JUNE 2020 # 88

the Analytical Scientist™

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Ice cores tell the tale of human history – and our shifting climate.

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Redistributing the Power (List)

Analytical chemistry supercharges science across the globe – a fact we want to celebrate with our 2020 Power List

Nominations for The Analytical Scientist Power List 2020 are now open – and, not for the first time, we've added a twist. In short, we want to take you on an analytical tour of the globe: "Around the World in 70 Analysts."

Please forgive the conspicuous paraphrasing of Phileas Fogg's fictitious 80-day journey; you see, we want to share the stories of 10 leading scientists from each of our planet's major continents. And yes, that includes Antarctica (ambitious, we know, but it felt wrong to exclude any colleagues working at the South Pole!)

In previous years, the Lists have been heavily skewed towards a certain demographic – and readers have (rightly) not hesitated to point out the inequality. The disparity is a symptom of wider societal issues – brought into sharp focus by unfolding events in the USA. The field of chemistry is just one lens through which to view all-pervasive inequity. An RSC article exploring the data behind the Nobel prizes paints a vivid picture of the problem (1): "The average chemistry Nobel laureate is an American man, probably called Richard, John or Paul. He is 57 or 58 years old and works at an institution in California (UC, Stanford or Caltech)."

Other facts: only five of the 183 winners of the Nobel Prize in Chemistry have been women, and no Nobel prize winners in any science have been black.

We hope that the fresh format of this year's List will allow us to celebrate more diversity than ever before. And, in that spirit, we hope you will consider the great and the good across the globe when submitting your nominations. Likewise, please don't forget your colleagues in industry.

To nominate an analytical scientist who is making a real difference, please complete the short form at https://bit.ly/2LMntTR. And if you've not already guessed from the (daring) inclusion of Antarctica, the nominees' place of work rather than place of birth will determine th continent represented.

I sincerely look forward to browsing through your nomination comments before handing the list over to our judging panel. As always, I am available at matthew.hallam@texerepublishing.com should you have any questions – or suggestions – ahead of publication in October.

Matthew Hallam
Editor

Reference

1. *RSC, "The data behind the Nobel prizes" (2019). Available at: https://bit.ly/3bVoL9w*

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The view from the Cole Gnifetti glacier in the European Alps, where Paul Mayewski and his team conducted their extensive work in ice core analysis

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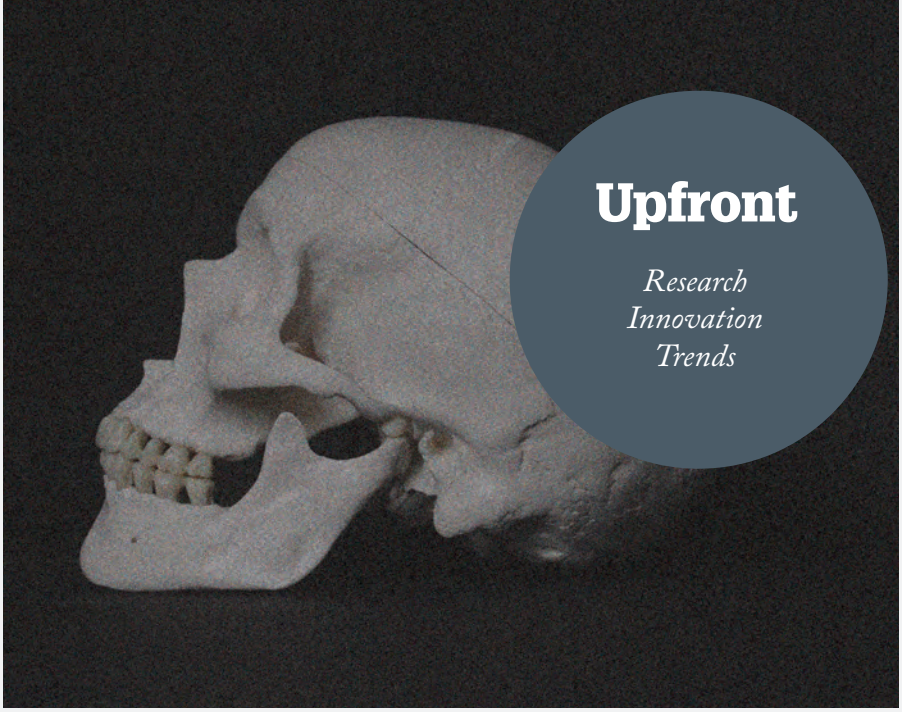


Clues from a Watery Grave

Bone proteomics could help investigators get to the bottom of drowning deaths

An estimated 320,000 deaths are caused by drowning each year (1), and determining the length of time a body has been underwater – the post-mortem submerged interval (PMSI) – can provide vital evidence in a forensic investigation. Unfortunately, current methods for estimating the PMSI – such as examining the decomposition stage of a corpse – require an almost-complete cadaver and are drastically influenced by the aquatic environment in which the body is found.

Though bone proteins have previously been studied for their use in estimating the post-mortem interval in terrestrial environments, Noemi Procopio and her colleagues at Northumbria University are the first to apply these forensic proteomic principles to bodies submerged in water (2).

The researchers examined whether four different types of water – tap water, saltwater, pond water or chlorinated water – affected the proteome of mouse bones. After a PMSI of 1 or 3 weeks, the team collected the mouse tibias and extracted proteins from the bone mineral matrix. These proteins were then enzymatically fragmented into peptides and separated using high-performance LC. MS analysis revealed the identity of the proteins, as well as their relative abundance in the sample.

"We found that different aquatic environments do not affect the proteomic result, meaning forensic proteomics has the potential to be applied to the unexplored field of aquatic decomposition with relative ease," says Procopio. Importantly, the team also identified novel biomarker candidates that could be used for estimating PMSI and the type of water environment a body was submerged in. For example, a protein called fetuin-A was more likely to undergo deamidation in pond water, which could help investigators determine whether a body was once submerged in pond water and later moved.

Further validation using human remains is needed before these findings can be applied to real forensic cases, but the team is hopeful about future applications. "I would like to explore the effects that temperature has on the proteome of submerged cadavers and look at other intrinsic variables, such as age and body size," says Procopio. "The more variables we can exclude as having an effect, the more applicable these results will be to real forensic scenarios."

References

1. *WHO (2020). Available at: https://bit.ly/2Wm2vRB*
2. *H Mizukami et al., J. Proteome Res. (2020) 19, 2122–2135. DOI: 10.1021/acs.jproteome.0c00060*

INFOGRAPHIC

Nobel Numbers

We break down the stats behind the most highly-acclaimed prize in science

Around the world

Top **3** countries with the most Nobel Laureates in Chemistry

(based on where they were working at the time)

USA: 76

Germany: 31

UK: 28

Age is just a number

97

The oldest person to receive a Nobel prize in Chemistry (and all categories) was John B Gooedenough in 2019

35

The youngest person to receive a Nobel prize in Chemistry was Frédéric Joliot-Curie in 1935 for the discovery of radioactivity

BUSINESS IN BRIEF

A round-up of this month's business news, from the world's most powerful NMR to continued COVID-19 testing

- Bruker has installed the world's most powerful commercial nuclear magnetic resonance spectrometer at the University of Florence's CERM research center. The 1.2 GHz NMR has a new magnet design that combines high- and low-temperature superconductors. CERM will use the NMR to study the structure and function of proteins, including those of SARS-CoV-2 (1).
- The FDA has provided Emergency Use Authorization to EUROIMMUN's (a PerkinElmer Company) Anti-SARS-CoV-2 ELISA (IgG) serology test; specific clinical laboratories will be able to use the ELISA test immediately for COVID-19 testing (2).
- In a bid to support global COVID-19 research, Thermo Fisher Scientific has announced it will provide 50 Ion Torrent Genexus Systems at a reduced price for research consortia and industry groups focused on mapping coronavirus spread and epidemiology (3).
- Renishaw has launched a new Raman system for forensic analysis: the inVia InSpect confocal microscope. Optimized for trace evidence analysis, it can be used to analyze samples that cannot be examined fully using other techniques or to obtain more detailed chemical information (4).
- The US Department of Homeland Security, Customs and Border Protection, has selected JEOL AccuTOF-DART mass spectrometers for five of its labs; the instruments provide a non-destructive, rapid method for analyzing forensic samples in real time, enhancing the current capabilities of the federal labs.

