MAY 2020 # 87

the Analytical Scientist™

COVID-19: Improvise, Adapt, Overcome

The COVID-19 pandemic has brought with it drastic changes to all aspects of our lives: how does this translate into our universities and conference programs?

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The Mind Matters

Mental health struggles represent a second pandemic in the wake of COVID-19 – we must stay connected as best we can, and extend a hand to those who need it

The coronavirus pandemic has repositioned health as public priority number one. Physical health, however, represents only one part of the whole. In this unprecedented age of social distancing, restricted movement, and economic uncertainty, we must also take care to protect our mental health.

I've faced my own struggles since the outbreak began, and I'd like to send a message of solidarity to those of you experiencing similar difficulties. Many of our usual coping mechanisms are closed to us now, and though we're fortunate to have digital tools like Zoom and WhatsApp, they are no substitute for real-life conversation – or hugs. Entering lockdown, I had good intentions of keeping a diary to document this strange moment in history. Eleven entries later, I felt more like a disheveled Bridget Jones than Captain Scott or Marco Polo…

Luckily, there is evidence that the analytical community is adapting rather more ably; Chris Harrison details out-of-classroom teaching solutions in his own (much less questionable) diary in our cover feature (page 16), alongside which Rick Yost shares digital conference solutions to keep our minds connected, despite our physical separation.

As time passes, science advances in our favor – a fact that can help lift our spirits. We reported on MS-based breath tests for coronavirus detection at key transport loci in our April edition; in this issue, we explore a wider view of analytical science's utility in ensuring optimal patient outcomes with Gareth McKeeman (page 33). As he says, "The next few years are likely to bring many challenges [...] and it has never been more important to work together to improve patient care."

Scientists have a rich history of overcoming daunting challenges. In 1915, Peyton Rous and JR Turner developed techniques for preserving whole blood, which, two years later, would allow a humble icebox to act as the world's first blood bank – saving soldiers who would have otherwise bled out on Belgium's battlefields.

I'm confident that our community – and that of the wider sciences – will produce equally innovative solutions to COVID-19. After all, we are armed with more knowledge today than Rous and Turner could have ever dreamed of. In the meantime, we must try to remain positive – and be (especially) kind to one another.

Abandoning my ill-fated diary, I have found solace in returning to my hobby of drawing cartoons. My latest creation, Elvish Presley (Middle Earth's premier Elvis impersonator), like many of us right now, is seeking fellowship (ideas welcome: matthew.hallam@texerepublishing.com)!

Matthew Hallam
Editor

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On The Cover

Michaelangelo's "The Creation of Adam," adapted in line with policies of social distancing amidst the coronavirus pandemic

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the Analytical Scientist

ISSUE 87 - MAY 2020

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Distribution: The Analytical Scientist (ISSN 2051-4077), is published monthly by Texere Publishing Limited, Booths Park 1, Chelford Road, Knutsford, Cheshire, WA16 8GS, UK. Single copy sales $15 (plus postage, cost available on request info@theanalyticalscientist.com). Non-qualified annual subscription cost is available on request.

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Upfront

Research
Innovation
Trends

Who's Our Daddy?

Paleoproteomics reveals the oldest human genetic evidence for our last common ancestor

Researchers at the University of Copenhagen, in collaboration with colleagues from the National Research Center on Human Evolution in Burgos, Spain, have retrieved human genetic information from an 800,000-year-old fossil for the first time. The fossilized tooth, belonging to the hominin species *Homo antecessor*, sheds light on a key branching point in our species' family tree (1).

The evolutionary relationship between *Homo sapiens*, Neanderthals and Denisovans has long been debated in paleoanthropology. Most recently, *H. antecessor* has been pegged as our last common ancestor – though there has been much debate regarding the validity of these claims, which are largely based on analyzing skeletal morphology.

Due to its degradation over time, the oldest human DNA analyzed is dated at no more than approximately 400,000 years – but ancient protein analysis could enable researchers to trace our evolutionary history much further back."Paleoproteomics is based on the analysis of ancient protein sequences preserved within archeological or paleontological tissues using MS," says Frido Welker, lead author of the paper. "As proteins survive longer than DNA, paleoproteomics can delve much deeper into human evolution."

Because our cells build proteins based on instructions found in our DNA, the order of amino acids in these protein sequences can tell us about the individual's genetic code. "By comparing the order of amino acids within these protein sequences with those from other hominins, we can gather evolutionary information to determine how they are genetically related," adds Welker.

The team analyzed several proteins from the ancient tooth enamel, including a protein sequence derived from a gene specific to the Y chromosome – telling us the fossil was from a male. "Our findings indicate that *H. antecessor* is closely related to the last common ancestor of *Homo sapiens*, Neanderthals, and Denisovans," says Welker. Although it is too early to confidently put *H. antecessor* as our last common ancestor, it is certainly a strong contender. Paleoproteomics offers researchers a whole new avenue to explore our genetic past – and close in on our true ancestor. "In the future, we want to analyze other hominin and animal fossils, to further our understanding of human evolution and the environments in which early hominins evolved."

Reference

1. *F Welker et al., Nature, 580, 235 (2020). DOI: 10.1038/s41586-020-2153-8*

INFOGRAPHIC

Progress Against a Pandemic

Quantifying published coronavirus research since 2002

997

planned or ongoing clinical trials

**According to clinicaltrials.gov*

Number of PubMed studies about COVID-19

2019: **156** articles published

Since Jan 1 2020: **7523** articles published

BUSINESS IN BRIEF

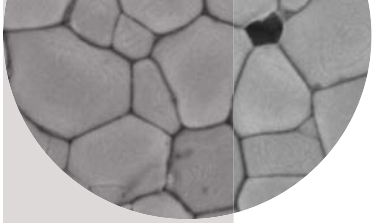
A round-up of this month's business news, from COVID-19 testing to new product launches

- Thermo Fisher Scientific announced the launch of its new iCAP PRO Series ICP-OES platform to accelerate the analysis of trace elements for routine laboratory applications (1).
- Health Canada approved the use of Spartan Bioscience's portable COVID-19 rapid molecular diagnostic test, Spartan Cube. This coffee cup-sized DNA analyzer can be used outside the lab in settings such as airports or remote communities (2).
- Agilent is working with My Green Lab to have their instruments independently audited for the Accountability, Consistency, and Transparency (ACT) label, which provides information about the environmental impact of manufacturing, using, and disposing of a product and its packaging (3).
- Biosero, in collaboration with Scripps Research Institute, is offering a free, automated lab workflow to accelerate the treatment of COVID-19. The Green Button Go automation scheduling software enables screening of 14,000 FDA-approved compounds for their therapeutic potential against the virus (4).
- PerkinElmer has expanded its analysis and automation portfolio to streamline workflows in pharmaceutical, semiconductor, biomonitoring, food, and materials labs. The new range includes multi-quadrupole inductively coupled plasma-MS, and Fourier-transform infrared (5).

Credit: Biosero, Inc.

References

1. *Thermo Fisher (2020). Available at: https://bit.ly/3aIWhPC*
2. *Spartan Bio (2020). Available at: https://bit.ly/2YarCbm*
3. *Business Wire (2020). Available at: https://bwnews.pr/2zzA1ek*
4. *Biosero (2020). Available at: https://bit.ly/2Y7s3Dh*
5. *PerkinElmer (2020). Available at: https://bit.ly/2KDjZCq*



On the Origin of Color

The 170-year-old mystery behind the first color photographs has been solved

In 1848, French physicist, Edmond Becquerel, produced "photochromatic images" of the solar spectrum, but the origin of these colors has since been widely debated. Now, we finally have an answer.

Using UV-Vis spectroscopy, a team of researchers, led by Victor de Seauve, found that visible light absorption by the images could be due to silver nanoparticles (1). They used scanning electron microscopy to visualize micrometric silver chloride grains and silver nanoparticles in the photochromatic material, and transmission electron microscopy pointed toward a plasmonic origin for the colors.

"When exposed to light, silver nanoparticles in the light-sensitized layer of the photographs reorganize, enabling it to absorb different colors," says de Seauve. "The color we see is the only one not absorbed – the one that caused this reorganization."

Reference

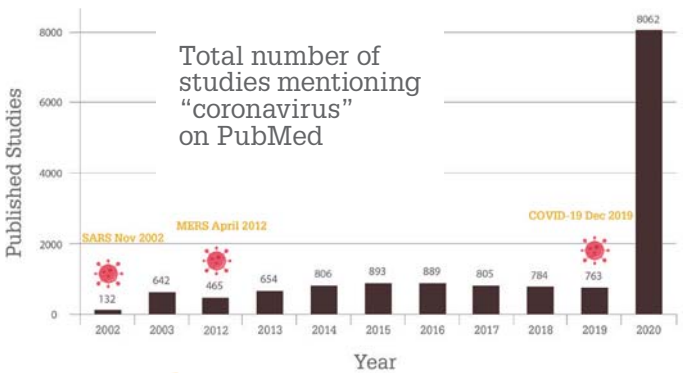
1. *V de Seauve et al., Angew Chem Int Ed. DOI: 10.1002/ange.202001241*

Number of pre-print studies about COVID-19.

Total articles

4115

** Using the terms "novel coronavirus" "ncov" "COVID-19" and "SARS-CoV-2" on the bioRxiv, medRxiv, ChemRxiv and ChinaXiv servers*



The Case of the Mysterious Maggots

Maggot analysis presents unique challenges – but a combination of molecular science and artificial intelligence is helping forensic researchers ID similar species

Fly and beetle larvae on a five-day-old animal corpse. *Credit: Paul Venter.*

Although academically interesting to some, it's difficult to see the relevance of maggots to the average analytical scientist. For those who work in forensics, though, the link is clear – maggots on a cadaver can help investigators determine when and where death occurred. In some cases, such as neglect, they can even help establish a person's physical condition prior to death.

The drawback? Maggot analysis is time-consuming, resource-intensive, and requires the input of expert entomologists who can distinguish between different species. In many cases, this requires raising living maggots to their mature fly form to make species distinction easier. But not all cadavers yield live maggots – and, even in those that do, identification can be subjective and different species may resemble one another too closely for reliable classification.

Is there a better way? That's the question researchers from the State University of New York and John Jay College of Criminal Justice sought to answer. By suspending combinations of maggots in ethanol and using direct analysis with real-time high-resolution MS (DART-HRMS), they were able to identify multiple species of maggot in combination, each with its own highly reproducible chemical signature (1).

Next, the investigators applied machine learning in the form of an aggregated hierarchical conformal predictor – a technique used to classify objects. After training on a hierarchical classification tree, the conformal predictor was able to identify individual species in mixtures of up to six different maggot species, with confidence limits between 80 and 99 percent.

The new method combines analytical science and artificial intelligence to both speed up and increase the objectivity of maggot analysis – and thus, hopefully, extract information from cadavers that could lead to more solved cases and fewer flies in the investigative ointment.

Reference

1. *S Beyramysoltan et al., Anal Chem, [Epub ahead of print] (2020). PMID: 32091197.*

Undiagnosed No Longer

A "metabolic fingerprint" for fibromyalgia

Fibromyalgia is a diagnosis of exclusion, relying on patient-reported symptoms, physical examinations, and tests to for identifiable pathologies. Patients can wait five years for diagnosis and other conditions might be missed.

A new study has revealed a "metabolic fingerprint" – a unique metabolite profile that can be detected by vibrational spectroscopy and may distinguish fibromyalgia from other rheumatological disorders (1). "We found clear, reproducible metabolic patterns in the blood of dozens of patients with fibromyalgia," said first author Kevin Hackshaw. "This brings us much closer to a blood test than we have ever been." Spectra also correlated well with patient-reported pain severity – a promising outlook, although the test still requires a large-scale trial.

References

1. *KV Hackshaw et al., J Biol Chem, 294, 2555 (2019). PMID: 30523152.*

IMAGE OF THE MONTH

The (Ugly) Face of Plastics

Say hello to *Eurythenes plasticus*. This newly described deep-sea amphipod has become the new face of the plastics crisis, after a team of researchers from Newcastle University discovered microplastic particles in its hindguts using Fourier-transform infrared spectroscopy. The team named the animal plasticus to send a message about the (quite literally) far-reaching consequences of plastic pollution.

Image credit: BBDO/ Newcastle University.

Reference: J Weston et al., Zootaxa, 4748 (2020). DOI: 10.11646/zootaxa.4748.1.9. Available at: https://bit.ly/3aGlDxQ

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QUOTE OF THE MONTH

"My advice? Have the courage to go and talk to the big names in any field. You'd be surprised how many people really love talking with young enthusiastic people who are just starting out."

Peter Griffiths, Emeritus Professor of Chemistry, University of Idaho, USA. Look out for the full conversation in an upcoming issue.

Proteins in Space?

The discovery of hemolithin in the Acfer 086 meteorite appears to be a world first

Three researchers from Harvard University, PLEX Corporation, and Bruker Scientific believe they have found the world's first extraterrestrial protein in a meteorite called Acfer 086 (1).

