management, maintenance and sharing of equipment. And, of course, modern technologies have a big part to play; for example, in containment and ventilation. New systems can reduce costs and energy usage while maintaining or increasing safety by using lower but more evidence-based air flows and more flexible operation in response to demand and ambient conditions.

"Big data" is a (big) shared theme and several conference sessions will investigate the potential of "joined up laboratories", focusing on consolidating, integrating and simplifying multiple data systems. A case study session will provide a real-world example of how this has been achieved at the awards-shortlisted Scottish Environmental Protection Agency, which has automated QA and analysis processes embedded within LIMS and database systems to deal with millions of air, waste and water samples.

Finally, a laboratory is only as good as its staff, but their personal development opportunities and career paths are often limited by specialization and lack of opportunity. That's why we have an entire conference stream to address personal development solutions, including Science Council Registration schemes, a Technical Workforce Planning initiative at the University of Cambridge, and a Laboratory Leadership masterclass.

In my view, we cannot escape or avoid the financial pressures, shifting needs, new technologies, and many other factors that demand change in all laboratories – we must learn about and embrace them by sharing stories and problems. The S-Lab Awards and Conference demonstrate ways that users, designers and others are rising to the challenge, but also show that there is great scope for further improvement.

See www.effectivelab.org.uk for more details of S-Lab, the Awards and the 2015 Conference.

CSR in Context

How much value do you put on corporate social responsibility (CSR) in your laboratory? Read this and you may change your mind.

By Elyssa Litchfield, LIMS Consultant at CSols Inc., Newark, Delaware, USA.

While I was studying for my master's degree, I became fixated on the intricacies of corporate social responsibility. In an attempt to merge my Master's degree study with my employment domain, I often searched for the terms "corporate social responsibility in laboratories" and regardless of whether I was searching in scholarly databases or Google, I always came up empty handed. The lack of awareness of this important concept bothered me to my core.

I have seen countless labs during my career and observed their CSR practices. But I found it troublesome that the term was not more frequently discussed; the fact that it was not a topic of conversation suggested to me that many labs were not, in fact, following good CSR practices.

CSR is an ethics policy that is most often associated with large corporations and perhaps less within research and academic analytical laboratories. For the former, it encompasses core business practices focused on sustainability for the larger community and environment as well as transparency between the company and its stakeholders. It also plays its part in calculating the total cost of a product from its origin as raw materials to disposal (the product life cycle). Lastly, the triple bottom line concept comes into play – or balancing profit, people, and the planet.

The key to making CSR policies work is finding the sustainable sweet spot. Savitz and Weber suggest that, "Sustainable companies find areas of mutual interest and ways to make doing good and 'doing well' synonymous, thus avoiding the implied conflict between society and stakeholders" (1). And they define the sustainability sweet spot as "the place where the pursuit of profit blends seamlessly with the pursuit of the common good".

Can this concept work for you in your laboratory? Some people will argue that CSR is only valid if you want nothing in return for it. But I disagree; it can be a strong part of the culture even when each business decision made in your laboratory must be justified numerically. Ethics must be woven into the framework of what you do; it needs to become a demanded practice (2).

One effective way is to have a written code of ethics, sometimes referred to as an ethics statement, which is further supported by a sustainability report. If you're a small business that's actively working on sustainable initiatives, there is value in publishing this publicly – a little good press can go a long way in attracting new customers.

Now that we've got a clearer picture of CSR, let's consider the factors that are unique to laboratories. With the growing use of laboratory automation software and instrument integration "fudging" results is becoming less of a concern, but it is still worth considering when implementing a CSR policy.

"CSR can be a strong part of the culture even when each business decision made in your laboratory must be justified numerically."

Moreover, hazardous or potentially hazardous materials must be disposed of properly to mitigate health risks and reduce environmental impact. Then there is the affect the laboratory has on the external environment, so testing outputs is a good way to monitor and reduce impact.

Finally, I think things are beginning to change – slowly. I am pleased to say that when I do the same "corporate social responsibility in laboratories" search today, I find that several companies appear in my query results. Although the number of organizations that have CSR policies is growing, it has not yet come to the forefront of consciousness. Even a small step towards greater CSR could begin to reinvent ethical standards for laboratory practices worldwide.

On page 40, several companies describe what CSR means to them.

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Multimodal Spectroscopy: Production Workhorse

Manufacturing is getting smarter; only a cross-discipline approach will ensure the success of tomorrow's processes.

By Rudolf Kessler, Professor of Chemistry at Reutlingen University and Head of a Steinbeis Technology Transfer Center, Germany.

The European Commission's smart manufacturing vision "Manufuture for 2020" and the US Food and Drug Administration's (FDA) PAT/QbD-platform (Process Analytical Technology, Quality by Design) are both helping to increase interest in the concept of intelligent manufacturing. It is a transdisciplinary technology where process chemists, process engineers, chemometricians and many other technologists must work together. In short, the holistic process analysis component will be the bedrock that supports the production of smart materials in smart factories! Indeed, process analytics by spectroscopy can improve understanding of how the process operates, and can be used to determine potential targets for process improvement by removing waste and increasing efficiency (1).

I have no doubt that optical spectroscopy – together with chemometrics – will play an important role in transforming industry from reactive to proactive production. Because spectroscopic techniques can detect morphological (from scatter) and chemical features (from absorption) simultaneously, the complete fundamental functionality of a compound is inherent in every spectrum.

However, we must recognize that sensitivity, selectivity and robustness of each individual technology, in combination with the wavelength range used, has limitations because of the structure of the measured species and the optical configuration selected. Furthermore, in any application, a key issue is finding the causal link between the measured spectral features and the final target quality. I believe multivariate data analysis of big data will be a key technology in the future. Proper process analysis means understanding the causal relation between measurement and response, and with spectral imaging, the spatial distribution in the x-, y- and, possibly, z-direction may also be of interest (1).

Many of you will know that ultraviolet- and visible (UV/Vis) spectroscopy is a highly sensitive technique for electronic transitions, while mid infrared (MIR) spectroscopy is specific for vibrational transitions. However, we also know that near infrared (NIR) spectroscopy is less sensitive than MIR due to lower cross sections of higher order vibrational transition probabilities. Clearly, the major advantage with NIR is that even at higher concentrations no sample preparation (for example, dilution) is necessary, but I think it is important to emphasize that both NIR and MIR spectroscopy are highly sensitive to water absorption. And in recent years, Raman spectroscopy has developed into a highly sensitive and versatile technique, proving to be a very good process-monitoring tool, especially in aqueous systems such as those found in biotechnology.

Currently, NIR- and Raman-spectroscopy are the workhorses in PAT applications, and multimodal spectroscopy will be the all-in-one sensor of the future. Samples containing phase boundaries that display simultaneous and superimposed wavelength dependent absorption and scattering effects cannot be characterized by a single measurement. Here, multimodal spectroscopy will come to the fore because of its ability to deal with combinations of measurements in different wavelength regions or in different optical set ups (for example, transmission and reflection).

In the future, special emphasis will be given to measuring not only the chemical entities but also their lateral distribution in an object. Spectral imaging (also known as chemical imaging) is an emerging field for a wide range of applications; for example, finding biomarkers in a tissue or controlling and qualifying pharmaceutical tablets or food. In addition, push broom imaging (line scanning) technology will allow multiplexing, thus reaction tomography or measurements in micro-reactor systems will be possible.

Therefore, I am very confident that process analysis, together with spectroscopy and intelligent data analysis, will play a more important role in modern manufacturing and processing. The German government's "Industry 4.0" concept describes the future of industrial automation as being arbitrarily modifiable and expandable (flexible), able to connect different components from multiple producers, enabling those components to perform tasks related to a context independently (self-organizational), with an emphasis on ease of use (user-oriented). Spectroscopy – particularly the workhorse techniques of vibrational spectroscopy – will be an important set of tools to realize this concept (2).

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Holistic Bioanalytics

Lawrence (Larry) Lesko is a bioanalytical veteran with many years of academic and FDA experience. Now, as director of the University of Florida's Center for Pharmacometrics and Systems Pharmacology, Larry uses metabolomics to discover biomarkers of drug toxicity.

Larry became a chemist at the age of seven with a Christmas gift that fired a growing interest in magic rocks, rockets and (by today's standards) dangerous chemical reactions. At high school, Larry's lifelong interest in pharmaceuticals began with a part-time job at the local pharmacy, where he was tasked with drug compounding – essentially, a continuation of his childhood chemistry set experience...

When did the serious learning begin?

I applied for – and received – a five-year scholarship at Temple University's School of Pharmacy from the Pennsylvania state senator. My dad was a former coal miner and my mum worked in a factory, so it really was the only option for me to get ahead. Pharmacy school seemed to be the natural choice – and I enjoyed it, but I realized that I wouldn't actually have the opportunity to practice much science if I continued down that path. In particular, I had become very interested in the scientific process of drug development. I recognized I needed an advanced degree to get into that field, so went back to graduate school and did summer internships at a couple of pharmaceutical companies. I worked at Roche in New Jersey and Wyeth Laboratories in Philadelphia and got exposed to many aspects of pharmaceutical development – and that included mass spectrometry and other analytical methodologies.

After weighing up my options, I decided to go into academia. I interviewed for a position at Texas Southern University, which was looking to improve pharmacy graduation rates. They offered me an intellectual challenge that I couldn't resist, and asked me to start a graduate research program, which sealed the deal. I succeeded in both areas – and set up an analytical laboratory – before moving up to the University of Maryland in Baltimore to become director of the Pfeiffer Clinical Pharmacokinetics Research Laboratory and an associate professor of pharmacy. A couple of years later, I found myself the director of what was essentially a fully-loaded analytical service laboratory.

What's driven your many career moves?

Looking back, I was passionate about building successful entities. My next move was to the University of Massachusetts Medical Center (director of its Clinical Pharmacokinetics Laboratory) and then onto a company called PharmaKinetics Laboratories, where I was vice-president of the Analytical Laboratory Services Division. We did contract work for the pharmaceutical industry and I headed up bioanalytical method development and validation – and that's where I seriously got into mass spectrometry. In the contract world, you're always competing with other laboratories, so you have to stay at the cutting edge in terms of sensitivity. It really was the analytical big time! We ran three shifts of analytical chemists – a real 24/7 analytical factory – to maintain the high throughput needed for industry customers.

And then nearly 20 years at the FDA?