References

1. *Bruker (2020). Available at: https://bit.ly/2XowebQ*
2. *PerkinElmer (2020). Available at: https://bit.ly/2WVNWER*
3. *Thermo Fisher Scientific (2020). Available at: https://bit.ly/2LQeQHH*
4. *Renishaw (2020). Available at: https://bit.ly/36tmPnK*

Battle of the Bronze Age

Unraveling encounters on bygone battlefields with fencing (and X-rays)

Researching historical combat is no simple task, but the Bronze Age Combat Project is making a good stab at it by investigating markings borne by prehistoric swords.

Their first port of call? Casting modern-day replicas of excavated weapons. Compositional analysis using scanning electron microscopy with energy-dispersive X-ray spectroscopy (SEM-EDX) was then used to demonstrate negligible alloy content deviation between artefacts and replicas; metallography and microhardness testing provided further confirmation.

Next: combat tests based on a 15th century fencing manual followed by painstaking microscopic analysis of use-related marks left on the archeological swords. Of the 23 marks observed, 14 were recreated on the replica swords through testing. "Some can be linked to specific combat actions or weapon encounters, such as sword versus spear," says principal investigator Andrea Dolfini. "This gives us first-hand insight into Bronze Age fencing styles." Let battle commence!

Reference

1. *R Hermann et al, J Archaeol Method Theory (2020). DOI: 10.1007/s10816-020-09451-0*

Where are all the women?

Of the **183** individuals to win a prize in Chemistry, only **5** have been women:

1911: Marie Curie (unshared)
1935: Irène Joliot-Curie
1964: Dorothy Crowfoot Hodgkin
2009: Ada Yonath
2018: Frances Arnold

An analytical perspective

Not many prizes have been awarded for contributions specific to analytical chemistry, as it forms parts of many other disciplines, but there have been a few:

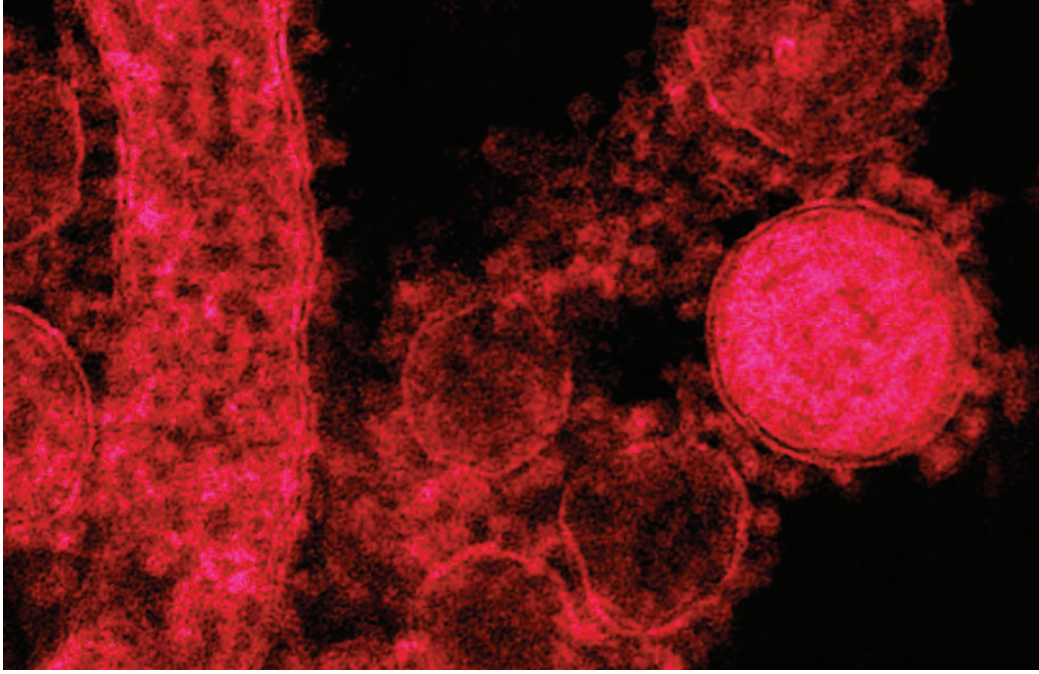
1923: Fritz Pregl for the development of organic microanalysis

1959: Jaroslav Heyrovsky for developing polargraphic methods of analysis

1926: The Svedburg, who developed ultracentrifugation, for his work on "disperse systems"

1948: Arne Tiselius for his research on electrophoresis and adsorption analysis, which demonstrated the complex nature of blood proteins

1952: Archer JP Martin and Richard LM Synge for their invention of partition chromatography



Joining the Fight

Analytical science's journey towards effective COVID-19 testing and treatment

A Point-of-Care Approach

Merlin Breuning (Notre Dame) and Jacqueline Linnes (Purdue) are working with their teams to develop methods for rapidly quantifying the COVID-19 immune response using novel lateral flow assay devices. The proposed devices will give high sensitivity and semiquantitative measurement of antibody levels. Why? To give inexpensive, point-of-care tests that make use of innovative membrane immobilization technology and thin-strip, microfluidic diagnostic devices.

National COVID-19 Institute?

The National Cancer Institute (NCI) is taking a three-pronged approach to supporting the fight against COVID-19: validation of serological tests, discovery of genetic elements of disease susceptibility, and screening of covalent inhibitors of SARS-CoV-2 proteinases (1). Their testing validation initiative – coordinated with the FDA, CDC and NIAID, as well as several academic centers – aims to supercharge serological testing, a crucial tool for identifying those who have been infected.

Neutralizing the Threat

Researchers from Utrecht University, the Erasmus Medical Center, and Harbour BioMed have identified a human monoclonal antibody (47D11) capable of preventing SARS-CoV-2 infection of cultured cells (2). How? By targeting the S1B receptor-binding domain of the trimeric spike glycoproteins that mediate viral cell infiltration. The observation of cross-reactivity with SARS-CoV – a spike protein with 77.5 percent amino acid sequence similarity – indicates 47D11 targeting of a conserved domain, which may offer a route to treating COVID-19…

MS Investigates

The team of David Clemmer and Martin Jarrold are employing charge-detection MS (CDMS) and ion-mobility MS (IMS) to explore the structure of developmental COVID-19 vaccines and therapies. It is hoped that these tools will allow direct-mass measurement of inactivated viruses, as well as "dummy" virus particles, bioconjugates containing immunogens, antibody-antigen complexes, and other targets. CDMS in particular should allow researchers across academia, industry and government to rapidly address challenging measurement issues encountered in the race to produce a vaccine.

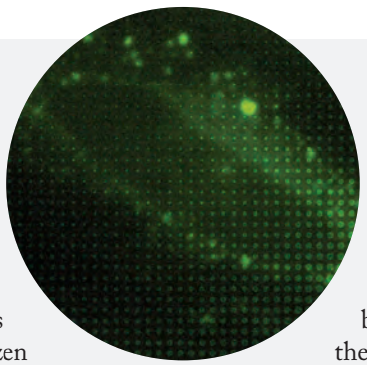
Reference

1. *National Cancer Institute (2020). Available at: https://bit.ly/35TPLFb*

Metabolons in Motion

GCIB-SIMS catches elusive clusters of enzymes in action

Multiple enzymes have long been known to form complexes, called metabolons, to combine sequential processes in metabolic pathways. But they've never been caught in the act – until now.



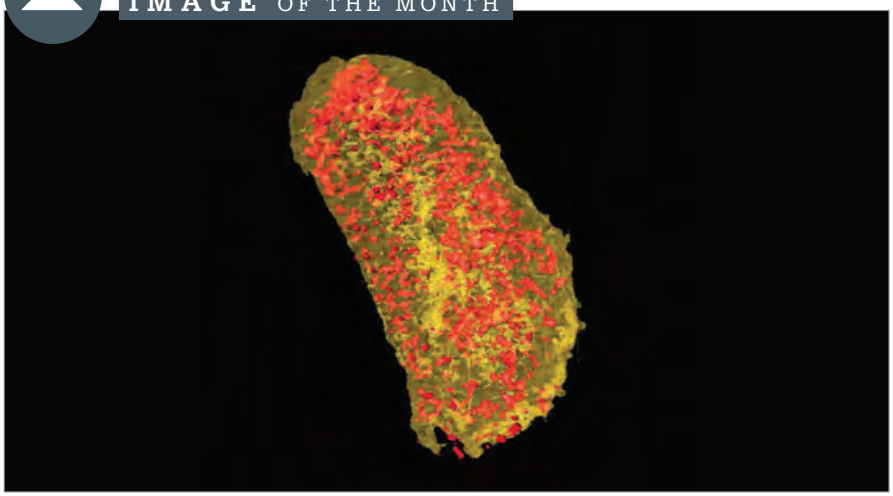
A team of researchers at Pennsylvania State University has used gas cluster ion beam secondary ion MS (GCIB-SIMS) to directly visualize *de novo* purine biosynthesis in the purinosomes of frozen HeLa cells. Purines – along with pyrimidines – are the building blocks of DNA and RNA.