The team was able to characterize the new 2320 Dalton protein – dubbed hemolithin – using high-precision matrix-assisted laser desorption/ionization (MALDI) MS. And based on the protein's high deuterium/hydrogen ratio, the researchers suggest it may have been formed in a protoplanetary disc at the start of our solar system – or in the interstellar molecular clouds that existed long before our sun was born.

The group is now working to determine hemolithin's 3D crystal structure and explore its other properties. If, as they suspect, hemolithin's iron-oxygen-iron grouping is able to absorb photons and split water into hydroxyl and hydrogen, it could provide insight into the biochemical processes that kickstarted life on planet Earth.

References

1. *MW McGeoch, "Hemolithin: a meteoric protein containing iron and lithium", Cornell University [submitted paper] (2020). Available at: https://bit.ly/3evWxob*

Whale (Shark) of a Time

Exploring the unlikely link between Cold War atomic bomb testing and whale shark conservation

By Mark Meekan

In the management of marine species, knowledge of growth rate is critical. Fast-growing species have superior rates of replacement and can withstand losses to threats, such as fishing. Slow-growing species, on the other hand, are less resilient, and conservation strategies must be adapted accordingly. Fish age is an essential factor in growth rate assessment.

In the case of whale sharks (*Rhincodon typus*) – the world's biggest fish – age estimates are obtained via growth bands from inside the vertebrae. Yet, there has been debate among researchers as to the intervals at which these bands are formed – some say one year per band, and others two.

Fast-forward to Karachi, Pakistan, 2012. A beached, 10-meter whale shark, alongside vertebrae from a (now closed) fishery for the creatures in Taiwan, afforded us the opportunity to finally solve this puzzle. C^{14} – a naturally occurring isotope – was also released in enormous quantities by atomic bombs during the Cold War, saturating the atmosphere and making its way into living organisms. By applying accelerator MS to quantify C^{14} levels within the growth rings of the vertebrae of the sharks, we can arrive at more accurate estimations of age (1).

We also needed to compare our samples of unknown age with a C^{14} reference chronology where ages had already been designated; for this we used a C^{14} chronology that had been reconstructed from the earbones (otoliths) of Atlantic fish. This had a pattern of increasing C^{14} values identical to the surface waters off Pakistan and Taiwan, where our whale sharks had once lived.

C^{14} peak comparison and the known date of vertebrae collection allowed us to age the shark in Pakistan at 50 years. We then recalculated growth curves for the species, and found that these sharks are very slow-growing. Perhaps this explains why fisheries targeting this species collapse and never recover – whale sharks simply aren't built to withstand the added pressure of human harvest.

To date, knowledge of whale shark life spans has been based largely on assumptions and evidence from other species. We thought they might reach ages as old as 100 years. Given that our 10-meter shark is thought to be 50, and whale sharks as long as 18 meters have been recorded, our study suggests that it's not unlikely that these creatures could live 100 years.

There is a Kenyan story that when God created whale sharks, he was so pleased with their form that he scattered silver dollars on their backs, which explains their beautiful white-spot patterning. But whale sharks are more than a charismatic part of the tropical ocean ecosystem; they are a significant contributor to the local economies of developing nations, such as the Philippines and Indonesia, where ecotourism surrounding whale sharks has lifted thousands out of poverty. And the more we know about these wonderful animals, the more hope we have of allowing future generations to also benefit from their presence.

Mark Meekan, Senior Principal Research Scientist, Australian Institute of Marine Science, The University of Western Australia, Crawley, Western Australia.

References

1. *JJ Ong et al., Frontiers in Marine Science, 7, 188 (2020). DOI: 10.3389/fmars.2020.00188*

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In My View

Experts from across the world share a single strongly held opinion or key idea.

HPLC Doctors and Nurses

Why spend time and money bringing in specialists to fix HPLC maladies, if we can learn the skills to remedy most ills ourselves?

By Victoria Samanidou, Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki, Greece

All high-performance LC (HPLC) practitioners will be aware of the need to overcome issues in both method development and routine analysis. Even the most sophisticated equipment can present unexpected chromatographic behavior. And though such issues certainly plague modern instruments less frequently, sooner or later, a problem will inevitably occur.

There are some preventative measures that can be taken to increase the chance of seamless operation and performance of HPLC instrumentation – the most common of these being:

- filtering of the mobile phase solvents,
- filtering of the samples prior to injection,
- using the right buffers and following instructions to remove or avoid precipitation of salts in the system due to organic solvent,
- preparing fresh buffer or aqueous solutions instead of storing in the fridge,
- proper washing of the column after use.

But issues occur – and recur – regardless of these measures, and chromatographic abnormalities can be difficult to spot. It is easier during analysis of standards than of unknown samples for sure, though, and injection of control samples can help us to spot aberrant outcomes.

Record keeping is a requirement in any analytical procedure, and it should be considered absolutely essential in HPLC. (It was actually one of the first lessons I learned in practicing HPLC, and it is one of the most important lessons I teach my students as they begin using the technique…). We should know how the system works when functioning properly; only then can we recognize any irregular signs and symptoms – allowing us to subsequently resolve the problem. Recording pressure and keeping typical chromatograms for comparison enable the recognition of a non-proper function.

Knowing how to confront the problems and solve them could be considered a prerequisite for efficient HPLC operators. HPLC is incredibly useful, but also highly complex. Analytical chemists must know the fundamental theory behind the simple act of sample injection. We are "analysts," not "analyzers," and – as practicing scientists – we must all have a firm grasp of this knowledge.

It is not easy to have the right answers to all problems in chromatographic analysis. HPLC troubleshooting manuals outline a vast number of potential irregular functions, and also many corrective actions – but not all lead to the right solution. And that's not to mention the fact that, although we all know the rule that we have to change one thing at a time, when we are in hurry, we sometimes ignore it and change many more...

But what happens when more "invasive therapy" is required? Are all HPLC practitioners able to proceed and fix the most common problems? Of course, we can call for assistance and technical support, but this is often time-consuming and associated with financial cost – nevertheless, we often find ourselves seeking an expert technician. But shouldn't chromatographers themselves be the expert technicians? Being "doctors" to our own HPLC systems – healing its symptoms when sick – could save us both time and money, allowing us to inject both of these resources back into our research, perhaps learning valuable lessons in the process.

"Knowing how to confront problems and solve them could be considered a prerequisite for efficient HPLC operators."

I suggest that analytical scientists – especially novices – using HPLC instrumentation should attend hands-on workshops to learn how to confront the problems arising in routine operation. And, at the very least, surely it would be better to invest time in actually reading the HPLC system's instruction manual rather than blindly paying an external technician to fix the problem.

Moore's Law and Crystal Balls

Can we predict our analytical capabilities 20 years from now? How single-molecule detection MS will deliver us the complete food metabolome by 2041

By Michael Rychlik, Department of Life Sciences Weihenstephan, Technical University of Munich, Germany

When developing analytical methods to quantify bioactive trace components in foods, I've always tried to work at the edge of current methodology. But for some time now, a big question has loomed over me: when can I expect to overcome the limitations of these methods? I set out to provide an answer by predicting when the whole food metabolome will be identifiable and detectable...

First, we separated the unknown components of the food metabolome into three different sets of "dark matter:"

- Set 1. Unknown metabolites not yet present in databases
- Set 2. The metabolites not yet detectable with current equipment
- Set 3. Molecules with unknown structures

We then looked at the most important compound databases from different organizations. The number of compounds included in these databases ranges from a few thousands (Golm Metabolome Database) to almost a hundred million (PubChem), running the full gamut from primary metabolites in humans to all man-made chemicals. In principle, all these compounds could be present in foods, but the majority of them are very unlikely to appear.

In fact, for our purposes, the databases of PubChem, ChemSpider and Metlin should not be included as they mainly contain xenobiotica. A much better estimation comes from the ~20,000 compounds in KEGG or the currently updated human metabolome database (HMDB), which contains around 114,000 compounds.

Considering that MS sensitivity and resolution appears to be increasing exponentially, we leaned on laws governing advances in general technological developments to make our predictions; namely, the laws of Moore (the number of transistors in an integrated circuit doubles every two years) and Kurzweil (the law of accelerating returns, estimating that the intelligence of artificial intelligence will surpass humans in around 2045 – an event he rather wonderfully refers to as the "technological singularity").

Our predictions? The unraveling of dark matter set 1 by 2025, set 2 by 2032, and set 3 by 2041.

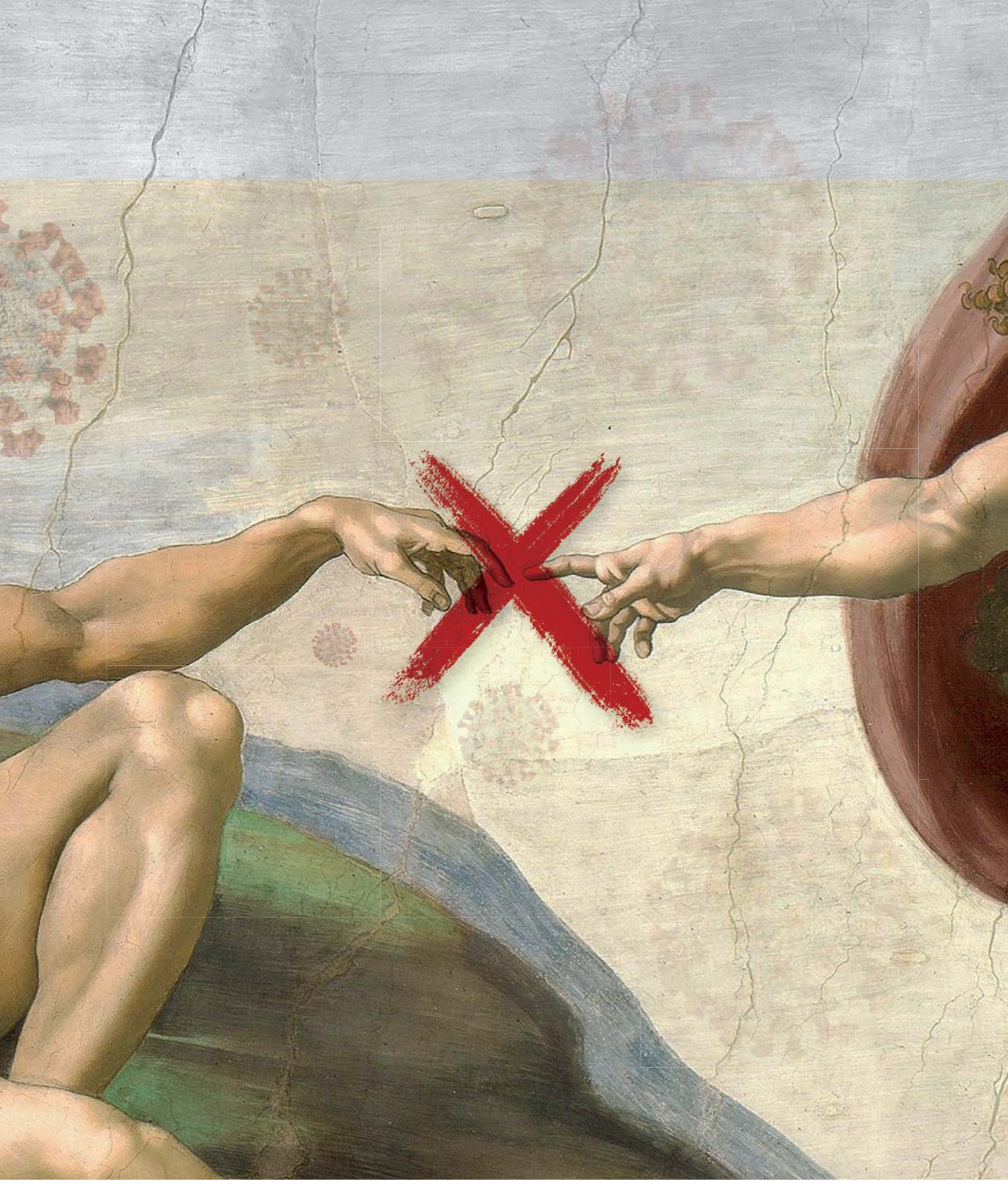
The important question in my eyes: when will these metabolites be detectable by analytical equipment as resolved features? To get there, we'll need an expansion of non-targeted metabolomics into single molecule detection. With the exponential development of current limits of detection (LOD) of 6 x10^{-18} mol to single molecule detection (1.66x10^{-24} mol) – we believe that single-molecule detection on routine MS equipment should be feasible around 2032.

"Such advances will allow us to uncover and assess what I would call the 'iceberg' of all food metabolites (we see but the tip at present)."

Such advances will allow us to uncover and assess what I would call the "iceberg" of all food metabolites (we see but the tip at present). As we move through our predicted timescale, researchers will be increasingly able to map the bioactive compounds – both toxic and health-promoting.

As we approach 2045, our coverage will be comprehensive – with a concomitant high impact in food safety and regulation. And so, in a way, our work could be seen as a valuable tool for proactive regulators and risk assessors...

The advancement of any other analytical field could be predicted in a similar way – perhaps even more easily; after all, food matrices are some of the most complex around. I would urge anyone that is capable of such extrapolation to give it a shot – the information gleaned could guide researchers forward with a clear view of the technical capability milestones we should expect to reach.