That's right. I knew a couple of well-known leaders – Carl Peck (Director of CDER) and Roger Williams (Director of the Office of Generic Drugs – OGD), and they invited me to develop a new research program. I joined the FDA in 1992 as director of research at OGD down in Rockville, Maryland. The position required a very broad-based view of analytics; the research revolved around finding new clinical and analytical methodologies to show bioequivalence of generic products in challenging areas. In 1995, the FDA opened the Office of Clinical Pharmacology and Biopharmaceutics – and I was asked to become the director and build the office from the ground up. We started with 20 people and I left in 2011 when we had nearly 180.

What were your FDA highlights?

We developed guidance for industry on bioanalytical method development and validation, which is the state of the art today. Another highlight was getting involved with personalized medicine in 2002. I was asked to look at approved drugs and determine in which cases genomics could be introduced into the label. We updated the labels of around 15 important drugs in that nine-year period. Perhaps more revolutionary was the Voluntary Genomics Data Submission Program that we started. We felt that the pharmaceutical industry was not always sharing the work they were doing in pharmacogenomics with the FDA – so we created a 'safe harbor.' Companies could submit data for advice rather than for review, preparing them (and us) for the future. We received around 100 voluntary submissions, which got our internal staff up the learning curve very quickly. Often, there is a perception that

regulatory agencies are followers and unlikely to adopt new science readily – I really wanted to change that perception and enabled FDA to lead the field.

How did you end up back in academia?

Well, that story is relevant to my current use of mass spectrometry. In 2010, I got interested in innovations related to drug safety – a paradigm that hadn't shifted in about 40 years. Safety evaluations tended to be retrospective; that is, companies tended to react to adverse events. I wondered, why do we react rather than predict? A question that led to my interest in integrated systems biology. I started the Mechanistic Drug Safety Program at FDA, which used software and analytical methodologies to investigate drug–adverse event pairs. For example, if you took a drug and had a skin reaction, we would use bioinformatics approaches to track the event back to a drug mechanism. And we could use the information gained to predict potential adverse events for new drugs. The program is now used in the review of new drug applications (NDAs) for safety. Anyway, I moved to the University of Florida in 2011 and wanted to continue my work on drug safety, so we purchased two Agilent LC-MS systems. One was the Agilent 6460 Triple Quadrupole MS for targeted metabolomics to enable the study of biomarkers at the cellular level and use them as a signature of a drug–toxic event relationship. And we needed the second system – a time-of-flight MS (the Agilent 6550 iFunnel Q-TOF LC/MS System) – for global metabolomics to identify new biomarkers of drug toxicity.

Yusuke Tanigawara at Keio University in Tokyo was studying the metabolomics of anti-cancer drugs from a therapeutic mechanisms perspective; I spent a week in his laboratory and was very impressed by his LC-MS instrumentation. And next door to us is the Sanford-Burnham Medical Research Institute – I also gained some recommendations from the scientists there on which models I should be looking at to match my needs; sensitivity is a huge driver for us, and given my long history of managing analytical labs, I also wanted efficiency – and that means robust instrumentation with little-to-no downtime. Notably, the Agilent systems are pretty kind to new users, and it was relatively easy to transfer assays from the literature. More importantly, the Agilent support team was always on hand should the need arise.

Can you share specific projects?

Right now there are two main projects. One is a study of drug-induced kidney damage; can the metabolome act as a "reporter" of toxicity ahead of a clinical laboratory test for serum creatinine (which only highlights a problem after 50 percent of the damage has already occurred)? If we can predict renal damage earlier, we can change the drug or drug dosage or introduce extra fluids and improve the patient's future quality of life. It's really an important unmet medical need. We've started out with a serious candidate that causes toxicity – the chemotherapy drug, cisplatin – which has an adverse event rate for renal damage as high as 35 percent for cancer patients in intensive care (around 7-10 percent for other patients). And that's a lot of people with kidney damage. We obviously want to move onto to other nephrotoxic drugs as the project moves forward; one of the interesting research questions is whether or not the metabolomic signature for cisplatin is drug specific or applicable to other drugs that can cause kidney damage.

The other project is focused on a rare and serious skin disease called Stevens-Johnson syndrome (SJS), which affects about one in 10,000 people (but has a much higher rate in Asian populations). A common drug that causes it is acetaminophen (or paracetamol) and we wanted to figure out the mechanism behind it. I'm happy to report that we have uncovered the pharmacological mechanism and also how to reduce its risk by using a protective agent. We're writing that up for publication at the moment.

How do you see your research ultimately being applied?

The end game is to employ integrated models that use biomarkers from metabolomics and so-called patient co-variates (like age, race, sex) to inform clinical decisions. For example, in the case of cisplatin, we might look at changes in a metabolomic profile based on 25-50 biomarkers and use that information to offer clinical options; for example, reducing the dose by half (since the patient still needs the drug) or minimizing toxicity by giving a concomitant medication that would block toxicity-causing pathways.

Your work on metabolomics appears very applied...

If you look at the broader world of metabolomics, it's very technology focused. A great deal of emphasis gets placed on the minutia of the analytical methods – and there's nothing wrong with that; it's important to drive the technical aspects of the field forward. It's a very similar scenario in personalized medicine, where half a conference can be devoted to next-gen sequencing and other technology. But the people at the technology end are not often clinically oriented. In many ways, I would say that technology has raced ahead of application in all the omics. We have the technology we need – let's put it to good use. As a clinical professor, I want to convert information from these new tools into valuable knowledge that can have a positive clinical impact – something I am very passionate about.

Listen to Larry Lesko's webinar for more details: tas.txp.to/0715/Lesko

Spectroscopy Brought Down to Size

New developments are mobilizing Raman, mid-infrared and near-infrared spectroscopy for a whole host of innovative handheld applications.

By Heinz Siesler

Since the early 1970s, I have been active in vibrational spectroscopy. And, for the last decade, I have made a point of following the continual development of miniaturized spectrometers for Raman, mid-infrared (mid-IR) and near-infrared spectroscopy (NIR). Forty years ago, Raman and Fourier transform infrared (FT-IR) spectrometers were huge, room-filling machines, and NIR spectrometers were just about to evolve from add-ons to ultraviolet-visible (UV-VIS) or IR spectrometers and appear as standalone instruments. Things began to change over the next four decades, with many exciting hardware and software developments for vibrational spectroscopy appearing. Nevertheless, apart from the introduction of light-fiber optics, special probes and chemometric evaluation routines enabling the technology to move out of the lab to the process, the techniques were still strictly for scientists. In contrast, the development of miniaturized, handheld instruments would not only lead to a further extension of the range of applications but also suggested that these instruments would eventually appear in non-traditional user environments.

Indeed, when handheld Raman and mid-IR spectrometers first appeared, the military adopted them much more quickly than industry for on-site chemical quality and process control in homeland security and antiterrorism applications. Since then, other important public services, such as fire and rescue services, environmental agencies, food control institutions, and law enforcement organizations, have also recognized the potential for handheld spectrometers.

In the majority of the above applications, the primary objective is rapid and safe on-site identification of unknown – often hazardous or toxic – materials or for authenticating the correct origin of goods by trained users – but not necessarily scientists. However, I think that the educational and conference activities planned for the 2015 "International Year of Light and Light-based Technologies" (www.light2015.org) will certainly help share the message that vibrational spectroscopy can significantly contribute towards improving safety and general standards in all areas of our lives.

Miniaturize technology; don't minimize performance

When miniaturizing an analytical instrument, one of the key objectives is to ensure that the reduction in size does not compromise measurement performance and precision. It therefore follows that handheld vibrational spectrometers will only have a real impact on quality and process control if the spectra obtained from them are comparable to those produced by larger bench-top instruments. However, numerous recent investigations (which included comparing miniaturized with conventional spectrometers for solving the same analytical problems) have shown that reliable and accurate results for qualitative as well

as quantitative applications are achievable with handheld instruments (1–3).

New developments are driven chiefly by the potential and advantages of micro-electro-mechanical systems (MEMS) production for building extremely miniaturized devices that can perform optical-mechanical functions. Handheld Raman systems are based generally on dispersive technology with 785-nm excitation, but recently 1064-nm excitation systems have been introduced for more efficient fluorescence suppression. Some instruments have orbital raster scan (ORS) technology for interrogating a larger sample area without loss of spectral resolution. Handheld mid-IR instruments are limited to attenuated total reflection (ATR) measurements and are offered as FT-IR systems or with a linear variable filter (LVF) monochromator. NIR spectrometers can operate in the diffuse-reflection, transmission or transflection mode and their enabling technology varies between dispersive and LVF or digital light processing (DLP) using digital mirror devices (DMD).

In general, handheld instruments come with measurement software and the manufacturers frequently offer additional software packages for qualitative and quantitative evaluation of the spectra. For most instruments, you can buy libraries for specific material classes (drugs, explosives, polymers) for fast and efficient identification. They do vary in weight, from approximately 1 kg down to 60 g for an ultra-compact system.

Testing times

For many years at the University of Duisburg-Essen, we have been testing various handheld Raman, mid-IR and NIR spectrometers for a broad range of interesting applications. During testing, we've had to revise our perception of the practical use of vibrational spectroscopy completely. We have discovered a number of interesting applications. Here's a small sample:

- We found that polymers and other additives present in bitumen could readily be determined quantitatively by on-site/on-the-road measurements. Taking into account the tremendous costs involved in road construction and, specifically, the importance of using the correct additive formula for improving the adhesive and rheological properties of bitumen, the impact of such measurements for road surface quality – and hence the safety of motorists – is clearly beneficial.
- In a feasibility study for a global mining company, we verified the possibility of quantifying milled rock samples for relevant minerals. For mine exploration studies, a fast on-site evaluation of geological test samples is essential and handheld instrumentation will certainly play a dominant role in such investigations in the near future.
- To address increasing public concern over fraud and deception in seafood marketing, we developed a fast and reliable analytical procedure for authenticating fish (4). Similar fish of superior/lower quality and higher/lower prices are difficult to distinguish by visual inspection. Instead, we used handheld NIR diffuse reflection spectroscopy and evaluated the spectral data using principal component analysis (PCA) and classified them by soft independent modeling of class analogies (SIMCA). Using this procedure, test fish could be identified unambiguously and assigned to the correct species.