Not only does the research offer an exciting glimpse into the little-explored world of metabolons, it also serves as an example of how high-resolution GCIB-SIMS could be applied to other biomolecular analyses at the single-cell level.

Reference

1. *V Pareek et al., Science, 368, 283 (2020). DOI: 10.1126/science.aaz6465*

IMAGE OF THE MONTH



X-Ray Vision

Using an X-ray-sensitive lanthanide-binding tag (LBT), scientists have demonstrated a new technique for imaging proteins in 3D at nanoscale resolution. By combining LBT with X-ray fluorescence, the method enables researchers to precisely locate proteins within individual cells, reaching the resolution of even the smallest subcellular organelles. In the above image, the technique reveals the concentrations of erbium (yellow) and zinc (red) in an E. coli cell expressing an LBT tag.

Image Brookhaven National Laboratory

***Reference**: TW Victor et al., (2020). DOI: 10.1021/jacs.9b11571*

Would you like your photo featured in Image of the Month? Send it to matthew.hallam@texerepublishing.com

QUOTE OF THE MONTH

"One of my first expeditions was to an area in the Himalayas that had only been climbed once before. We had no form of communication or maps, and it took six weeks of traveling through wild villages on the border of Pakistan during the Soviet war in Afghanistan just to get to the drilling site!"

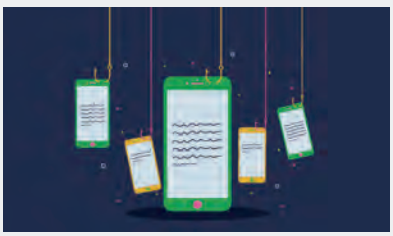
Paul Mayewski, Director of the Climate Change Institute at the University of Maine, USA

Contributor to our cover feature; quote taken from a future article.

Nasal Swabs for your Mobile

A low-cost smartphone test can identify pathogens in 30 minutes

Current point-of-care systems for nucleic acid-based detection of pathogens require highly trained users and results can take days. Now, Brian Cunningham and his team at the University of Illinois have created a smartphone device that can detect viruses and bacteria within 30 minutes in animal trials. If the device works in humans, it could be used for rapid detection of pathogens like SARS-CoV-2.



Within 15 minutes of inserting a nasal swab into the device, the microbe's RNA is amplified into millions of copies. Fluorescent dye stains these copies and glows green when excited by the blue light from a smartphone, which is then picked up by the camera.

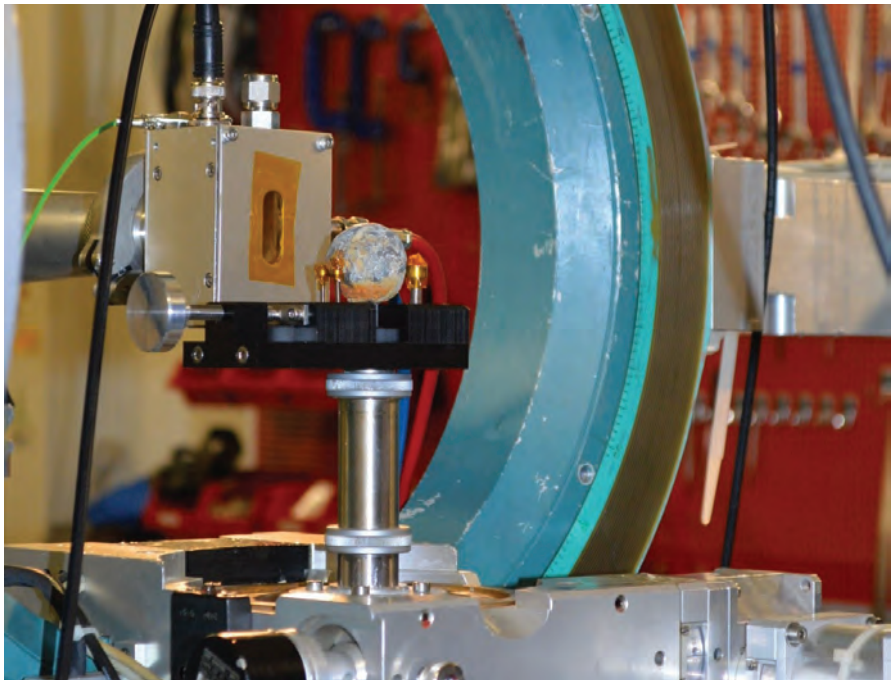
"By using a smartphone for detection, our goal is to make the instrument as low-cost as possible so millions of systems can be deployed," says Cunningham. "The data can also be shared with healthcare providers so they can more accurately identify trends and perform contact tracing."

Reference

1. *F Sun et al., Lab on a Chip, 20, 1621 (2020). DOI: 10.1039/D0LC00304B*

Secrets of the Mary Rose

X-ray analysis of artefacts recovered from Henry VIII's favored warship reveals surprising details about armor production and conservation efforts



The business end: a lead shot from the Mary rose mounted in the analysis position. The X-ray beam comes from the Kapton foil covered slot to the left.

Coinciding almost exactly with the reign of Henry VIII, the life of the Mary Rose has fascinated historians for years. Having fought many successful battles for the infamous royal, the prized flagship's career finally came to an end in July 1545, at the Battle of the Solent. It was eventually raised from the seabed in 1982 – along with some 19,000 artefacts – and has since been housed in its own dedicated museum in Portsmouth, UK .

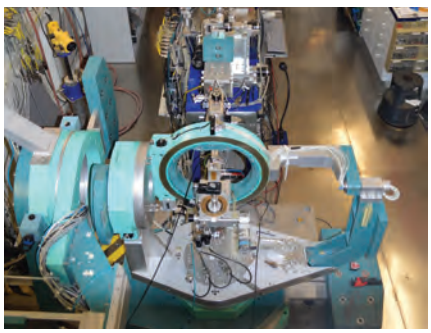
Scientists from the Universities of Warwick and Ghent have now analyzed three artefacts using the XMaS (X-ray Materials Science) beamline facility (1). "Our analysis revealed that the three brass links, believed to be chain mail fragments, were manufactured from an alloy of 73 percent copper and 27 percent zinc," says Mark Dowsett, lead author of the resulting paper. "This modern alloy composition was consistent across the three samples, indicating that Tudor brass production techniques were very well developed and controlled," he adds.

The links had also undergone different cleaning and anti-corrosion treatments, enabling the researchers to compare the effectiveness of different conservation efforts. By looking for chemical species that signal corrosion (such as nantokite), the team was able to show that soaking and coating of the artefacts with inhibitors – combined with their storage conditions – had effectively prevented corrosion. "Analysis of this kind can not only inform the overall conservation of the Mary Rose, but also future projects too," says Eleanor Schofield, Head of Conservation at the Mary Rose.

The increase in X-ray flux available on the XMaS beamline, combined with its Pilatus camera, facilitated extraordinary sensitivity. "X-ray diffraction doesn't normally give you a sensitivity of parts per million," says co-author Mieke Adriaens. "But our unique approach allowed us to merge thousands of camera pixels into each data point in the diffraction pattern, which allowed us to identify low-intensity features that would have otherwise been buried in background noise."

The overall aim for the research team is to devise new analytical methods using electrochemistry as a means of inducing controlled chemical modifications that can be studied in real time using techniques such as synchrotron X-ray diffraction or X-ray absorption spectroscopy.

Currently, the XMaS beamline is being rebuilt in a bid to reduce beam size and increase the X-ray energy range. "This is very exciting for us – we hope to win beam time on the new instrument for further work on other Mary Rose samples," says Dowsett.



The XMaS beam line – a UK national facility supported by EPSRC – at the European Synchrotron Radiation Facility in Grenoble. The Huber goniometer is in the foreground and the black acetal copolymer vice made to hold the Mary Rose samples can be seen at the center of the green circle.

Reference

1. *MG Dowsett et al., J Synchrotron Rad (2020) 27, 653–663. DOI: 10.1107/S1600577520001812*

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In My View

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

Trust, but Verify!

Open method sharing – through online repositories – could finally put an end to niggling issues of method irreproducibility

By Pierre-Hugues Stefanuto, Senior Scientist and Lecturer, Liège University, Belgium

Analytical scientists, like most scientists, are driven by the research process: being inspired, translating this inspiration into an experiment, analyzing results, and drawing conclusions.