COVID-19: *Improvise,* ADAPT, OVERCOME

From the moment COVID-19 hit, scientists across disciplines have been combining their expertise, racing to adapt to the evolving situation. The pandemic has brought with it countless changes to both our personal and professional lives, but how are education and communication platforms adapting – and for how long will this be the case? In this special feature, we hear from professors testing new tech to keep students informed and engaged, and explore how Mary Wirth, Luigi Mondello and Rick Yost wrestled with dramatic changes to our approach to conferences in 2020.

By Lauren Robertson and Frank van Geel

ALL QUIET *on the* UNIVERSITY FRONT

A day-by-day perspective from the midst of a pandemic

By Chris Harrison, San Diego State University, CA, USA

MARCH 9

The campus seems a bit quiet for a mid-semester Monday. With COVID-19 gradually spreading towards San Diego, the University of California has decided to move courses online for the remainder of their quarter. They only have a couple of weeks left; we've just crossed the halfway point of our semester.

MARCH 10

The campus seems even quieter today. I'm not sure if students are staying in their dorms or being called home by parents... An emergency meeting of the University Senate was held this afternoon to discuss the outbreak. The plan is to use the time up to spring break – a little over two weeks – to transition all courses into online-only formats, but there are many concerns. What happens to students getting financial aid through work study programs? What about courses with required internship hours? And what about students who are living on campus, or don't have access to the necessary technology at home?

MARCH 11–13

The rest of the week has been a blur. Almost as soon as we concluded our meeting to discuss our plan moving forward, we received an email indicating that those plans would change once again. Throughout the week, we saw a number of incremental changes regarding when in-person classes and labs would end, with the dates being brought forward from spring break to the end of the week. All in-person meetings (including labs) were now to end after March 13.

The students in my research lab have been great. Those feeling ill for any reason have been staying home and those who came in brought hand sanitizer and disinfectant wipes to share. We all also took precautions to wipe down instruments and communal surfaces; morale was high, despite undercurrents of uncertainty. By March 12, none of my research students were coming to the lab. And by Friday, I had shut down all the vital computers and instruments. Fortunately, this was pretty simple given I run a lab with primarily capillary electrophoresis instruments!

MARCH 14–15

The weekend brought with it a warning to make plans for continuity in the case that the campus is shut down. By Sunday the orders were updated again. Undergraduate students were no longer allowed to conduct in-person research, but graduate students were still permitted to come to the labs.

MARCH 16

Campus feels like a ghost town. It isn't shut, per se, but is empty nonetheless. We received an email last night directing faculty or staff over 65 or with underlying health conditions to stay home. I'm here, but I'm not entirely certain why? I'm not conducting lab work, and I'm going to be teaching online later in the day anyway. It's a strange day. But one benefit of my being here is that I can discuss plans for digital teaching with my colleagues – I'm the department expert on digital technologies.

MARCH 17

I was feeling a little uneasy yesterday, and I realized why this morning: I hadn't received a revised campus plan. This has become so routine that I got used to having plans altered every day. But fear not, I did indeed receive an email late in the evening indicating that all non-essential staff should telework from March 17. I really should have checked my email this morning before cycling to work…

MARCH 18

My office is now the kitchen table in my condo. It's not the best situation in the world, but at least I have good Internet. And the dogs are over the moon!

Yet another new directive was issued today, indicating that the buildings will be locked and access restricted. Residence halls will also be closing by the end of the week and all students who can go home must do so. Only a few international students, and others with extenuating circumstances, are allowed to stay.

"Teaching is still a challenge, with motivation being a real struggle for both faculty and students. After all, how important is 'this assignment' or 'that test' in light of a pandemic?"

MARCH 23

It's getting harder to distinguish one day from the next. My commute is much shorter, but I have more meetings than ever, and seem to be getting less work done. There are daily faculty meetings in our department, including discussions of the challenges we are facing, how to teach labs online, how to run fair exams, questions about who has access to the labs to maintain crucial instruments, and who has research projects that cannot be left unattended?

WHERE ARE WE NOW?

Over time, many questions have been resolved. A small number of faculty were given limited access to the labs, while a couple of staff are allowed daily access to care for the equipment and handle issues for those of us at home.

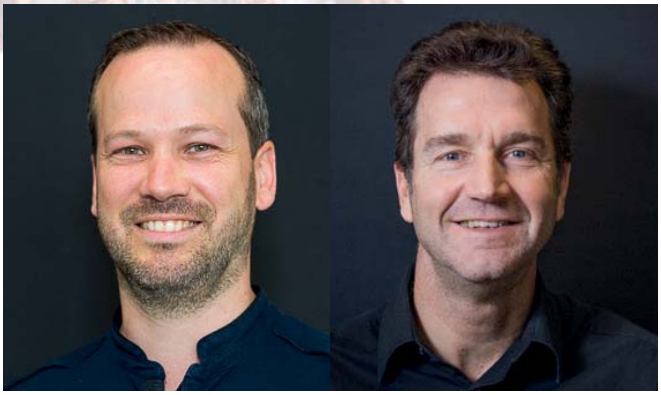
Teaching is still a challenge, with motivation being a real struggle for both faculty and students. After all, how important is "this assignment" or "that test" in light of a pandemic? Along with the introductory analytical chemistry course, I'm also teaching the second half of our upper division analytical lab course. Finding a meaningful way to teach MS, GC, and high-performance LC (HPLC) online is a challenge. We have some past data that can be given to the students for an analysis project, but the hands-on side of things is absent. There are very few good simulation programs available online, but I'm making the most of those that I can, along with videos from manufacturers and others that describe the function and operation of instruments. It's not great, but it's the best we can do.

I had initially presumed that by June we could start to get back into the lab. Now I'm not so sure. It's good to see that our state has a clear set of metrics that need to be met before the shelter-in-place order will be lifted, but those goals may be further off than I anticipated. The university has already decided that the summer session will be online only, and we are being given guidance to plan for a full fall semester of online teaching as well.

And that's where the unknowns get even greater for our department. At least this semester our students got to do half the labs in-person, but how do you teach real chemistry lab skills online? If I can't get to the lab over the summer, I guess you'll find me at home – trying to figure out how I can conduct HPLC in my kitchen!

A *Moment* OF REFLECTION

Revisiting teaching during the COVID-19 pandemic



By Davy Guillarme and Jean-Luc Veuthey, School of Pharmaceutical Sciences, University of Geneva, Switzerland

On March 16, 2020, the University of Geneva decided to suspend all classroom teaching and move courses online. Our second year "Pharmaceutical analysis and spectroscopy" course is typically taught for two hours per week, with the entirety of the practical lab work undertaken in the spring semester. Clearly, our course would look a little different for the remainder of the year...

GOING DIGITAL

Some years ago, we began to introduce short videos into our teaching to help explain particularly difficult concepts to students – these are now coming in handy. As for practical work, corresponding videos were available to present the theoretical bases of experiments, with additional videos offering practical demonstrations of the equipment and techniques.

As of March 16, several options were suggested by the University of Geneva to record videos. Eventually, PowerPoint was selected because staff were already familiar with it, it's easy to use, the quality of the video is excellent, and it's available on most computers. With our slides prepared, the faculty set about recording the accompanying audio and transforming this into video lessons of around thirty minutes.

We quickly recorded and made all our courses from March 16 onwards available, so that students could organize activities according to their availability until the end of the semester. Initially, we used a secure cloud called SwitchDrive to store, synchronize, share and edit files quickly. However, the platform was rapidly overloaded, so our IT staff instead developed a dedicated platform specifically for the School of Pharmaceutical Sciences, where the videos can be uploaded by teachers and downloaded by students with ease.

We have also incorporated quizzes into our teaching to make it more interactive – and to assess understanding. We provide the students with a set of multiple-choice questions using a Votamatic platform – an online application that integrates voting tools with teaching. The teacher can then access the results, and detailed answers are uploaded to the Moodle application, as well as statistics on correct answers. A discussion forum in Moodle allows us to receive students' questions and comments, which have – so far – been extremely positive!

(IM)PRACTICAL?

The greater challenge was to ensure that students still received the same level of practical education needed for pharmaceutical analysis. Though lecture content can be delivered effectively online, there is an undeniable need for hands-on experience in any science curriculum.

We are lucky to have already developed a few practical lessons based on computer simulation for some of the more expensive and complex devices. For capillary electrophoresis, we are using the freeware program, Peakmaster, to simulate experiments and predict parameters of background electrolytes and analyte peaks. For HPLC, we are using the HPLC Simulator software – a web-based HPLC simulation, where the user can adjust a range of experimental parameters and see their effect on chromatographic parameters, including retention time, column efficiency, and backpressure.

Where no simulation tools are available, we have asked our PhD students, who are normally supervising the labs, to find some data from previous groups. The students then have to treat the data and provide answers to general questions related to the practical work. Our PhD students mark the results, and are available to answer any questions. Fortunately, our students already practiced some analytical techniques during their first year – more of which awaits them in their third year.

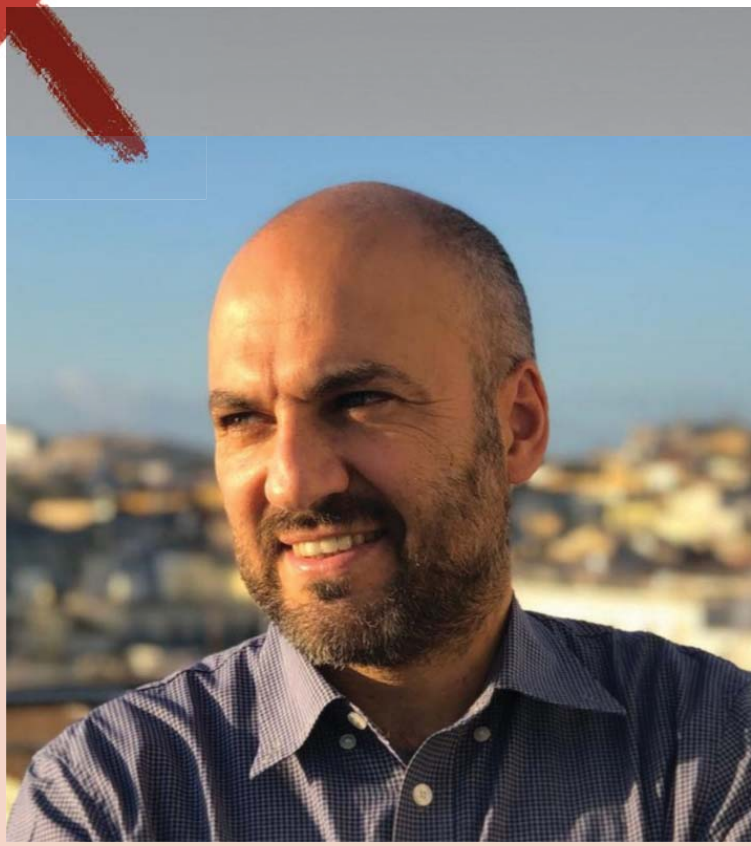
POST-PANDEMIC

It is clear that COVID-19 has drastically affected university education. Before this crisis, a lot of professors were reluctant to use innovative teaching tools (videos and the like), despite the fact that such tools have proved to be highly beneficial for students. Now, a number of teachers have been forced to implement these resources. Although we are convinced that face-to-face lectures remain the most effective way of teaching at university, and that hands-on laboratory experimentation is vital to training a scientist, we do believe – and hope – that a greater number of teachers will integrate modern teaching procedures into their future courses.

MEANWHILE *in* ITALY...

In unprecedented times, unprecedented action is ensuring student success

By Alberto Cavazzini, Professor of Analytical Chemistry, Department of Chemistry and Pharmaceutical Sciences, University of Ferrara, Italy



Our university came face-to-face with COVID-19 at the end of February. Thanks to a well-organized and efficient communication and technology department, we were ready to start teaching remotely in about a week. Teaching could be done either by streaming or recording classes in Google classrooms, with Q&A sessions organized once a week with our students through Google Meet. Despite initial reservations, the process has worked quite well.

OUR SOLUTION

The focus at a university level is ensuring students can graduate according to their initial plans. We opted for so-called "virtual laboratories" to explain lab activities. Thankfully, there are a number of tools available to facilitate this, including free digital editions of published books on the topic. As for thesis preparations, students are requested to critically review scientific papers and data from literature. Exams are performed through the web, either as written or oral tests.

Students are reacting positively to these changes. Many may prefer traditional teaching methods, but they appreciate the enormous effort made by professors to stay in touch with them in these uncertain times. I truly believe this has reinforced the empathy between students and teachers, as is evidenced not only by the assiduous participation in online classes – despite my lack of affiliation with video resources (!) – but also in their quasi-military discipline during them. I believe there is a sense of mutual responsibility that has dramatically increased in students during the pandemic.

LOOKING FORWARD

Hopefully, we'll start to see a return to research activities in the near future. In the longer term, we have the resources in place to be online-ready for courses starting in September. Personally, I don't think teaching will ever be the same again. Although the physical presence of students at university cannot be replicated or replaced, it is clear now that there are so many incredible tools that can improve the way we teach. For example, as professors, we all know too well the difficulty of scheduling classes and lab experiments with such a large number of students. With these new technologies, it would be possible to have part of the teaching provided as electronic material, leaving more time for practical experience.

