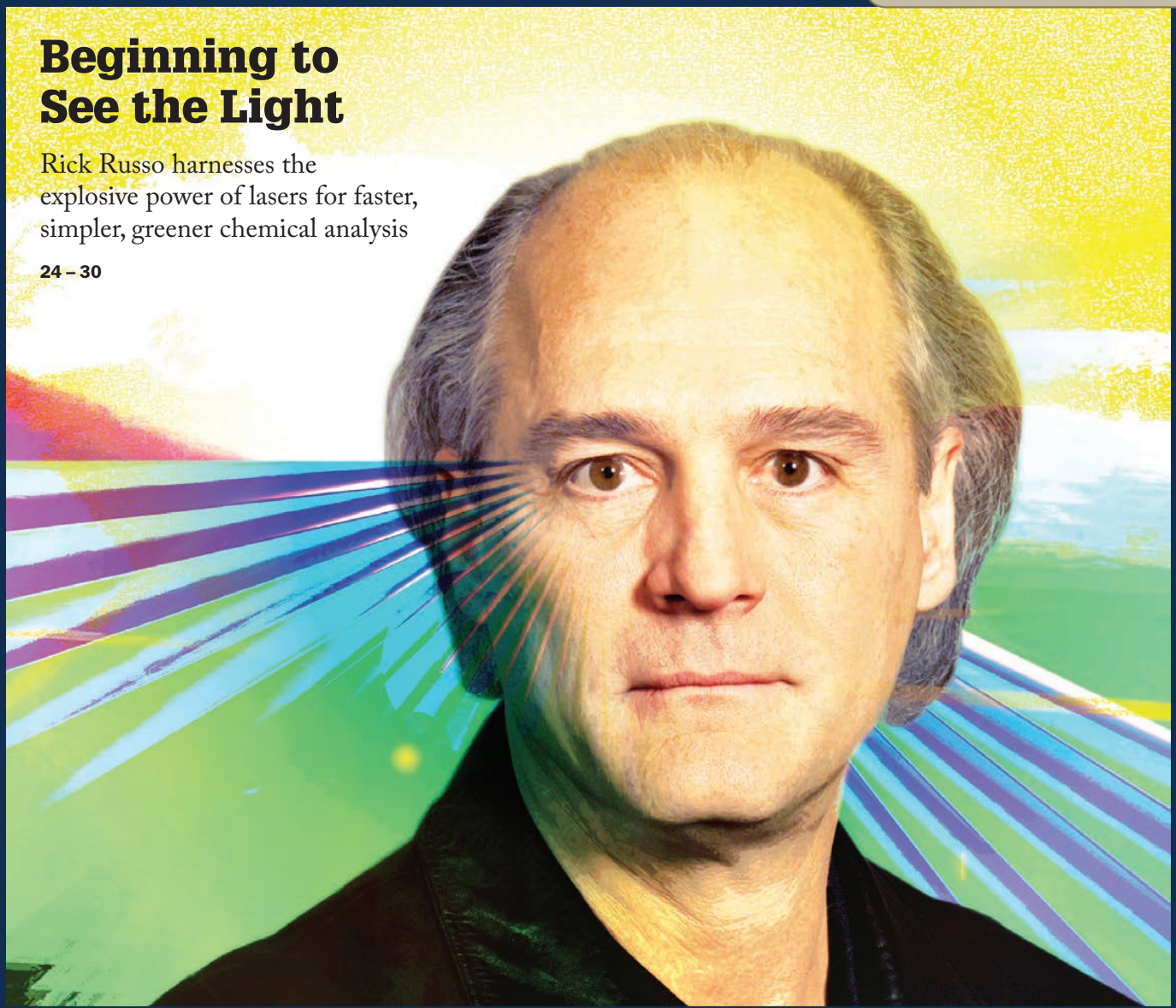
FEBRUARY 2014 # 13

the Analytical Scientist

Beginning to See the Light

Rick Russo harnesses the explosive power of lasers for faster, simpler, greener chemical analysis



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Comparison of Column Inertness

- Solid-core columns from leading manufacturers investigated
- Comparison of column efficiency for pyridine, a basic molecule
- Efficiency measured at 50% peak height

Peak Efficiency Comparison

Application # 1802

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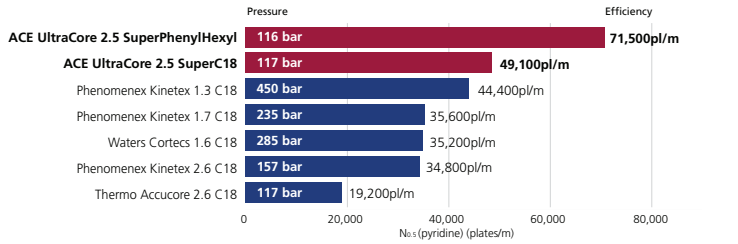

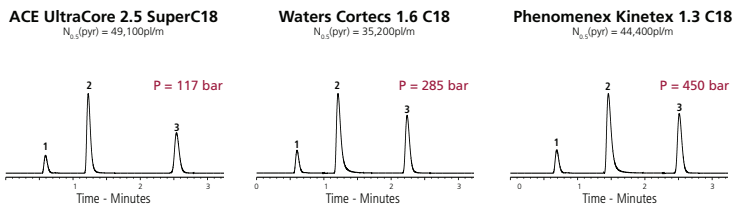

Column Dimensions: 50 x 2.1mm Sample: 1) uracil 2) pyridine 3) phenol
Mobile Phase: 30:70 (v/v) MeOH/10mM NH_4OAc in H_2O (pH 5.8) Flow Rate: 0.20ml/min Temperature: 22°C Wavelength: 254nm
Comparative data may not be representative of all applications.

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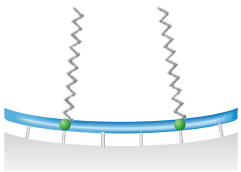

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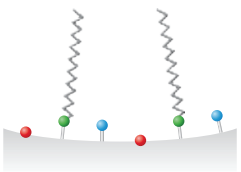
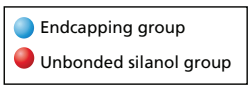
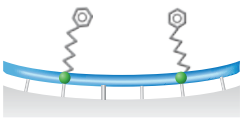


Traditional C18 Bonding





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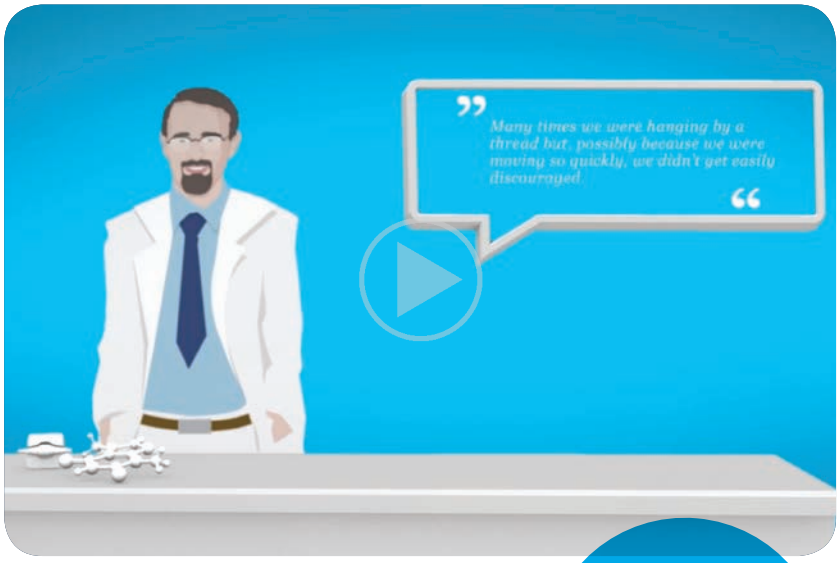


Watch the video here: tas.txp.to/0214/video

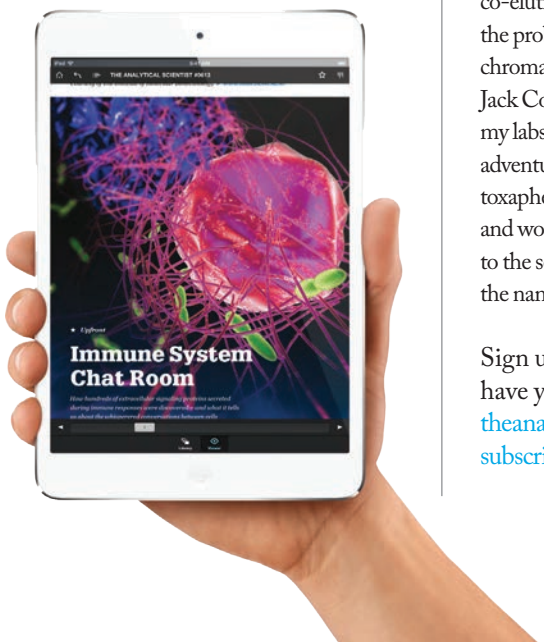
Five Minutes of Fame

To celebrate our first year anniversary, we have commissioned a short video that highlights what The Analytical Scientist is all about.

In the video, you'll see that we feature four contributors to the magazine and two members of the editorial team.

Now, all you need to do is enjoy (analyze) the video and put a name to the scientists included – one is very easy; he's already identified for you. Some of the others are decidely more difficult...

"What's in it for me?" you ask. Well, email edit@theanalyticalscientist.com with six (correct) names and you'll be entered into a prize draw for an iPad mini. Good luck.



Don't Ignore GC! (tas.txp.to/0214/2DGC)

"There seems to be a push centered on MS as a near 'cure all' analytical technique by some investigators – with almost disdain for GC. I hold out hope for the promise of three column identification as a technique with the legitimacy and respect that MS holds today." – *Kenny, California, USA*

"There should be more emphasis placed on actual GC separation and column chemistry. Youngsters today seem happy to just load a GC method with no clue as to why the separation is inadequate or why there is wrap around or co-elution. There is a lack of thinking through the problem or knowing how to utilize the chromatographic space (to coin a phrase from Jack Cochran). Jack has spent a lot of time in my labs where we have had many hilarious adventures separating pesticides, playing with a toxaphene separations, or making some weird and wonderful attempt at adding a new tweak to the separation of a new compound - all in the name of science!" – *B-J, South Africa*

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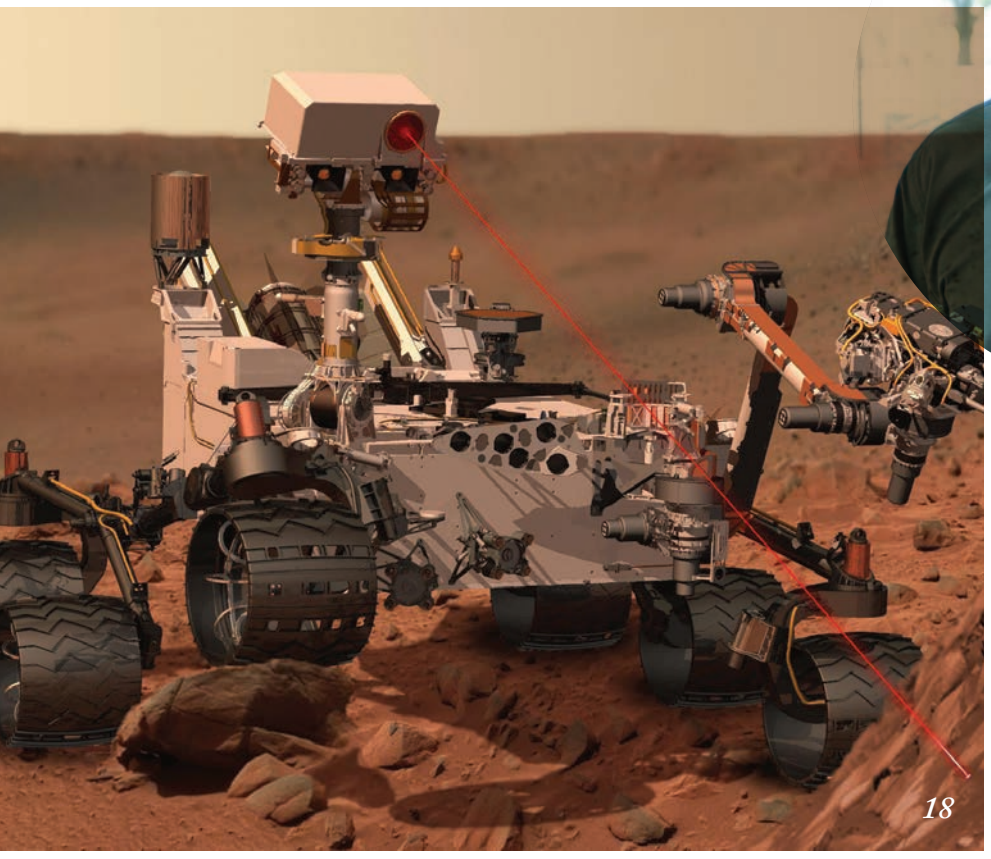

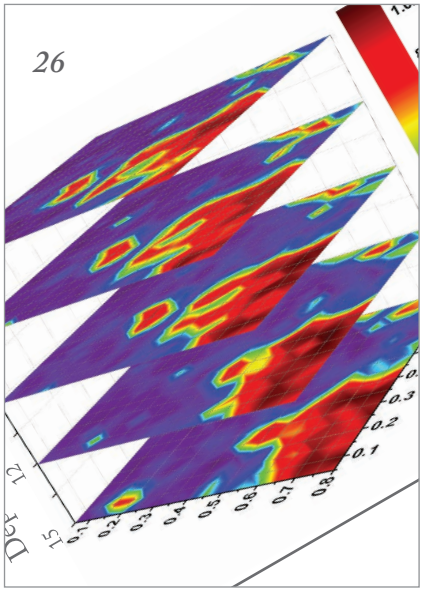

On The Cover

Rick Russo blinds us with laser science.

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Departments

Sitting Down With

the **Analytical Scientist**

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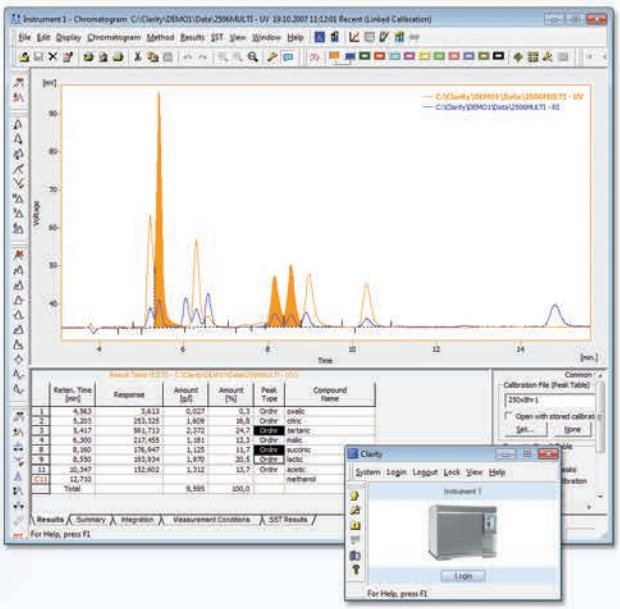

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Internet Etiquette for Researchers

New sites devoted to post-publication peer review open up great opportunities for dialog; so long as we can all agree on a clear code of conduct.

The Internet is a fantastic forum for interaction. For example, although I am based in California, I recently felt moved to comment on the issue of independence for Scotland on a newspaper website – it was exhilarating to play just a small part in a passionate and important debate, especially so far from home.

The downside is that many contributions on such forums are not worth reading; a good chunk are either depressing or simply offensive. But that's the price we currently pay for mass interaction/free speech.

Surely this doesn't apply to a group like scientists? Online forums are the perfect venue to debate the quality and meaning of data in real-time, with almost no chance of any infantile name-calling. But is the research community mature enough to handle the responsibility?