Clearly, these miniature handheld spectrometers are enabling a new population of users in new measurement environments to gain important benefits. In addition, I can foresee the use of such instruments beyond police forces, food inspection agents or military personnel. Just as mobile phones have become essential in every-day-life (irrespective of gender and social or financial status of the users), so why shouldn't a user-friendly handheld spectrometer of similar technical complexity, equipped with evaluation software, gain the same public pervasiveness? Black market goods like bastard amber, fake ivory and silk shirts could be consigned to the past, together with the issues we now have with food quality, adulteration and authentication, as well as healthcare technology.

Despite these bright future prospects, let me end with some words of caution. If I've sparked your interest in handheld instruments and you've decided to investigate them further, be sure to critically scrutinize the technical background of new, elaborately advertised products – particularly those offering investment opportunities and life-science applications – because many of these, in my opinion, appear to lack feasibility.

Heinz Siesler is an Emeritus Professor in the Department of Physical Chemistry at the University of Duisburg-Essen, Essen, Germany.

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Spec Snapshot II: Bringing Home the Harvest

Experience:
Our research group has been using handheld NIR devices since 2011.

Objectives:
One of our current projects aims to determine the optimum harvest time of medicinal plant materials using handheld NIR instrumentation.

Opinion:
Top three benefits (compared with benchtop instruments):

- Easier to handle; often they are small enough to carry in a pocket
- Easy data transfer via Wifi or Bluetooth
- Extremely attractive for taking measurements "in the field"

Spec Snapshot I: Authenticating the Authentic

Experience:
I have been using handheld analytical instruments for seven years, starting with Raman.

I routinely use handheld Fourier transform infrared (FTIR), NIR, Raman and X-ray fluorescence (XRF) spectrometry because they provide a minimal footprint and can be used in the field as well as in the laboratory.

My company, Authenticate Limited (www.nwbspectroscopy.co.uk) assesses suspect counterfeit pharmaceuticals and luxury goods. The technologies listed above are all part of a toolbox of chemical identification options, for rapid, often non-destructive sample assessment.

Opinion:
Handheld instrument performance is definitely good enough for qualitative assessment of suspect goods. Quantification is possible but less utilized. I would say in general, handhelds are not quite as good as benchtop instruments; however, their resolution and performance are sufficient to provide cost-effective results. In reality, they are complementary tools and not intended to replace superior technology, or more specific analytical techniques, such as mass spectrometry for the confirmation of unknowns.

Neville Broad, Managing Director, Authenticate Ltd, Sittingbourne, Kent.

Manel Alcalà Bernàrdez, Associate Professor, Applied Chemometrics Research Group, Faculty of Sciences, Universitat Autònoma de Barcelona (Autonomous University of Barcelona), Spain.

Spec Snapshot III: Process Monitoring in Hand

Experience:
My research group studies applied chemometrics for the pharmaceutical and chemical industry and we have been using benchtop instruments for many years. Our development and validation of analytical methods using benchtop spectrometers focuses on installing the technology in QC/QA facilities, where the environmental conditions are suitable for such instruments. However, over the last decade – with the growth in process analytical technology (PAT) applications – the need for small, rugged technology for in-process monitoring is increasing.

Our first experience with handheld spectrometers followed the International Conference on Near Infrared Spectroscopy 2011 (Cape Town, South Africa), when JDSU and I began to collaborate on developing the "MicroNIR" spectrometer. We contributed to spectral acquisition configuration, specifically during the development of a spectral library for identifying pharmaceutical raw materials, and to developing and validating multivariate calibration models for quantitation of active principle ingredients in a pharmaceutical formulation. Our experience with this technology contributed to a feasibility study that demonstrated the performance of the instrument in a real world scenario.

Opinion:
Handheld instrumentation is a good choice for both qualitative and quantitative applications, where technical limitations do not allow the use of traditional benchtop spectrometers. The major benefits are clear: their size, portability, internal power supply and the ability to transmit data wirelessly.

The biggest challenge is to achieve accuracy, repeatability and robustness of spectral response compared with the validation guidelines. This is important; because of the miniaturization and highly integrated setup, the optimization of each part of the spectrometer is highly specific.

I wouldn't define handheld spectroscopy to be better or worse than traditional benchtop approaches. It is most definitely a complementary technology that provides very specific solutions that are difficult to achieve using traditional instruments.

Countering Counterfeit Medicine Little by Little

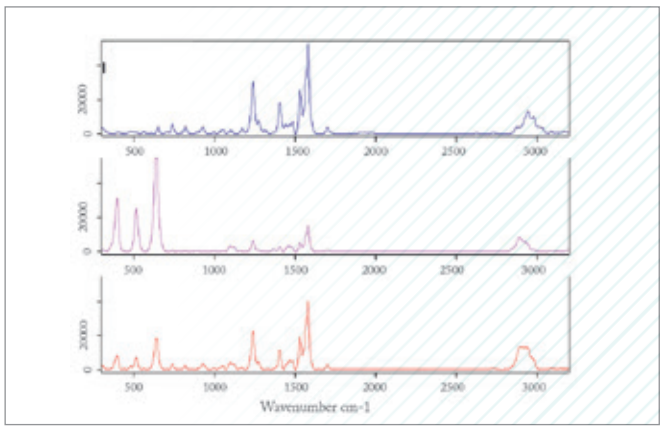
Sulaf Assi is a lecturer in forensic sciences at the Faculty of Science and Technology at Bournemouth University, UK. With an extensive background in pharmaceutical analysis, she brings her knowledge and skills to bear on instructing the forensic investigators of tomorrow in the use of handheld vibrational spectroscopy, Raman, near-infrared and infrared. Assi is also involved in the research of different aspects of forensic sciences: counterfeit products (medicines, cosmetics, tobacco and alcohol), drug abuse and misuse, novel psychoactive substances, analytical (chromatographic and spectroscopic) techniques, handheld instruments and multivariate data analysis.

"Handheld spectroscopy is excellent for counterfeit medicine analysis. It is simple, non-destructive and quick. Being fully portable, you have no trailing cables and you can generally get around four hours out of a single charge of the on-board battery. This is important particularly when you are analyzing samples taken from street markets, for example. You do not want to destroy them, as the counterfeits are evidence. You can take the instruments to precisely where you need to be," says Assi.

"Admittedly, you do need to do a lot of chemometrics; building spectral libraries, particularly for counterfeit medicines is challenging. So far, we have about 300 examples we have taken from the world market – and then you have to optimize your algorithms – both linear and probability-based algorithms – according to the sample you are analyzing."

Assi says that Viagra and Valium (benzodiazepine) are among the most counterfeited medicines on the world's black market. However, counterfeiting could still be encountered with any medicine class and any formulation type. The World Health Organization (WHO) typically defines counterfeit drugs as those that contain no active pharmaceutical ingredient (API), low/excess API, no API or even fake packaging.

"We found one particular Viagra tablet where the concentration of sildenafil citrate was much higher than the authentic medicines. I could tell all of this using the handheld Raman spectroscopy. By correlating the tablet's spectra to the sildenafil citrate spectrum in the library, I could see that the counterfeit had more peaks corresponding to the high sildenafil citrate concentration. Likewise, I could tell that these counterfeit tablets had a thin coating which was clear when correlating their spectra to the spectrum of titanium dioxide (a main ingredient in the coating of Viagra tablets)," says Assi.



Raman spectra of authentic Viagra tablet (pink), counterfeit Viagra tablet (red) and sildenafil citrate (blue) measured using a handheld Raman spectrometer equipped with a dual laser power.

"I currently use a handheld Raman spectrometer (Bruker Bravo) that subtracts the fluorescence you get with both thick and thin tablet coatings. The spectral resolution is very good and the range extends to around 3200 cm-1, which is critical. When dealing with counterfeit medicines, everything counts – every peak is an important characteristic and can indicate something important."

In chromatography, analytical scientists may focus on a single peak of interest and disregard the rest, but with spectral analysis of a counterfeit product the whole spectrum is a signature of the material.

Assi uses the handheld instrument in both the laboratories and onsite. She teaches second year forensic science students, supporting another lecturer's unit. She also makes use of the technology with Master's degree students studying crime scene management and forensic science.

"Students get trained as forensic investigators and on the Master's course they have to take part in a simulation exercise at Bournemouth airport where they investigate suspicious powders and fibers found on board an airplane. We also offer three-year forensic science, forensic investigation and forensic biology courses where students have placements throughout. They also get a final project, with many of them choosing to use Raman and/or infrared spectroscopy. For example, a year one student has been comparing Raman with infrared to optimize our cosmetic library and another used Raman for detecting herbal sleep remedies in alcoholic beverages used as date rape drugs," says Assi.

FTIR Takes the Heat for Aerospace

Handheld FTIR spectrometers have proven capable of measuring thermal damage in various carbon fiber composites used in modern aerospace applications. In this case, Boeing used a handheld FTIR (Agilent 4300) to support a partner company that manufactures and supplies large composite parts after a thermal exposure incident occurred during a routine composite repair.

According to Paul Vahey, an analytical chemist at Boeing, "A faulty heat blanket subjected a portion of a large composite part to substantial excess heat. Based on a visual inspection alone a hole would have been cut through the part to remove all the affected composite material. Though the large part was worth several hundred thousand dollars, it would have been scrapped because a through-thickness patch would have been unacceptable to the airline customer."

The solution was to use handheld FTIR directly at the site to evaluate the composite material on both the inner and outer surfaces. Vahey explains, "While effects of heating were visible on both sides, objective information from the FTIR indicated the resin was not weakened in the discolored back side of the heated area. By scarfing one layer at a time and measuring the underlying layer, it was necessary to remove less than half of the plies under the runaway heat blanket. Non-destructive FTIR data was confirmed by thermal analysis, such as glass transition temperature and differential scanning calorimetry."

Composites are now replacing metal components in other industries too, such as sports cars, motor racing, and boating. These booming composite applications demand more refined diagnostic tools to detect problems and confirm the chemical integrity of the material. Handheld FTIR instruments, like the one used by Boeing, are optimized for such tasks and provide the capability of at-site, non-destructive measurements, enabling users to make real-time decisions about quality, performance, damage and degradation.

Vahey says handheld technology provides several benefits. "One important advantage of FTIR was the immediate availability of the data, which allowed the repair to move forward. The portable nature of the handheld FTIR also allowed us to respond quickly, especially as the facility did not have on-site spectroscopy equipment. Indeed, FTIR provided objective data for the engineering department to base decisions upon, instead of making educated guesses on visual information alone. If we had to wait for thermal analysis of each layer, the repair process would have required days for the analysis, instead of hours. In the end, we saved time and money by not scrapping a large composite part that would have added substantial amount of flow time, labor, and materials to replace."