My favorite part: the inspiration. We are inspired by our surroundings, and scientific inspiration can come through any medium, from an interesting paper to a talk, webinar, or even a tweet. After your initial idea comes a period of intense method development, trying to tweak every parameter to get the best results. Sometimes it works. Sometimes we learn – that is part of the game. But what follows a successful experiment?

We publish! As scientists, we have to communicate our findings, primarily to share with the community, and also to support our career development. (One may argue against the last reason, but that's another topic for another time.) When we begin the writing process, we must ask an important question: what information is essential for reporting my methods?

In answering this question, I find it useful to ask another: "If my method inspires another scientist, have I provided all the information to allow them to implement it directly in their lab?" We are well placed to ease the future experiments of our peers by providing such "plug-and-play" solutions.

Method reporting guidelines represent a growing topic of discussion in the scientific community. Heather Bean even explored this problem in The Analytical Scientist fairly recently, emphasizing the need to improve repeatability. "Give a senior scientist a paper and ask him to reproduce the study based on the method section… he will fail," she wrote. The sentence is shocking because it is true. What is the purpose of the method section if it does not allow you to replicate the study?

"Scientific inspiration can come through any medium, from an interesting paper to a talk, webinar, or even a tweet."

But the reality is that providing such a method walkthrough is easier said than done. Even if you were to communicate all the experimental details, how could you do it efficiently? Initiatives like the Metabolomics Standard Initiative have defined some guidelines to help provide an answer (lots of lists is one answer). Yet it is difficult to generate relevant lists with so many different techniques (and combinations of techniques) being used.

"I don't believe that adding an extra 10 pages of tables and lists to the supplementary materials is a real solution… A perfect solution would allow direct transfer of the required information from instruments and software, with automatic manuscript format checking."

I work mostly in GC×GC-MS. For the last two years, we have organized focus groups on this topic during the Multidimensional Chromatography Workshop and the ISCC and GC×GC symposium. The main output: trying to list all required parameters is a challenge; between instrument specificities, sample preparation steps, separation parameters, detection, and data processing, it's a near-impossible task to include all the necessary information.

I don't believe that adding an extra 10 pages of tables and lists to the supplementary materials is a real solution. It would be difficult to review and implement in another lab, even if the same instruments are used. A perfect solution would allow direct transfer of the required information from instruments and software, with automatic manuscript format checking.

The automatic format checking is mandatory. You cannot ask reviewers to verify every single parameter of an entire method. Software, however, could check that every value is listed. We could even add advanced screening to request comment if a value is out of a given range (such as a high temperature value). Templates to check parameters against could even be generated directly from instrument or processing software; these files could be then uploaded in online repositories. And these repositories could also keep track of replication studies, which would in turn demonstrate the robustness of the published method. Instrument providers could even establish instrument-specific open repositories, where you could find a method relating to a specific sample via a specific method and import it directly. In such cases, the method section could be a brief summary of the protocol, which references the relevant repository files.

Put simply, open method sharing has the potential to improve our trust in publications, as well as allowing replication and cross-laboratory validation. So what are we waiting for?

Analytical Education: a Joint Responsibility

The current educational focus in analytical chemistry and instrumental analysis neglects the power of the youth and non-academic craftsmen: we have to rethink our strategies!

By Thomas Letzel, Executive Director, AFIN-TS GmbH, Augsburg, and University Teacher at the Technical University of Munich, Germany

I followed the discussion surrounding education in instrumental and analytical chemistry in The Analytical Scientist throughout 2019. By the time the December issue hit my desk, I felt a need to express my own opinion on the matter.

I absolutely agree with Editor Matthew Hallam's statements about an unengaged public in his editorial, "A Call to Communicate," and also with Michelle Misselwitz's points regarding lost education from instrumental vendors in her piece "The Principle of the Thing" – not to mention Terry Berger's points on the dominance of research over industry (in The Power List and beyond). These are significant issues, stemming from public separation from science and a lack of experienced experts in instrumental analysis, and also academic dominance in that area. However, other important drivers are rarely addressed, such as the loss of youth and non-academic apprentices to the analytical sector – the so-called "craftsmen dilemma."

I am a researcher, (university) teacher, and consultant of more than 20 years, specializing in the sophisticated (and expensive) world of chromatography and MS. I came in contact with many analytical systems during my apprenticeship in the 1990s and while studying chemistry, but mass spectrometers were never allowed to be touched! When doing research for my dissertation, I began working in high-performance LC-MS, and had the luxury of access to three MS systems in my postdoc. In that period, I realized that MS has intense power, but for the most part, almost exclusively available to PhD students and academic staff. It was also clear 20 years ago that MS use, and thus the need for experienced operators, would increase drastically in the future – meaning a need for improved education on the topic.

I formed my first independent research group in 2003, and we immediately started to give students, pupils and chemical apprentices hands-on experience with our chromatographic systems and mass spectrometers, as well as key learnings in these instrumental analyses. Doing so allowed us to build a group of experienced chromatographic and MS specialists from non-academic backgrounds for our institution and others. We consequently set up national and international consortia for such non-academic educational initiatives over the past two decades, and these have been very fruitful; for example, the EU-CHEMLAB consortium (https://bit.ly/35hc8Uo) and the open access e-learning platform Analytics+ (https://bit.ly/2Sh9IjC).

"Long-term education is needed not only before, but also during employment in a lab…"

Yet, the momentum of this sophisticated education would never survive long in the industrial analytical community. Why? There are two main reasons. First, employers still hire academics as operators for such sophisticated systems; second, employers still do not invest enough in the qualification of their non-academic employees to become experts in such operating systems.

Though today's life is somewhat hectic, we need to invest more into our development than is provided by 15-minute YouTube clips and online tutorials. As an institution for education and teaching, we notice that courses of only a single day, or workshops of two days, are provided to many analytical employees. Long-term education is needed not only before, but also during employment in a lab – the necessary skills could be gifted in this way, but only given that employers and colleagues are willing to inject the required time and finance to do so.

As long as we are not willing to invest more in excellent education, we will continue to lose our connection to the digitized generation and science interested (non-academic) youth. E-Learning tools, webinars and short courses cannot be the solution – they are only a starting point. Let us all begin to invest more resources (especially time) for a glorious future of experts in analytical chemistry!

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FROZEN
in Time

THE COLLE GNIFETTI HISTORICAL ICE CORE PROJECT APPLIES STATE-OF-THE-ART ANALYTICAL TECHNOLOGY TO EXPLORE THE INTRICATE INTERACTIONS BETWEEN HUMANS AND THE ENVIRONMENT

By Lauren Robertson

The year is 1980. Paul Mayewski is standing atop the Nun Kun glacier preparing to extract one of the first ice cores recovered from the Himalayas. But this is just the beginning of many such expeditions in his illustrious career. In 2013, along with colleagues from the Climate Change Institute at the University of Maine and the Initiative for the Science of the Human Past (SoHP) at Harvard, he will focus his attentions on Europe. His target: the Colle Gnifetti glacier in the Alps. Using a 72-meter section of ice from this glacier, the group will map the first detailed record of 4,000 years of climate history for the region.

Although there are many ways to study the climate of the past – for example, using marine sediments, tree rings or peat bogs – ice cores offer the most robust record. Formed through the annual accumulation of snowfall and melt, each layer compresses the one below, capturing chemical fingerprints that can tell us about the climate and environment – and the events that triggered change.

Though clearly valuable, such cores can only be retrieved from certain parts of the world – namely highly elevated areas or the polar regions. And the deeper the ice, the more compact the timeline becomes, making analysis difficult. There is a considerable amount of historical information contained within European cores when compared with those from more remote regions. But few regions in the Alps have the height necessary to preserve high-quality ice cores, so extraction sites are limited – and dwindling with rapid warming. The Colle Gnifetti glacier on the Swiss-Italian border is one remaining and well-worked example.

We spoke to Paul Mayewski, Alexander More, Michael McCormick, and Christopher Loveluck about their ambitious project studying ice cores from Colle Gnifetti as part of our environmental mini-series: "The Complexities of Saving our Planet."

So, now that we've broken the ice, let's drill deeper into what the project could tell us about the future of our species – and our planet.

CORE PRINCIPLES

The primary aim of the Colle Gnifetti Historical Ice Core Project is to study the intricate relationship between humans and the climate by tracking past events. Ice cores detailing a long history have previously been taken from polar regions, but Colle Gnifetti offers glimpses into Europe's past that others cannot.

Typically, ice core researchers are able to resolve 100 samples per meter – fine if your sample is from a region with ample snowfall, where the timeline is adequately stretched. But in areas with less snowfall, or if you are drilling into old ice – where layers have become increasingly compressed – 10 mm resolution does not offer sufficient detail. In Colle Gnifetti samples, approximately 4,000 years of history are compressed into a 72-meter core; to access information at sufficient resolution, the team turned to laser ablation inductively coupled plasma-MS (LA-ICP-MS) (1).