Despite the many negative impacts, this pandemic has given us an opportunity to rethink traditional teaching activities, and it would be a real pity not to take advantage.

"Although the physical presence of students at university cannot be replicated or replaced, it is clear now that there are so many incredible tools that can improve the way we teach."

ASMS 2020 *gets a* REBOOT

By Rick Yost, Professor at the University of Florida and President of the American Society for Mass Spectrometry

This year's ASMS Conference had been planned for May 31–June 4 in Houston, Texas, with an anticipated attendance of almost 7,000 attendees – not to mention the 384 oral presentations and 3,000 poster presentations.

On February 24, we posted a statement about COVID-19 and promised regular updates. Just over a month later, on April 1, the scale of the COVID-19 pandemic in the USA and elsewhere became clear, and the ASMS Board voted to cancel the face-to-face conference. We opted for an online program instead. In my view, ASMS is about a community of scientists from diverse disciplines coming together every year not only to present and see great science, but to connect and engage. Our goal was to keep this tradition going.

We announced our plans for the ASMS 2020 Reboot on April 14, with all talks and posters to be presented in a virtual and interactive format over a two-week period – June 1 through 12. There will be live webinars for plenary lectures, tutorials, and award lectures, plus 50 interactive workshops. We will also have a "watch party" for each of the 64 oral sessions, including a live Q&A webinar with the speakers. A variety of corporate events will occur each day before and after the live conference program, plus about a dozen short courses the following week. All conference content will be available to registrants for three months – all at a fee of just $50 for ASMS members.

The response from presenters, individual and corporate members, and attendees has been uniformly positive. Though they are all looking forward to the next face-to-face conference in Philadelphia in June 2021, they fully support our online approach to maximize engagement. Some presenters may have to modify or withdraw their presentations due to lab closures and reduced data, but others who couldn't make the trip to Houston now have the opportunity to attend the online conference!

Beyond ASMS, the COVID-19 pandemic will have a major impact on teaching, research, and on sharing our best science with each other. When will it be safe to resume large face-to-face conferences, such as ASMS? This fall? Next spring? The answers require a better crystal ball than I have. But I know that I'm looking forward to getting back into the classroom to teach, back into the lab with my graduate students, and to attending conferences in person – as soon as that's sensible and practical. And I look forward to seeing everyone at ASMS 2021 in Philadelphia next June!

HPLC *on* HOLD

By Mary Wirth, W. Brooks Fortune Distinguished Professor, Purdue University, USA and HPLC 2020 Symposium Chair

I attended the Pittcon 2020 meeting at McCormick Place in Chicago in the first week of March. I would never have imagined that, just a few weeks later, McCormick Place would be converted into a field hospital...

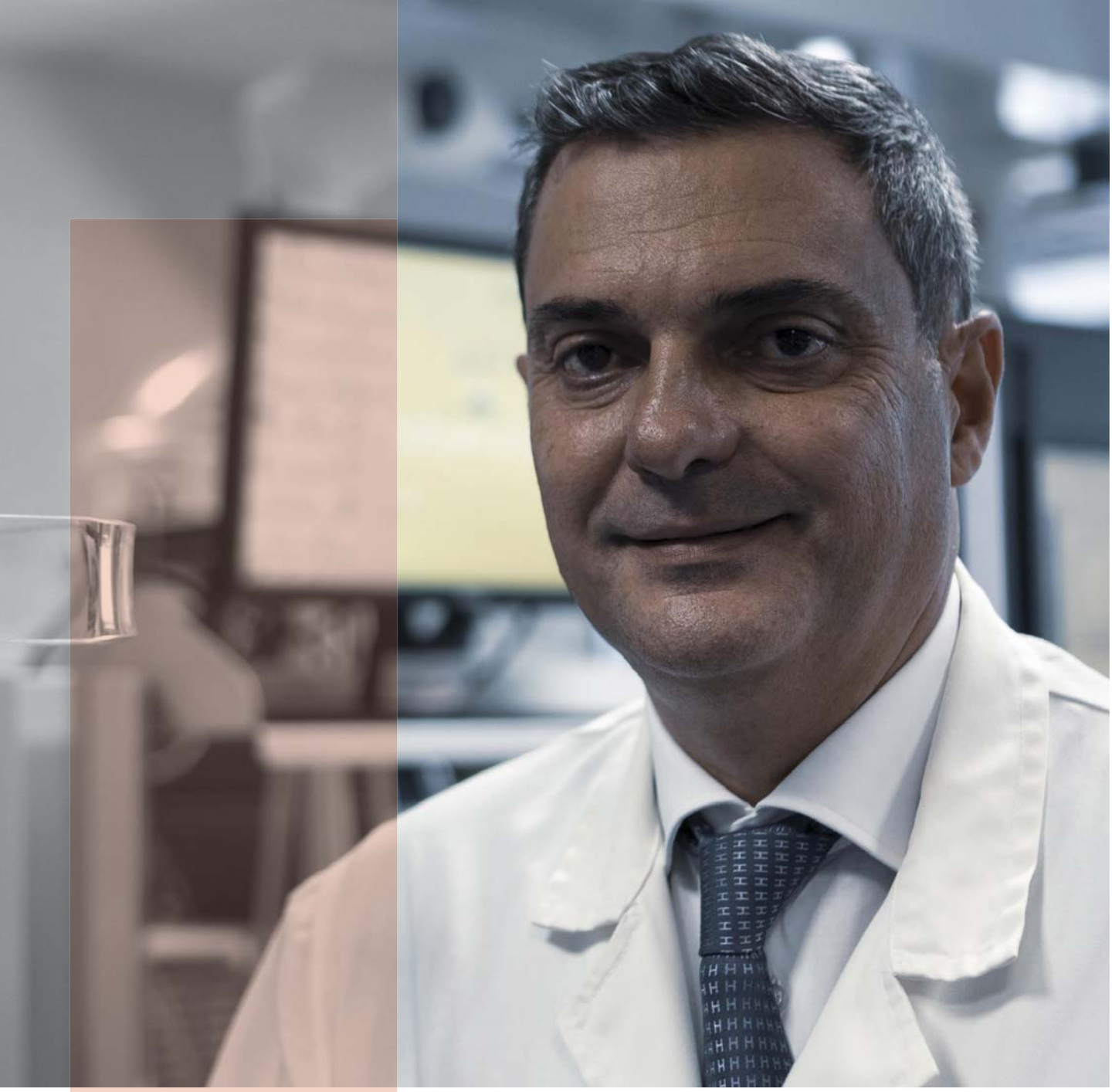
The first inkling I had that HPLC 2020 might be postponed was a message from Ed Yeung at the end of Pittcon suggesting we talk about this possibility. I was taken aback at first and wondered if we were being overly cautious, as the virus had diminished in Wuhan in a matter of months. If we did cancel, would the venue keep the hefty deposit and bankrupt HPLC, Inc.? I started getting messages from people overseas saying that they could not travel – large companies banned travel altogether, and my own university soon followed suit. It soon became clear that the safe decision was to cancel the 2020 meeting and shift all plans to 2022. The work we did on organizing 2020 is not wasted – its fruits are just on hold for two years!

We initially discussed the possibility of hosting the meeting as webinars, but the value of HPLC goes well beyond the content of the talks. Q&A sessions continue informally all week, people expand their scientific networks, students and prospective employers meet, and ideas about future research and best practices are exchanged informally. HPLC 2020 was designed to enhance these beyond-content experiences by including programming on career development, with successful entrepreneurs sharing their insights – thanks to The Analytical Scientist for helping us plan and advertise this part of the meeting! We also had interesting interactive discussions on academic-industrial collaborations planned, including industry needs, the basic research that would underscore these needs, and the entrepreneurial and vendor capabilities that will ensure its success.

"We initially discussed the possibility of hosting the meeting as webinars, but the value of HPLC goes well beyond the content of the talks."

In the end, we decided to postpone the event until 2022 because you simply can't get the same level of value online. However, timeliness is also a key consideration in terms of the content of the talks – we are hoping webinars can fill this void.

The long-term impact of this pandemic presents more questions and uncertainties. Will there be an economic depression? Will there be changes in our behavior and infrastructure? Will there be permanent changes in social obligations? We live in unique times in the USA; the governors of the states took the lead in imposing stay-at-home orders, but the federal government has threatened to sue some states over these measures. There are people traveling to state capitals to demand that the stay-at-home orders are lifted, while health experts warn that there will be a second wave if the orders are lifted too quickly. I do not know what will happen in the long run, but I find the possibility of social strife more worrisome than the virus...



RIVA: *the sun will rise* TOMORROW

By Luigi Mondello, Full Professor of Analytical Chemistry, University of Messina, Italy and Chairman of the 44th ISCC and 17th GCxGC (Riva 2020)

I was aware from early on that lockdown would inevitably impact all my activities, each at a different level. Two weeks after the first coronavirus case in Italy, our government took aggressive action to confront the danger. The whole University in Messina was put in lockdown, and all our facilities were closed by March 8.

As a teacher of analytical chemistry for undergraduate and PhD students, I was committed to ensuring these activities – from lectures and lab sessions to college meetings and graduation sessions – could continue without too much disruption. As chairman of Riva 2020, I have realized that, despite taking early precautions, the truth is that you will never truly be ready to face such events.

Pat Sandra passed the baton to me in 2012, and I have since

"In 2020, we were on track to surpass the attendance of past years, but with the outbreak becoming increasingly pandemic in nature, it was clear a short-term postponing of the conference was not feasible."

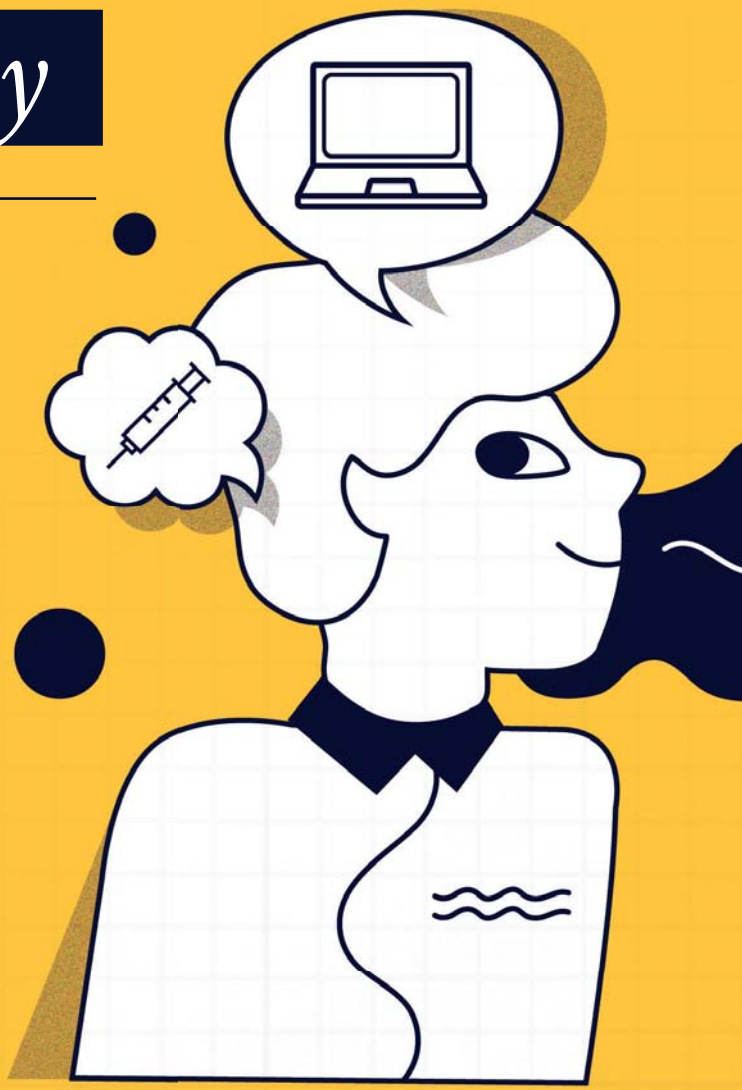
committed myself to ensuring Riva's success, dedicating substantial effort and energy to every phase of organization and planning. It has been a challenging but rewarding experience; after all, Riva del Garda is widely regarded as one of the premier meetings in the field. In 2020, we were on track to surpass the attendance of past years, but with the outbreak becoming increasingly pandemic in nature, it was clear a short-term postponing of the conference was not feasible. Finally, I made one of the most difficult decisions of my life – to cancel Riva 2020.

We were very close to the conference date, and most of the groundwork was already done. In addition, we had already processed hundreds of abstract submissions and applications for the awards and grants dedicated to encouraging young students' participation. I wholeheartedly appreciate the understanding and dedication demonstrated by everyone involved. Their willingness to help in any way, and the sincere and positive proposals I received from the members of the Scientific and Organizing Committees, is representative of a truly heartfelt attempt to save a much-loved conference.