Faster Raw Material Analysis

In the pharmaceutical industry, one mistake can be fatal, which is why the industry is regulated so heavily. In fact, the world is moving toward stronger regulations with the implementation of PIC/S (The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme), which requires 100 percent inspection of incoming raw materials – a significant challenge.

Hetero Drugs Limited in Hyderabad, India, is a research-based global pharmaceutical company that focuses on developing, manufacturing and marketing active pharmaceutical ingredients (APIs), intermediate chemicals and finished dosages. Hetero's manufacturing facilities are cGMP compliant, meeting global standards in terms of infrastructure and systems. Given the fact that Hetero markets its products in over 138 countries worldwide, PIC/S required serious consideration.

Hetero's quality manager, K.V. Ramana Reddy, says, "With traditional methods of HPLC and other lab-based analytical techniques, our materials were being held up in quarantine for long periods of time. I cannot imagine how much time we would lose, if we used such method for 100 percent inspection."

Using handheld Raman spectroscopy (B&W Tek NanoRam), Reddy says it is now possible to complete 100 percent inspection and actually accelerate the process of releasing raw materials into production – repurposing the lab for more important duties in the process. Instead of sending all of the raw materials to the labs for testing, they are inspected as they are unloaded. Moreover, because Raman can test directly through transparent packaging materials, workers no longer need to conduct sampling, which potentially exposes them to dangerous chemicals or contaminating the very raw materials being sent for testing. What's the turnaround per sample? Reddy says each scan now only takes a few seconds for the operator to complete, and the uniqueness of individual raw material Raman signatures allows for a positive identification.

According to Reddy, a device with an easy-to-use touch screen interface allows users to quickly navigate and complete sampling procedures. Various sampling adaptors also mean that the team can work with different types of raw materials, such as solids, liquids, powders, or slurries. And different algorithms allow users to not only identify, but also verify raw materials that may be contaminated or mislabeled.

Guiding Lights

Have your graduate students discovered all of the career paths open to them? Have you recognized the demands and realities of an evolving job market? In short, is it time to become a better mentor and guide students to real opportunities in industry?

Harold McNair (Professor Emeritus, Analytical Chemistry, Department of Chemistry, Virginia Tech, Blacksburg, Virginia, USA) and Vincent Remcho (Professor and Patricia Valian Reser Faculty Scholar, Department of Chemistry, Oregon State University, USA) discuss the need to re-examine the role of academicians.

What's the problem?

Harold McNair: In North America, there's no problem in general with graduate chemistry programs – although decreasing government funding makes research more difficult. There's a strong increase in international students, particularly those coming from China and India, so our reputation remains very high both at home and abroad.

I do however see a problem with mentoring – and this affects our students. Only 10 percent of PhD students in the USA will remain in academia after they graduate because there aren't many jobs; in fact, academic jobs are on the decline due to the aforementioned cuts in government funding. Nevertheless, most students are mentored in graduate schools to become professors. According to my own research, about 80 percent of US graduate students take up employment in industry. However, very few are mentored or encouraged, or actually taught about what industry will be like.

I believe that the best way to learn about industry and attain reasonable first-hand knowledge is to get an industrial job during the summer. But this does not happen. Indeed, few faculty members have industrial experience, and some look down on industrial jobs; they think such work is menial because it is applied rather than fundamental.

Also, very few professors want their students gone for three months in the summer time. As for me, I gained many years of industrial experience in different companies during and after my student years, so I know what it is like and I realize the advantages. That's why I encouraged all my students to take internships in the summer time. And when I think of all my graduate students from Virginia Tech, only about eight of them are in the academic world. So actually it's just a problem of mentoring by the faculty members themselves.

Vincent Remcho: Harold is correct in saying there is no fundamental, critical problem with the technical education that students receive in graduate school today. The disconnect is in how we inform graduate students about various career opportunities and paths, and how we prepare them to make good decisions regarding which paths to follow.

Graduate students are the drivers of academic research, and they are exposed to many aspects of the "inner workings" of the academic career field – research, teaching and service.

They are often sheltered, though, from the finer details: how professors actually accomplish their work. We should engage graduate students in more of our daily activities: proposal authorship, budgeting, preparation of teaching materials, outreach activities. It would be good for courses on these topics to be taught as well.

I also agree with Harold's assertion that we do not typically provide students with insights into career opportunities in industry and in government labs. Summer internships are a great way to provide this insight and to help students connect with prospective employers. Yes, this does come at the cost of having them disengage from the academic research lab for a period, but it is a price worth paying. We also could do a better job of inviting seminar speakers from industry to provide students with an opportunity to hear more about what PhD chemists do in industry.

In academia, professors largely work independently, though they are of course subject to periodic review. They are required to be highly self-motivated and historically have not had much mentorship – they entered as assistant professors and were left to figure it out on their own. Now, we are seeing some new efforts in the direction of mentorship. This is wise: universities make a large investment in recruiting and hiring these promising scientists, and it is smart to mentor them toward success yet to ensure that they retain their full academic and creative freedoms.

In industry, mentorship is more the norm, yet the research horizons are typically more limited; after all, the needs of the company must be met. There is room for each field to learn from the other.

What are the key issues?

VR: The key barriers to providing graduate students with these new opportunities are simple to define but challenging to address:

1. Convincing faculty that research productivity will not plummet (in fact, it is more likely that productivity after the internship will increase appreciably) if one or two students a year head off for summer internships.
2. Convincing partners in industry to fund summer internships and bring students into the research, QA/QC, and development labs.
3. Convincing university administrators to fund (and provide appropriate teaching credit for) career preparation classes that are specific to the field of chemistry.

Universities need to offer a good course on careers in chemistry taught by a blend of professionals from industry – both start-up companies and established companies, national laboratories and academia. The course should address everything from researching the options to building networks to preparing application materials, and then move into the details of what these careers entail.

HM: I think that some academics have real prejudice against summer jobs. Some professors say, "No. I need my students here 24/7 in the lab, 12 months a year for five or six years" or for however long it takes. But when 80 percent of our students go into industry, the best thing you could do is to encourage them to take summer jobs. I say: let them learn about industry, learn about the advantages and disadvantages. Good mentors will talk to their students about the need for both academic and industrial experience, in addition to the pros and cons of gaining it.

How urgent is the issue?

HM: If we don't do this, we're guilty of wasting students' time. For example, think about those students who are finishing their PhDs right now and have been writing proposals and interviewing for academic positions that really don't exist. I suggested to one student not so long ago to think about going into industry and the response was "Oh, I don't want to go to industry, I don't know anything about it." They hadn't even considered getting an industrial job – and that's the problem.

Industry in America is recovering and hiring new people. On one hand, I believe companies would love to recruit skilled PhD graduates who have some industrial experience gained through internships and summer jobs. So, I think industry is suffering a little bit because they need the best people. However, on the other hand, we see graduates who are confused about their future prospects and are unemployed. Then there are many graduates taking a post-doctoral position on low pay and then, after two or three years, they discover they won't get a permanent academic position.

VR: I don't think this is necessarily a new problem, but it is more acute than it was previously. As Harold mentioned, people move from job to job more regularly now than was the case 20 or 30 years ago. Therefore, these skills are more critical – and called upon more often – than they were before. I can say that the academic enterprise in the US is changing at a rate that is unprecedented, and that traditional academic career opportunities in the USA seem to be more limited than before. Conversely, new opportunities are arising in China, for instance, where there is a lot of investment in academic research.

What are you doing to improve mentoring?

HM: Last year, I gave a seminar at Virginia Tech that compared and contrasted industry and academic jobs. It raised many issues, which are probably common to all universities throughout the USA. For example, people expect to make a lot more money in industry (and indeed, starting salary will be 30 to 40 percent higher in industry). Normally, you'll have a limit on what you earn in industry until you pick up more skills and are promoted to manager. In academia, however, your salary will be low initially and it will increase continually. And if you're a good researcher, you can technically pay yourself a 30 percent salary in the summer time to boost your academic salary, which pays well for nine months of the year. Salary is a personal choice, but you cannot assume either one is going to be exactly the salary you want. One thing's for sure: both jobs will demand hard work!

Another issue for graduates is geographic location. Many of them will have a strict preference: "I'm from Virginia, I grew up here, I want to stay in Virginia or maybe Maryland". However, there are so few academic positions that you have no choice in reality. You have to go where the jobs are, and whether it's Buffalo, New York, or Sacramento, California – in truth, it could be the only academic opening for you that year. On the other hand, in industry there are probably 30 jobs in every state throughout North America.

One thing that bothers many people is job security. They think that once they get tenure at university they're set for life and they can't be fired. In general, industry is more brutal, and if the company is doing poorly, the worst performers are fired. In academia, people are reluctant to let faculty members go during difficult financial times.

I'm not sure of the actual numbers, but I imagine that only about 60 to 70 percent of PhD students who get an academic position actually end up with a permanent job. I know several cases of would-be academics resorting to either part-time or post-doctoral positions five, six – even 10 years after their PhD. One of the factors is the benefit of long vacation time. Academics will say that they only work nine months of the year, but I'm telling you – having been a professor for 45 years – if you only work nine months of the year, you're wasting a lot of time. During those long summer months, you need to do a lot of work, read papers and in many cases do an industrial internship to gain some job experience. So, vacation time is not something you should be thinking about as a young scientist.

Also, in industry you'll have a boss. He can fire you, give you a good salary raise, present you with problems, and he can mentor you. In the academic world, your boss is usually a committee of full professors and once a year they review you on your teaching, research, and service. (The large American universities with PhD programs have research as a major objective and if you don't bring in money, you won't get tenure.) At Virginia Tech, research counts as 45 percent, teaching 45 percent and service or outreach 10 percent.

In industry, your responsibilities are simpler: solve this problem and solve it as quickly as you can. It doesn't have to be 80 percent perfect – the product will ship in two weeks and you've get 10 days to do the best you can.

In other words, we are talking about very different jobs with very different opportunities. Students don't have exposure to that kind of information but they truly need it. Universities should hire industry speakers to tell the students about what they're doing and to offer summer internships. Also, we need to encourage the faculty to realize that some of their best students actually don't want to go into the academic world – nor will they find an academic position – which means they would be better served by real-world advice.

"Some look down on industrial jobs; they think such work is menial because it is applied rather than fundamental."

And if we don't solve the problem?