The establishment says, "No." A quick scan found no comment facility on Analytical Chemistry, Journal of Chromatography A, Nature Materials or Journal of Proteomics. To their credit, Science and PLOS One do allow comments. But, in the main, science publishers and editors want to retain the status quo, that is, they want to keep control. This is nicely illustrated by a recent editorial in ACS Nano (1), which suggests that you kindly lodge any comments with the authorities (them) rather than through social media.

Thankfully, a number of newish sites do promote vigorous scientific discourse on the published literature. Among these are Retraction Watch (2), which, I should declare, is co- run by my friend and former colleague Ivan Oransky, and PubPeer (3). To see PubPeer in action, look at "Anonymous cowards vs the scientific establishment", which questions the veracity of an ultrasensitive assay called plasmonic ELIZA (4). Another new site, PubMed Commons (5) is run by the US National Center for Biotechnology Information, part of NIH, bringing post-publication review into the mainstream. Kudos to them.

PubPeer allows posters to remain anonymous; PubMed Commons does not. It will be interesting to see how that affects the character of the two sites as they develop.

The only potential issue raised by increased engagement is the need to ensure that all parties are treated fairly; one author whose work was criticized online (6) has already claimed to "…have been subject to chemical cyberbullying," even stating, "I understand what kids that commit suicide go through."

I felt this was an overreaction having read the comments; however, the question of community standards is something that all scientists should have their say on, so that an agreed code of behavior emerges.

Richard Gallagher
Editorial Director

References

1. *pubs.acs.org/doi/full/10.1021/nn405306e*
2. *retractionwatch.com*
3. *pubpeer.com*
4. *blog.pubpeer.com/?p=53*
5. *ncbi.nlm.nih.gov/pubmedcommons*
6. *R.F. Service, "Nano-Imaging Feud Sets Online Sites Sizzling," Science, 343, 6169 (2014)*

Contributors:

Nick Kim

Nick Kim's background is in applied environmental chemistry. Now a senior lecturer at Massey University Wellington, New Zealand, his main research interests lies in the diffuse contamination of natural and built environments. "I was employed as a scientist in one of New Zealand's regulatory agencies for about 10 years. The agency was in charge of environmental controls and was actually a weird mix of EPA-style licensing and local government politics, with the odd court case thrown in," he says. From an artistic point of view, Nick says he sees every physical thing as a dynamic variation of the Periodic Table. "Students look perplexed when I compare them to the desks that they're sitting at. Of course, some students are a closer match than others..."

Nick shares this very analytical view of the world on page 14.

Elizabeth Treher

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

Liz explains how to manage career transitions on page 46.

Albert Heck and Reinout Raaijmakers

Albert J. R. Heck is a professor at the Science Faculty of Utrecht University in The Netherlands. Heck is also scientific director of the Netherlands Proteomics Centre and coordinator of the European proteomics infrastructure PRIME-XS and the NWO roadmap funded Proteins At Work. "I'm interested in implementing innovative mass spectrometric methods, with an emphasis on protein interactions and post-translational modifications," he says.

Reinout Raijmakers is the managing director of the Bijvoet Center for Biomolecular Research also in The Netherlands. There, he is responsible for the coordination of EU funded research and infrastructure projects. "Addiontally, I'm in charge of the organization of the educational programme for students in the center, which includes courses, a seminar series and a yearly symposium," he says. Reinout has also been working on the analysis of post-translational modifications and interactions of proteins – and their relation with diseases. "In particular, I concentrate on analysis by liquid chromatography and mass spectrometry."

Albert and Reinout team up on page 21 to extoll the virtues of solid proteomics infrastructure.

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Upfront

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

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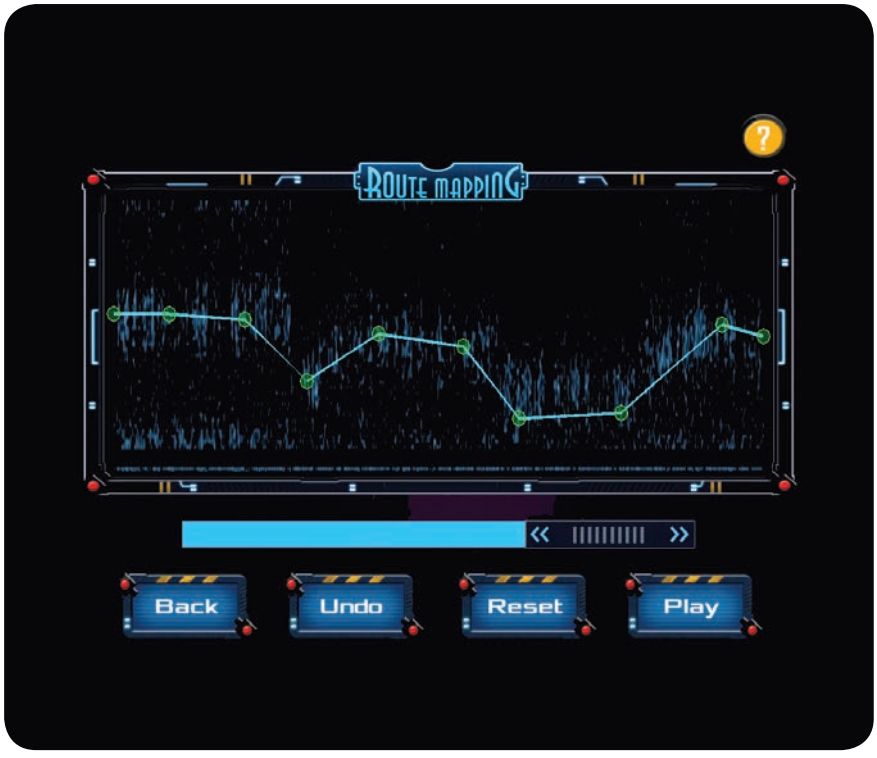


Gains from Games

Gamers are better at identifying certain patterns than computer algorithms, so why not use them to pick out breast cancer-related gene profiles?

If you've ever dreamed of piloting your own spaceship through an asteroid belt while simultaneously performing cutting edge cancer research, then "Play to Cure: Genes in Space" is the app for you.

While you're busy plotting your course and harvesting "Element Alpha" in the intergalactic (genetic) landscape, what you are actually doing is inspecting gene copy number variation from state-of-the-art data gathered from the 2012 METABRIC (Molecular Taxonomy of Breast Cancer International Consortium) study (1).

METABRIC looked at patterns in the tumors of nearly two thousand women and concluded that there were at least ten different subtypes of breast cancer, each with its own genetic fingerprint (Figure 1) But that left an ocean of genetic data to crunch.

Oscar Rueda from Carlos Caldas' group

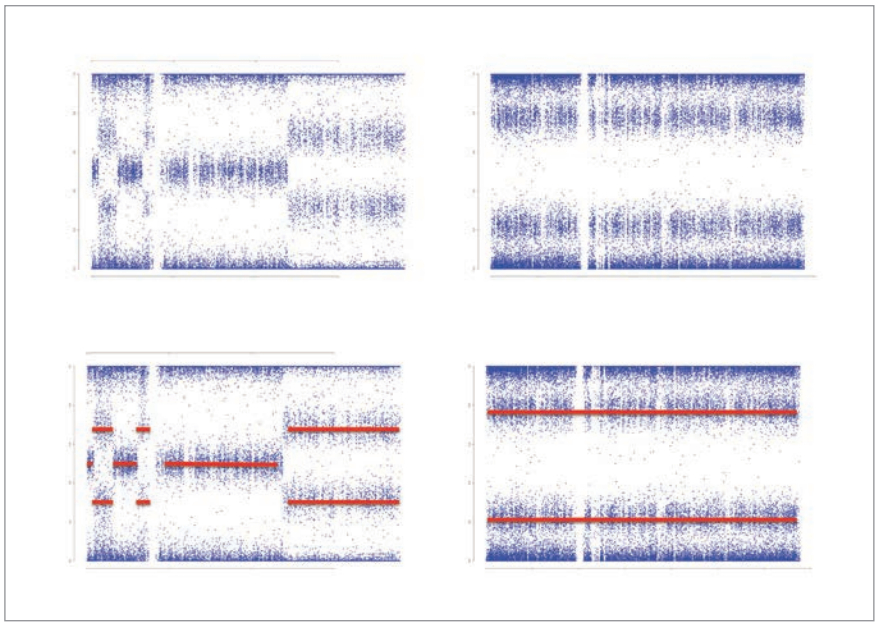
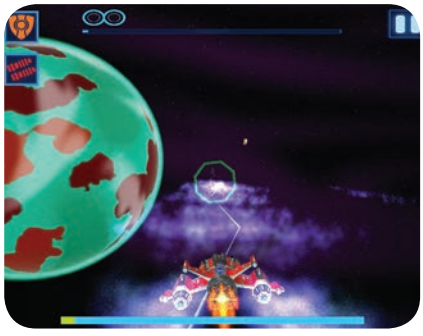


Figure 1. Raw data from the METABRIC study (above) was converted into "Element Alpha" to create an interactive space-scape (left and below).



(Breast Cancer Functional Genomics, University of Cambridge) was involved in the project. He explains that, "The cancer types have different DNA copy number profiles. In some cases these form a narrow peak that describes the driver gene in that particular subtype; in other cases it is not so clear." Current statistical methods can detect copy-number aberrations in the genome with an accuracy of 90-95 percent, Rueda says, "But for difficult cases, the human eye usually does a better job. It can spot the patterns in the copy number profile and distinguish whether a real copy number change is happening or if it is just noise."

The problem is, manual curation of 46,000 plots is not feasible. "Plus, we would still have problems with the inter-rater agreement, due to subjective scoring," says Reuda. And so, the idea of a video game was born, tapping into the inexhaustible passion for tablets and smartphone games.

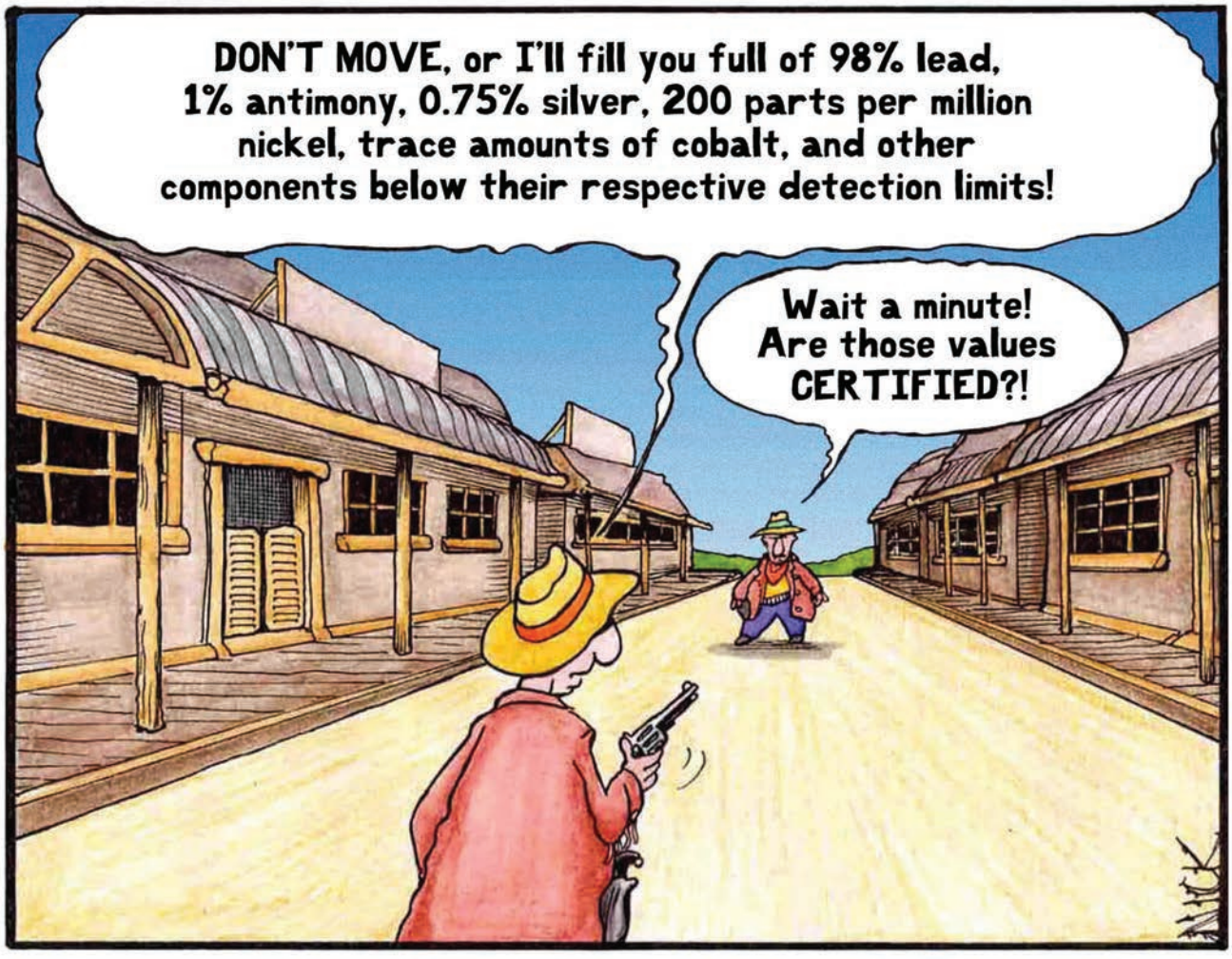
"Play to Cure" is available from Apple and Google Play stores and it's fair to say that it's addictive – consider it as a much more useful replacement for Flappy Bird. "We expect that with a large number of people analyzing each case, the average results will be more accurate than any statistical method," says Reuda, "but of course we will have to formally prove it."

If the project is a success, look out for more opportunities to put your game addiction to good use. "I think it will open the door to many other problems that can benefit from crowd sourcing initiatives," Rueda says. *RW*

Can you beat the (meager) success of The Analytical Scientist's first mission? Asteroids destroyed: 10, Element Alpha: 7120. Post your scores online: tas.txp.to/0214/spacegenes. And may the force be with you.

Reference

1. *Christina Curtis et al., "The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups", Nature 486, 346–352 (2012). DOI:10.1038/nature10983*



Courtesy of www.scienceandink.com

Analytical Chemists in the Wild West

Herbal Bubble Toil and Trouble

DNA barcoding highlights a disturbing trend in the composition of herb-based health products – contamination, substitution, and unlabeled fillers make up your daily dose

It is easy to take accurate labeling of goods for granted. For instance, the meals we devour – as well as the indigestion tablets that follow – come from highly regulated industries. When you walk into a store stocked with "healthy" herbal supplements, which in most countries are monitored by health authorities, you may assume that a similar level of regulation applies. How wrong you'd be.

Steven Newmaster, botanical director of the Biodiversity Institute of Ontario, and his colleagues at the University of Guelph, Canada, have used DNA barcoding (DNA extraction and sequencing) to conduct blind authenticity testing of 44 herbal products from 12 different companies, representing 30 different species of herbs. The results, represented in Figure 1, are quite shocking.

Newmaster told us more about the study that appears in an Open Access journal (1).

Why did you study natural health products (NHPs)?

Problems with product contamination and substitution have been identified in other sectors – we felt it was important to extend testing to the NHP marketplace.

What did you expect to find?