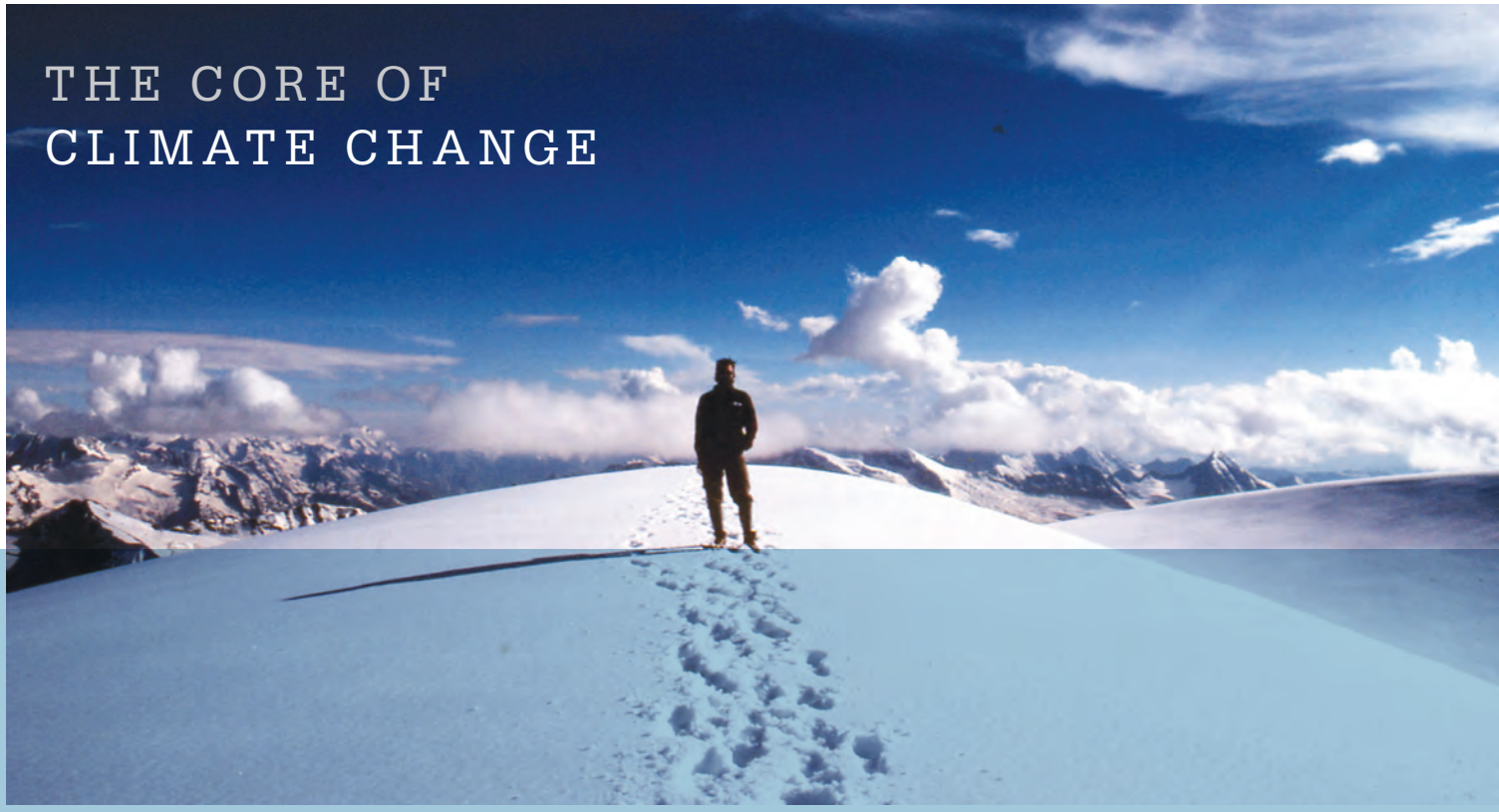
LA-ICP-MS has "revolutionized" sample resolution for ice cores, allowing Mayewski's team to take not 100 samples per meter, but up to 20,000. "The first day using LA-ICP-MS, we took more measurements than I had collected in my entire career," says Mayewski. "We went from collecting hundreds or thousands of measurements to millions."

The number of samples scientists can retrieve per year depends on how compressed the ice is, but even when tested at a depth of 1,800 meters in the Greenland ice sheet, the team was able to obtain the equivalent of roughly one sample for every day of the year. Such high temporal resolution meant that the team could not only identify specific years in the ice core, but also track specific weather events, such as storms.

In the initial stages, LA-ICP-MS analysis of glacier ice could only measure one element per ablation pass or spot – but now the team has improved application of the technique to enable multi-element analysis (2).

The technique has also allowed the team to overcome a key challenge in the study of ice cores – melting. "We are already losing a record of climate change *because* of climate change, so it

THE CORE OF CLIMATE CHANGE



The Colle Gnifetti Historical Ice Core Project was a long time in the making. In the early 1990s, Paul Mayewski played a key role in one of the most important modern discoveries concerning our interaction with the environment: the concept of abrupt climate change.

It may come as a surprise now, but prior to 1990, the majority of climate scientists believed the climate changed very slowly – and that humans had little impact on it. As leader of the Greenland Ice Sheet Project 2, Mayewski and his team demonstrated that the climate could in fact shift to a completely new state in just a few years, potentially leading to the collapse of entire civilizations.

But while the media was quick to recognize the importance of this discovery, it was not accepted by all. If the general consensus held that the climate changed slowly, greenhouse gases and other pollutants could be poured into the atmosphere without us having to face the consequences for hundreds, or even thousands, of years – an attractive "get out of jail free card" for climate change sceptics. Even those who did accept the findings may have assumed abrupt climate events were a thing of the past.

Fast forward to today. We are faced with the first abrupt climate change event in the modern era – a rapidly warming Arctic. "We're seeing an unprecedented melting of Arctic permafrost and, as this continues, a huge amount of methane – which is 30 to 60 times more effective at trapping heat than carbon dioxide – will be released into the atmosphere," says Mayewski. This change is already having severe consequences for people and ecosystems across the polar regions, he says, altering the thermal balance from the North Pole to the mid-latitudes and triggering changes in atmospheric circulation patterns that have intensified droughts, floods, and storms. "Global warming is a nice soundbite, but the reality is that the planet is not warming evenly all over, and this uneven warming triggers abrupt changes."

The project in Greenland snowballed into many other areas of research, and Mayewski now directs one of the oldest climate research units in North America: the Climate Change Institute. Priding themselves on their multidisciplinary approach to studying the environment, they have teamed up with the Initiative for the Science of the Human Past at Harvard (SoHP) to study the impact of climate change on society.

"There are multiple reasons for this multidisciplinary approach," says Michael McCormick, Chair of SoHP. "Importantly, natural proxies such as ice cores offer invaluable new data to inform our incomplete written records of environmental change and the human response to it in the past."

For Mayewski, it is this collaborative element that really sets the project apart from others. "Without getting these different disciplines together, you can't make the sort of discoveries necessary to understand really complex systems," he says. "It's really a two-way relationship. We provide them with climate information and they correlate this with significant historical events – it's extremely useful to be able to calibrate the ice core record with known historical events."

seemed crazy to melt the ice and destroy it for further analysis," said Alexander More, a member of SoHP and the Climate Change Institute. The new technology is non-destructive, using a unique laser ablation cryocell capable of holding up to 1 meter of ice – and it also requires less sample preparation than standard core-melting methods. "You can't even see a scratch on the ice with this new technique," says Mayewski. The laser moves slowly over the ice, creating a 10-micrometer groove, while argon carrier gas transfers the sublimated "ice" from the core to the ICP-MS system for analysis. For the researchers, the main advantage is the ability to continually go back over the same area and take new measurements, while preserving the core for further studies.

Another advantage is that the method allows the researchers to visualize exactly where they are taking samples from in the ice core – in real time. Using a video camera attached to a microscope, the team can see if they are taking samples between multiple ice crystals – the so-called "triple point," where chemistry can differ slightly to its surroundings, allowing for bias assessment in sample acquisition.

ANOTHER ONE BITES THE DUST

Heather Clifford – at the time a Master's student at the Climate Change Institute – put the team's new laser technology to work by analyzing the Colle Gnifetti ice records of Saharan dust storms (3). Historically referred to as "blood rain," these dust events occur frequently and have a notable impact on natural weather systems, altering the frequency of hurricanes, accelerating the melting of glaciers, and generally exacerbating the effects of climate change around the world.