VR: I don't think the sky will fall if we continue on the path we are on, but I also don't think that "muddling through" is a very compelling alternative. To ensure that our students move on into vibrant, rewarding, enjoyable and productive careers, we need to prepare them for a changing job market. As academics, this means building new and more substantial mentoring relationships with students; asking them critical questions about their interests that cause them to carefully consider a variety of career alternatives, and listening effectively to their responses so that we can more effectively help them as they make career decisions.

HM: We definitely need further discussion on what to do about the lack of understanding about industry in academia, and we need to find the best way to enthuse the faculty and the best way to educate the students. I don't know what the answer is – yet. But I'm sure other people have equally strong views – and I would love to hear all potential solutions.

Is the Next Generation Ready?

By Lawrence Lesko, Director, Center for Pharmacometrics and Systems Pharmacology, University of Florida.

All of us older guys look at the next generation of scientists coming through the system and wonder about the future. I agree with Harold McNair and Vincent Remcho – it's an important part of our profession and job to mentor people. But it's easier said than done for some; I've seen terrible mentors and very good mentors. Clearly, it's incumbent on all of us – especially in academia – to make our students "job ready". But let's be more specific: it's imperative that we focus on developing people for careers where jobs actually exist.

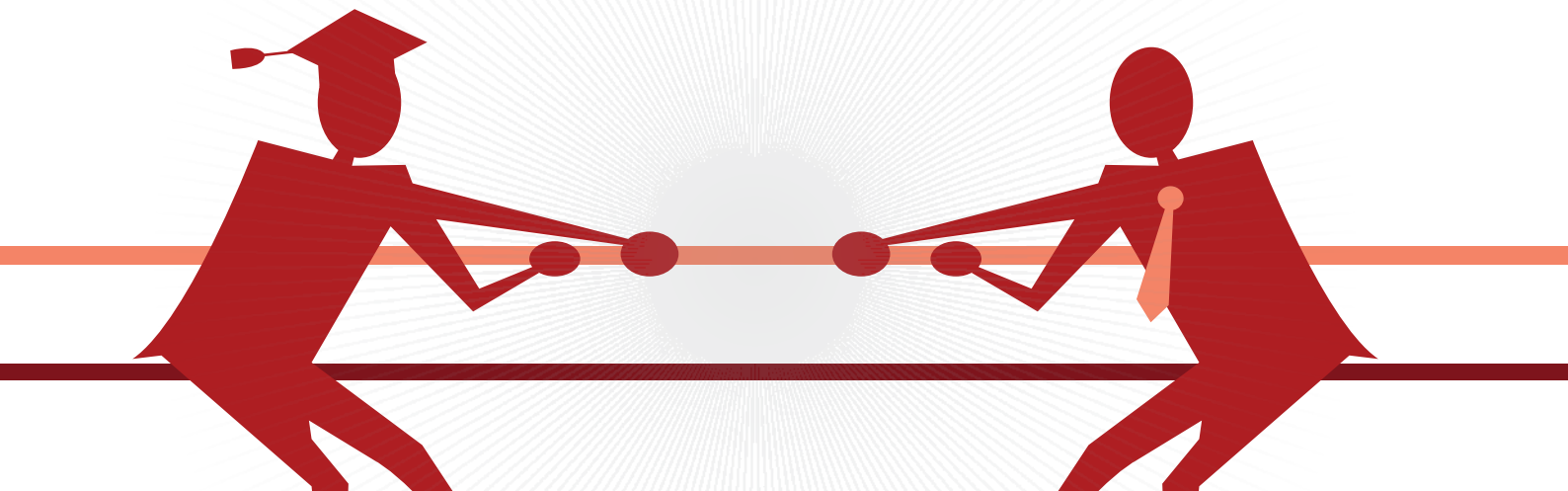
As professors, we have access to very bright people – great post docs and talented PhD students – and we shouldn't only be giving them the technical training they want (or the technical training we impose upon them for our own goals) – we must also create a context for the application of that technology. Why? So that when these people exit a graduate or post-doc training program, they can easily segue into a position in a pharmaceutical company or the FDA, and not be restricted to following a traditional path through an increasingly competitive academic environment.

Indeed, we need to train people differently. We can't simply focus on the basic science, whether it be analytics, omics or whatever, but take it a good step beyond that. And if you can't offer the additional expertise in context yourself, why not look outside to collaborators who can? In either case, we must make people job ready.

Take the FDA. There are very few jobs in the entire regulatory agency of over 14,000 individuals or so for a pure mass spectrometrist. However, there are many opportunities for someone with mass spectrometry experience and the capability to apply it to public health questions that come up in a regulatory context.

I've been around the circuit a couple of times when it comes to jobs, and during nearly 20 years at the FDA, I interviewed many PhDs and post docs. The majority were totally unprepared for a career in the FDA, more than likely because of the program that was laid out for them in the academic world. We have to be very cognizant about training the next generation in a much more meaningful way. Especially when we consider that success in the academic model is an arcane endeavor. Academicians are encouraged to constantly seek funding (most likely from the NIH) and don't necessarily end up doing the research they want to do; rather they do research that is fundable by the federal government. Consequently, post docs and graduates end up doing basic research rather than applied science. But even research funded by the NIH needs to be translatable; for example, enabling a pharmaceutical company or a regulatory agency to do something differently – and better than the status quo.

There are certainly plenty of jobs out there in applied sciences. I just got a call from someone at a major pharmaceutical company. He said, "I need five people, and I can't find anyone – I'm calling you because I know you train your people to solve drug development problems." I sent him three resumes. I believe there needs to be a groundswell in these kinds of interactions with private industry. We need to shake up the academic world a little bit – from the inside.



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Shouldering Responsibility with Science

More than likely, you are already doing your part to improve lives and make the world a better place – you're an analytical scientist, after all. Here, four companies that represent the diversity of business in our field share how they go above and beyond what's expected when it comes to corporate social responsibility. In short, we consider and then celebrate CSR.

Full Markes for Awareness

Markes International connects with the local community – and gets the wider community to connect with analytical science.

Markes International is a relatively small company – just over 100 people – and that means the cofounders have been able to successfully foster a culture of social responsibility that echoes their own ethics and roots.

Typically, those involved in analytical science are inherently socially responsible – assisting as they do in endeavors focused on ensuring a safer and healthier world – and that's an excellent cornerstone for CSR. Markes is certainly proud that its products have a positive effect on society; they help scientists to detect chemicals in materials, products and the environment and in doing so, make the world a better place. But Markes go one step further, honing in on the activities of less responsible companies with a long-term focus on trace-level volatile and semi-volatile organic compounds released by industry. Indeed, providing straightforward and reliable detection of such chemicals is the first step in gaining knowledge, increasing pressure, and finally driving legislation – thus minimizing the impact on public health. What could be more socially responsible than that?

Grass roots support

Markes is also committed to advanced research with several ongoing collaborations, such as the University of York's pollution monitoring CAPACITIE project at the York Environmental Sustainability Institute (YESI), and the European-funded QUAFETY project (www.quafety.eu), which aims to improve the safety and quality of fresh produce by developing new methods to quantify and manage spoilage. Outside of the food and environmental fields, Markes has teamed up with an Austrian healthcare company that aims to use volatile compounds as biomarkers in exhaled breath to distinguish potentially aggressive lung cancer from more benign illnesses.

But is doing 'the day job' enough to satisfy true CSR needs? Probably, but Markes International also recognizes the value in getting involved in the local community at a grass-roots level. It supports several employment initiatives at the local and national level, offers summer placements and work experience to undergraduates and local schoolchildren, respectively, and even sponsors the Pontyclun under-12s rugby team (co-founder Alun Cole is a former player!).

The founders are also very passionate about education and the next generation. "We also take time out to visit high schools," says marketing manager Gavin Davies, "But we don't just send scientists, we also discuss other job functions to help spread the word that working for a 'daunting' science company can be a very rewarding career choice." Bridging the gap in this way is unlikely to help Markes directly, instead it's part of a bigger strategy to help "the average person in the pub" relate to the hidden science all around them.

To that end, recognizing the great work done by our field and acknowledging just how unrecognized and misunderstood those efforts can be – Davies turned an interesting marketing opportunity on its head.

Campaigning for science

In what is believed to be a first for a small laboratory instrument company, Markes has been plastering train stations in the UK with poster advertisements that simply and concisely inform the general public how Markes – but, more importantly, chemical analysis as a whole – makes our world "healthier and safer through science".

Davies explains the concept of the campaign: "We are trying to join the dots between the equipment we make and its place in society – that is to say, the positive impact it is having on everyone's lives. To do that, we need to help people feel more at ease with chemistry as a whole." The campaign fits nicely into the overarching goal. "In short, we want to raise the profile of analytical science – that's got to be good for society in the long run. If we can just trigger the imagination of a few individuals and get them interested in chemical analysis, we might, in some small way, be responsible for the Francis William Astons of tomorrow."

Light Years Ahead

Using spectroscopy to protect and improve the quality of life for people worldwide.

Fueled by a passion for science, Ocean Optics created the industry's first line of miniature, modular spectrometers and accessories over 20 years ago. The dream? To enable researchers to make measurements at the sample and in the field – experiments that simply couldn't be performed in the lab. In essence, Ocean Optics wanted to make spectroscopy flexible, cost-effective and accessible to new scientific fields and technology markets.

Those researchers went on to create new techniques for solving problems with spectroscopy, and their students graduated and joined the ranks of industry. That second generation began to use Ocean Optics spectrometers as well, leveraging the instruments' small footprints and high performance-to-cost ratios to create innovative new devices for applications in medicine, the environment, process, food, safety and more.

Today, Ocean Optics embraces the philosophy that building partnerships with those who share a passion for the bold and the innovative will pay dividends that go beyond the bottom line, creating a world where spectroscopy helps to protect and improve the quality of life.

Embracing the light

It all begins with light. Light transcends boundaries imposed by geography, politics and even time.

In its own little corner of the world, Ocean Optics experiences firsthand how customers around the globe are connected by light – measuring it, moving it, applying it – in pursuit of research, education and applications that solve problems and often elevate us all. "It's exciting to be a part of that exploration and, in our own small way, to help folks to achieve great works," says David Creasey, Vice President of sales and marketing at Ocean Optics.

Light has always played an integral role in man's development. Today, light is being used in creative ways to solve many of the challenges facing our world, with photonics technologies like spectroscopy driving those solutions. Indeed, from early man and the first astronomers to James Clerk Maxwell and Albert Einstein, great thinkers, scientists and dreamers have pondered, explored and experimented with ways to harness the power and beauty of light.