You can't approach this work with set expectations; rather, you must follow the data. Having said that, there have been several smaller studies, referenced in our paper, that identified contamination in herbal teas and medicinal plant products. And a recent scientific review (2) listed 60 publications that have used DNA barcoding of medicinal plants;

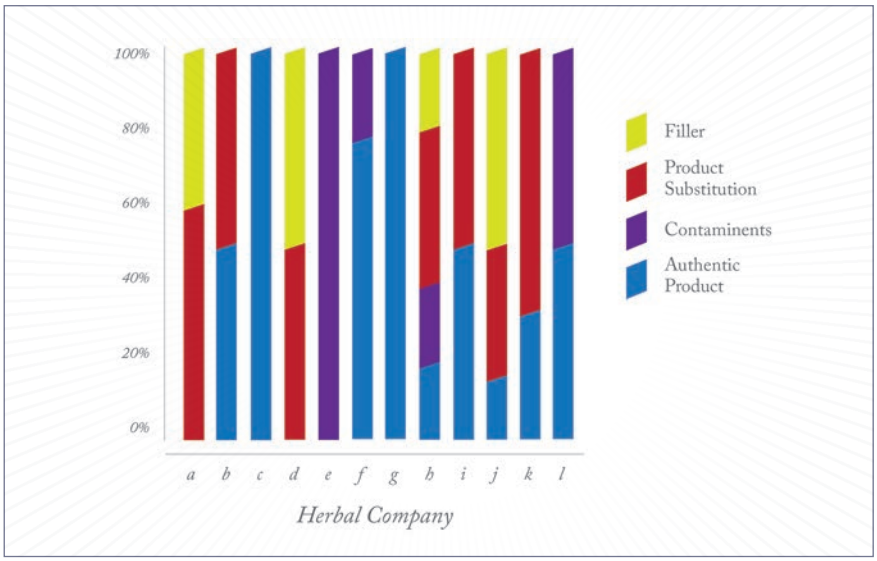


Figure 1. DNA barcoding highlights the consituents of several herbal products from 12 companies.

many of them reported positive tests for contamination.

Were the results surprising to you?

Our real surprise came previously, when we revealed the level of mislabeling in seafood. The reaction this time was more one of disappointment that the same problems exist in NHPs, especially considering the risks to consumer health that have been identified.

How far has the rot spread?

This problem appears to be very widespread. We have now tested NHPs from India, China, UK and Australia, and we found substitution, contamination, and use of fillers across the board. When we tested goods in other sectors, such as herbs, spices, and other plant products used in food (oils for example), we found that the issue is systemic in the marketplace. With fish products, trade reports suggest that perhaps 10 percent of products are subject to some form of fraud; from our work on NHPs and seafood, I'd say that 10 percent is a very conservative estimate. I am sure you will hear of more studies in the near future, so stay tuned.

Where do we go from here?

We suggested in our paper that testing would not cost that much for the industry, if they tested the bulk containers used to manufacture products. This approach has been embraced by some industry members and we are working with them. Remember that manufacturers can be victims of fraudulent substitution and contamination as well as perpetrators of it; they trust their suppliers, who claim their products are authentic. We are currently working with manufacturers and testing labs to set up protocols for proper testing, as well as working with existing product authentication and traceability systems. For us, working to clean up the marketplace is a rewarding activity. *RW*

Reference

1. *S. G. Newmaster et al., "DNA Barcoding Detects Contamination and Substitution in North American Herbal Products", BMC Medicine (2013). DOI: 10.1186/1741-7015-11-222*
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Two trucks with (very) different purpose.

Laughing Gas Laser

QEPAS offers highly sensitive portable sensing of nitrous oxide and methane – two of the nastier greenhouse gases

A landfill site in Houston, Texas is not the most glamorous of locations for academic research but that didn't prevent a team from Rice University taking its new quartz-enhanced photoacoustic absorption spectroscopy (QEPAS) sensor out for a spin. The portable device was installed in the mobile laboratory as part of NASA's DISCOVER-AQ campaign, which stands for Deriving Information on Surface Conditions from Column and Vertically Resolved Observations Relevant to Air Quality. QEPAS was able to detect methane at 13 parts per billion by volume (ppbv), reaching down to 6 ppbv for nitrous oxide in a one second acquisition time (1), findings that are comparable to much larger instruments currently used.

QEPAS makes use of a thumbnail-sized quantum cascade laser (QCL) whose beam is focused between two prongs of a millimetre-sized piezoelectric quartz tuning fork (QTF). In (very) simple terms, localized heating of molecules between the prongs at a certain wavelength generates an acoustic wave, which excites the QTF – the vibration produces a detectable voltage that is proportional to the concentration of the gas.

Why the interest from DISCOVER-AQ in methane and nitrous oxide? The global warming effects of CH_4 and N_2O are 21- and 310-times greater than CO_2, respectively (pound for pound on the 100-year global warming potential scale), according to the US Environmental Protection Agency.

Portable sensing equals better environmental control, allowing for improved monitoring of certain industries, such as agriculture, that are emitting both gases in increasing quantities. From a more short-term perspective, N_2O exposure can decrease mental performance and manual dexterity (this is laughing gas after all) – given its use as a processing gas in medicine and aerospace, it would seem wise to monitor leaks.

The team is now working on further miniaturization of the sensor and plans to install a smaller version on another mobile monitoring van that is carrying out a Rice/University of Houston survey of pollutants in the city. Apparently, the tuning fork costs no more than a dime; however, the cost of the continuous wave, thermoelectric cooled, distributed feedback quantum cascade laser is not mentioned. *RW*

Reference

M. Jahjah et al., "A Compact QCL Based Methane and Nitrous Oxide Sensor for Environmental and Medical Applications", The Analyst, advance article online (2014). DOI: 10.1039/C3AN01452E

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Maintaining Curiosity of Mars

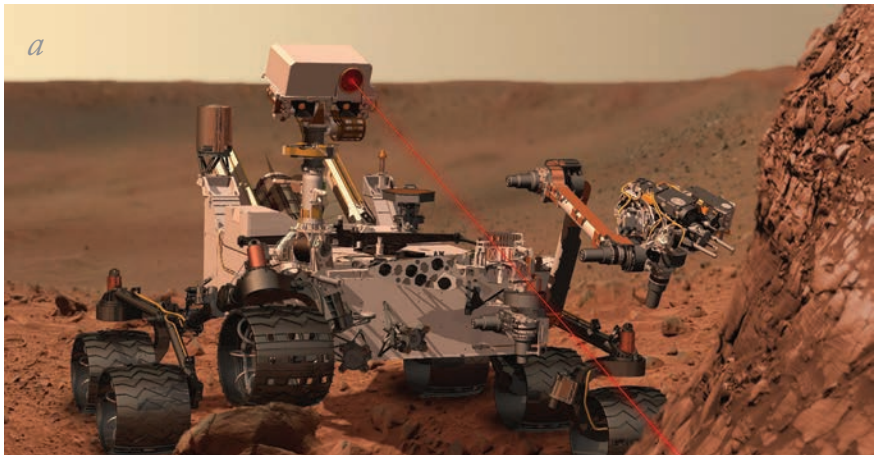
What is the ever-inquisitive Rover digging up now?

NASA's Curiosity Rover (Figure 1 (a)) recently raised its head (camera) to the night sky to take its first photograph of Earth from the surface of the Red Planet (Figure 1 (b)). The picture postcard shot strongly evokes the words of Carl Sagan:

"From this distant vantage point, the Earth might not seem of any particular interest. But for us, it's different. Consider again that dot. That's here. That's home. That's us. On it everyone you love, everyone you know, everyone you ever heard of, every human being who ever was, lived out their lives." – Pale Blue Dot: A Vision of the Human Future in Space.

But, apart from snapping photos of Earth and taking "selfies," has Curiosity provided any analytical insight? Towards the end of 2013, Curiosity passed the milestone of 100,000 "zaps" of its ChemCam laser ablation breakdown spectroscopy (LIBS) instrument. The landmark infrared laser blast was fired from distance of 4.04 meters at a rock called "Ithaca" (naming rocks on Mars is a bit of a pastime for NASA – tas.txp.to/0214/rocks). Each pulse delivers more than one million watts of power for a tiny fraction of a second – roughly five one-billionths. The resulting plasma spark is observed by ChemCam's "telescope" to gain spectroscopic information about rock composition (see Figure 1c). The international team pouring over the resulting data is interested in learning about the diversity of materials inside Mars' Gale Crater and the geology involved in their formation. *RW*

To learn more about LIBS, please see "Beginning to See the Light" on page 26.



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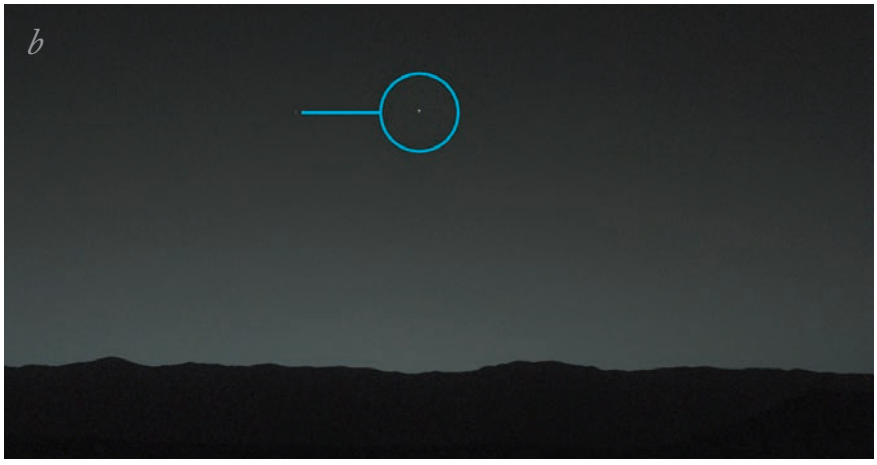

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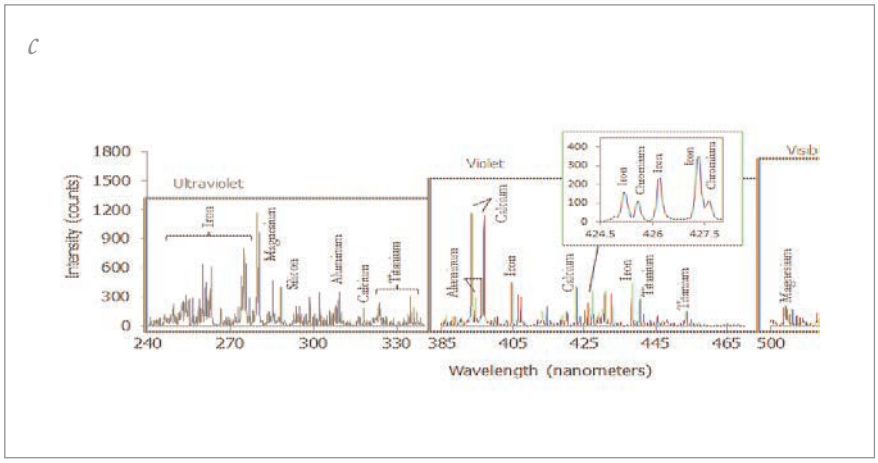

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Figure 1. a) Artist's impression of the Curiosity Rover. b) Earth – the brightest spot in the Martian twilight. c) Spectrum recorded by ChemCam's LIBS instrument. The spectrum averages data from multiple laser firings from the same rock sample spot and is typical of Martian volcanic material, and identifies a standard major-element suite of silicon, magnesium, aluminum, calcium, sodium, potassium, oxygen and titanium.

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Greening Analytical Science

How we might reduce environmental impact without reducing capability – and why we should try.

By Miguel de la Guardia Cirugeda, Department of Analytical Chemistry, University of Valencia, Spain

The greenest method of analysis is one that solves an analytical problem properly but with zero, or minimal, deleterious effect on the environment and operators. Sustainability must take into consideration, perhaps in equal measures, the environment, economic factors and other potential benefits. If it is cheaper to perform green analytical chemistry then it is more likely to be accepted by the big players in industry. In short, a marriage of ethics and economics is the most likely route to sustainability.

All methods can be improved and in time, we should endeavor to make improvements across the board. But the place to start is with those disciplines that are high-risk, that consume large volumes of reagents and that generate a lot of waste – sample preparation and sampling are good examples. The greenest approach would be to obtain the data in-situ without the need of sample treatment at all, something that would probably also please a lot of analysts… However, this is not always practical. Measurement techniques should be considered alongside sample prep for potential improvements.

The crux of the greening issue is the need to reduce the impact of unsustainable side effects without reducing the capability of our methodologies. A green alternative that cannot maintain (or, even better, improve) the current accuracy level or if it reduces sensitivity to an undesired level, then it is simply the wrong strategy. Consider two focus areas for green analytical chemistry, namely automation and miniaturization. It is not evident that automation reduces sensitivity and, in many cases, it improves the selectivity. Miniaturization by its very nature can lead to decreased sensitivity (an area of research focus), but is acceptable in most cases. Automation and miniaturization are actually relatively easy (though initially expensive) tasks that can dramatically reduce the deleterious environmental side effects of commonly used methods.

The generation of waste products is unavoidable in most analysis and we must take as much responsibility for the waste that we generate as we do for the important data that we produce. I believe that the accumulation of waste for collection and external treatment is a mistake; instead, I advocate online decontamination of waste products by incorporating a final decontamination step into lab methods. For example, photo-catalysis can mineralize organic waste, and precipitation steps can passivate toxic metals and reduce the amount of waste.

Thinking on a more creative level, one might consider alternative direct methodologies to obtain sample information; remote sensing or image

"We must take as much responsibility for the waste that we generate as we do for the important data that we produce."

analysis are examples that show potential. Advanced chemometrics is capable of enhancing and optimizing the information obtained using these alternative methods.

Some instrument vendors have begun to incorporate automated or mechanized systems for sample introduction, and these are often green. Other companies and research groups offer miniaturized systems or portable technologies. An example of this is the portable microwave system to extract essential oils that Farid Chemat and I have developed. Software developers can also join the party by increasing the amount of useful information obtained from (smaller) samples.

As an added bonus, the development of simpler, cheaper and side effect-free methods will extend their use, particularly in developing countries. This is another reason that green methods of analysis will become increasingly important in the future.

It is often said that, in the grand scheme of things, the scale of analytical chemistry's impact on the environment is minor when compared with industrial processes. This does not absolve us of responsibility. On the contrary, since the goal of analytical science is to improve people's lives, it is incumbent upon us to do so with the minimum environmental impact.

Turn to page 38 for a full discussion on the greening of analytical science.

Proteins At Work

How we can best provide state-of-the-art proteomics technology to the biomedical community.

By Albert J.R. Heck and Reinout Raijmakers, Netherlands Proteomics Center & Utrecht University, The Netherlands

Proteomics is an essential technology for research in the life sciences; it provides the crucial link between physical information presented by gene sequencing and structural biology, and the dynamic picture generated from cellular signaling and other biological processes. Integration of all these sources of knowledge gives us a broad systems biology approach that has applications in biology, medicine and biotechnology, both in academic research and in industrial development. Thus, the availability of state-of-the-art proteomics technology is crucial for life sciences research worldwide. But what is the optimal way of providing this technology?

The research questions being asked by the life sciences community are becoming increasingly complex and to

"A coordinated effort to build a large-scale proteomics infrastructure is more efficient"

answer them we need multidisciplinary teams of well-trained scientists with access to cutting-edge enabling technologies. Inevitably, there are bottlenecks. The two bottlenecks in state-of-the-art proteomics are (1) the availability of (rather expensive) hardware and (2) a shortage of the expertise required for the efficient and innovative use of that hardware. The second one is, arguably, the bigger problem. For an infrastructure to be optimal it requires three things: a critical mass of researchers with advanced analytical and biochemical skills; bioinformatics support; and expertise in various areas of molecular biology and medicine.

One way to fulfil the proteomics needs of life science researchers is by providing local proteomics facilities. Often, however, these services are set up with just a single instrument. They lack the support required to be valuable in the long term and they tend to offer standard proteomics technology, lacking the resources to provide customized and cutting-edge services.

A coordinated effort to build a large-scale infrastructure is more efficient and allows the provision of both new technologies and the expert guidance required for state-of-the-art proteomics. Organizing that infrastructure at the national level ensures a tight link with the national life sciences research communities that will benefit most.