The impact of these storms is felt not just in Africa, or even Europe; the dust can make its way right across the Atlantic Ocean to the USA, and beyond. (A little-known fact: Saharan dust storms fertilize the Amazon rainforest with key nutrients...)

Clifford and her colleagues were able to not only trace the history of Saharan dust events, but also identify the atmospheric conditions that promote them. The resulting paper (3) demonstrated that there are significant markers of atmospheric circulation patterns in the ice, showing how what happens on one continent can impact on another. The data also showed that increased dust transport has occurred over time, correlating with more high-pressure systems over the Mediterranean and drier conditions in North Africa. And with many climate change models predicting these conditions will become more frequent with global warming, the future looks very dusty indeed.

"I think we forget, as humans, that the planet existed before us in a state of equilibrium. We've polluted that equilibrium for at least the last 2,000 years."

THE BLACK DEATH

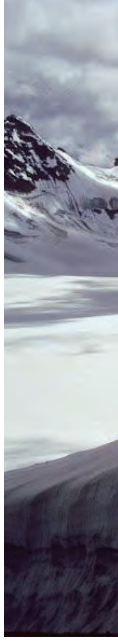
The applications of the LA-ICP-MS method don't end at studying dust. The team also analyzed historical lead pollution levels as a marker for human impact on the climate.

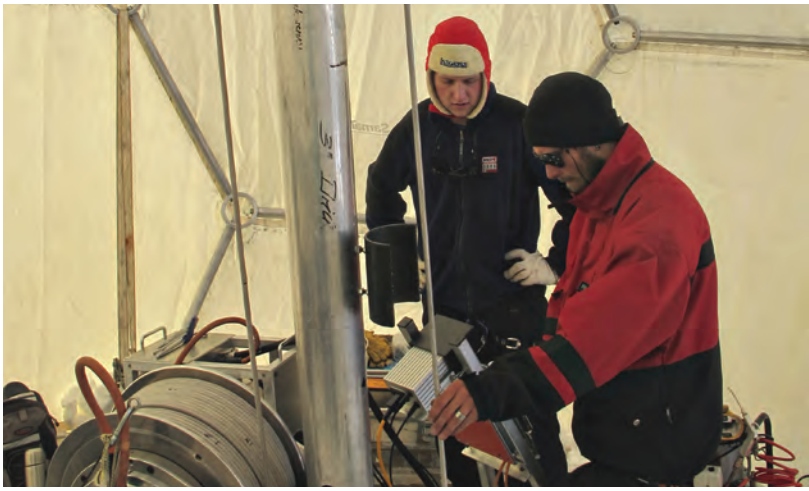
Nowadays, the health effects of lead are well known – exposure to high levels causes kidney and brain damage, for example. But this is (relatively) contemporary knowledge; lead-silver ores have been mined for centuries for use in coins, roofs, water pipes and paint, with little thought given to the long-term impact of this pollutant on our environment – or human health.

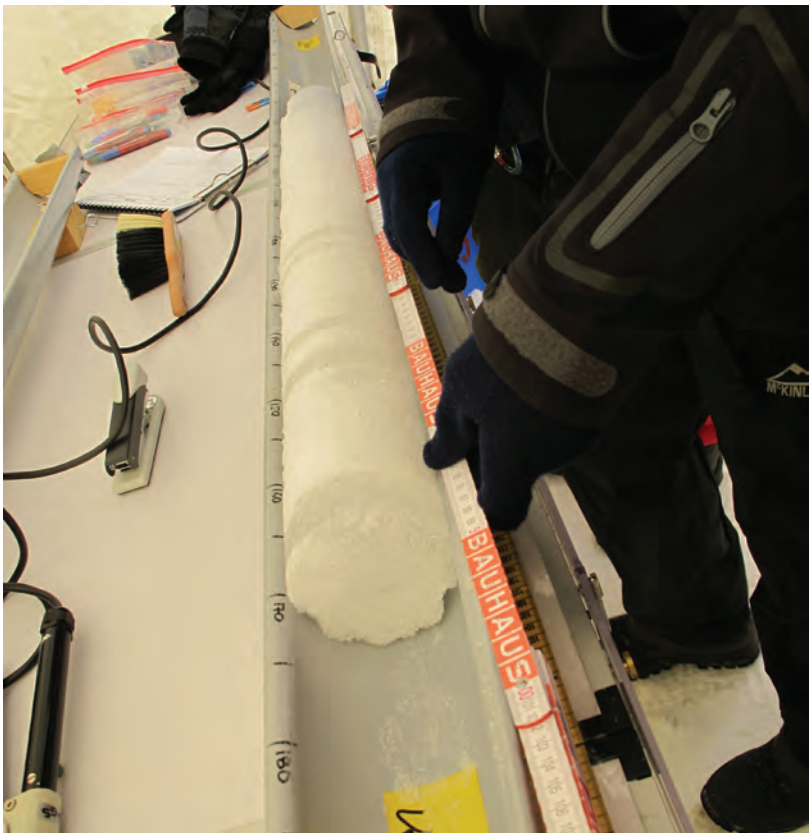
Because some natural events, such as volcanic eruptions, can release lead into the atmosphere, it was previously believed that the atmosphere had a "natural" background level of lead, even before the industrial revolution. Even today's policies to reduce lead pollution are based on this assumption.

Alexander More used the Colle Gnifetti ice core to disprove this theory, showing that lead pollution has been elevated for the past 2,000 years – excluding a four-year period starting in 1349 A.D. when lead dropped to undetectable levels in Europe (4). "This is what I wanted to hear, because it confirmed our chronology was accurate," says Michael McCormick, Chair of SoHP. "The funny thing is, the postdoc taking these measurements had no idea the trough in the data lined up with a huge historical event – I kept challenging him to make sure he had the date right. Eventually he asked, 'Did something happen in 1349?' If your history is similarly rusty, the period coincides perfectly with the onslaught of the Black Death in the 14th century."

The devastating pandemic reduced Europe's population by 40 to 50 percent – and put a stop to lead mining activities,






BAUHAUS

"One surprising trough, dated circa 1170, corresponds to the year Thomas Becket, the Archbishop of Canterbury, was murdered by King Henry II's knights..."

causing lead pollution to plummet. "Levels this low suggest there is no 'natural' level of lead (at least not a measurable one), and that anything higher must be caused by human activity," says More.

But will such knowledge inform environmental policies? "The frustrating part about our work is that it's like watching an accident in slow motion," says More. "I think we forget, as humans, that the planet existed before us in a state of equilibrium. We've polluted that equilibrium for at least the last 2,000 years, so our environmental standards cannot be based on just pre-industrial levels, 200 to 300 years ago."

MURDER, WAR AND THE MAGNA CARTA

With a baseline of lead firmly established, the team went on to analyze an 800-year-old section of the core in more detail. This phase was led by Christopher Loveluck from the University of Nottingham, and revealed new details about 12th century life (and death) in Britain and France through key events that impacted lead production (5).

Using atmospheric circulation analysis – modeling how pollution travels on wind currents throughout Europe – and other geoarcheological records, the team were able to determine that the lead was deposited by winds carrying pollution from the UK. The information from LA-ICP-MS analysis was then compared with the only detailed yearly lead record from the same period: the English Pipe rolls from 1167 to 1216. These documents record the taxes paid on lead mines during the reign of the Angevin Kings.

Remarkably, the team were able to show that the annual pollution levels reaching the Alps between 1170 and 1216 mirror the records of annual lead and silver production in England – the first time that the environmental impact of a medieval macroeconomy has been demonstrated in an ice core at this resolution. "The correlation between evidence of fluctuating lead pollution found in the ice core deposits and the fluctuating levels of lead production in Britain – seen in taxes paid on lead mines and directly requisitioned 'cart-loads' of lead – is astonishing," says Loveluck. From the royal successions of Angevin monarchs to periods of instability and major construction projects, peaks and troughs in the ice core show how lead production was impacted by these historical events. "We can see the deaths of King Henry II, Richard the Lionheart, and King John right there in the ice."