As we celebrate the International Year of Light 2015 (www.light2015.org), Ocean Optics wants the scientific community to promote the use of light to improve the quality of life. It's certainly exhilarating to consider the impact of light in so many areas: illumination and restoration of art and cultural works; light-based applications in life sciences and laser-based therapies in medical diagnostics; light-measurement methods applied to farm-to-table technologies; and light used to monitor the health of the environment.

Celebrating the journey

No technological discovery or advance – be it a great scientific achievement or a small but meaningful improvement to a technique or process – has taken place without collaboration. The most brilliant scientists and technologists have colleagues, observers and even rivals with whom to share ideas.

"When we think about being socially responsible, we first consider how collaboration can produce great things: new ideas, big concepts, and visionary landscapes. From direct support of students and researchers through funding initiatives to sharing of knowledge and insight with prospects and customers, Ocean Optics is committed to furthering the cause of science and its role in our society," says Creasey.

Motivation for Ocean Optics is simple. In the future, what we eat, drink and breathe, and what dose of medicine we take to improve our health, will all be determined through better analytics. And spectroscopy will play a leading role in helping us navigate important choices regarding our health, our quality of life and the environment. Providing our children with clean water to drink and safe medicine to take will be the greatest legacy of analytical science, allowing future generations to not just survive, but thrive.

Photo: Markus Schmidt Stabstelle Foto-Grafik-Video Universitätsklinik Mainz

Thirty Years Young

PSS is celebrating its 30th anniversary this year. And growing steadily over that time from two to more than 50 people has ensured that its core principle remains unchanged: a passion for sharing knowledge that helps make the world a better place.

Daniela Held is marketing and sales manager and has been with PSS since 2000. She feels that her reasons for joining – and staying – with the company are echoed throughout its staff. "I decided that I wanted to be part of a smaller company; and PSS offered me a better opportunity to develop myself. I already knew that they were not just trying to make as much money as possible – they wanted to make something long lasting, which focuses more on people than money. Of course, we need money to make a living, but many people feel more strongly about making a difference."

Going back 30 years, PSS started out as a spin off set up by two PhD students from the University of Mainz. They began by producing synthetic polymers with special properties and subsequently expanded the product portfolio over time to today's offering: all supplies and services for the analysis of macromolecules with liquid chromatography.

CSR at its core

Corporate social responsibility at a small company tends to be a much more personal endeavour, and PSS is no different. "CSR is very important to all the founders and owners; all of whom are still working at the company. It gives PSS the freedom to create the perfect framework to support employees who really believe in what we are doing as a company," says Held. And she believes that if people are happy in their positions, they can, in turn, better support customers and collaborators. "We often say that we are passionate about macromolecule characterization – and I think that is what sets us apart. We really believe that what we do helps others to develop better products to, for example, find new cures for diseases and provide other benefits to humanity."

Moreover, a small company with passionate and well-supported employees doesn't need to waste time and energy on negativity, instead finding time to be charitable. Held says, "We are involved in many charity projects. Most of them are projects that the company owners are involved in; for example, PSS supports orphanages in Africa and Romania. Actually, we do not spend money on Christmas cards or gifts for our customers each year – instead, we donate extra money to charity projects."

The importance of being educated

What especially comes across from the people at PSS is their passion for education at all levels. From fully supporting the German dual-education system, to offering work experience to school children, to providing training to analytical labs in Africa, PSS are trying to spread the word about the importance of macromolecule analysis and analytical chemistry in general.

And given the complicated nature of the field, PSS are all too aware that excellent training is absolutely essential inside the company to make good on its promises to promote knowledge about macromolecules. Daniela says, "Because our subject is so specialized, we're not able to employ fully-trained people from universities; instead, we seek the right personalities for the company and give them training on the job, so that they can understand macromolecules and pass on that knowledge to our clients. There are no easy answers in analytics. And there is no easy way to find the right people – it requires time, training and passion!"

PSS is a relatively young company with a mature – even unusually philanthropic – philosophy. "We don't want to make millions of Euros in the next five years. We just want to grow the company organically at the rate we can find and train good people so that we can support more people worldwide," says Daniela. "After all, the market for macromolecules is increasing but knowledge about macromolecules is decreasing. And we want to do our best to help."

Improving Life Through Science – Responsibly

Sigma-Aldrich places "global-citizenship" at the heart of its business.

"We aim to improve the quality of life through science, so being committed to 'Global Citizenship' is in our DNA. We work to enable our employees, customers and the greater community to continue to benefit from these fundamental beliefs," says Jeffrey Whitford, Director, Global Citizenship at Sigma-Aldrich.

"We are constantly finding new ways to increase the sustainability of our business from procurement to production to consumption by our customers. With a global environmental management system for all of our facilities, we have invaluable data that helps guide our decisions and investments to reach the next level of sustainability."

Shrinking the problem of waste

Sigma-Aldrich has improved transparency and reporting of waste generation through its local Environmental Health & Safety and Facilities teams, which has helped to identify opportunities for waste reduction or beneficial reuse. Sigma-Aldrich will soon announce the completion of its initial 20% waste intensity reduction target.

Sheri Williams, Facilities Team Leader, at the company's Teutonia facility (Milwaukee, Wisconsin, USA) says, "By 2012, our Teutonia facility in Milwaukee was Sigma-Aldrich's main central distribution center, handling an increased volume of shipments from all around the world. This inevitably resulting in increased recycling volumes – almost four times the amount of cardboard, plus other waste materials."

Sheri decided to focus on waste shrink-wrap. She partnered with a local waste provider to investigate possible ways to recycle shrink wrap since the company could not recycle it in-house. "After a very successful trial we now recycle more than 20 tonnes of shrink wrap each year." This is just one example of the individual contributions employees are making to decrease our impact.

Acting on climate change

Sigma-Aldrich also recognizes the challenges that climate change poses. "We continue to make progress toward our 20 percent CO2 emissions intensity. We are working hard to mitigate annual increases and finding innovative ways to grow our business and manage our carbon footprint. We are about evaluating ground breaking technology to make our energy use more efficient and helping to reduce our impact," said Whitford.

Water is another major issue for a large-scale company. Sigma-Aldrich has mapped each of its large production, R&D and distribution sites using the World Resources Institute Aqueduct tool and found limited risk, with facilities in high-risk areas requiring limited amounts of water for production. In fact, seventeen percent of the company's sites are located in designated biodiversity hotspots, but they only account for 6.3 percent of its total CO_2 emissions and three percent of total water use.

People make the difference

"The only sustainable way to earn the unwavering trust of our customers is by demanding a high standard of behavior and unquestionable integrity from every Sigma-Aldrich employee," says Whitford. "Continued honest and ethical business conduct is a cornerstone of our 'One Company' values – the articulation of our commitment to transparency, responsibility and compliance at all times."

Nobody working for Sigma-Aldrich is above the law, and ethical violations are never acceptable. "A single violation by even one employee can cause great harm to our company's reputation and ability to carry on our operations, and can compromise the work of many others," says Whitford. "And, whenever there is any doubt about legal obligations or the appropriateness of conduct in any situation, employees have access to experts who can offer instruction or advice."

Being socially responsible

Sigma-Aldrich has focused its philanthropic investments in three key areas: science, technology, engineering and math (STEM) education, scientific research, and economic development through science. These three key areas are also supported by Sigma-Aldrich employees through skills based volunteerism; local initiatives help build a growing network of projects that have a positive impact. In 2014, Sigma-Aldrich invested more than $2.2 million through cash investments and $1.9 million in product donations in the communities in which they maintain offices around the world. There were also 163 employee-led events (126 percent growth in activity since 2004), with employees donating time (13,689 hours – 70 percent increase) and money (US $234,000 – 17 percent growth).

Some charitable works involve collaborating with schools, community organizations, and other corporations to address the growing need for individuals proficient in STEM subjects. The company also supports research focused on diseases, greener chemistry and other areas of interest to its overall mission – "enabling science to improve the quality of life."

A Wonderful Sense of Perspective

The 'ph' in Phenomenex stands for philanthropy and drives a very 'giving' culture.

When Fasha Mahjoor started Phenomenex over 33 years ago, he envisaged a colorful, high-energy culture that would differentiate the company from all others. His architectural roots allowed him to build an aesthetically pleasing, environmentally conscious, safe and efficient space, which included gyms, game rooms and many other benefits long before such ideas became mainstream. Employee welfare, promoting from within, and cross training to provide advancement opportunities are still top priorities, and Mahjoor has always actively supported the passions of his staff through a deep commitment to philanthropy, sport, the environment, and continued education. Indeed, to attract the brightest and best people – and retain them – Mahjoor knew he had to place a genuine focus on their welfare, that of their families, and on humanity.

Today, the company still provides unique benefits to its employees, including stipends for adoptive parents and staff adventure trips. But it also provides paid time off for volunteer work and on-site philanthropic events.

Fostering the right company culture

The Phenomenex company mission statement reads, "…it is our responsibility and foremost mission to promote the growth, prosperity, and well-being of those we serve – our customers, our employees, and humanity." Over two decades ago, Mahjoor launched a global Red Cross bone marrow drive – Save Simon – to help a colleague with leukemia. It was sadly too late for Simon, but the drive has since ignited a flame within the company – a deep and emotional commitment to philanthropy that continues to grow.

At Phenomenex, 'giving back' is a part of daily life – and all employees must share the same passion. Sponsored events are held on-site during working hours so that everyone can participate. And, each of its companies around the globe have active Philanthropy Groups who plan, organize, and execute volunteer activities.

Looking after Mother Earth

For Phenomenex, reducing its carbon footprint, recycling, and saving resources (especially water at its HQ in California!) is taken very seriously. About a decade ago, Phenomenex strived to reduce the environmental impact of its products and now uses 100 percent recycled paper, soy-based inks, and post-consumer recycled fibers in reduced amounts of packaging.

And by setting up a recycling program with its neighbors – the Switzer Learning Center for Autistic Children – Phenomenex not only gets to clean up its act, but it also gives young adults work experience and the opportunity to be environmental guardians, which they love; a real win-win.

Getting hands dirty – in a good way

Phenomenex India is deeply committed to the Cheers Foundation Orphanage, a non-profit organization that provides shelter, food, education, good health and a lovable family atmosphere to underprivileged children. The Phenomenex team is hands-on with the children, hosting gatherings, field trips, and learning activities. The company also provides financial support for food, tuition and books, shoes and clothing.