We have a working example of this. The Netherlands Proteomics Centre (NPC; www.netherlandsproteomicscentre.nl), founded in 2003, combines research in proteomics technology with localized "research hotels" that provide access to technology alongside an integrated program to enhance and improve the use of bioinformatics in proteomics. In 2011, the European Union began funding PRIME-XS (www.prime-xs.eu), a pan-European program that funds access to multiple national infrastructures, including the NPC. PRIME-XS, provides proteomics expertise to many European scientists who would not otherwise have access to the technology.

The NPC is now firmly established in the national research community, and is also recognized internationally because of its high-quality contributions to the field. In the coming year, access to state-of-the-art proteomics technology will be further boosted by the Proteins At Work project (www.proteinsatwork.nl), which has received 13.5 million Euros in funding. Proteins At Work is a close collaboration between our core facility at Utrecht University, and several biomedical research centers, such as the Netherlands Cancer Institute, the Hubrecht Institute and the academic hospitals of Utrecht and Rotterdam. In addition to providing local proteomics support to the affiliated institutes, Proteins At Work acts as a conduit to any future enabling technologies pioneered at the core in Utrecht. Furthermore, Proteins At Work offers improved proteomics capability to all biomedical and biology-oriented researchers in the Netherlands.

Given the proven importance of proteomics in life science research, we hope that other countries – and the European Union – will place the continuity of access to state-of-the-art proteomics expertise higher on their agendas; to not do so would deprive genuine efforts to tackle today's societal challenges of vital support.

The Biologics Boost

Without the rise of biopharmaceuticals, would separation science and mass spectrometry be where they are today?

By Davy Guillarme, School of Pharmaceutical Sciences, University of Geneva, University of Lausanne, Geneva, Switzerland

Small chemical molecules are the classic active pharmaceutical ingredients and – despite the buzz about biologics and personalized medicine – still account for about 90 percent of all commercialized drugs. However, while biologics represent the minority in terms of sheer number, the financial story is somewhat different. Of the top ten selling drugs of 2012, seven were biologics. And so, for good reason, over the last few years,

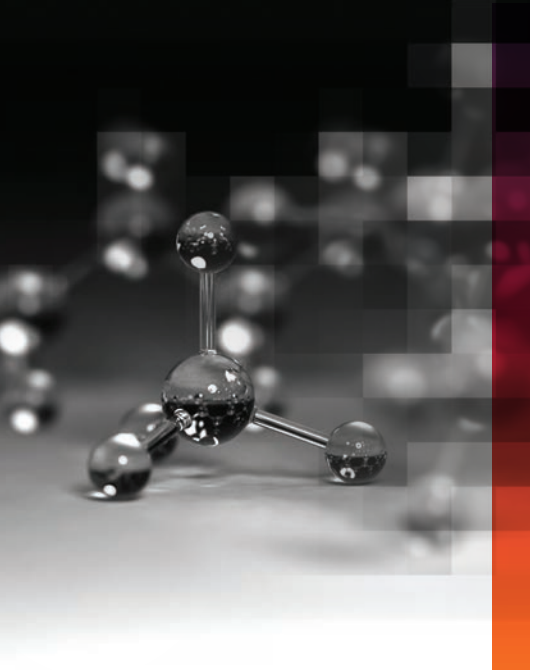
industry has concentrated much of its efforts on targeted therapies and more clinically efficacious drugs in the form of biologics – or biopharmaceuticals, if you're old school.

Within the field of biologics, the majority of research and product development is currently focused on recombinant proteins and monoclonal antibodies (mAbs, which accounted for five of the top ten selling drugs of 2012). These large molecule therapeutic proteins are composed of amino acids and can have a size of up to 150 kDa, and are essentially copies or optimized versions of endogenous human proteins. They are used for multiple indications, including cardiovascular diseases, infectious diseases, immune disorders, and cancer. For the treatment of cancers, mAbs have really hit the mark because of their ability to selectively bind to the receptors of cancer cells while leaving healthy cells untargeted and, therefore, safe from attack – the so called "magic bullet". It is for this reason that biologics often cause fewer side effects than chemotherapy.

In the last 20 years, there have been a total of 40 antibody products and derivatives approved by the European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA), and the growth in approved mAbs in the last few years has been exponential. Today, more than 400 antibodies, primarily involving immunological and oncological targets, are under pre-clinical development and clinical trials. These are exciting times to be in the pharmaceutical field.

"Today, more than 400 antibodies are under pre-clinical development and clinical trials. These are exciting times."

Working, as I do, in a university laboratory that focuses on pharmaceutical analysis, part of my work has transitioned from the analysis



of small molecules to the detailed characterization of biopharmaceuticals, logically mirroring the general trend outlined above. Because biologics exhibit high molecular complexity, they tend to be sensitive to changes in the manufacturing processes, which can lead to considerable micro-heterogeneity. Of course, such heterogeneity must be critically evaluated – levels of impurities (as with any pharmaceutical) and degradation (extremely complex in biologics) have serious health implications.

To meet this essential need, a large panel of separation techniques based on both liquid chromatography (reversed phase, ion exchange, size exclusion, hydrophobic interaction, affinity) and electrophoresis (capillary zone, capillary isoelectric focusing, capillary gel, SDS-PAGE) is being employed for biopharmaceutical characterization and comparability studies. Mass spectrometry (MS) also plays a pivotal role in the structural elucidation of mAbs because it offers an additional degree of separation by mass/charge ratio, greatly facilitating the identification of variants. Indeed, the full characterization of biopharmaceuticals is highly challenging and necessitates high-resolution separation techniques and powerful MS systems.

Despite the challenges and complexity, a study from Tufts University back in 2010 (1) noted (with caveats) that clinical trial success rates for large molecules were more than double that of their small molecule counterparts (survival rates from Phase I to approval of 32 percent and 13 percent, respectively). Why? I believe that it is in part because of the impetus that biologics have provided to the chromatography, electrophoresis, and mass spectrometry communities. The urgent requirement for new solutions generated a spirit of collaboration that has revitalized "snoozing" academic, governmental and industrial laboratories around the world. Examples include many recent advances in LC (widepore RPLC phases, core-shell technology, inert instrument and columns to limit adsorption, size exclusion and ion exchange materials packed with smaller particles) that aim to meet the requirements of biomolecular analysis. MS devices are also being increasingly adapted for the analysis of large biopolymers (for example, more accurate and higher resolution devices, implementation of new data-dependent acquisition modes, and dedicated software for deconvolution).

"The urgent requirement for new solutions has generated a spirit of collaboration"

The big question is, how can we continue to improve on the Phase I survival rates for the 400 antibodies out there, and the hundreds of other potential biologics that will appear over the next few years? The answer is that we must translate even more of our hard analytical work into product success. In doing so, we will be contributing to something very special – the development of new medicines that save lives.

Reference

1. *J. A. DiMasi et al., "Trends in Risks Associated With New Drug Development: Success Rates for Investigational Drugs", Clin. Pharmacol. Ther. 87, 272–277 (2010).*

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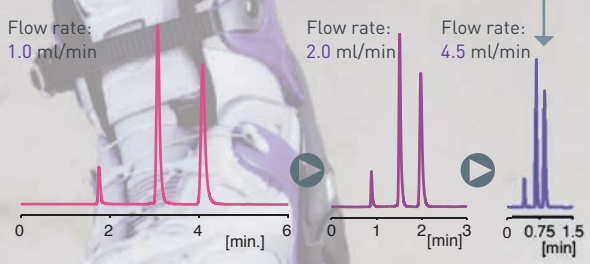

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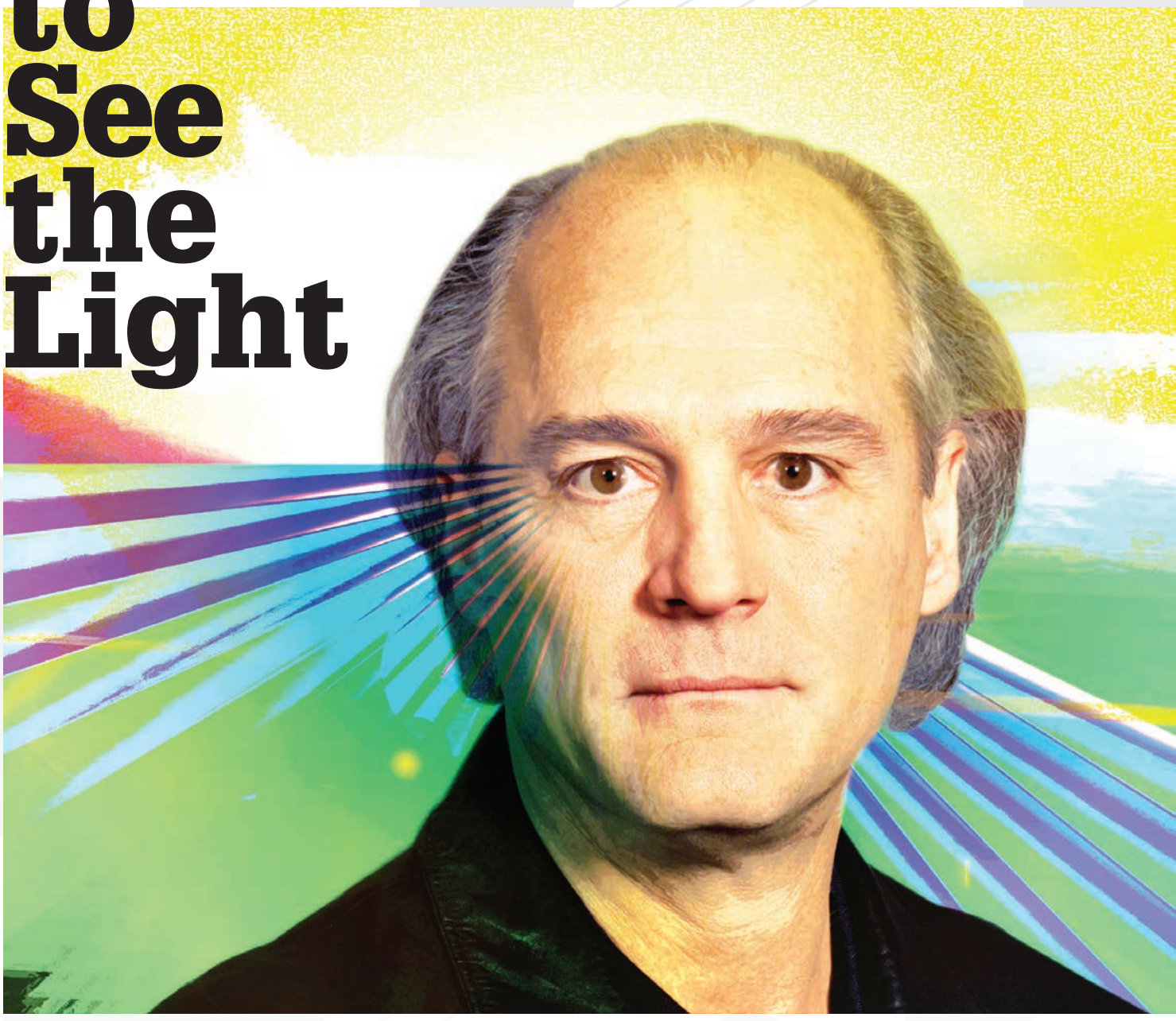


Laser ablation already has multiple applications in the analysis of chemical composition but even after three decades of devotion to the cause, I know that we've only scratched the surface so far. Here's my journey through science, and my personal view on the transformative potential of laser technologies.

By Rick Russo

Mass spectrometry is riding high at the moment; increasingly, it is the method of choice for identification, characterization, and quantification of all kinds. But I know of a simpler, faster, cheaper and greener method; an approach that can "do the mass spec" without using a mass spectrometer; a mass-spec killer! It is called laser ablation molecular isotopic spectroscopy (LAMIS) and is the culmination of a career spent in the pursuit of new analytical methods using lasers. More details later.

LAMIS is the latest chapter in a career in laser research that dates back to the 1970s. It really began when two of the pioneers of atomic spectroscopy – James Winefordner and Gary Hieftje – impressed upon me in my undergraduate and PhD years that direct solid sample analysis was the 'Holy Grail'. I became aware that others had proposed (as early as 1962) that a viable method of achieving that goal was laser ablation, which is the process of removing minute particles of mass from a sample via a highly focused laser beam. By combining these two pieces of information, I secured funding from the US Department of Energy (DoE) to study laser ablation for chemical analysis. This was at the Lawrence Berkeley National Laboratory (LBNL) in 1982. My proposal was that a green technology (which at the time was an emerging issue) could be developed for rapid, direct, solid-sample chemical analysis, eliminating laborious sample dissolution procedures. But, looking back, that was just the tag line – my real desire was to unravel the fascinating physics behind the micro-explosion that occurs when you blow things up with a high-powered laser. In those first years, I was just completely enamored by the process and having a real ball.

Back in the early 80s, commercial instruments were rudimentary and more like laser beam delivery devices than analytical measurement instruments. Instead, you sourced a laser, found a detector and set it all up on an optical table, aligned everything by hand (there was no software, as such) and recorded most of the data on an oscilloscope. And we say "those were the days"? Nevertheless, that early work laid the foundation for understanding the parameters that affect the ablation process.

Over the subsequent 30-some years, my group at LBNL has immersed itself in the fundamental mechanisms of the explosive ablation processes. We have described mass removal rates, fractionation (in the form of preferential vaporization), matrix effects and plasma spectrochemistry. Perhaps the most important advance was when we demonstrated the influence of laser-pulse duration on analytical performance; this in particular, and our work overall, convinced people that laser ablation could not be treated as a "black box". It is a delicate process in which each of the fundamental parameters can have a tremendous impact on chemical analysis; as with any other analytical instrument, a stable system and a reliable method are essential.

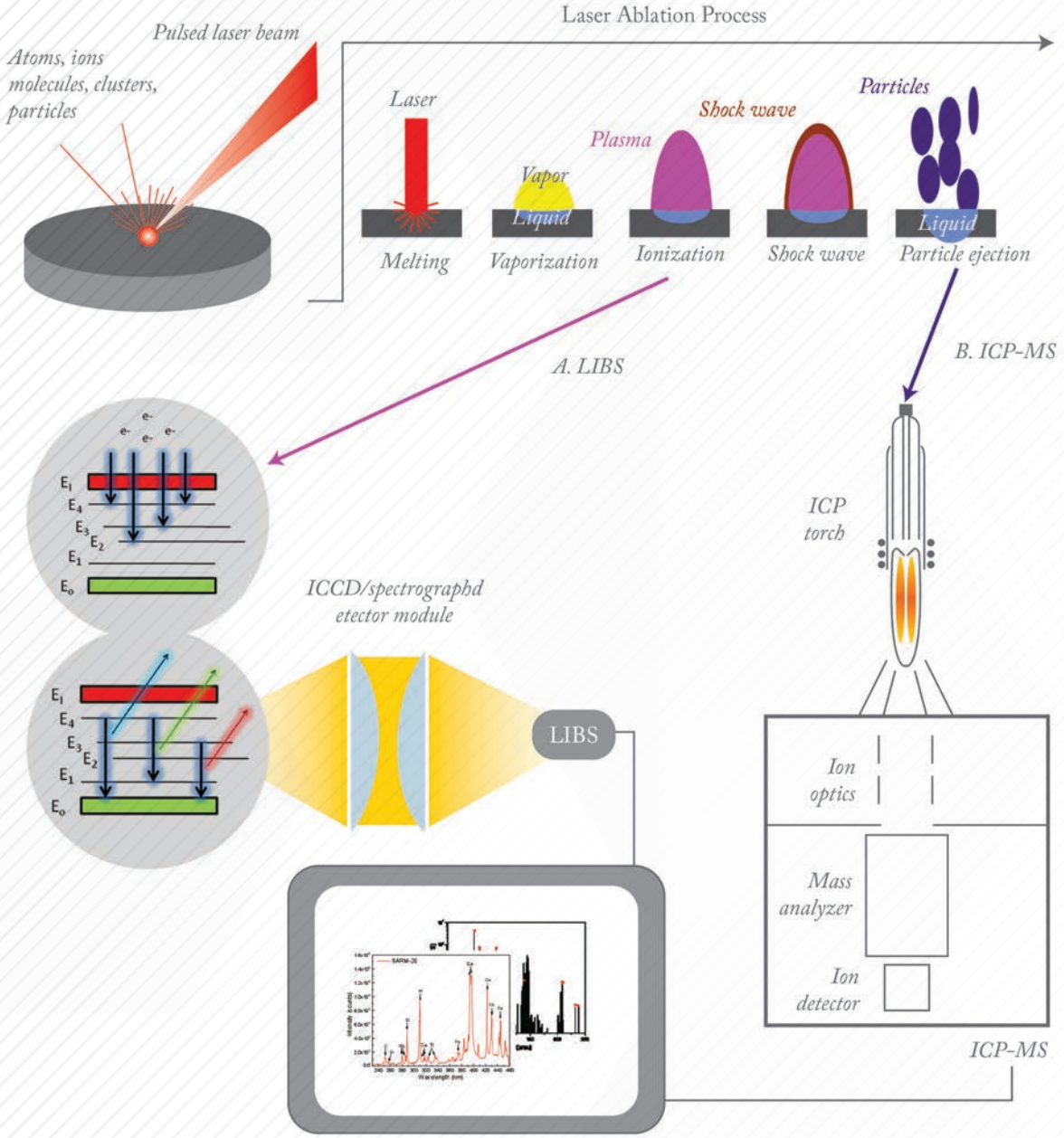
Data for skeptics

The whole laser ablation chemical analysis field has been criticized from the beginning. You know, some people just don't like change or progress – it took almost 20 years for typewriters to be replaced by computers, because the masses just couldn't accept that computers were going to be so useful. So, when laser ablation technologies (see sidebar, "Laser Ablation Chemical Analysis") threatened to replace traditional chemical dissolution techniques - there was a lot of resistance.