One surprising trough, dated circa 1170, corresponds to the year Thomas Becket, the Archbishop of Canterbury, was murdered by King Henry II's knights. Henry was subsequently excommunicated. The dip in lead pollution is likely to reflect the impasse between Church and State running up to Becket's murder, when royal government demands for lead and taxes, largely transmitted by clerics, were disrupted. A decade later, there is a clear peak in lead that correlates with Henry reconciling his differences with the Pope and ordering new construction work, using British lead for key monasteries

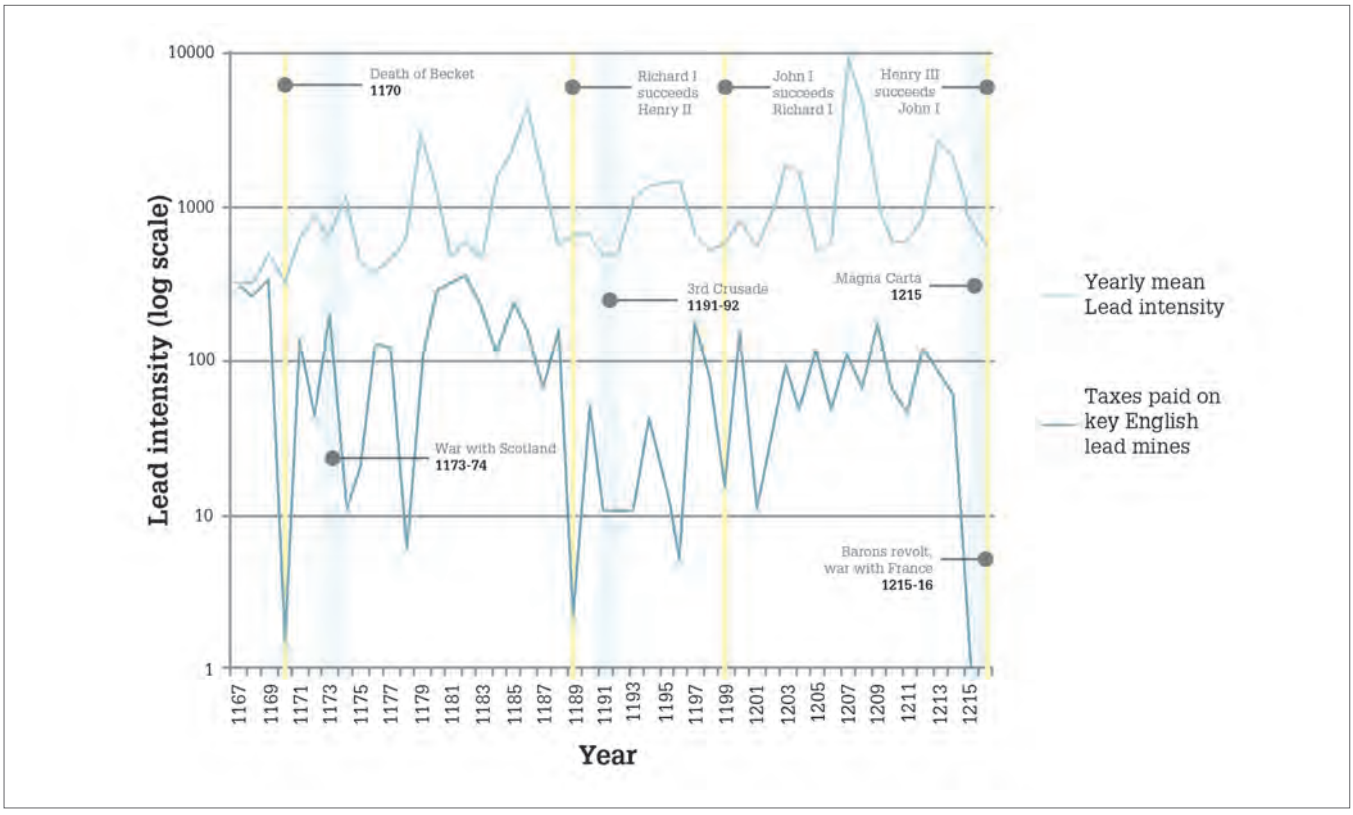


Figure 1. A proxy for British lead production, AD 1167-1216. The dark blue line represents combined totals of farm payments for two key mines in Britain and the cart-loads from all mines per year, and the light blue line represents the Colle Gnifetti yearly lead record.

in England and France in atonement. Similarly, following the civil war of 1215, when the Magna Carta was signed, and the continuing war through 1216, when the French invaded England, silver and lead mining was halted once again, due to lack of government demand and transport insecurity. These events too can be visualized in the ice (Figure 1).

Up to this point, the team has focused on the upper 2,000 years of the ice core record. The lower 2,000 years is compressed into just a few meters of ice. And though the team has already tested the technique on this precious three meters of ancient history, further improvements to their technique will be required to extract as much information as possible.

Beyond Colle Gnifetti, many other fascinating combinations of history and climate are starting to present themselves. "We're beginning to involve more and more people, as we realize there are so many more stories to be told," says Mayewski. The team hopes to gain access to ice cores from Asia and the Middle East, to expand their work beyond European history.

"We're beginning to involve more and more people, as we realize there are so many more stories to be told."

PANDEMICS VERSUS POLLUTION

You might be wondering at this point, if we can see the Black Death in these ice core records, will we be able to see COVID-19 too? "Yes, of course," says Mayewski. "We've already seen the short-term impact of worldwide lockdowns on environmental pollutants, and I am in no doubt that this will be recorded in ice cores around the globe."

Meanwhile, the team's immediate concern is what coronavirus means for efforts to combat climate change. "It is extremely important that governments and global organizations do not try to tackle these crises one at a time," says Mayewski. "I can only speak for the USA, but all I hear in the news at the moment is the impact of the current pandemic in our country, and a little about other parts of the world – everything else is being forgotten about. All of the other politics still going on, particularly around climate change, are being swept under the carpet."

But you don't work in this field if you're a pessimist. "I do believe there's a silver lining to the terrible COVID-19 situation. Prior to the pandemic, there was a growing anti-science movement, particularly in the USA, and a scourge of misinformation. Since the crisis, the polls indicate that around 80 percent of individuals believe that what we are being told – not by the government I might add, but by science and healthcare providers – is exactly what we should be doing," he says.

Mayewski also notes that the pandemic has offered people a first-hand glimpse into the short-term impact of certain actions on the environment. People around the world can now walk outside and see the stars more clearly, or breathe more freely. As More puts it, "We need to be mindful that, as humans, our perception of the planet has been skewed for a long time – it's arrogant to believe we can predict every impact we have on the climate. We must learn from the past and realize that we cannot control our environment. It's imperative that we learn to live more sustainably."

International organizations have historically operated within distinct areas, from health and the environment to trade and human rights, notes Mayewski; since the dawn of the COVID-19 era, these organizations have sought to work outside of these silos. "I hope this crisis will serve as a reminder that, when faced with global disasters, it is critical for everyone to work together – and follow the science."

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PUTTING SAMPLE PREP *Centerstage*

We are the EuChemS-DAC Sample Preparation Task Force and Network. Our mission? To secure a starring role for a crucial but often-neglected phase of the analysis process.

By Elia Psillakis, Manuel Miró, and Stig Pedersen-Bjergaard

Sample preparation has achieved exceptional progress over the past few decades; we've seen the introduction of powerful technologies, advances in fundamental knowledge, and a plethora of breakthrough applications. However, enthusiasm for sample preparation is not necessarily shared by all members of the analytical chemistry community – let alone other scientific disciplines.

The idea that sample preparation is an "art" and not a "science" or that the discipline relies on application-driven research remains well-entrenched in the minds of many academics and non-academics. Indeed, sample preparation scientists have, on the whole, done a poor job of communicating contemporary advances and celebrating the successes of the field. There has been a lack of communication with external platforms, and an absence of credible and influential voices to articulate sample preparation's importance and contributions.

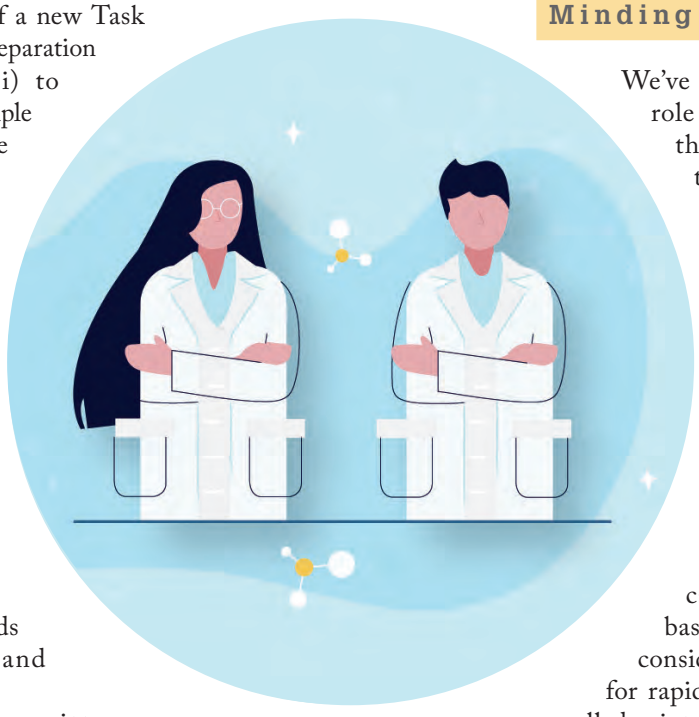
Until very recently, internal communication within the sample preparation community has also been lacking. And a coherent strategy, outlining the goals, expectations, successes and future directions, did not exist. Moreover, a systems approach is rarely applied in sample preparation, meaning that it was often separated from the context in which it was conducted – and that its practice was not always considered in relation to its impact on many interconnected systems.