In Europe, Phenomenex Italy, Stop Hunger Now Italia Onlus (SHNIO) and Phenomenex Inc. have made it their mission to feed hungry children in developing countries. SHNIO has made an astounding 780,000 meals, giving hope and a brighter future to communities in Africa. And since "Save Simon", Phenomenex USA has continuously hosted on-site blood drives and raised money for global disaster relief efforts, and now also supports a program called Ready When the Time Comes, which trains volunteers to respond to local disasters.

What's next? Mahjoor's City Three Peaks challenge (see page 15), a London-to-Paris Cycling Challenge, and Happy Hats for Kids in Hospitals, a project that aims to bring joy to children with cancer and other life threatening diseases.

Phenomenex truly strives to set the best example. Imagine if all companies focused just as hard on being responsible global citizens...

State-of-the-Art TLC-MS

TLC-MS is here and still evolving – continual advances in coupling techniques and ambient mass spectrometry are giving rise to a renaissance. Here, we share the most promising techniques and open your eyes to the powerful – and flexible – combinations of TLC and MS.

By Michael Schulz, Head of R&D Instrumental Analytics, and Hans Griesinger, Analytical R&D Engineer, Merck Millipore, Germany.

Over the last few years, several coupling techniques for mass spectrometry have emerged to broaden the scope of TLC-MS analysis beyond elution-based sampling. Though some ambient MS techniques were not developed specifically for TLC, they offer additional flexibility and a number of advantages. However, with choice comes the potential for confusion! We hope to shed light on what is available, comment on the level of "commercialization" or development, and also indicate the most appropriate choice, depending on your objective or application.

TLC-MALDI-MS

Matrix-assisted laser desorption/ionization (MALDI)-MS is well respected and has found widespread use in a number of areas, such as tissue imaging and proteomics. MALDI's ability to scan an area of interest make it a natural partner for TLC; to that end, Bruker Daltonics introduced an adapter that allows you to directly insert your TLC plate into a MALDI instrument. The fully automated measurement process allows an entire plate to be scanned and produces a visual representation of separations. Indeed, the data evaluation software enables so called MALDI chromatograms that plot molecular mass against TLC position, producing a two-dimensional view; analytes that overlap on the TLC plate are separated by mass and shown in a different color.

From an application perspective, TLC-MALDI-MS is strongly suited to proteins, peptides and lipids, especially when analyzing less complex mixtures. And though it is unlikely to overthrow gel electrophoresis methods, in certain applications it is a compelling additional analytical tool. Notably, MALDI matrix must be applied ahead of analysis, and only aluminum backed plates may be used because of the need for plate conductivity.

TLC-DART-MS and TLC-DESI-MS

Like MALDI, direct analysis in real time (DART) and desorption electrospray ionization (DESI) are general surface analysis techniques and therefore also lend themselves to TLC analysis. The mode of operation at the surface of the plate is somewhat similar, but in DART-MS a gas stream is focused on the TLC plate; in DESI, the stream hitting the surface is a solvent mixture. Also like MALDI, both techniques are able to scan the entire plate, which offers distinct advantages.

Gertrud Morlock has published a number of papers on TLC-DART-MS (1). Morlock is a real advocate of TLC-MS in general, and you can read her opinions in the first article of this series online: tas.txp.to/0715/missinglink.

We haven't done a great deal of work with TLC-DART-MS or TLC-DESI-MS (2) yet, but that's not to say they are uninteresting techniques – to the contrary. However, while the sources are commercially available, right now there are simply no complete systems available to enable straight-forward coupling, which is why academics like Morlock are leading the way. Our experience of these techniques comes from collaboration with such groups and we have been impressed with the results. Certainly, these two techniques are seriously worth following.

Liquid Extraction Surface Analysis

LESA™ technology was originally developed to investigate tissue slices, but it can analyze almost any surface with its nano-robotic ESI source – and that includes TLC plates. The TriVersa® NanoMate (Advion) automatically works its way across the plate, taking a fresh pipette tip to analyze each "zone," which practically eliminates carry over. In actual fact, the robot is capable of multiple modes of operation, but for LESA the robot picks up a pipette tip, draws extraction solvent from a reservoir, moves to the zone of interest, allows a small droplet of solvent to mix with the sample spot for a preset time, and draws up the mixture before nanospray injection into any high-end MS system.

LESA is an elegant solution that offers high sensitivity. And the high level of automation is welcome for high-throughput studies. The system does however require hydrophobic plates to operate effectively, so reverse-phase (RP) modified TLC plates are needed. Fortunately, RP plates are suitable for most separations. In fact, we have run a number of applications using LESA and in 80-90 percent of cases, it works very well.

There is, however, a sort of paradox: the nanospray infusion of the TriVersa NanoMate works best coupled with high-end mass spectrometers – but in general, laboratories that have such instruments do not typically perform TLC analysis. That said, because the technique is so promising, we are keeping a keen eye on further developments. Certainly, as the TLC-MS user base expands, we can imagine a number of advanced labs adopting this approach.

Elution-based TLC-MS

Two commercial systems are available for elution-based TLC-MS, both of which

were developed specifically for the task. Morlock introduced the concept (and the background) to CAMAG's Interface in the article noted earlier, and very recently Advion released its Plate Express. Plate Express operates on a similar principal to CAMAG's Interface – both utilize a head that seals to the plate with a cutting edge. A capillary channel introduces solvent to the spot within the seal, and another channel extracts the analytes and solvent for introduction into a mass spectrometer.

Perhaps the strongest feature of elution-based coupling is its complete independence from the mass spectrometer – any MS system can be used, in principal. Plus, offline extraction into vials is possible, if additional analysis (with NMR, for example) is needed. In online TLC-MS mode, the interface sits between the HPLC pump and the MS system, and is pretty much "plug and play". It's fair to say that such systems offer the lowest entry barriers into TLC-MS, and can be used with almost any kind of plate.

However, unlike MALDI, DART and DESI, these elution-based approaches don't allow scanning of the whole plate, instead taking measurements from each sample zone within the head's cutting edge.

TLC's renaissance

Hopefully, a clear picture is emerging: TLC-MS is a growing and evolving field. With a number of very promising – but quite different – solutions on the market, it's clear that there is great value in combining the power of TLC and MS in a number of different application areas. Indeed, the number of publications focusing on TLC-MS is steadily increasing, and as the technique becomes more affordable (the price – and size – of MS systems is coming down) we expect the upward trend to continue. TLC is already a very low-cost analysis method – add low cost mass spectrometry, and it becomes an compelling orthogonal tool that is hard to ignore.

A strong driver for more rapid development will simply be increased uptake of TLC-MS – although there is growing interest, many people are still not aware of the potential of the technique, which impedes progress. But things are changing. We recently held a (national) TLC-MS user meeting in Darmstadt, Germany, and although it was relatively small, it still drew a similar number of delegates – more than 100 – to the last HPTLC symposium in Lyon. Why? Because it attracted both TLC and MS users, particularly those who are interested in high-quality quantitative screens or orthogonal analytical methods.

Likewise, at mass spectrometry conferences it's very interesting to follow new developments in ambient ionization for MS – in principal, many of these can most likely be applied to TLC in innovative ways.

Are we at the beginning of a virtuous cycle of dedicated instrument development for TLC-MS? We think so and believe a thriving community will quickly emerge.

Find out "what you've been missing" with Michael Schulz's comprehensive webinar tour of TLC–MS, moderated by Rich Whitworth (Editor): tas.txp.to/0715/TLCwebinar

Hot TLC Research

Broadly speaking, TLC-MS offers three key benefits: the ability to handle matrix rich samples, orthogonality to HPLC, and parallelization. Here, we share some interesting research from the past few years that highlights the potential of applying TLC-MS in your lab.

TLC-DART-MS

"Combined multivariate data analysis of HPTLC fingerprints and direct analysis in real time mass spectra for profiling of natural products like propolis"
G. E. Morlock et al., J. Chromatogr. A, 1328, 104–112 (2014). tas.txp.to/0715/TLC1

Elution-based TLC-MS

"Characterization of saponins in peas (Pisum sativum L.) by HPTLC coupled to MS and a hemolysis assay"
V. Reim and S. Rohn, Food Res.Int. (2014). tas.txp.to/0715/TLC2

Elution-based TLC for sample preparation

"Planar solid phase extraction clean-up for pesticide residue analysis in tea by liquid chromatography–mass spectrometry"
C. Oellig and W. Schwack, J. Chromatogr. A, 1260, 42–53 (2012). tas.txp.to/0715/TLC3