Two particular criticisms kept being repeated. One was, "You don't get representative sampling." We addressed this objection with very high repetition rates using femtosecond pulse lasers. This allowed us to sample more mass, take a signal average, and integrate any inhomogeneity. Not only could we describe the bulk sample composition, we also provided information on those inhomogeneities – knowledge that can be very valuable to industry. The second criticism was, "You don't have standards." Our response was that in most industries the same product is made continuously and the desired tolerances are set; thus, the process contains its own standards.

Besides overcoming these practical challenges, we have used more powerful data analysis and chemometrics to address other challenges. For example, we – like everyone else – had to rely on univariate analysis, using the area under the curve to calculate the concentration. Now, we have complex spectra with thousands of lines and software can determine whether those lines really are iron or, say, iron being interfered with by titanium. Of course, this is a general phenomenon. The power of modern computers and chemometric algorithms mean we can all do so much more with our data, allowing us to address what were previously considered to be problems. Take nuclear magnetic resonance or near-infrared spectroscopy: neither would be viable without sophisticated algorithms behind them.

People have criticized the technology my entire career and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Laser Ablation for Chemical Analysis

Laser ablation is the removal of a small quantity of mass from a sample surface using a focused, pulsed laser beam. After the laser pulse, a high-temperature (>15,000 K) plasma rapidly rises from sample surface and into the ambient medium followed by fine particle ejection.

A. Laser Induced Breakdown Spectroscopy (LIBS) is a rapid chemical analysis technology that analyses the light emitted from the micro-plasma explosion. Continuum light is emitted during the early stages of plasma cooling process (< 200–300 nsec) followed by discrete atomic lines at around 1 µsec. Light emissions are collected by the ICCD/spectrograph detector module, followed by spectral analysis by system software. LIBS spectra are displayed and subjected to qualitative and quantitative elemental analysis.

B. Laser ablation (LA)-inductively coupled plasma (ICP)-MS analyzes the ablated particles by transporting them to the secondary excitation source of the ICP-MS instrument for digestion and ionization. The excited ions in the plasma torch are subsequently introduced to a MS detector for both elemental and isotopic analysis.

"The whole laser ablation chemical analysis field has been criticized from the beginning. You know, some people just don't like change or progress"

you can talk until you're blue in the face, but they won't believe you. The only way to win the arguments is with data. So we made measurements and we shared results and, as the number of published papers grew, it became harder and harder to deny that the technology has distinct merits.

Amongst other successes, my group has achieved world records. for spatial resolution (450 nm) and for detection of 220 attograms for elements in geological samples using a single femtosecond laser pulse with LIBS. That's no mean feat. No other technology can provide such detection capability at atmospheric pressure, without sample preparation, and in real time. I rest my case!

In the process of academically proving the veracity of laser ablation, I began to understand its real significance and potential from an application point of view. Our understanding of the parameter space coupled with the improvements to laser and detector hardware created the perfect storm. And so, in 2004, a few of my PhD students helped me found Applied Spectra (see sidebar "Commercially Applying Spectra", page 29) to commercialize the technology. We had expertise in laser ablation chemical analysis using LIBS, in addition to laser ablation with ICP-OES and ICP-MS and successfully transitioned this knowledge into the manufacture of chemical analysis instruments.

I'm doing exactly what I set out to do when I submitted that funding proposal to the DoE; selling instruments around the

"Telling people that LAMIS is mass spectroscopy without a mass spectrometer raises a lot of eyebrows..."

world that address some significant analytical problems. That's despite the fact that I started with an obsession for blowing things up with a laser beam and had no real clue initially about how to fulfill the aims set out in the grant application.

In truth, we still don't fully understand the physics. But we can accurately replicate the process and that's key. Once you define a method and achieve reproducibility, you have a viable analytical technique, which can finally be treated as a black box by the customer. We help our customers to set up reproducible methods for their application and, for the most part, they are not interested in what laser and what detector is used - they just want to be sure that it will quickly measure 10 ppm mercury in soil or warn them of sodium contamination. Industrial analysis has clear demand: simplicity and speed.

In a wonderful role reversal, I'm learning more and more about potential markets from my old PhD student Jong Yoo, who is now Vice President of Technology and Marketing at Applied Spectra. LIBS is gaining real traction in a number of industrial sectors, such as solar, semiconductor, environmental and materials, and the list is growing. That's not too surprising since the technology is able to measure pretty much any element on the periodic table. Put simply, if you shine a laser beam at something, you get an answer. NASA have used the same technology on the Mars Curiosity Rover (see page 16) and, while I wasn't directly involved in that project, many of my colleagues were. I visited Los Alamos to see the prototype and discuss it with the team and now, my group is working with NASA to look at the next generation of this capability. Which brings me to LAMIS.

Mass spec killer

Most of my career has been pretty fortuitous: my approach is to delve blindly into something that I know very little about, learn from others, and see what happens. That's exactly how, two years ago now, we made a breakthrough in the ability to measure isotope ratios in our ablation plasmas. Everything just seemed to fall into place.

When you create a laser spark, you get a lot of background – white light plasma – which changes as a function of time after the initial spark. We usually try to set our detector gate or timing to get good signal-to-noise for the elements, whether we want either atomic or ionic lines, but there are always background molecular spectra. As hot ions and atoms collide with the oxygen and nitrogen in air or different species within the sample, they form molecular species, as the plasma cools. We were brainstorming about this and someone reminded the group that there is good isotopic information in molecular spectra (a fact that is well known); instead of trying to get rid of this "noise", we said, why not try and enhance it? Sure enough, when we got down to understanding the fundamentals of molecular spectra, tweaked the system and used samples with different isotope ratios, we saw beautiful isotope splitting.

Telling people that "LAMIS is mass spectroscopy without a mass spectrometer" raises a lot of eyebrows. Do I believe it? I think that I do - you just never know what's possible (for instance, who would have ever thought that we would have a laser on Mars?) In reality, we have a long way to go with our technology. Mass spec has been around for a hundred years, ICP-MS since the 1970s, but LAMIS is only two years old. We're certainly going in the right direction. We've published seven papers in those two years (the first three papers published in 2011 won best papers in Spectrochimica Acta) and LAMIS won a 2012 R&D100 Award and technology recognition from NASA.

Right now, we're trying to tailor the laser plasma for particular molecular species in order to improve the precision and sensitivity of our analysis. We've seen the potential of measuring isotope ratios, and simply must gain a better understanding of the chemistry. We are investigating how these molecules form in the laser plasma and how we can prevent interference. These are big hurdles, but the very same problems had to be overcome in mass spec: that's why collision cells were developed.

Commercially Applying Spectra

Stress, sales and satisfaction: how we've gone beyond research to make products for real customers.

We took a leap of faith in 2004 by founding Applied Spectra Inc., and have survived (perhaps too harsh a word!) to celebrate the tenth anniversary this year. We made it through "The Valley of Death" (a term I never knew when I was strictly interested in pure physics) by following the mantra from the movie, Apollo 13: "Failure is not an option." We made a lot of mistakes, as all start-ups do, and sometimes we didn't have the money to pay the electricity bill or the wages, but we kept pushing forward. The company has some really good people who never flinched; they are phenomenally dedicated. Two of them are former PhD students who have been with the company since the beginning, working day and night. In fact, they were the ones who had the entrepreneurial verve to push me into founding the company in the first place.

Our earliest customers were in the semiconductor packaging industry. The Restriction of Hazardous Substances (RoHS) Directive required them to make compositional measurements of several different elements, such as mercury and lead. And when you're sending hundreds of samples a day to be analyzed at a lab, the costs mount up very fast. If you simply need to measure mercury, day in day out, LIBS is a no brainer; however, you still need a forward-thinker at the company who believes in the technology and convinces management to buy the instrument. We are grateful to those early adopters.

Now, the story is repeating itself, and new early adopters are coming to us with requests. We recently signed up major new customers who are interested in integrating our technology into their manufacturing processes. They can see that faster analysis means increased efficiency and higher profits. One company told us they've been waiting 30 years to be able to do this sort of analysis, and they're willing to work with us to develop the technology and make it happen. We've also sold instruments into forensics (and other analytical) laboratories that do the leg work in development because they want to be leaders in the field. They are starting to prove that the technology has tremendous validity within their application.

You can sit there, steadily publishing papers, but they don't even make it onto a library shelf these days. I still love the physics, but seeing our technology being adopted and used in diverse applications is so rewarding and fun. After selling our first instrument in 2009, I thought: "Oh my God – they actually believed us!" We'd put some components together, packaged them, written a bit of software, and a customer decided to join us for the ride. That moment proved the technology's credibility in my own mind – I wasn't just making this up. Laser ablation chemical analysis had real value to people. We supported that first customer absolutely and were at their beck and call, totally devoted to making it work for them.

We've grown from there. Last year we sold more instruments than we'd sold in the previous five years combined (the whole time we've been selling instruments). That gives me real pleasure.

To infinity and beyond…

Like all new technologies, LAMIS will have to prove itself; the scientific community and time bear the challenge. The advantages are clear – measure isotope ratios in real time, without sample preparation, and without a mass spectrometer (measuring isotopes at atmospheric pressure). Initial interest has come from within nuclear, geological and medical applications. With improvements in precision and sensitivity allowing measurements in these applications areas, it will not be long before commercial LAMIS instruments will be available to these (and other) industries, as modifications to our existing LIBS systems.

In addition to analytical technologies, I've participated in several esoteric projects. One was the discovery of the world's smallest 'nanowire' laser. Another was development of an on-line laser ultrasonic sensor to help the paper industry. I even got involved in fabrication of high temperature superconducting (HTSC) thin films using pulsed laser deposition (PLD). In

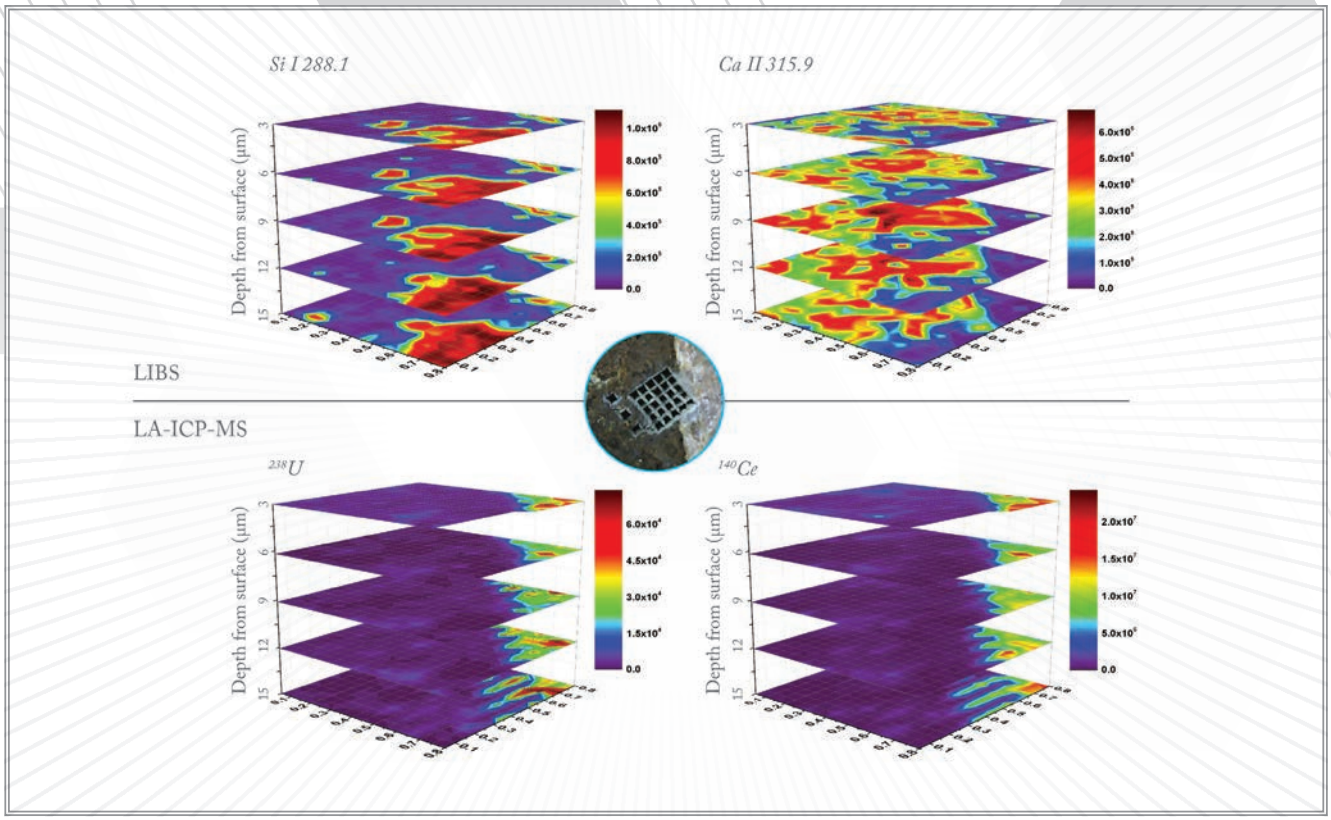

Figure 1. 2D and 3D imaging of a geological sample at the boundary of two minerals using LIBS and LA-ICP-MS. 2D and 3D mapping takes advantage of the lateral and depth resolution of laser ablation chemical analysis.

two years, my team achieved a world record critical current in one of our superconductor films. All further evidence of my love affair with lasers...

Looking to the future of LIBS, I can see laser ablation being taken into a whole new realm by harnessing near-field scanning optical microscopy. Pretty much everything that I've done has been in far-field optics, where focusing the laser down to spot sizes of half the wavelength is pretty difficult. With near-field optics, the technology (whether it's LIBS or laser ablation with some secondary source) can be used on the nanoscale. That's a whole new world of physics that someone is going to need a lot of time to study and understand – and it probably won't be me.