This crisis has dramatically changed our lives, both private and professional. Our university has made impressive efforts to digitize courses, exams and academic activities that do not require lab work, with very positive feedback from our students. From the beginning my priority has been to keep my research activities as unaffected as possible, with social contact severely limited. Luckily, my lab team has always relied on strong communication, and this has enabled us to better navigate the lockdown. We currently share our outcomes and presentations in remote meetings, on an almost daily basis, very successfully.

As for the future, the new rhythm of home working has given me the chance to devote more time to projects dear to my heart – such as rebuilding the labs of the Mediterranean Separation Science Foundation Research and Training Center destroyed in a fire five years ago, and updating research and training activities to make use of new technologies to allow for remote operation and training.

CONVERSATIONS ABOUT *Chromatography*



HPLC is a crucial technique in many application areas, but where did it all begin? And what lurks over the horizon? Sit back as we eavesdrop on a coffee break catch-up between separation experts (and longtime friends and colleagues) Peter Schoenmakers and Bib Pirok.

By Peter Schoenmakers, Professor of Analytical Chemistry and Applications in Forensic Science & Bob Pirok, Van 't Hoff Institute for Molecular Sciences, Analytical Chemistry Group, University of Amsterdam, the Netherlands

Peter: Hi Bob! The Analytical Scientist wants to get our thoughts on separation science - shall we talk now?

Bob: Let's do it!

Peter: Sure. I guess I'll start by saying that separation science constitutes arguably the most important group of techniques available to analytical chemists. These methods find a home in most application areas, but – as my job title indicates – I lend some focus to forensics. Separation techniques are uniquely important in this field… After all, DNA analysis also relies on these tools.

Bob: I couldn't agree more. And, with the increasing volumes of data we are producing with such methods, my research focus – the interfacing of separation science with chemometrics – becomes ever-more important. HPLC is a particularly robust and reliable technique across application areas, and our equipment demonstrates an incredibly low downtime.

Peter: Less than ten percent, right?

Bob: Yes, and this compares favorably with our other equipment, such as our mass spectrometers. Overall, though, what I love about working in LC is the expertise and knowledge it requires. New challenges arise constantly, even for experts, and we are constantly provided with new puzzles to solve from industry.

Peter: Absolutely. And how do we keep our knowledge up to scratch? By visiting key conferences, like the annual HPLC meeting. I always take a number of students and postdocs to the event – it's essential to get young scientists involved, and the culture for this group is particularly strong at EU meetings. And you also attend, Bob?

Bob: Of course! I always bring the research of both myself and the wider team. Given the coronavirus situation, I've implemented a chromatography journal club between our lab and further groups, and this has been great – almost better than a real conference at times! But the great thing about HPLC is the shared interests and opportunities to exchange innovative ideas. We should prevent ourselves from working on islands – so to speak – wherever possible, and bringing the community together is the best way to avoid this. This is especially the case with the crowd at HPLC, which consists of both HPLC technology specialists and specialist users, who apply the technique to specific application areas.

Peter: And these application areas are so diverse, from pharmaceuticals (where high-performance LC [HPLC] has a major role in safe drug development), to medical diagnosis, food quality and safety, industrial materials (such as polymers), and so on. In fact, our own research in multidimensional separations actually feeds right into these polymer applications; comprehensive 2D-LC contributes significantly to this field, and is now an indispensable tool.

Bob: Right, and on this front, development of retention modeling of LC separations to rapidly compute optimal method parameters for 2D-LC is surely one of the greatest breakthroughs in the field thus far?

Peter: Absolutely!

Bob: Well, that and unique couplings of different instruments. For example, using reaction modulation for nanoparticle characterization.

Peter: And let's not forget your own contributions to multidimensional separations, which now also encompass GC×GC.

Bob: Thanks, Peter – I'm flattered. Ultra-HPLC (UHPLC) has also been an indispensable tool in most of our 2D-LC research, both for high-resolution separations (dimension one) and for very fast separations (dimension two). Without UHPLC, 2D-LC would not be as powerful as it is today.

Peter: I couldn't agree more… But let's not forget where this all started some 50 years ago.

Fifty Years of HPLC

By František Švec, Department of Analytical Chemistry, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic

My first encounter with chromatography dates back more than 30 years. My first projects focused on the application of polymers in separation science by developing a classic format of stationary phase – beads. But this format was soon replaced by a new approach: monoliths, of which we knew very little at the time.

The monolith boom came in the 1990s, and has continued growing since. My current position, supported by the STARSS (Specialized Team for Advanced Research in Separation Science) project, is exceptionally well placed for applying subtleties of separation science, and particularly chromatography.

This project means not only conducting excellent research using high-end instrumentation, but also teaching our students and postdocs. They are the next generation to whom we will hand over the baton, expecting them to love chromatography just as we do, and to discover creative solutions to society's significant challenges, including environmental issues, food safety, affordable health care, and the development of drugs against new targets.

HPLC has developed significantly since its advent more than 50 years ago. Focusing just on the column technologies:

- 1966: Horvath and Lipsky used stationary phases with a particle size of around 50 µm packed in up to 275 cm long columns. The particle size has decreased ever since.
- 1990s: New columns format – monoliths – invented. Monoliths allowed HPLC separation at unprecedented speed – separating molecules as large as proteins in mere seconds.
- Today: Sub-2 µm particles are a current industry standard. Horvath's idea of pellicular beads has transformed to give today's core-shell particles. These developments have led to a significant increase in column efficiency, meaning excellent separations could be achieved with much shorter columns.
- Tomorrow: What can we expect to see in the future?
  - Even smaller particles? This would require chromatographic hardware capable of tolerating higher pressures and dealing with associated challenges.
  - Narrower columns? Perhaps, since narrower columns require smaller flow rates to achieve desired velocity, thus reducing consumption of the mobile phase and attempting "green" chromatography.
  - Micromachined columns? Using processes typical of microelectronics, the preparation of columns containing arrays of pillars in a channel are emerging.
  - 3D printing? I anticipate that columns will be produced this way. Early birds are already emerging on this front; printed monolithic columns will be designed in silico. However, high-resolution and rapid 3D printers are as of yet are unavailable.

Alongside column breakthroughs, detection methods have also taken impressive strides. The introduction of electrospray ionization to support MS by Fenn in the 1980s is a great example, and an essential breakthrough for the field of proteomics. Despite the availability of several approaches in the detection area, MS has become the most frequently used characterization technique for multistep analytical procedures. Significant improvements in MS instrumentation have been achieved in recent years, meaning spectrometers are both more accurate and more sensitive.

Yet, numerous sample preparation steps precede the chromatographic analysis. This area will remain a major target of studies for the foreseeable future, as the diversity of samples to be analyzed is close to infinite. Their preparation will require tailor-made, integrated, and high-throughput methods, alongside a decrease in both sample and instrument sizes, as well as automation, robotics, and multiplexing.

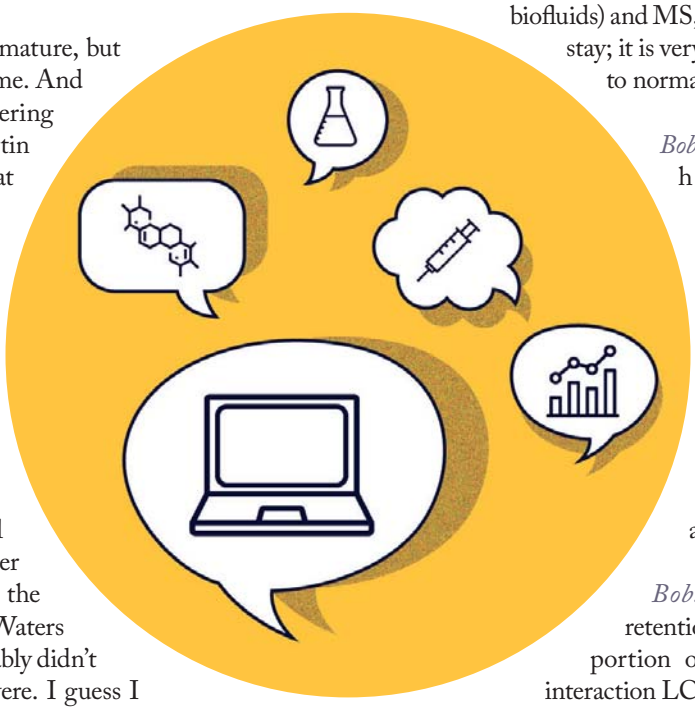
In short, there is much that must be achieved. Thus, the problems we face will not only keep us busy, but provide ongoing challenges for the next generations of analytical scientists and engineers.

"DECADES OF RESEARCH HAVE GONE INTO POSITIONING (RP)LC AS THE RELIABLE AND ROBUST TECHNIQUE WE KNOW TODAY."

Bob: Hey I've got a question: how old would you say LC is in "human years?"

Peter: 40 years.

Bob: Really? I'd say 30 – it's mature, but there's still much more to come. And it all started with the pioneering work of Nobel Laureates Martin and Synge, who showed that HPLC required small particles to compensate for the low diffusion coefficients of liquids. This requires some pressure to give a reasonable flow rate and led to a great debate of high-pressure versus high-performance LC.



Peter: I was in high school back then, but a few years later began performing HPLC in the lab myself. We had a few Waters (M6000) pumps, and I probably didn't appreciate how great they were. I guess I was spoiled from the beginning, and you'd need to ask people (even) older than me about the early ordeals. In any case though, the 1970s were a revolutionary time in LC – gradient elution was still a new concept, and so were chemically bonded phases. LC-MS was difficult, and we had multiple manual ways to integrate peaks, including a planimeter (a fabulous instrument), followed by cutting out and weighing the peaks after photocopying the recorder trace.

Bob: I read about those! All kinds of columns (stationary phases) and mobile-phase mixtures were tried with variable success. The development of chemically bonded phases was actually a major breakthrough. This culminated in a focus on non-polar octadecyl-silica (C18 or RP-18) phases and polar (water-based) eluents. This combination of polarities was opposite to the earliest HPLC studies (polar adsorbent and apolar mobile-phase), and thus became known as reversed-phase liquid chromatography (RPLC). The conventional normal-phase (or straight-phase) LC systems soon became an anomaly.

Peter: It's no wonder – RPLC has many advantages. It offers immense flexibility (fully miscible solvents ranging from water to tetrahydrofuran), high selectivity and efficiency, rapid column equilibration, compatibility with aqueous samples (including biofluids) and MS, and many more. RPLC is there to stay; it is very unlikely that LC will ever return to normality.

Bob: Indeed, and decades of research have gone into positioning (RP)LC as the reliable and robust technique we know today. Even before your first dive into HPLC in the 70s, great scientists like Huber, Kirkland, Knox, Giddings and Horvath first laid the foundations for the technique.

Peter: And let's not forget Guiochon and Snyder!

Bob: Of course! Today, alternate retention mechanisms steal only a small portion of the limelight. Hydrophilic-interaction LC is fashionable, but it is useful only for very polar analytes. Ion-exchange chromatography remains important for ionic compounds, size-exclusion chromatography for polymers, hydrophobic-interaction chromatography for the separation of intact proteins, and supercritical-fluid chromatography has made a bit of a comeback, especially for the separation of chiral compounds. All these techniques have their niches, but RPLC occupies most of the playing field.

My Life in HPLC

By Monika Dittmann

I worked at Agilent Technologies in Waldbronn, Germany, from August 1988 to November 2019 as a research scientist, specializing in HPLC, capillary electrophoresis and microfluidics. In this position I largely applied the fundamentals of separation science to the development of analytical instrumentation to serve as a consultant to the engineers (hardware, software and the like).

HPLC is the essential analytical technique used to develop and test drugs, test the safety of food, enable doping control, monitor the environment, and much more. Without HPLC, our modern life would be much less safe.

A number of breakthroughs have pushed the technique to this point: the application of high pressure (up to 400 bar) to LC some 40–50 years ago, which enabled the use of much smaller (5 µm) particles; development of reversed-phase stationary phases in the early 80s; the advent of ultra-high pressure instruments by Jorgenson in the late 90s; and the first commercial UHPLC instrument (Waters) in 2004 – others soon followed suit.

I am especially interested in modern UHPLC instruments – they are extremely versatile, and can be applied to almost any analytical problem. Over the past 15 years, we've witnessed vastly improved speed and resolution in these analyses, as well as those in LC×LC. Combined with MS detection, very challenging problems are now solved with relative ease, such as analysis of biological drugs. And, at present, it's believed that further increases in operational pressure or reduced particle size will have only marginal benefits.

Today, LC instruments are becoming increasingly usable by non-experts, and may eventually become a common commodity, like a TV or a car. This, of course, requires easy-to-use, smart instruments, improved diagnostic features and support in application areas. In line with my work, prediction and simulation of separations could lend support to application development and user training, but large databases of retention data are required – this is maybe best collected through an open-source project.

Open-source projects could also support us in overcoming current bottlenecks in research – particularly, method development and data analysis – that can be solved computationally and require close collaboration between analysts and computer scientists. This is already happening in some academic groups and companies. The coronavirus pandemic is clearly a testing time, but perhaps it has something to teach us about the true value of collaboration and data sharing to speed up progress – in LC and elsewhere.