TLC-MALDI-MS

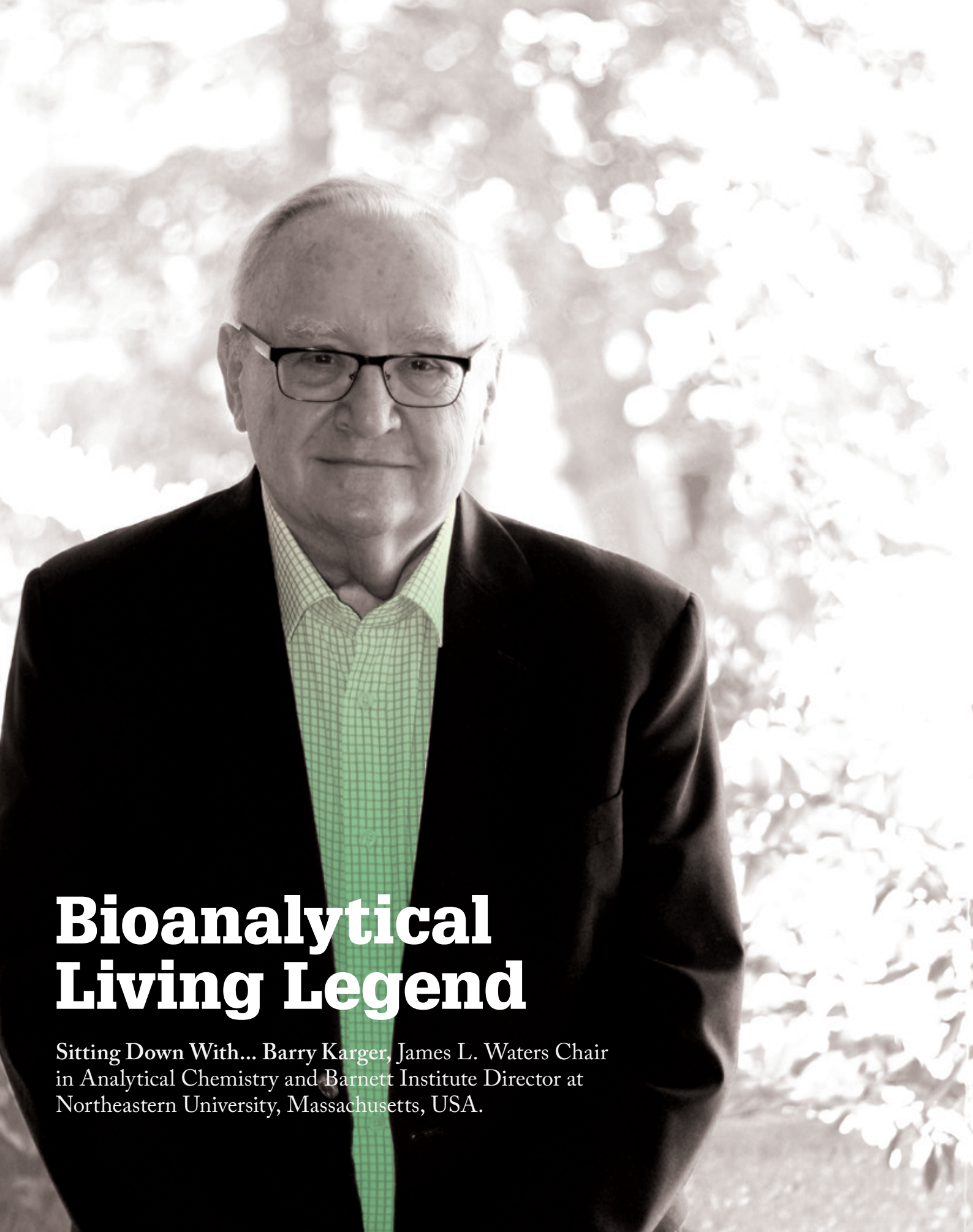
"Stationary phase thickness determines the quality of TLC-MALDI-MS of lipids"
H. Griesinger et al., Anal. Biochem., 451, 45–47 (2014). tas.txp.to/0715/TLC4

TLC-MS still evolving: "direct spray" MS

"Identification and semi-quantitative determination of anti-oxidants in lubricants employing TLC-spray MS"
G. Kreisberger, J. Chromatogr. A, 1383, 169–174 (2015).

Reference

1. *E. S. Chernetsova, A. I. Revelsky, and G. E. Morlock, "Some New Features of Direct Analysis in Real Time Mass Spectrometry Utilizing the Desorption at an Angle Option", Rapid Commun. Mass Spectrom. 25: 2275–2282 (2011). DOI: 10.1002/rcm.5112*
2. *S. P. Pasilis et al., "Using HPTLC/DESI-MS for Peptide Identification in 1D Separations of Tryptic Protein Digests", Anal. Bioanal. Chem. 391(1), 317-24 (2008). DOI: 10.1007/s00216-008-1874-6*



Bioanalytical Living Legend

Sitting Down With... Barry Karger, James L. Waters Chair in Analytical Chemistry and Barnett Institute Director at Northeastern University, Massachusetts, USA.

Take us back to the beginning...

I got my undergraduate degree in 1960. And I guess the main reason I chose to enter the world of analytical chemistry was the influence of my senior thesis professor at MIT – L. B. "Buck" Rogers. He passed away more than 20 years ago, but he was a very well respected analytical chemist, particularly in separations. I then went onto Cornell University and worked for another big name – Donald Cooke. The field of gas chromatography was just beginning, and I built my own flame ionization detector triggered by work Jim Lovelock had published in 1961. The other part of my thesis was fundamental work on optimization separations using time normalization. Around that time, a guy I'd never heard of from Ecole Polytechnique in Paris wrote to me in broken English and started using some of my data. I finally met Georges Guiochon in 1964.

And then you moved to Northeastern University?

In those days, the universities in the US were expanding because of the impending war-baby boom, and it meant that I was essentially free to go anywhere. My wife is from Boston, so there was pretty strong pressure to go back there... I began at Northeastern University in 1963. I worked on two areas – gas chromatography and foam fractionation (a method to separate by adsorption on bubbles). One of the big discussion points of the day was the battle between packed and capillary GC columns (the latter introduced by Marcel Golay in the late 50s). We all know how that story ended: capillary columns won the day. Chiral separations, in particular diastereomers, were another focus in those early years. Then in 1964, I met Csaba Horváth who was doing a post-doc at Harvard Medical School ahead of Yale. He told me I really should start looking at aqueous systems, both for GC and liquid chromatography. I agreed, and we began early work on LC. Of course, when a new method comes along with the potential to displace an existing method, some experts start getting defensive; it was an interesting time.

So you found yourself in an exciting and burgeoning field?

Yes - and with the right people. We connected with István Halász (Csaba's PhD mentor), who doesn't get enough credit today; he had a major impact on Csaba, Georges Guiochon and myself, and he actually introduced bonded phases. We made a major effort in C18 bonded phases and got into reversed phase LC early, in part because of Csaba's insistence. It was an interesting era – initially, the technique was not robust at all. Columns were shipped in foam rubber because the packing would settle leaving an empty space.. For a couple of years, we did a training course for FDA scientists on LC, and I remember receiving some columns, installing them, and then discovering there was a void at the top – useless (I won't mention the vendor).

Fortunately, the technique quickly evolved. I think it was in 1973 when everyone got excited because the first LC method had been accepted into the US Pharmacopeia. Also in 1973, we had the first international HPLC meeting in Interlaken (I was there). In some ways, that first generation is like mass spectrometry today – with hot new ideas and applications constantly pouring forth.

And you continued to connect with the right people?

In the 70s, I got friendly with Josef Huber and Lloyd Snyder – we wrote several papers together. It felt like we'd formed a real community. In fact, Csaba, Lloyd and I published a textbook – Introduction to Separation Science – and it was used as a graduate text for the next 25 years. HPLC really improved over the decades that followed – and the fundamental understanding kept pace, which was hugely important. It's fun looking back; the fundamentals in our book are still good – but the rest of it is woefully behind. I'd describe it now as an historical document...

"I've always felt that analytical chemistry should be at the center of a wheel, with the spokes being various application areas."

How did the Barnett Institute come about?

I've always felt that analytical chemistry should be at the center of a wheel, with the spokes being various application areas. Working alongside the NU's College of Criminal Justice, we got funding from the Department of Justice (which stopped when Jimmy Carter became President) and the opportunity arose to form an analytical institute with a focus on forensics – one of the spokes. Later, the Barnett family offered a naming gift, and that was the beginning of the Barnett Institute – I've been director there for over 40 years. As a side story, Jim Waters helped me out in my early days by giving me an injector and pump. And in 1985, he endowed

the James L. Waters Chair in Analytical Chemistry at NU, which I am very proud to hold. He's 89 now, but he still comes to Institute board meetings.

We began filling out the wheel with spokes from other areas; for example, the 80s had an environmental focus, and the Human Genome Project dominated in the 90s – we developed the linear polyacrylamide matrix that was used extensively in the sequencing. In the 2000s, I saw next-gen sequencing being introduced by dedicated and well-funded companies, and made a smart decision to refocus on chromatography and bioanalysis.

"Without an application you've got nothing. And there are plenty of questions left to solve, they just need to be understood."

What would you consider to be your main legacy?

People. Over the years, the Barnett Institute has seen 375 academicians pass through its doors, with many big names among them. My first post doc was Heinz Engelhardt. Wolfgang Lindner you know... There are obviously far too many to mention here. But I'll say this: none of them found it difficult to get jobs!

Of course, we've licensed a great deal of technology over the years as well... I already mentioned our impact on the Human Genome Project. But I think most academics will share my thoughts that it is the people you shape – and watch go onto great things – that give you the most pride.

Why do you think so many top people gravitated towards you?

Well, it wasn't just me – it was also the institute. But I think my focus on not only the fundamentals but also on applications was very important. Without an application, you've got nothing. And there are plenty of problems left to solve, they just need to be understood. Indeed, one of the grand challenges right now is being able to analyze intact proteins. Every biopharmaceutical is a mixture – and to tackle that, we're going to need improved mass spectrometry and improved separations. There are many opportunities, but to see them, you need to come out of your shell. Forming real collaborations is a big part of that.

You've been in the field longer than most – how do you maintain a fresh perspective?

Keeping an open mind helps. When I started, analytical chemistry was suffering a real loss of prestige, so being aware of opportunities was important. Today, the situation has dramatically improved. If you have something new and can solve a problem that hasn't been solved before, people will be knocking down your door. The term "analytical chemist" is less used these days – people are described as bioengineers, clinicians and so on – and that's a good thing because we need a collaborative approach; the problems we're tackling now are much more complex than ever before – in part because we now have the tools to tackle them. I actually think we'll see more and more academic–industry collaborations as the decade plays out. Industry keeps your head straight and offers a true link to what is required. Some people would suggest that such work is scientifically less creative, but that's totally wrong. In many cases, it actually drives the fundamentals.

Finally, take us into the future...

I see several major areas out in front. Protein analysis is not going away – sheer complexity has made progress slower than perhaps expected, but its importance will only grow. Bioinformatics will become hugely important – we're getting serious amounts of data; what can and should we do with it? And we need advanced statistics to ensure relevance amongst all this complexity.

Another major trend will be our need to deal with limited amounts of sample. In the clinic, for example, liquid biopsies are fast emerging, particularly in our search for early cancer diagnostics. We clearly can't take a liter of blood, so our ability to handle and analyze such limited amounts of material will be a big driver. Amy Herr was at HPLC in Geneva presenting on single-cell proteomics, Renato Zenobi is working on single cell metabolomics. And for all of these things we need separations. How can we deal with picogram quantities of material? The people answering these sorts of questions will be the leaders of tomorrow.

In recognition of Barry Karger's scientific contributions and his establishment of the Barnett Institute, Northeastern University initiated a medal in his name, awarded biannually, for outstanding advancements in the field of bioanalysis. The inaugural awardee will be Matthias Mann, Director of Proteomics and Signal Transduction at the Max Planck Institute of Biochemistry in Munich. The Karger Medal will be presented in October 2015 in Boston, an event that coincides with Barry's celebration of 50 years at Northeastern University.

PSS

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