Near-field optics is a different way of using light; the laser is focused through an optical fiber that must be nanometers away from the surface. While we have been working on it for about five years and can perform ablation at the nanoscale, we have not yet been able to detect a signal. We don't even know if the physics are the same. This is the next generation – literally; it's for the young people who have a lot more time and patience to dedicate their careers to understanding this complex and exciting science.

As for me, I will continue to approach technologies, concepts, and devices in my own way. That usually means without a huge amount of expertise but with the attitude that I can do whatever anyone else can do but in my own different (not necessarily better) way. I owe my accomplishments to the many people that have entered my life and tolerated my craziness, from my initial mentors to the many students and colleagues who continue to make sense of my passions for learning and lasers. My devotion to lasers is ongoing: when you see the ways that they have changed society, from surgery to manufacturing to cutting, welding, and scribing, I see no reason why they will not play a dominant role in analytical chemistry. People are beginning to see the light.

Rick Russo is leader of the Laser Spectroscopy and Applied Materials Group at LBNL (teamd.lbl.gov), and CEO and founder of Applied Spectra Inc. (www.appliedspectra.com).

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WHO'S FIGHTING THE ATHLETE'S CORNER?

Performance-enhancing drug expert Douwe de Boer (in the blue corner) goes toe-to-toe with the Dutch Doping Authority's Herman Ram (in the red corner) on the big issues in sports doping.

Round 1: The Biological Passport

Is this individual, electronic record of results from doping tests helpful or unhelpful to sport and to athletes?

We know from the past that athletes who dope do not simply stop doping when a new detection method is introduced; rather, the nature and magnitude of their doping is altered. The biological passport seems to be an effective tool in counteracting prohibited blood manipulations.

The Union Cycliste Internationale (UCI) has reported that the percentage of anomalous blood values dropped after the passport was introduced in cycling. Overall in sport, the consensus is that there is less doping now than there used to be; while many factors contribute to this, the biological passport is undoubtedly an important one.

The passport is not just a tool to gather information on which a new doping case can be built (such decisions are not taken lightly; a lot of information is needed to build a concrete doping case). The passport does help to select athletes who deserve to be monitored more intensely. In doing so, the process is improving 'regular' doping controls that determine the presence of a specific substance. An example is that the number of EPO-related positives has increased since the introduction of the biological passport.

To successfully apply the biological passport, one must be able to guarantee that factors other than doping compounds or methods do not result in a sanction. Unfortunately, nobody can give such a guarantee.

Some factors are covered; the anti-doping authorities ask for relevant information during sample collection, such as the altitude of performance, gender, and information on blood loss. However, for other potentially confounding factors, the legal responsibility rests with the accused athletes. If athletes do not give an explanation for abnormalities in their biological passport, it is considered that those abnormalities are caused by so-called doping manipulation. Not every accused athlete is in a position to investigate such unknown factors, which limits defense and weakens their legal position.

Another reason why athletes are not currently in a strong legal position is because they tend to assume that doping is only a problem for other athletes – they are not always proactive about standing up for their rights when the anti-doping authorities write or revise regulations. Those in a better position to do so should protect the rights of athletes, but they – the anti-doping authorities and analytical chemists – are primarily concerned with their own position, and not that of the athletes.

We must be extremely careful. The anti-doping testing system should not be hell-bent on catching every guilty athlete at the expense of convicting innocent athletes too. Currently, there are question marks over what risks are reasonable.

Round 2: Banned substances

What should the criteria be? And how should thresholds be applied?

The list of prohibited substances and methods need greater gradation in the form of threshold values. Only if the concentration of a given compound in a biological sample is above a certain threshold value should a disciplinary process be started. Today, threshold values are in place for a very limited number of compounds, meaning that analytical detection of extremely low concentrations can start the disciplinary process. Legally, the detection of one molecule (if possible) would be sufficient. That's crazy. As analytical developments enable lower and lower limits of detection, regulations should shift towards setting reasonable thresholds. Pollution of drinking water with waste medication and contamination of food with veterinary drugs have led to situations where unconscious intake of compounds that are prohibited leave athletes in a perilous situation.

Prohibition of substances should have a sound scientific basis, which first requires a clear definition of the performance-enhancing effect. That's assuming that we focus only on performance enhancing effect rather than ethical or health considerations. The current list of banned substances, which was developed over the last 50 years ago, set out to protect "doping victims." In other words, the rationale for banning things at the outset was impact on health; subsequently, health, fairness and performance

"We must be extremely careful – the anti-doping testing system should not be hell-bent on catching every guilty athlete at the expense of convicting the innocent."

enhancement contributed jointly to the rationale; and now some of us may prefer a purely performance-enhancement rationale. Such a shift would present a significant challenge and it may prove difficult to find consensus worldwide.

I agree on this one: a list that is based on science would be preferable – a list that puts an emphasis on performance-enhancing properties. We state so every year in our reaction to WADA's draft List of Prohibited Substances and Methods, but the fact of the matter is that in a World Anti-Doping program the opinion from The Netherlands is just one of many. We favor in-depth discussions on the performance enhancing properties of, for example, opiates, alcohol and cannabis.

Regarding thresholds, the current rules allow for one lab to report lower concentrations of a banned metabolite than another lab. From a "catch as many dopers as you can" point of view this makes sense: you do not want to let a cheater get away with remnants of exogenous banned substances when you have verified the presence of them in a scientifically correct way. But we should be careful not to report too low concentrations, as the clenbuterol-in-meat experiences have shown. And we have had experiences like this before, for example, when it was found that the anabolic steroid boldenone can be produced endogenously as well. You are bound to run into problems when you lower the detection limit on a continuous basis, but these sorts of new findings will also advance science.

Round 3: The role of doping labs

Are all accredited labs up to the job? If not, how can they be improved?

Doping analysis is a special topic. It engages forensics, medicine and law in a very specific environment: the world of athletics. But doping laboratories also share a lot with other types of analytical labs: all analytical experts can learn from each other, with open dialogue being the key to improvement.

We need the following: agreed-upon guidelines, equivalent to the International Standard for Testing and its Technical Documents; double-blind EQAS samples to secure proficiency; and an innate scientific interest to understand the results. I believe that these criteria are largely being met, but this does not mean that improvements are not possible.

All WADA-accredited labs are strong – the mere fact that labs sometimes lose their accreditation proves that there is a strict monitoring system in place. Revoking the accreditation of the lab in Rio de Janeiro almost on the eve of the football World Cup and ahead of the Olympic Games shows that the system is working.

One improvement would be inter-laboratory exchanges of samples; this would strengthen the program from both scientific and PR points of view. But the current approach has a long history: the B-analysis is always performed in the same lab as the A-analysis, which means that many practical issues would need to be resolved.

Analytical laboratories have an important role and there is no reason to suspect that they are not doing their utmost to fulfill their mission. However, some analytical laboratories are limited, based on budgets and/or local expertise. The anti-doping authorities should invest in those laboratories. Analytical laboratories can apply for investigation grants but, in practice, the high-level labs are in a better position to receive funding – WADA's system punishes even relatively low-level operating laboratories. Adequate support to increase the overall level of analytical laboratories might help create a uniform, standardized level of testing. Right now, that is not the case.

Analytical chemists must contribute actively to discussions

on doping policy; they are part of the anti-doping problem/solution. At the same time, the tendency for politicians to have an increasing amount of influence on doping policy should be addressed.

Round 4: Jamaica Gate

What are the implications of the Jadco resignations in November 2013?

Some athletes are not being tested adequately; those of Jamaica might be a good example of that. If the ongoing investigations prove the media claims to be correct, the Jamaican Anti-Doping Commission (Jadco) did not have an adequate testing program. Eleven of its commissioners resigned as the news broke. Such testing disparity is not fair, period. As stated, adequate support of relatively low-level national anti-doping authorities might be an effective way to deal with such unfairness.

First of all, Jamaican athletes are not under any extra suspicion in comparison with other well-performing athletes. It will be a fatal blow to sports when every extraordinary performance becomes synonymous with doping suspicions – that is exactly why the anti-doping system needs to be at the highest possible level.

We cope with all sorts of doping continuously. If 'old-style' doping gets the reputation of being 'old and forgotten', it will automatically turn into 'interesting and thus new' doping. That's one of the specific aspects of this field. Our goal is to supervise possible doping habits of all elite athletes, so the overall suspicion of doping use in elite sports will be at the lowest level possible.

Round 5: The war on drugs approach

How far should the pursuit of doping athletes be taken? Are there any limits?

"Certainly, the harder you push, the more resistance you feel. But, if there is clear evidence that an athlete is using doping deliberately, we will push."

Without a doubt, there are parallels between our approach to the wider drug problem and sports doping. In both cases, the more we try to achieve the goal, the more difficulties appear. The difficulties may stem from a lack of financial resources (more effort requires more money), the right to privacy (increased unannounced testing at any time of day undermines the privacy of athletes), or inequalities in testing in different places (see previous answers). Wider society should decide how much effort is appropriate and what priority the doping issue should receive. Anti-doping authorities and analytical chemists obviously consider their tasks and roles to be high-priority, but this may not be in line with the majority opinion.

The phrase 'War on Doping' has been used before, but not by us. This is not a war; it is a continuous effort to defend sports, and those who compete, and perhaps to retain a certain sense of morality, even though morality may change over time (and so, therefore, may the doping regulations.)

Certainly, the harder you push, the more resistance you feel. But, if there is clear evidence that an athlete is using doping deliberately, we will push. Do not forget that analysis is just one side of our work. We also try to educate athletes and their support personnel to think about the effects of their decisions. Elite athletic achievements are possible without doping and, in the end, both individual athletes and sports in general are better off in an environment where they are not forced to take potentially harmful substances. That is why we will keep on doing our work.

We invite you to contribute your views and ideas at: tas.txp.to/0214/green.

WHAT WILL IT TAKE TO CLEAN UP OUR ACT?

Could – and should – analytical science be more environmentally friendly? Thought leaders from academia and industry weigh in on the opportunities and the trade-offs. The clear message is that sustainability and cost-effectiveness often go hand in hand.

By Iestyn Armstrong-Smith

When the key methods of analytical science were first developed, the goal was accurate, reliable, reproducible and cost-effective analysis; there was little if any consideration given to the long-term impact on the environment. This has changed slowly over the years: researchers have proposed alternative techniques and revised popular methods to reduce the use of resources and lessen pollution. But have we done enough to make analytical science green?

In this article, we seek answers to the following questions:

- Do analytical technologies have a substantial environmental impact?
- If they do, with whom does the responsibility lie to reduce this impact?
- What technology developments will help us to clean up our act?
- What is being done to incentivize these technologies?

The answers are provided by thought-leaders from academia, industry and the equipment manufacturers.

Academic Analysis

Three of Europe's leading advocates for greener analytical chemistry offer their views on issues such as how to reduce solvent use, the parameters for successful green technologies and the possibility of replacing instrument testing with environment-friendly alternatives.

Pat Sandra

How committed are you to sustainability?

Sustainability is of utmost importance. We use a range of green techniques in our daily work and try to reduce the use of solvents, reagents, and additives, as much as possible, and to select benign solvents (for example, acetone, ethanol, and CO_2).

I'm a member of the EU scientific advisory council and sustainability is a hot topic in our discussions.

What steps have you taken to implement greener analytical science?

Part of our research is dedicated to the development of green sample preparation and chromatographic techniques. We have published several articles describing these approaches. Miniaturization is the key.

Ultra high performance liquid chromatography (UHPLC) is a convenient and efficient way to reduce solvent consumption. I recommend short, narrow-bore columns and sub-2 µm packing material; this can reduce solvent consumption by as much as 90 percent. You can, of course, miniaturize further, using capillaries or chips, down to µL to nL/min flow rates. On the other hand, switching to more benign solvents compared to those presently used is much more complicated – but it is possible.

We also use gas chromatography (GC) and supercritical fluid chromatography (SFC). GC is greener than LC – notwithstanding the shortage of helium and its cost. SFC is considered to be green because it uses less toxic organic solvent and fewer additives than LC; on the other side of the coin, there is an argument that carbon dioxide-based techniques are not environmentally friendly as they produce greenhouse gases. However, the CO_2 used in SFC is reclaimed from the atmosphere and when it is used for preparative processes it is recycled.

Finally, we are also taking a greener approach to sample pretreatment techniques, approaches that enable miniaturization and solventless operation. What we are finding is that these are often much more productive and cost-effective than the classical enrichment methods.

How easy was it to make the changes?

Well, it is not difficult to make changes. However, one has to take care not to violate the guidelines and the norms! This can be a particular problem for industry: changing a validated method to a green method is often rather expensive.

Do greener technologies and techniques provide the quality and efficiency required?

They must, otherwise it makes no sense to develop them. Having said this, I note that some so-called greener methods have been published that are less robust than conventional methods, that are too difficult to be implemented in routine laboratories, or that are impossible to automate. These contentious issues have appeared in recent literature.

Pat Sandra is at the Department of Organic Chemistry, Ghent University and Founder and President of the Research Institute for Chromatography, Kortrijk, Belgium.

Mihkel Kaljurand

How did you get into greener analytical science?

My interest in green analytical chemistry developed as something of a happy accident. We were HPLC users until about 15 years ago, when the economic situation in Estonia forced us to switch to capillary electrophoresis (CE). It was cheap – we used our own instrumentation – and it required a negligible amount of solvent. Given this, Mihkel Koel and I published a paper hailing capillary electrophoresis (CE) as a green analytical method. The article attracted a lot of attention, which led to invitations to write books and papers on the topic.

Recently, we introduced simple colorimetric assays using paper to test wine and herbal tea for antioxidant activity.

Designing paper-based colorimetric tests is rather easy; the only challenge is finding the right reaction. But you need funding; you need to be able to convince financing agencies and proposal referees that green analytical chemistry is a serious research topic. Sometimes we have succeeded in this, and sometimes we have not.

Is "being green" a sufficient goal for new technologies?

No. I am afraid that if the only motivation to introduce green analytical methods is commitment to sustainability, very few laboratories will succeed in introducing them. There must also be a financial incentive. CE running costs are small compared to HPLC; likewise, the cost of colorimetric testing using paper is negligible compared to instrumental methods.

How do they compare in terms of accuracy and sensitivity?

In general, green tests are less accurate and less sensitive, and they are not as efficient. However, it is often the case that the accuracy, detection limits and efficiency provided by modern instrumentation is greatly in excess of what is actually required. What we need is accurate information and our methods meet this requirement.

Where do you see green analytical chemistry going?

The two biggest issues are how to use less harmful solvents and how to reduce cost of experiments.

Another thing I'd point out is that the production of instruments generates a substantial ecological footprint, a fact that's often overlooked in green analytical chemistry publications. I suggest that the aim of green analytical chemistry research should be to find approaches that replace instrumental testing. Unfortunately, little is being done in this respect and I do not believe that the instrument companies would be happy about such an aim!

"THE TWO BIGGEST ISSUES ARE HOW TO USE LESS HARMFUL SOLVENTS AND HOW TO REDUCE COST OF EXPERIMENTS."

Mihkel Kaljurand is at the Department of Chemistry, Tallinn University of Technology, Estonia.

Caroline West

How committed are you to sustainability?

In my everyday life, as well as in my work as an analytical scientist, I try to select solutions that are more sustainable and take steps to change habits.

I would like all chromatographers to be greener, but I am realistic; I understand that progress is far quicker when change produces other benefits, such as an economic advantage. The greener way is not always feasible – and rarely easy. Also, getting people to change their habits is always a huge challenge.

What's your approach to green analytical chemistry?

I work a lot with supercritical fluid chromatography (SFC). Its reduced solvent consumption make SFC inherently greener than HPLC methods on comparable scales; however, how the technique is practiced can make a big difference. For example, methods that consume even less solvent can be developed by careful selection of stationary phases and choosing ethanol over methanol.

I try to educate my students about greener methods, especially in terms of sample preparation and experimental designs that avoid wasting solvents and energy.