Peter Schoenmakers (left) and Bob Pirok (center)

"WE NEED INTELLIGENT SOFTWARE TO COMBAT THE FACT THAT THE NUMBER OF LC INSTRUMENTS IS GROWING MUCH FASTER THAN THE NUMBER OF TRAINED SPECIALISTS."

Peter: Very true – and likely because of the continued input given to improving the various aspects of HPLC technology. An impressive development on this front has been open-tubular LC (OTLC). Fundamentally, OTLC is attractive, provided efficient columns can be made with diameters of 10 mm or (preferably) less. Poppe's group were among those that showed it was feasible, but the dynamic working range was grossly inadequate...

Bob: Which is why efforts in the field then mainly focused on effective, alternative packing materials, like monolithic columns and – eventually – pillar-array columns. Overall, packings have become much more efficient, reproducible and stable, and core-shell particles were developed to further enhance performance.

Peter: On the topic of enhancing performance, the advent of UHPLC spurred a major jump in technology and applications. With higher pressures, UHPLC allowed smaller (sub-2 µm)

particles to be used for very fast analysis, and also forced overall improvements in instrumentation. Like you said before, Bob, the technique is now...

Bob: Indispensable!

Peter: Yes, indispensable – and found in virtually every analytical lab today.

Bob: And what about the future?

Peter: First, we need to open the door to LC for non-specialists.

Bob: You said it. But this is – obviously – a major challenge for instrument and software manufacturers alike. We need intelligent software to combat the fact that the number of LC instruments is growing much faster than the number of trained specialists.

Peter: Plus, the expertise required is becoming increasingly complex. On one hand we require more expertise, but we cannot train experts at the rate at which they are needed. This dilemma we have to address with very smart artificial intelligence.

Bob: Smaller systems are also a priority. The volumes of organic solvents we use right now are too large, so that movement towards miniaturization is inevitable. Simpler, automated systems are also desirable, as you say, but in this case, we must sacrifice some efficiency for a selectivity benefit. Separation science must also move out of the lab to help protect against environmental issues and improve society.

Peter: I agree – just look at the coronavirus pandemic, for example. Separation science will surely play a pivotal role in finding a solution, just as it does in the monitoring of environmental pollutants.

Bob: Well, it's been great chatting, Peter. But it looks like it's time to get back to the lab!

Peter: Is that the time already? We should do this again sometime.

Bob: Absolutely.

SPECIAL SERIES
Advanced Clinical Analytics

ANALYTICAL SCIENCE *and* Patient Safety

Clinical scientists have the power to improve patient safety – and it's our job to help

Michael Schubert, Editor of The Pathologist, interviews Gareth McKeeman

WHAT IS YOUR ROLE IN THE LAB?

I'm a consultant clinical scientist specializing in clinical biochemistry. I work at a National Health Service (NHS) hospital laboratory within the Belfast Health and Social Care Trust. As a Clinical Scientist, I'm responsible for providing clinical and scientific leadership and oversight across different areas of clinical biochemistry, including the General Chemistry (Automation Laboratory) and Regional Immunoproteins lab. Clinical biochemistry is one of many disciplines within pathology, and incorporates a number of specialist areas, such as toxicology, pediatric metabolics and screening, endocrinology, and trace elements, as well as the two areas mentioned above.

There are three hospitals incorporated within my Trust. We have a general biochemistry (automated) lab across each of the three sites, set up as a hub-and-spoke model, with two smaller "hot" labs and a main site where regional services are based. We handle approximately 130,000 samples per month in our clinical biochemistry lab, and approximately 5,000 samples on a normal working day in the general biochemistry (automated) section.

We use variations of spectrophotometric analysis (endpoint and rate assays), electrochemistry (using ion-specific electrodes), immunoturbidimetry, and immunoassays (competitive and sandwich), as well as osmometry, electrophoresis, high-performance LC- and GC-MS, and inductively coupled plasma-tandem MS, to report on samples across primary and secondary care. One of my main roles is to ensure that appropriate methods are used, and that they are performed to the standards required for patient management. I must maintain insight into the common problems that can occur with such analyses to provide appropriate guidance to both laboratory staff and service users.

Many of the tasks we perform in the hospital laboratory focus on quality management and service monitoring and review. Daily internal quality control (IQC) monitoring is key, and we have different IQC regimes for different tests. In fact, our general automation lab produces up to 2,500 IQC data points per day – a significant amount of information for review. Development and implementation of software to assist with the collation and review of IQC data has significantly improved the process, allowing us to track and trend analyzer performance across all three lab sites.

Important components of this work include regular monitoring of potential differences in results for the same test across the lab network, assessing measurement uncertainty, and using a scientific approach to develop goals for acceptable performance for many of our quantitative tests (taking into account analytical performance, biological variation, and clinical need). We can also use the data we obtain to develop and review appropriate Westgard rules for IQC acceptance and rejection using sigma metrics methodology.

The validation and verification of new tests or equipment is another important task that requires assessment of assay precision, bias, and linearity to ensure tests meet performance targets. Once methods have been developed and introduced, we initiate appropriate quality assurance procedures, incorporating IQC and external monitoring. We also set key performance and assurance indicators, monitor them frequently, and perform regular audits to assess ongoing compliance against set standards.

WHAT DOES "PATIENT SAFETY" MEAN TO YOU?

Patient safety is an integral component of my job. Many of the strands of my work are linked to ensuring the ongoing provision of accurate patient test results, which are used to assess their general health, diagnose any disease or condition, and guide treatments. But I believe that there is much more to patient safety than oversight of the internal lab processes around sample analysis and producing results. As a laboratory medicine professional, when I think about patient safety, I think of the total testing pathway – that is, the complete sample journey from the patient's first appointment with the doctor to the final test result and its impact on treatment decisions. The lab has a role to play in every aspect of this pathway. It's up to us to ensure that all the steps in the sample journey are carried out correctly and in line with proper standards and guidelines. Each process carries a risk of error, so a key aspect of patient safety is continually reviewing and monitoring, and then taking steps to reduce risk and errors that would negatively affect the patient.

I feel that patient safety is also linked to patient experience. It's about making the patient feel that they have had a positive and effective experience – and increasing awareness of what goes on in pathology labs is part of that. I think a part of our role as laboratory medicine professionals is to consider what information we

"I am proud to work in a laboratory where many staff are engaged in safety and quality, working to deliver an effective laboratory service."

could provide to particular groups of patients to improve transparency and provide them with more ownership over the processes surrounding sample collection and result reporting, perhaps including the timelines involved. I believe that when service users feel calm and content with laboratory testing, we are enhancing patient safety.

HOW DO YOU CONTRIBUTE TO PATIENT SAFETY?

Much of the work we do in the lab has an important impact on the patient. I am proud to work in a laboratory where many staff are engaged in safety and quality, working to deliver an effective laboratory service. We senior lab professionals have to be willing to take responsibility for every result that is produced and reported. We must do everything we can to ensure that the result we report is accurate and reflects the clinical state of the patient at that time. My work contributes to patient safety on a daily basis. I provide oversight and leadership of the quality management processes within my work areas, which includes ensuring that we have appropriate policies and procedures – built on evidence-based standards – in place to support staff and provide guidance on all areas associated with the analysis and reporting of accurate test results. To maintain high levels of safe working practice, we make sure procedures are followed, reviewed, and updated on a regular basis as we evaluate the service and receive feedback. We also ensure that we have an accurate audit trail surrounding analysis and reporting of results. Ultimately, these practices are in place to promote safe

Top Tips for Improving Patient Safety

- Start talking! Meet clinicians, service users, and patients so that you can all learn from one another.
- Demystify the lab. Offer tours to colleagues, patients, and the public – and, if possible, tour your colleagues' spaces as well.
- Attend other departments' meetings when you can. This will give you insight into their patient safety needs and initiatives.
- Every step is vital! The total testing process begins before a sample reaches the lab and ends after it leaves – so make sure to consider the entire pathway.
- Find champions in other departments who can help implement and promote patient safety and experience improvement initiatives.
- Knowledge is power. If you can provide helpful information to others – whether clinicians, patients, or otherwise – it's your duty to do so.

working practices and to protect our patients.

Our laboratory is currently accredited under ISO15189 standards, many of which impact patient safety; part of my role is to review ongoing compliance. We have quality indicators that we set and review regularly, which include monitoring the time it takes us to report results for urgent medical tests and ensuring such results are reported within stated timeframes. We also have a systematic approach to reporting performance issues; we record them as occurrences (a failure to fulfil a requirement that has not led to a system failure) or as incidents (any event or circumstance that could have or did lead to harm, loss, or damage to people, property, environment, or reputation). Recently, our quality team and I have developed an improved system for logging and coding occurrences to allow for more robust tracking and root cause analysis. We've introduced new codes to capture data across the total testing process and empowered all staff to log occurrences and incidents. We review these regularly and have now started to trend them as involving human, mechanical, or external factors and discuss them at risk management meetings, where there is oversight from the senior lab and governance team. All of these endeavors allow our lab to proactively reduce risk by implementing appropriate corrective and preventative actions, making a significant contribution to patient safety overall. Ongoing staff training and engagement is a key element, so we're continuing to work on it by providing regular training and promoting open discussions about overall improvement.

I also liaise with clinical colleagues to provide guidance on test results; for example, assisting with the clinical interpretation of tests results by advising on what might cause a result to change, when this is significant, advice on further testing, and possible treatment. This layer of communication is particularly important when a new test is introduced, because my role involves developing relevant user information and ensuring all staff and clinical users have access to it so that they can accurately interpret results and follow up with patients. An important aspect of this liaison is meeting service users to review current services and to see where improvements can be made. Recently, we have piloted a small sample reception area within our emergency department (ED) where one of our medical laboratory scientists (MLSes) centrifuges and processes samples before sending them to the laboratory. The reception allows urgent samples to bypass the lab's busy sample acceptance area and go straight to analysis. We showed some improvements in result turnaround time but, more significantly, a reduction in the number of samples rejected due to preanalytical problems (such as hemolysis). I have also worked with a consultant cardiologist, ED consultant, and specialist chest nurses to develop and implement a new one-

"Having a robust quality management system in which all staff are engaged is important in any lab, but especially in the case of patient care."

hour chest pain pathway to improve triage of patients with suspected acute coronary syndrome, leading to faster discharge or referral.

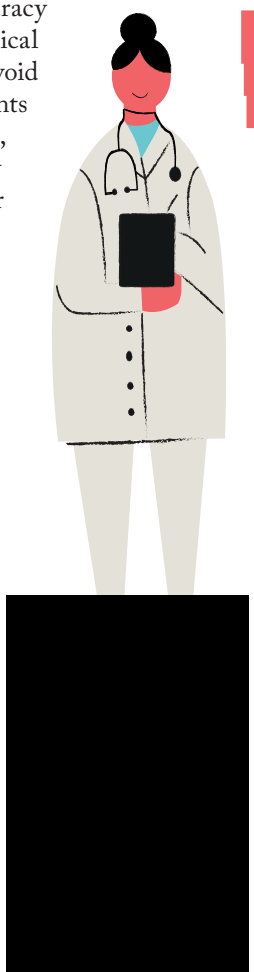
One of our recent projects has been a safety campaign promoting full labeling of patient and sample details. When all Blood Sciences samples have all the essential information, it allows escalation of critical results to the correct person or team and to ensure sample integrity and accuracy of reported results. Here, the onus is on the clinical staff taking the sample to get it right first time to avoid inappropriate sample rejection. Such improvements have a significant impact on patient safety. Overall, other senior lab professionals and I constantly review and monitor the services we provide within our governance and management structures, which all work together to enhance patient safety.

HOW CAN OTHER ANALYTICAL SCIENTISTS CONTRIBUTE TO PATIENT SAFETY, AND TO PATIENT CARE IN GENERAL?

We must ensure that all analyses undertaken in the hospital laboratory are performed to a high standard, taking into account the clinical need for each result and how it is used to guide the patient's journey. Having a robust quality management system in which all staff are engaged is important in any lab, but especially in the case of patient care.

Research and development are also linked to improving patient safety. The development of new and improved markers for assessing different biochemical functions and translating those markers into laboratory tests is important. We can also have a positive impact by developing improved analytical methods for current tests, or by automating them to enhance capability and throughput. That way, we contribute to service improvements that can expedite the clinical decision-making process.

There have been significant developments in MS technologies in recent years, including the ability to automate different aspects of sample processing, allowing the introduction of improved methods for biochemistry tests (for instance, hormone or vitamin D tests) into the routine clinical laboratory. It is important that analytical methods continue to evolve – especially for tests that currently use only spectrophotometric methods, which are affected by known interferences (for instance, by certain medications). As new drugs and compounds proliferate, studying potential interferences with existing assays is a key aspect of ensuring patient safety; analytical research and development must continually evolve to improve medical testing.



HOW DO YOU SEE THE INTERACTION BETWEEN ANALYTICAL AND MEDICAL SCIENCES GOING FORWARD?