Caroline West is at the Institute of Organic and Analytical Chemistry (ICOA), University of Orléans, France.

Industry Insights

A number of large organizations in the private and public sectors rely heavily on analytical science, contributing significantly to its overall impact on the environment. Here, Wayde Konze (Dow Chemical Company, and Nikki Dalby (UK Food and Environment Research Agency) share insights, from more sustainable industrial processes to energy efficiency measures in the lab.

Wayde Konze

How does Dow approach sustainability?

In research and development, Dow applies the principles of sustainable chemistry and engineering across all areas. This typically translates into four main themes:

- Reduced hazard
- Atom economy (maximize the utilization of every atom)
- Energy footprint
- Holistic design (lifecycle approach quantifying energy, water and emission footprints).

The analytical science team plays a big part in making products and processes safer, more economical, and more sustainable (from the raw material standpoint). This is not a recent adjustment; we've evolved as we learned from experience, research findings, publications, and other sources.

We are also carrying out hypothesis-driven research to minimize the number of studies while maximizing the impact to businesses; this is reducing the number of samples that we process.

In addition, we have implemented several initiatives within our analytical labs to reduce our utilization of solvents, materials and inert gases, and to minimize waste and improve safety. New technologies have been introduced that have had a substantial impact in this regard. These include micro-column liquid separations, to reduce solvent consumption; microwave digestion, to avoid large quantities of acids in inductively-coupled plasma (ICP) analysis; and size exclusion chromatography (SEC) and SFC, which reduce solvent and waste costs by 80 percent. We have also refurbished our helium manifolds to improve our usage efficiency.

So you use analytical science to make other processes more efficient?

Yes. The point is less about "greening analytical science" than understanding the critical role it can play in reducing waste, energy and resources over the long term. If we develop a more sustainable process by using hypothesis-driven research, we ultimately perform fewer experiments at greater speed.

We have done a lot of internal research on coupling high-throughput capabilities with appropriate analytical techniques to answer the right questions with a significantly smaller sample size. This has been challenging and required a lot of combined expertise to accomplish. However, we are now using these workflows to find new solutions faster and with less solvent utilization. The big impact at Dow is using analytical science to support good, sustainable decisions. Saving a few liters of solvent in the lab pales in comparison.

We come out of the lab with a much better fundamental understanding of the chemical process, kinetics, mass transfer, and so on, so innovations can be scaled up much more reliably. This creates a lot less waste in pilot plants and in initial production runs. Furthermore, we can optimize components, such as catalysts, to drive more efficient and sustainable processes in our production plants.

Regarding analytical instrumentation, we recently partnered with a vendor to co-develop new ultra-high performance SEC technology for polymer separations – a critical aspect for our company. This was a great success. The instrument reduces solvent and waste costs by about 80 percent, while providing the same or better quality and efficiency of analysis.

Wayde Konze is Director of Analytical Sciences at The Dow Chemical Company, Saginaw, MI, USA.

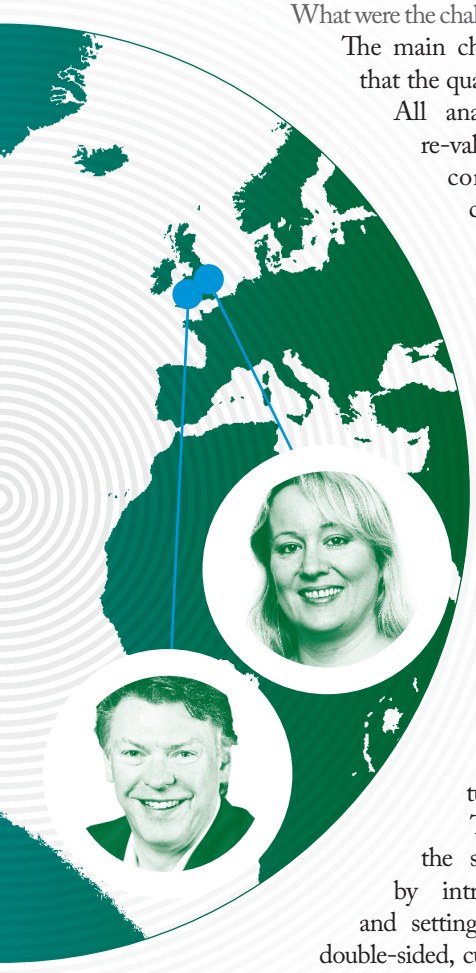
Nikki Dalby

How have FERA's methods become greener?

Many of our analytical methods have been consolidated into multi-analyte approaches, which reduces solvent, column, consumable, and reference standard usage. We also maximize the number of batches per run, which has the same effect. A number of our analytical methods have been redeveloped to reduce dichloromethane and acetonitrile usage wherever possible.

What were the challenges in making those changes?

The main challenge comes from ensuring that the quality of data is uncompromised. All analytical methods had to be re-validated, of course, to check consistency before and after changes were implemented.



FERA is quite a big site – how have you tackled energy usage?

We've put in a lot of effort in recent years. Smart meters were used to assess the running costs of laboratory equipment and studies were carried out to evaluate optimal settings, enabling us to adjust operating temperatures for fridges and freezers, water bath temperatures and drying cabinets. We added timers to ensure equipment was turned off when not required.

The number of printers across the site was significantly reduced by introducing networked printers and setting these to automatically print double-sided, cutting the paper usage by half. Dishwashers have been switched to cold feed instead of hot, light sensors have been added to the majority of rooms, and a number of water saving initiatives were implemented, including installing water purifiers instead of buying bottled water with an associated shelf life.

Nikki Dalby is Team Leader at the Pesticides and Veterinary Medicines Group, Food and Environment Research Agency, UK.

GOING GREEN FROM THE GROUND UP

By Howard Handley

Dŵr Cymru Welsh Water is a company that supplies drinking water and wastewater services to most of Wales and parts of western England. In early 2012, Welsh Water had the rare opportunity to design and build a new state-of-the-art potable water testing laboratory. While the quality of data was the foremost priority for any decision, reducing impact on the environment was a key factor in determining the choice of design, process and equipment.

Welsh Water worked with a number of instrument manufacturers to design the processes required. Of these, Agilent were particularly supportive in providing the technology needed to implement more environmentally-sustainable solutions. Among the equipment purchased was highly sensitive LC and GC instrumentation capable of achieving extremely low limits of detection with greatly reduced solvent extraction methods. High sensitivity ICP-MS instruments allowed methods to be developed for metals testing that halved the energy usage normally associated with such analysis. This was achieved by combining suites of analysis to enable more than 30 elements to be analyzed from less than 10ml of sample.

As part of the building design, solar panels were added to the roof to reduce reliance on the grid. Rainwater is collected from the roof and diverted into a grass swale rather than into the sewerage system. While this doesn't impact the laboratory directly, it delivers reduced water treatment costs and a reduced risk of flooding.

As the company was opening a new laboratory, it was relatively easy to incorporate sustainable choices from the outset. It can be very difficult to change accredited and regulated methods once in use and often the development resource needed to bring about change is in very short supply. Welsh Water recruited a team of specialist scientists to create a more sustainable laboratory model from the beginning. There was also a huge economical benefit: the technologies selected for the new laboratory have made annual savings of more than £1M in ongoing operational costs.

Howard Handley is Laboratory Services Manager at Dwr Cymru Welsh Water, Newport, Wales.

Meticulous Manufacturers

Shifting blame is common in issues of environmental sustainability and some believe instrument manufacturers should shoulder much of the responsibility. Here, upper-management from Waters Corporation and Thermo Fisher Scientific describe how they are both pulling their weight.

Dan McCormick and James McCabe

How does your company tackle the green issue?

The Waters strategy is to develop products that are not only intrinsically green, but that enable a move into a greener world. For example, our products are evolving to smaller footprints, higher productivity, lower solvent use and lower sample volumes, coupled with design simplification for more efficient manufacturing and increased lifespan.

We have a series of initiatives in place to support the migration to greener products. In addition to Waste Electrical and Electronic Equipment (WEEE) and Restriction of Hazardous Substances (RoHS) directives, we have implemented two other practices. Firstly, Waters continually works towards extending the lifespan of its products, either through the design of more reliable components and subassemblies, or through modular designs that simplify worn part replacement. Secondly, we employ a cross-discipline approach to the reduction of energy consumption. Low voltage, low power digital design practices are coupled with software that manages load sharing within the product to further save power.

Which Waters products exemplify this approach?

The search for meaningful impact has given us a number of products that offer environmental benefits while ensuring analytical performance. To name a couple, our ACQUITY systems reduce solvent and energy consumption by reducing analysis time, and the UPC2 employs "convergence chromatography," which uses compressed gas and liquids for solvent flow, which simplifies the transition of samples to chromatographic systems and also reduces solvent use.

How do you promote greener analytical science to the market?

A significant selling point for UPLC and SFC is the reduction in solvent usage as compared with conventional liquid chromatography. For the most part, clients are as motivated as Waters to reduce costs and carbon footprints. We estimate that our installed base of UPLC instruments has eliminated more than five million liters of solvent from the global waste stream since 2004.

Where do you see the highest uptake of green technology?

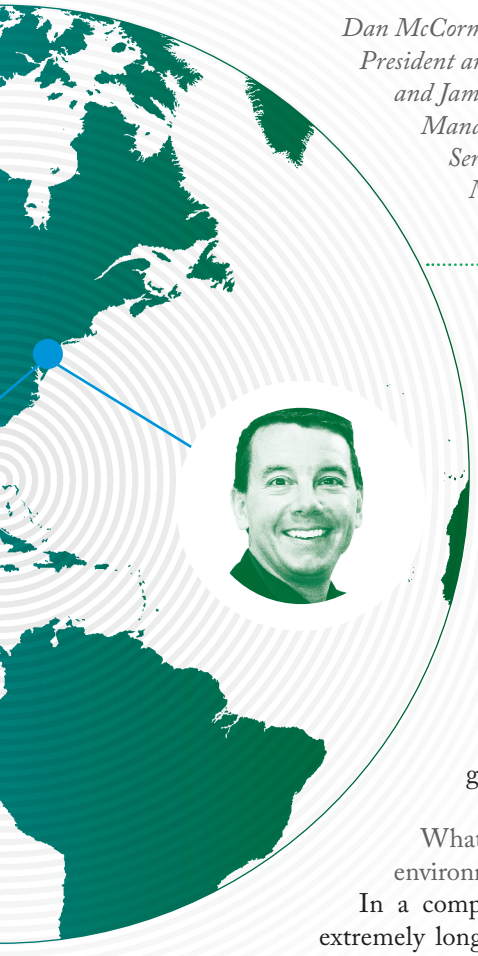
It can be easier for those markets that are not subject to scrutiny by government agencies to make the change; those in the chemical industry can adopt this type of technology more easily than the pharmaceutical industry, for example. This is not a conflict but juxtaposition of the needs of today being subjected to the regulations of yesterday – and the slow nature of change that can reduce the impact of new technologies. Uptake for more regulated industries will likely be accomplished through significantly improved analytical benefits and the use of more efficient technologies.

What would you say to convince analytical scientists to move to greener technology?

In today's marketplace there is increasing pressure for everyone to participate at some level to make a contribution. Pharmaceutical and chemical companies are reaching Carbon Disclosure Project scores that indicate they are actively

pursuing an improvement within their companies – and telling the world about their efforts. Lab managers should not ignore the need to participate in greener technology. If they do not direct it today they may find it imposed on them in the future.

Dan McCormick (pictured) is Senior Vice President and Chief Technology Officer, and James McCabe is Sustainability Manager, Global Operations/ Services, at Waters Corporation, Milford, MA, USA.



Daryl Belock

How does Thermo Fisher Scientific approach sustainability?

Generally, we look at ways to reduce the amounts of consumables necessary to operate analytical instruments, in addition to addressing waste, energy consumption, and specialty gas requirements.

What in your portfolio is most environmentally friendly?

In a company of our size, the list is extremely long. A few that come to mind are the "reagent-free ion chromatography" instrument that uses water as its mobile phase rather than strong solvents; our Trace 1300 Series GC system with a helium-conserving enhancement; SOLA solid phase extraction components that reduce solvent waste and extend column life. The latest generation of nano, capillary and microbore HPLC systems also use less solvent, reducing organic waste streams.

"OUR UPLC INSTRUMENTS HAVE ELIMINATED MORE THAN 5 MILLION LITERS OF SOLVENT FROM THE GLOBAL WASTE STREAM SINCE 2004."

Aside from producing instruments that reduce the impact of general analysis on the environment, Thermo has a passion for raising the bar in environmental monitoring. Our portfolio of solutions includes air quality instruments to measure primary atmospheric pollutants, such as nitrogen oxide, sulfur oxide and particulate matter concentrations; instruments to measure water quality, such as pH, conductivity, dissolved oxygen; trace element analysis instruments to measure elemental pollutants, such as lead, arsenic, chromium; and chromatography-mass spectrometry instruments to measure such qualities or pollutants, such as anions/cations, pesticides, and polyaromatic hydrocarbons.

What are the challenges for labs that want to be more environmentally efficient?

Many labs use approved methods. Unfortunately, it's not always cost-effective to alter and revalidate a method on the basis of environmental impact alone.

What would you say to inspire commitment to the environment?

Society as a whole is recognizing the importance of protecting the environment and conserving increasingly precious natural resources. The scientific community is an integral part of this scenario; analytical scientists should choose technology and techniques that facilitate their important work whilst also reducing environmental impact.

Daryl Belock is Vice-President, Innovation and R&D Collaboration at Thermo Fisher Scientific in Waltham, MA, USA.

Profession

Leadership
Talent Development
Career Planning

Tackling Transitions

Did you leap at the chance of a supervisory role or do you dread the idea of managing a former peer or an entire lab? Here, I outline how you can make each professional transition work for you.

By Elizabeth Treher

If we think of supervisory transitions at all, it is usually that first big step into a "managing role." However, as we advance and receive promotions, we continue to face significant transitions with each change in our position. Such transitions happen many times during a career and aren't limited to "new" technical supervisors. Even those who have supervised others successfully can struggle with further advancement as their role changes. Understanding these transitions can help make them easier and more successful.

Transitions into new roles and responsibilities often mean increased compensation and prestige. Unfortunately, this entices some of us to take roles for which we are not prepared, suited, or even skilled. In fact, the technical skills that lead to promotion can also be the skills that undermine supervisory success. That's because, as professionals in analytical science, the recognition of our skills and abilities by others (that is, getting credit for results) is important. This is true not just for advancement or for changing jobs; it is also a key factor in building our self-esteem and security. The perceived threat of losing that recognition can be strong. Therefore, we need to adjust our motivations and work values to bring us fulfillment when we manage the work of others.

There are four key requirements to making a successful transition and you need to meet them all. Ask yourself:

- Am I willing to give credit to others?
- Am I motivated to help others succeed?
- Do I listen openly to others' ideas?
- Am I interested in taking on new roles?

Your behavior in response to these questions affects your relationships, your style of communication, and how you utilize supervisory skills, such as delegation and coaching.

If the lure of additional compensation,

a new title, or organizational prestige is your main motivation for seeking a new position, ask and answer the four questions again.

If one of your reports solves a critical problem, will you ensure that he or she gets the recognition? If staff members who report to you struggle, will you spend time helping them? If there is a problem with an analytical procedure, will you first ask your team member for input and listen carefully, or will you start by explaining your own views and expecting people to follow your approach? The latter is more efficient, but asking questions and requesting input will help your staff to grow. As you teach the people that you supervise to think through and analyze their ideas, you will also learn and perhaps discover an even better solution.

Some of us are naturally suited to supervisory roles and enjoy communicating and working with others. Indeed, research into differences between managers and scientists shows distinct behavior patterns and preferences (see sidebar "Manager or Scientist?", page 46).

That said, our preferences change with time and circumstance. I worked for a period at Los Alamos National Laboratory where, at first, I resisted taking a supervisory role. I had previous experience in managing others, when I set up an electron microscopy lab and trained new technicians, but at Los Alamos I loved my work. I was productive and I feared that supervising others would slow me down. It wasn't until someone pointed out that I could try many more of my ideas if I managed others that I agreed to the new role – and I never regretted it. In contrast, at about the same time one of my colleagues took a senior manager position at another organization; he missed his former role so much that he returned to it after a few months, and never again applied for a management role. He did the right thing. Unfortunately, most of the individuals who make the transition and find that they regret it never go back. Both they and their employees suffer.

Three important transitions

During career development, managers pass through transitions that reflect their knowledge and ability relative to the people that they supervise. Each of these three transitions presents new challenges; they are:

- Supervising former peer(s) where your skills and experience are greater than theirs.
- Managing those whose skills and experience levels are very similar to yours.
- Leading groups with varied technical skills, including individuals who have more experience or perhaps greater and entirely different skills.

The first transition could be taking on supervision of one or more lab technicians. Typically, when a technical professional receives a first supervisory assignment, junior staff act as assistants or simple extensions of the professional, similar to relationships in universities. Initially your technical skills and experience are probably greater than those of the individual(s) you supervise. It is, in fact, this expertise that probably earned you the promotion.

For many first-time supervisors, a major concern is about supervising individuals who were previously peers or may be older (or even more experienced). The key here is to have frank discussions about your new role and expectations. Listen and stay open to others' ideas. Learn from those who have been with the organization longer

Manager or Scientist?

Using data from the literature and from our own experience, Gus Walker and I developed the "Manager or Scientist: Attribute Inventory" (1, 2). The inventory lists thirty statements to be rated on a scale of 1 to 6 between two preferences (there are no right and wrong answers). A selection of the statements are shown opposite.

The inventory includes scoring and interpreting of results. A strong profile in either direction does not preclude or imply success as a manager or scientist but suggests transition may be difficult. This is particularly true with continued advancement, as the roles of manager and scientist/technical specialist become more distinct.

The indicator has helped many people to understand some of the issues they have experienced as managers – or may face, if they become one. It often helps to clarify internal struggles, so that they can be recognized and addressed.

a	*I enjoy working with people from different departments and functions*			*I enjoy working with people with similar backgrounds and interests.*		
	1	*2*	*3*	*4*	*5*	*6*
b	*The most important thing is to understand and solve the problem*			*The most important thing is to meet goals and objectives.*		
	1	*2*	*3*	*4*	*5*	*6*
c	*In solving non-routine problems, the leader should provide support*			*In solving non-routine problems, the leader should give directions and ideas*		
	1	*2*	*3*	*4*	*5*	*6*
d	*I like to generate new information and results on problems*			*I like to see that available information is found and used effectively*		
	1	*2*	*3*	*4*	*5*	*6*
e	*People and decisions interest me more than things and ideas*			*Things and ideas interest me more than people or decisions*		
	1	*2*	*3*	*4*	*5*	*6*
f	*Decisions should be made analytically on the basis of the facts*			*Political and human considerations should influence all decisions*		
	1	*2*	*3*	*4*	*5*	*6*

and recognize their contributions. This first transition won't take you far from your technical roots. You may be working alongside your supervisee in the lab, but this is not the case for subsequent transitions.

As you advance, you will no longer be the individual best able to handle a specific technical task. In a second transition, you may be supervising people with equivalent technical capabilities. They may even have greater experience or perhaps a more advanced degree in another area. Giving up a degree of control to people that you manage can be a major challenge. The ability to handle these interactions is a key test of managerial aptitude, and delegation is important to success.

Unfortunately, more skill or experience in one area convinces some supervisors that they are superior in other skills as well. This often leads to over-direction and micromanagement, leading to a frustrated staff. It can also mean you don't recognize special abilities in the people who report to you.

For those who relied on giving close direction in their initial supervisory role, this transition can be especially difficult. One's experience and training can create strong feelings about the best approach to a problem; however, if you continue to promote only your own solutions, your staff may resent their lack of influence. To those with knowledge beyond your own, such behavior is seen as incompetence. Instead, you should rely on the skills and abilities that they bring, and work collaboratively to generate creative solutions. Use the tools available (for example, lab notebooks and technical data) to review and assess results and procedures – even PhD scientists often do not have good experimental design skills. Protect your staff from interruptions (including your own) and guide them through meaningful review and questions.

The third major type of transition occurs when you have responsibility for a large organization or must deal with interdisciplinary teams that

include people who have management responsibilities themselves. Compared with the two previous transitions, you need less technical competence for this role; instead, general knowledge and the ability to manage resources and integrate and prioritize tasks are crucial. You must understand and achieve your goals by trusting and relying upon your staff and creating a motivating climate. This does not mean that you should ignore the technical work; use your ability to evaluate approaches and results and to guide progress via thoughtful questions and meaningful discussions.

Research and development managers can face each of these three transition stages multiple times in their careers. They are handled best when they are recognized and carefully considered. Failure on the part of many people to do so may explain why only 25 percent of the scientists and engineers I've met over the years say they have worked for an outstanding boss.

Rarely is there organizational support to help you focus on the important transitions needed for managing other professionals. At best, you will receive training in delegation, performance management, communication, and other supervisory skills; the importance of recognizing and helping with the behavioral and psychological elements of a transition is rarely considered. And yet, if we reflect upon and expect transition issues, we are better prepared to handle them.

Liz Treher managed R&D groups in academia, a national laboratory, and in the pharmaceutical industry before cofounding The Learning Key.

Join her March 5 at Pittcon 2014 Short Course #139 to take the Manager or Scientist Attribute Inventory and focus on supervisory skills.

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1. *E. N. Treher and A. C. Walker, "Manager or Scientist: An Attribute inventory" in The 2000 Annual: Vol 1, Training, 153–166 (Josey-Bass/Pfeiffer, San Francisco, 2000).*
2. *E. N. Treher, D. Piltz, and S. Jacobs, "A Guide to Success for Technical Managers." (John Wiley and Sons, Inc., Hoboken, NJ, 2011).*

High Speed and High Resolution SEC Analysis of mAbs Using TSKgel SuperSW mAb columns

Size exclusion chromatography (SEC) is the standard method for aggregate and fragment analysis of monoclonal antibodies in biopharmaceutical QC. A new series of silica-based SEC columns was engineered to provide shorter analysis time or higher resolution than standard columns for the separation of fragments, monomers and dimers.

Introduction

Antibody therapeutics are enjoying high growth rates in the biopharmaceutical market; the major areas of therapeutic applications being cancer and immune/inflammation-related disorders including arthritis and multiple sclerosis. In 2010, four of the top ten best-selling global drug brands were monoclonal antibodies (mAbs). The characterization of these complex biomolecules is a major challenge in process monitoring and quality control. The main product characteristics to be monitored are aggregate and fragment content, glycosylation pattern and charged isoforms. The standard method used in biopharmaceutical QC for mAb aggregate and fragment analysis is SEC. A new series of silica based HPLC columns can be applied to either increase speed or improve resolution of the separation of antibody fragments, monomers and dimers.

Experimental

IgG was digested with papain over 24 hours. The fragmentation process was monitored by analyzing 10 or 5 µl aliquots of the sample.

Mobile phase: *200 mmol/L phosphate buffer + 0.05% NaN3, pH 6.7*
Flow rate: *A & B: 1.0 ml/min C: 0.35 mL/min*
Injection vol.: *A & B: 10 µl; C: 5 µL*
Temperature: *25°C* *Detection:* *UV @280 nm*
Samples: *10 g/L IgG digested with papain for 0–24 hr*
Columns: *A: TSKgel G3000SWXL, 7.8 mm ID x 30 cm*
B: TSKgel SuperSW mAb HR, 7.8 mm ID x 30 cm
C: TSKgel SuperSW mAb HTP, 4.6 mm ID x 15 cm

Results

Figure 1A shows the separation of a papain digested immunoglobulin G sample on a TSKgel G3000SWXL column, which is applied as the standard SEC column in routine analysis of aggregates in many QC and R&D labs. Figure 1B demonstrates that the resolution of the separation can be improved by using the new TSKgel SuperSW mAb HR (HR stands for 'High Resolution') with 4 micron silica particles. This column provides higher resolution than the conventional column at the same analysis time. Using the TSKgel SuperSW mAb HTP (HTP stands for 'High Throughput'), a short semi-micro column packed with the same 4 micron particles as SuperSW mAb HR, dimer/ monomer/ and fragments were separated at the same resolving power as on the conventional column but in half the analysis time (Figure 1C).

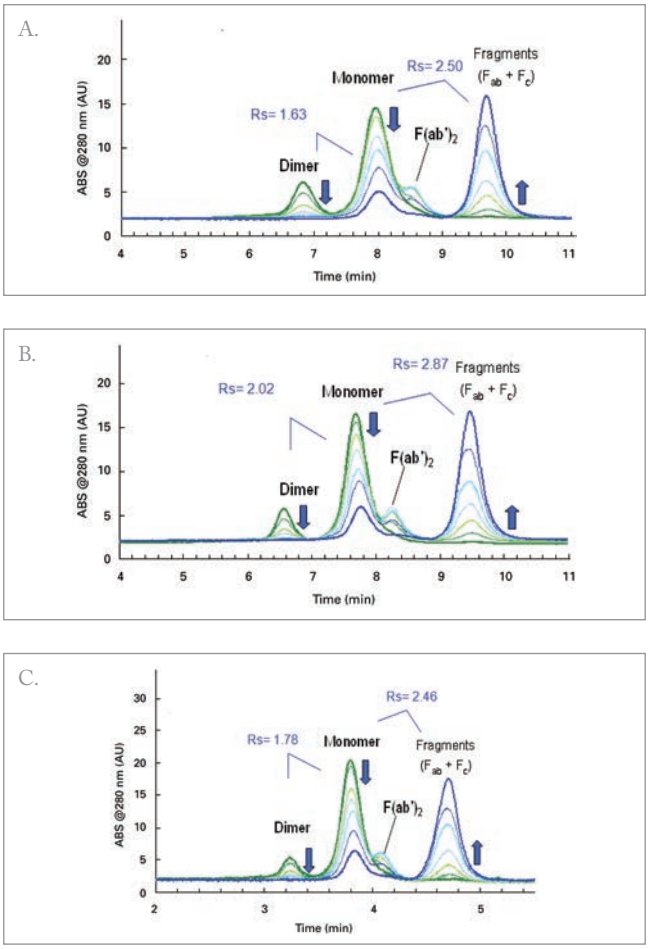

Figure 1. Separation of antibody fragments, monomers and dimers by SEC. A: TSKgel G3000SWXL, 7.8 mm ID x 30 cm; B: TSKgel SuperSW mAb HR, 7.8 mm ID x 30 cm; C: TSKgel SuperSW mAb HTP, 4.6 mm ID x 15 cm.

Summary

Size exclusion chromatography (SEC) is a common method for the separation of antibody monomer from dimer, aggregates, or degradation products on the basis of molecular size. Two novel SEC columns designed for antibody separation exhibit reduced analysis time while achieving baseline separation or enhanced resolution between monomer and dimer.

TOSOH

Webinar

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Register Free at:
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1

Event Overview:
QuEChERS Sample Preparation 101 will provide a basic understanding of the QuEChERS extraction procedure. More importantly, it will also show you how it can be best implemented, and help you understand the analysis and results to be expected.

Date: 27 March 2014, 12pm CET / 11am GMT

2

Event Overview:
Advanced QuEChERS Techniques: Extending QuEChERS Beyond Fruits and Vegetables. Given its proven benefits, QuEChERS is rapidly expanding into other matrices and compound classes; however, because it does not entirely remove the matrix, your analysis will be affected by ion suppression or enhancement. In this webinar, you will learn the parameters that affect analyte recovery using the QuEChERS extraction procedure and discover a straightforward approach that optimizes QuEChERS extraction for unique sample matrices.

Date: 10 April 2014 ,12pm CEST / 11am BST

Speaker
Joni Stevens, PhD
Sample Preparation Application Scientist
Agilent Technologies

Moderator
Rich Whitworth
Editor, The Analytical Scientist

Presented By

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Proteomics for the People

Sitting Down With… Steven Carr, Proteomics Platform Director at the Broad Institute of MIT and Harvard.

You're giving Pittcon's Wallace H. Coulter Plenary lecture – how about a sneak preview?

Essentially, I'll be "taking the temperature of proteomics" – where the field is today, how it is being applied, and where it is going. I'll describe how it fits in with our partners in genomics, and why it's so critical. I'd also like to highlight that, for the very first time, I feel we can put hand over heart and say we are actually 'doing proteomics.'

Could you qualify that last point?

In genomics, we can define all of the genes in the organism being studied and the expression levels of those genes. In proteomics, up until quite recently, large portions of the proteome as well as post-translational modifications of those proteins (such as phosphorylation, glycosylation, and so on), were undetectable 'dark matter' for proteomics. Improvements in sample handling and instrumentation as well as the introduction of quantitative approaches in discovery proteomics now enables us to confidently measure a high percentage of the proteome and to define differences between one cell or tissue condition and another, which gives us much better information about biological states, disease presence or aggressiveness, or response to treatment – all of which are areas of focus at the Broad Institute.

Where have advances been made?

The dynamic range of proteins has been a huge analytical challenge, but materials science, chromatography and instrumentation have all seen vast improvement. Combined, these have enabled us to ramp up coverage to 50-80 percent of the expressed mammalian proteome. In some microbial systems, we can measure the whole thing. So now the bottleneck is gradually shifting downstream: now, we must make sense of all the information.

As we generate high quality data, we simply must, in parallel, develop high-throughput methods for building biological understanding. The computational approaches for integrating information from proteomics (including the many tens of thousands of modifications we can now detect) with genomics and ultimately metabolite profiling, are woefully behind.

What is it like working at the Broad Institute?

It's incredibly interesting. Every day I interact with top scientists in biology and clinical medicine: arriving at new biological insights requires collaborative interaction, and that's what I enjoy most in my current position. The Broad is unique in the academic world in that we apply technologies and capabilities on a scale similar to a biotechnology or pharmaceutical company, with whom we share many of the same questions: what are the right targets, how do we drug them, why do current drugs stop working? The difference is that our main objective is to solve scientific questions, such as the response and resistance to cancer therapy, though group collaboration within the Broad's matrix of capabilities.

What part do you play in the matrix?

I run the Proteomics Platform. Platforms sit alongside the institute's programs (in cancer, infectious disease, chemical biology, and so on) and are led by people with a long history and deep understanding of a particular field. My team and I keep the Proteomics Platform moving forward to address current needs and anticipate future requirements of the entire Broad community. Groups come to me to discuss projects that require proteomics input, but we also connect them with other groups or platforms: not all pieces of their puzzle will be solved by proteomics. In that sense, I help knit the community together.

Proteomics is rapidly evolving, so we need to be amenable to innovation. That means being well connected with technology, data analysis, biological, clinical and software development fields. And our field is only just catching up with statistical data analysis, so expertise is needed there also.

What are you currently working on?

The Broad's mission is to leverage the genome to improve patient treatment and quality of life. Knowledge of the proteome (and all its modifications) provides an essential and orthogonal view into cellular function and physiology, and is entirely complementary to the genomic-based approaches. Much of our research focuses on how the proteome changes under different perturbational conditions. As an example, we just published a paper in Science that describes the mechanism of action of an anticancer drug and, unexpectedly, revealed a new way to develop targeted therapies for this cancer.

Is the collaborative approach sometimes limiting?

In modern science, there's less and less room for a "my lab does it all" mentality. Disease mechanisms are far too complex. A rich mix of technologists, biologists and clinicians working collaboratively is needed to provide solutions to improve patient outcomes – and that is what we have at the Broad. This notion will resonate with anyone working in a biotech or pharma. And even with all the right skills being applied in collaboration, human biology remains human biology. What works in cell culture or an animal model, may not translate to patients.