It is important that we continue to maintain close links and learn together. Clinical labs need to continually review their test repertoire and the services they provide in line with new evidence-based guidelines. They must also increase their visibility to both medical colleagues and other service users to highlight the services they can provide – for instance, information on analytical platforms and laboratory methods and experience with specific methodologies.

Laboratory professionals should be included in clinical discussions and reviews of patient care pathways that involve laboratory testing, so that they can provide scientific input into the best available test methods and how to most efficiently implement them.

There is now an increasing focus on "big data" and how we can better use the information we generate to improve healthcare. To transform

patient services, clinical and scientific leadership is vital – and a key aspect is linking laboratory data and test results to patient outcomes.

Clinical hospital laboratories must also provide feedback to assay manufacturers about test performance and identify tests that need improvement – particularly with respect to assay sensitivity and interference. We must foster research and development opportunities with industry to improve point-of-care and remote testing technologies that can safely enhance patient care. This is where senior laboratory leaders must be involved. And we must nurture interactions between analytical and medical sciences. The next few years are likely to bring many challenges, particularly with respect to COVID-19 testing, tracking, and monitoring, and it has never been more important to establish connections between our disciplines as we work together to improve patient care.

DO YOU INTERACT WITH PATIENTS?

As part of Patient Safety Week 2020, I was privileged to be involved in developing a podcast that features a conversation between a laboratorian (me) and a patient. We discuss what blood testing means for a patient in treatment for cancer, explore their thoughts around laboratory medicine, and discuss pathology services to highlight the crucial role they play in the patient journey. It has been interesting to hear what really matters to a patient when it comes to blood testing – it's not all about the speed of result reporting, like I had assumed. The main message that came from this conversation is the need for more patient information about what happens to their samples, the lab processes that lead to a result, and some of the common errors. For example, the patient I spoke to had never realized that a hemolyzed sample could result from sample collection or preanalytical handling errors. They had wrongly assumed that it was something to do with them – something they had done or something wrong with them – and this caused anxiety when they were asked to return for a repeat blood sample. And that's an important message for those of us who work in pathology labs. How may our lab reports be interpreted in the absence of appropriate explanations?

I believe we have an important role in providing useful information to patient groups to increase knowledge about the processes within the sample journey and what can affect the results to reduce anxiety. This conversation has also highlighted

"We laboratory professionals have a role to play in reducing some stresses and fears about changing numbers – perhaps by providing better information about expected levels of variation in test results."

how much our work means to a patient whose results are used to guide treatment. It was fascinating to hear that some patients focus a lot on numbers and, when a result for an important test (such as a tumor marker) changes, it can cause a lot of stress even if it never leaves the reference range. In the laboratory, we may not pay attention to small variations in results, because we know that there is a level of uncertainty associated with all of our tests. However, it is important for us to realize that a patient may not have this same level of insight. The key message I have taken from this discussion is that we laboratory professionals have a role to play in reducing some stresses and fears about changing numbers – perhaps by providing better information about expected levels of variation in test results.

I believe it is important for laboratories to increase their visibility and transparency to improve the links between the lab and the patient. We need to raise awareness of the laboratory and promote our role in the patient journey – and that means we need to understand what matters to the patient. Our local Trust now emphasizes Personal and Public Involvement (PPI) initiatives in which service users, caregivers, and the general public get involved in service design and development. For instance, some colleagues and I have invited patients from a cancer services PPI group to visit the labs and work with us on developing an information sheet for cancer patients that will provide useful information on blood sampling and testing. I would recommend other labs develop links with patients and use them to promote pathology, improve the patient experience, and enhance patient safety.

It's important for labs to improve visibility to clinical users and colleagues as well. We have held lab open days for doctors and nurses in the past, and these have been successful in building links, sharing experiences, and coming up with ideas for improvement. To affect patient safety, we need to meet other teams and seek feedback from our users. A key part of this is ensuring that the laboratory is considered in changes to patient services and represented during investigations into incidents and serious events. Too often, we are only included at the final stages – if at all – despite the fact that seeking our feedback can have an important impact on improvements to patient safety. Our pathology labs have a good safety culture and our staff feel able to report errors without blame. This openness needs to be continually encouraged as part of daily practice – and especially when staff change over time.

One final important element is to talk to all staff in pathology labs who handle samples and encourage them to consider the

"We know that errors in these processes can significantly impact the quality of the reported result and, ultimately, patient safety."

patient at the end of the sample. We have a dedicated team of MLSes in our Blood Sciences sample reception who work hard receipting and processing samples for analysis. Within clinical biochemistry, we have a number of logic rules set up to hold or release results once they have been analyzed and evaluated. The majority of these results are within normal reference limits and are released automatically or auto-validated to allow quick lookup by clinicians. And so for a significant number of samples, our MLSes are the only people interacting (indirectly) with the patient and assisting them on their journey. It is important for staff to hear this. They are in a privileged position and, hopefully, by telling all staff what happens to the results once they have completed their work, we can remind them how important their job is and how essential it is to follow all procedures and policies.

WHAT ADVICE DO YOU HAVE ON IMPROVING PATIENT SAFETY?

Go out and meet clinicians and service users (and patient groups, if possible) and learn from each other. My involvement in quality improvement work has been a useful way to network with other colleagues in the hospitals where our labs are based, and has led to projects with an emphasis on patient safety. We have also given lab tours to staff from the ED and the neonatal unit and, in turn, toured their areas. Such networking has improved the link between lab and patient by allowing us all to see the challenges at both ends of the sample journey. It's important to see how our processes impact patients, especially if we want to make service changes.

It's also good to see what other hospital sites and labs are doing around patient safety by attending relevant meetings. I also invite external speakers to provide talks on interesting cases, improvement work, and lessons learned from past incidents.

Developing effective networks and teams is vital. It's also important to consider the total testing pathway – especially preanalytical processes. We know that errors in these processes can significantly impact the quality of the reported result and, ultimately, patient safety. It is very difficult for us to make and enforce changes to the processes before a sample reaches us. We must find local champions working at the frontline who can implement and continually promote improvement initiatives to their colleagues. This point was particularly apparent during the implementation of our new chest pain pathway; the specialist chest pain nursing team played an instrumental role in training and updating ED staff to ensure that everyone was aware of – and used – the pathway.

Overall, remember that knowledge is paramount. Providing a little information to patients about what happens to their samples – and what goes on behind the lab doors while they are sitting in the ED or clinic waiting for important test results to come back – can have a huge positive impact on their experience and can reduce their fears. It's within our power to improve not only patient safety, but also the patient experience – and I believe it's our duty to do everything we can.

Gareth McKeeman is a Consultant Clinical Scientist at Belfast Health and Social Care Trust, Belfast, UK. The Pathologist (www.thepathologist.com) is a sister magazine of The Analytical Scientist.

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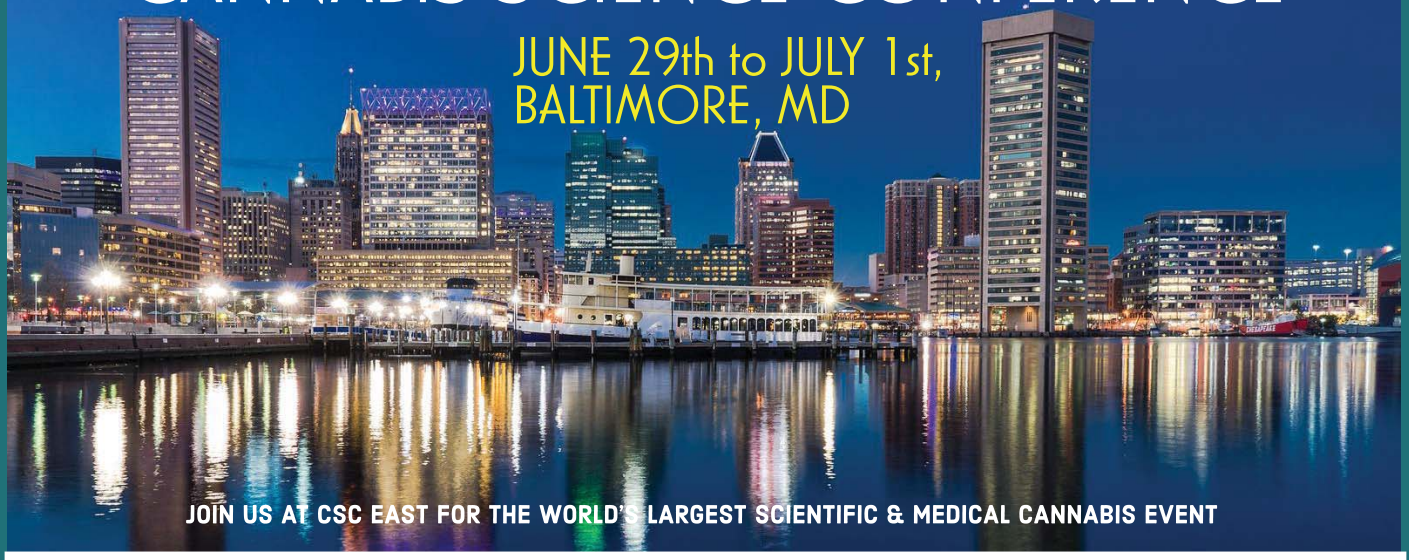

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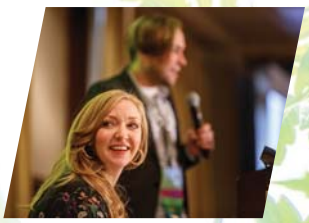

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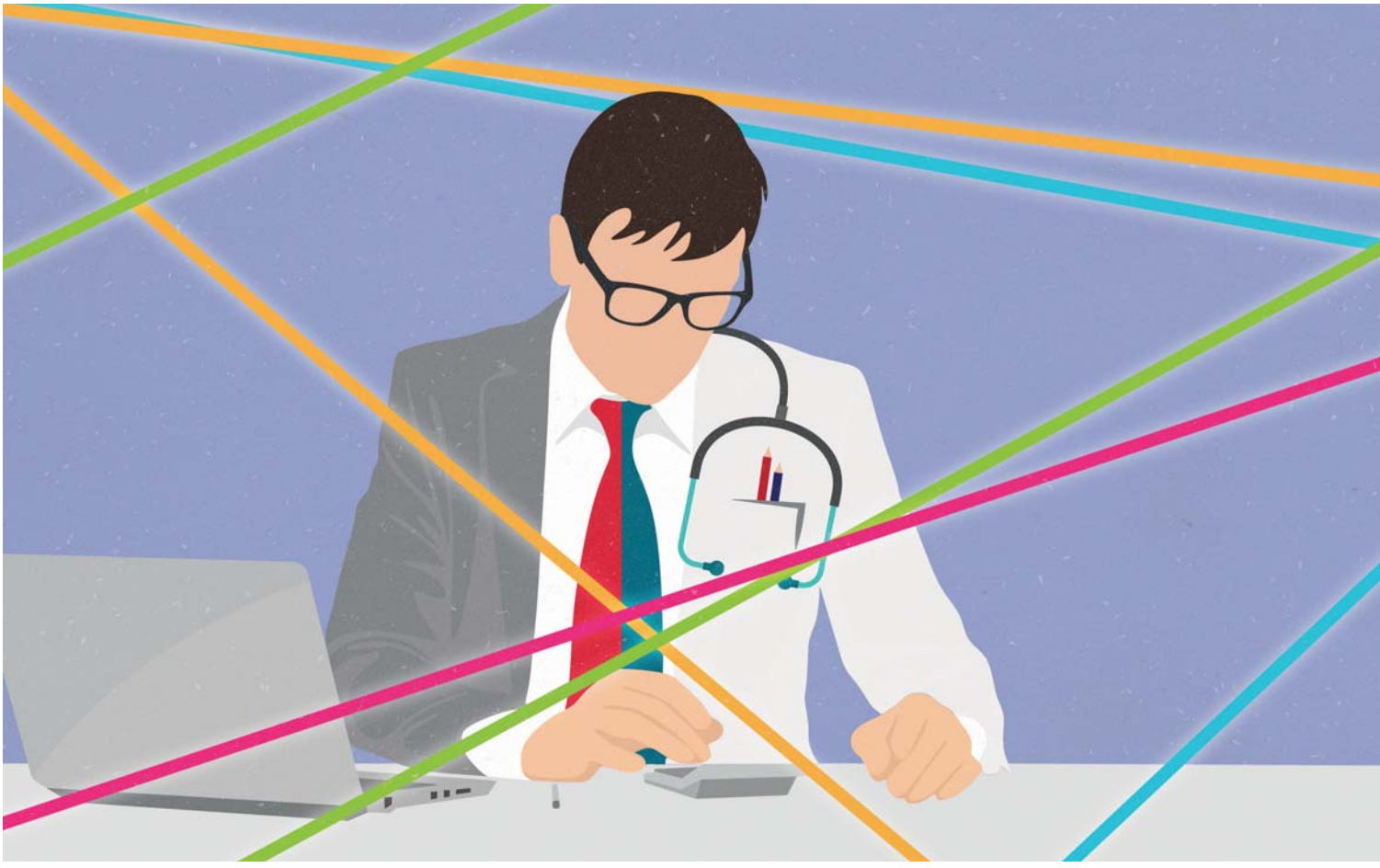

Swapping Optical Benches for Boardrooms

Transitioning from research spectroscopy into the business world can be a daunting prospect – here I offer some tips from my journey with Innovative Photonic Solutions to help you on your way

By Scott Rudder, co-founder and VP Sales and Marketing, Innovative Photonic Solutions, New Jersey, USA

Discussions of business and entrepreneurship are not all that common in the scientific field. Like many of you, I dreamed of starting my own business, but was afraid to quit my stable job to "take the leap" into start something of my own from scratch. To most analytical thinkers, it's a scary concept to make such a big change in our lives, I guess most people in our field are largely risk averse, and – despite their great ideas and clear talent – are hesitant to take the plunge without some sort of guidance. As it stands (at least in my own experience), career scientists are often not given the appropriate skills to traverse easily into the world of entrepreneurship. When kickstarting a business, there are a number of questions you should consider…

Jump – don't step!

Sometimes it is easier to explain a concept with a metaphor… That's the purpose of this section's title. When starting a business, it is important to recognize that the founder needs to "jump out of a window" – they need to commit themselves fully to their plan. They cannot "step-out" carefully – stepping out of the window allows for reflection, and fear and doubt can creep in. It is impossible to fully commit to a path when you have a safe alternative to retreat to when times get tough (which they inevitably will). The key point in this metaphor is that an entrepreneur needs to take a leap of faith – jump out of a window – but this is not done

blindly. The entrepreneur needs to "know what floor they are on before they jump." Just how risky is this business opportunity? Is it a leap out of a first or second floor window? Or is it a bigger risk – a leap from a higher floor. This refers to a more challenging business plan that requires a lot of capital investment to be successful. In this case, you need a parachute, by which I mean investors are needed to help you mitigate the risk of the fall. No matter the plan, however, the entrepreneur needs to take the jump out of the window in order to be successful!

Is my idea the right one?

Step one in any business plan is to decide on the product or service you will be providing. Once you understand this basic requirement and expose it to entirely different views from peers, it can open the door to untold opportunities for the analytical community. I think this question can be particularly tricky to answer for us analytical thinkers.

My business training came from my time in the army. I worked for the United States army for 12 years or so, and my boss at the time sent me to business school, where I was exposed to lots of professionals with financial backgrounds and incredible worldviews. These people seemed to speak a completely different language to that I was used to, and I learned a lot about myself through mixing with them. The biggest lesson I learned there: there's not always one answer to a question, there are many, and each is right for completely different reasons. Be sure to speak with people from both engineering and science – as well as finance and marketing or sales backgrounds – to truly understand the different ways that your business plan could be successful – then pick the one that suits your exit strategy.

"No matter what exit strategy you decide to adopt, it should be a main priority in your business plan. You're much more likely to get to where you need to be if you mold your strategy around that endpoint from the beginning."

What do I want to get out of it?

When starting a business, you should know exactly what your exit plan is: will you run the business for the foreseeable future, would you like to sell it once you reach a certain stage, or would you like to take the company public? It is important to define your exit strategy when starting a business, because this decision will drive the way the business is organized and managed. For example, it makes no sense to try to raise capital from an investor if there is no plan to ever sell the business. Furthermore, the type of corporation you establish (S-Corp, C-Corp, LLC., etc.) needs to align with your exit plans in order to minimize both tax consequences and paperwork issues in the future. If you'd like to take your company public, then you'd best prepare for this far in advance; you'll need at least three years' worth of books to successfully pass a financial audit. Ultimately, no matter what exit strategy you decide to adopt, it should be a main priority in your business plan. You're much more likely to get to where you need to be if you mold your strategy around that endpoint from the beginning. In some ways, defining and documenting the exit strategy when you start the business is more important than the idea itself.

Who should I go into business with? "The rule of three"

That's up to you! But one thing I will say is that I think it's important to go into business with a minimum of three people (yourself included) – something

I call my "rule of three." It's important that the three of you have differing mindsets that work well together to avoid mistakes in key decisions, and if one of you has to take a step back for a short while or has a difficult day, then you have two close partners who can support you and continue dealing with important affairs. This emotional support is just as important as the business knowledge itself – there will always be difficult days, and it means a great deal to have somebody there to reassure you that everything will be okay.

"From the beginning to the end, the business plan is one of your most valuable resources. Think of it as a living document – it must evolve constantly, both with yourself and the business."

In addition to the three business founders, you also need a board of directors to help guide the business. I believe that there should once again be a minimum of three members on the initial board of directors. This assures that there are others with which to socialize ideas, and that there are no "ties" when difficult decisions need to be made.

Where can I obtain financial support for my business?

Larger ideas require access to venture or investment capital. Smaller ideas, however, can be "boot-strapped" and self-funded. But what is the difference between "small" and "big" idea? This is an integrally financial question. Many in our community would think that an investment of $250,000 to $1M would be a large sum, but this is far too small of a figure to be of interest to a venture capital or private equity firm – and even most Angel investors would not express interest. Realistically, you must be looking to raise figures of $10 million or higher to interest the commercial investment community.

So, what do you do if your idea just isn't that big? You "boot-strap" the company, of course. In this case, each of the founders put in their own money and search for a company that would be willing to put up some small investment in your firm in exchange for first mover advantage and equity.

When my partners and I started Innovative Photonic Solutions (IPS), we put our own money into the company, and we identified a commercial partner who supplied some equipment and a small amount of money in exchange for access to the product and a small equity stake. We had no safety net whatsoever, and we didn't take salary for around nine months – but we had our first customer! In terms of investment, we took the smallest amount of angel investment we probably could to keep us going at the start. It took a year and a half or so for us to become financially stable and stop worrying about making our own payroll, and the rest, as they say, is "history!"

How important is my business plan?

From the beginning to the end, the business plan is one of your most valuable resources. Think of it as a living document – it must evolve constantly, both with yourself and the business. Use it to continuously check whether or not you are on track for your original (or adapted) aims, and adjust your approach accordingly. It is important to recognize that your business plan can change… But these changes should be conscious, not fallen into. If, upon periodic review, you find that you have strayed from the original plan, try not to worry too much. Compare the new plan with the original, and decide which is better and correct your strategy. Sometimes your new path may be better than the original – but it's important that you constantly reassess if this is the case.

In the case of our business, I was on a skiing holiday when I suddenly realized that there was a

huge problem with our current business plan – the time that we had projected for adoption of our technology into the market was not at all realistic. The customer base was going to take longer to develop than we anticipated; by the time the customers were ready to adopt our idea, there would likely be a fair amount of competition and we would have run out of funding. We adjusted our plan by focusing in on a smaller market. That allowed us to target buyers with an immediate need more effectively, and our new product offering was much less price-sensitive than we had initially envisioned. Ultimately, the business changed direction toward a smaller opportunity, but we survived, whereas we might well have perished if we stuck to the original plan.

When should I sell the business?

It depends! In our case, we sold IPS to Metrohm two years ago, almost 14 years after starting up. In that intervening period, I learned that the exit is less about the money offered, and more about the culture match between the acquirer and the acquiree. You must consider carefully at this stage exactly to whom you are going to sell your company; there's no point making a lot of money if an overly demanding company takes over and makes your life miserable. No amount of money is worth that. For this reason (any many others), it's important that you choose your "dance partner" wisely – you will likely be required to stay on and help with the transition for quite a while, and you might as well be happy during that period!

Give yourself "real options" and "date around"!

When faced with difficult decisions, analytical thinkers often go with the lower-risk option, which can seriously limit (and frequently eliminate) the upside potential of an opportunity. In this situation, you need a "real option" to take a risk and allow yourself to say YES! People often deprive themselves of this option. For example, you see a job listing that sounds interesting, but before applying you complete a list of potential negatives (bad location, poor money, and so on) and never apply for the position – you never really had a decision to make in this example, as you said NO to the job before it was even offered. Instead, you should allow yourself the option to say YES. This concept is critical when starting your own venture; you need to leave all possible options available in order to choose the best fit.

My final piece of advice I often share is to "date around." Involve yourself in many different types of technologies or business before committing to one – find out what you don't like. And, like with dating, avoid what you already know is not a good fit for your personality or goals.

I urge you to "jump out of the window." Entrepreneurship is exciting and rewarding. If you can overcome the barrier of fear of "falling," you can open the doors to untold opportunity for yourself and your colleagues.

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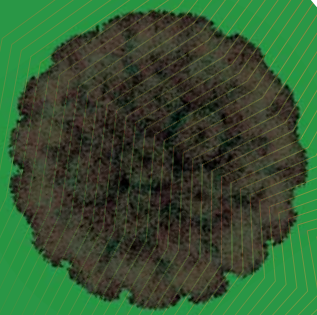

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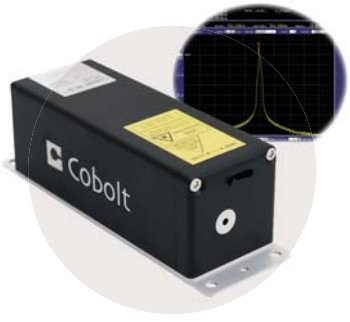

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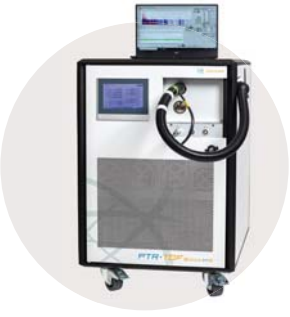

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Blurring the Boundaries

Sitting Down With … Caroline West, Associate Professor at the Institut de Chimie Organique et Analytique, Université d'Orléans, France

Why did you gravitate towards analytical science?

I initially wanted to work in forensics, but analytical chemistry soon drew my attention. Even if you specialize in just one technique, there are so many different applications areas that you could never grow tired of it.

When students are considering analytical chemistry, I'll try to convince them by saying: "Whatever your personal interests or drive – whether it is sports, health or the environment – there is something for everyone!"

What first drew you to supercritical fluid chromatography (SFC)?

More chance than anything. I completed my PhD in SFC, but knew little about it when starting my studies. It was exciting to explore such an "unknown." Today, I tell my students that SFC is a technique worth learning purely because of its complexity – there are so many optimization parameters and unusual effects. If you take the time to learn SFC, it's going to be beneficial to your understanding of any other separation method.

In terms of added value to analytical science, the relevance of SFC at the preparative scale has been recognized for about 20 years – especially for chiral separations in the pharmaceutical industry – because of its economic and ecological advantages. But where SFC comes into its own is its ability to complement other techniques. For example, in drug impurity profiling, you want to make sure that you visualize all components of the sample. If you use just one method, you may miss something important. Orthogonal methods like SFC shine for such applications.

Why is Orleans such a great environment for SFC?

Orleans is in the "French cosmetics valley." There are plenty of big names around us, such as LVMH Research, who's most famous brand is probably Dior, meaning that our institute is involved in cosmetics research, as well as in therapeutics and diagnostic innovations. For my part, I am mostly involved in pharmaceutical analysis, especially with Servier, a French pharmaceutical company. I've been fortunate to work with people who are very open to new ideas in this space, and are willing to share their experiences. And that allows us to tailor methods to optimize their success. Cosmetics are also less tightly regulated than the pharmaceutical industry, so it's often easier to get new techniques accepted.

How has analytical science changed over the last few decades?

People have become increasingly aware that they need analytical scientists. How "good" is the food they eat? What's the quality of their tap water? How pure is the air they're breathing? All in all, it's a great time to be an analytical scientist! Other scientists are now starting to realize our potential in their own projects, which encompasses a huge amount of effort in areas such as method development. Knowledge of these complexities is really changing the way our field is viewed.

Another key change is the increasing amount of data generated by the analytical sciences. Data analysis has become an essential part of the analytical process, making huge progress over the last 10 years. Our methods are more powerful – because we can do things faster and in multiple dimensions – and we are able to compare huge numbers of samples, each with massive amounts of data, with relative ease.

What's in the future for SFC?

I've mostly worked with chemicals and small molecules so far, but we are moving slowly towards biological molecules. This shift brings many more unknowns that I'm excited to explore.

"[SFC] is changing the way we operate by opening the doors to new applications."

Old perceptions of SFC are no longer valid. We are beginning to blur the boundaries between different techniques – performing experiments with wide gradients that start in SFC conditions and end in high-performance LC. The future of SFC is constantly evolving. Strictly speaking, the name "supercritical fluid chromatography" may no longer apply, but I'm not concerned about the name. The important thing is that it's changing the way we operate by opening the doors to new applications.

What are your interests outside the realm of SFC?

Something I'm working on currently – and which probably matters the most to me – is helping to improve the integration of disabled students in university. In 2005, President Chirac introduced a law encouraging the integration of disabled children into French schools. Since then, the number of students with disabilities entering university has been growing exponentially.

In my opinion, we aren't as prepared as we could be. As well as physical disabilities, we also need to learn how to properly approach psychological disabilities and other neurodevelopmental disorders. We need to discover how best to teach these students and encourage universities to better adapt because it would be beneficial to all. It's a big task, but it's an area I'm passionate about and learning a lot from.

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