We believe the time is right for sample preparation to cast off its image as a "follower" discipline and take up its rightful place as a leader in discovery.

Using the force

In 2019, the European Chemical Society-Division of Analytical Chemistry (EuChemS-DAC), approved the formation of a new Task Force focusing on sample preparation with three objectives: i) to increase the visibility of sample preparation, ii) to raise awareness of its importance and contributions, and iii) to provide a coherent strategy for external and internal communication. To achieve these ambitious goals, the Sample Preparation Network was created as a space for academic and non-academic members of the sample preparation community to work collectively towards promoting, improving, and synchronizing activities.

Several European Committee Members were invited – and the participation of non-European experts was also encouraged to allow transparency and dissemination of the combined efforts. Today, the network includes regular members from 23 countries working in academia, institutes, industry, and private laboratories. Since its inception, three working groups have been created: "Science and Fundamentals," "Automation, Innovation and Entrepreneurship," and "Information Exchange and Networking."



Minding the gap

We've seen a tremendous shift in the role of sample preparation from the early years of this century to the present. Initially, the focus was on determining trace-level concentrations of target contaminants in a large number of environmental or biological samples. Today, our efforts are more commonly directed toward more complex tasks, such as human exposomics – multidisciplinary and holistic approaches for untargeted and targeted workflows to uncover cancer biomarkers using MS-based omics techniques. And also consider preliminary screening tests for rapid diagnosis at the bedside (so-called point-of-care analysis), which typically rely on affinity microextraction methods.

To achieve better results in these new areas, fabrication of new sorptive phases that improve selectivity towards class compounds or enhance sample clean-up in eliminating matrix-interfering compounds is critical. To meet the need, there are a plethora of novel composite materials described in the

"WE WILL SEE THE RISE OF POST-PANDEMIC EFFORTS TO IMPROVE ROBUSTNESS AND INDEPENDENCE – AN IMPORTANT TREND THAT MUST BE REFLECTED IN ANALYTICAL CHEMISTRY LABORATORIES."

literature and applied to complex samples; however, the majority do not perform better than commercially available materials – and validation across sufficient numbers of samples is rarely performed. Consequently, a gap has opened up between promising research results and sample preparation products that actually make it to the market. Efforts in our Task Force and Network are directed toward filling that gap by gearing research efforts in Europe and the rest of the world towards actual needs; for example, the reliable detection of COVID-19 virus at low-level concentrations by exploiting bioaffinity sorptive platforms.

The COVID-19 pandemic teaches us that modern society is fragile, and supply chains are not as reliable as we may like to think. Therefore, we will see the rise of post-pandemic efforts to improve robustness and independence – an important trend that must be reflected in analytical chemistry laboratories. Society depends heavily on our measurements, and labs must be able to stay fully operational during future crises. One scenario is to downscale analytical methods, reducing our consumption of chemicals and reagents. Another scenario is to analyze samples on-site with smartphones, operated by non-trained personnel, and connected to a network for digital or manual interpretation. In a more pessimistic scenario, sampling and analysis may have to become contactless; for example, using drones for field sampling and automated laboratory methods with all sample preparation steps fully integrated. All these scenarios rely on extensive sample preparation research, and development of new micro-extraction technologies.

Braving a new world

Digital technology is already having a major impact on sample preparation. The breadth of materials and composites now available, each with distinct chemical composition and sorptive properties, opens new possibilities for 3D-printing tailor-designed sorbent materials, membranes and scaffolds for point-of-use devices. By the year 2040, analytical chemistry will likely be staffed with scientists born with a smartphone or tablet in their hands and a 3D printer at home. The thirst for data will unite them with wider societal forces, and members of the public will be actively engaged with "citizen science," transforming analytical research. The rise of connectedness and low-cost sensor technologies used for chemical measurements, as well as the push to improve the transparency and accessibility of science, will require many enabling technologies, including advances in smartphone cameras and printer resolution; new (open source) software; detectors/detection principles compatible with the 3D-printed (open source) objects; smartphone-compatible microchips; lab-on-paper; and, last but not least, sample preparation. The latter has to be microscale to adapt to the microchip format and highly selective to circumvent the limited selectivity of smartphone sensors.

Much of this future relies on extensive sample preparation research – and we must find new ways to reinvigorate the area by bringing in other disciplines, while still maintaining the field's identity.

Reaching for the stars

Sample preparation needs to become increasingly interdisciplinary, if we are to increase opportunities for innovation. The Sample Preparation Task Force and Network will increase interaction with other sciences and promote problem-driven research to address the world's increasingly complex and interconnected problems.

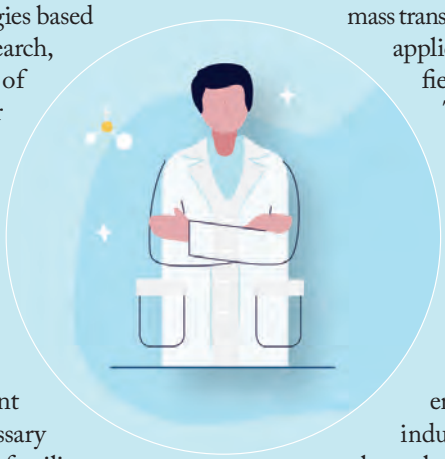
Breaking down the single-discipline silos of sample preparation will also allow transferal of knowledge from other "distant" disciplines and will increase current understanding of the underlying processes. Indeed, compared with other physicochemically simpler systems, such as GC, sample preparation is less developed and understood. Focusing on the science is not about giving academics the freedom to explore their intellectual curiosities – it is the bedrock for future advances. We simply do not understand the technologies we use well enough to predict everything we need or might need; studying the fundamentals will future-proof the field and allow us to tackle problems we can't yet foresee.

GLOBAL IMPACT

EuChemS-DAC Sample Preparation Task Force first launched in Europe, but soon expanded to include international members. Here, four international committee members from around the world share their hopes for the initiative.

Janusz Pawliszyn, University of Waterloo, Canada

The EuChemS-DAC Sample Prep Task Force and Network will engage committed individuals to move the analytical science towards a greener, more sustainable future. There are a number of new, efficient extraction technologies based on fundamental research, but the majority of scientists are either not aware of these developments or do not understand them. When chemists get involved in a project involving a quantification step, they typically want to provide the necessary data ASAP. As such, familiar approaches are preferred, and newer, more powerful, and greener techniques are ignored in favor of standard technologies that may not fully address the challenge at hand. In an ideal world, scientists would consider the utility of all approaches when tackling a problem; however, this is rarely done in practice. This phenomenon is not limited to analytical chemistry or even chemistry but is observed whenever new technologies are introduced. However, we are living in times when swift and decisive action is needed towards a sustainable future. We have many technologies already available or under development that can support human existence on the Earth for millions of years to come, and we must make use of them if future generations are to enjoy life as we have experienced it. The leadership provided by the Task Force towards cost-effective and faster screening methods will prove central to address these challenges.



Gangfeng Ouyang, Sun Yat-sen University, China

Sample preparation is a classical research field, which has exerted wide and deep impacts on our modern society. However, even as the importance of the field grows, there is waning interest from the scientific community; many scientists appear to be convinced that the fundamentals of sample preparation can be addressed by the classical theories and laws of thermodynamics and mass transfer, and treat it as a purely application-driven research field. The Sample Prep Task Force and Network will be an invaluable international effort to raise awareness of the importance of sample preparation, promote scientific research in this field, and solve the problems encountered by different industries. China arguably has the largest number of researchers in this field, and we have seen similar initiatives on a national level, with regular academic meetings. Nonetheless, the clear and ambitious goals proposed by the EuChemS-DAC will certainly inspire researchers in China to organize more effective communication among research groups and individuals, as well as between industry and academia.

Fernando M. Lanças, University of São Paulo at São Carlos, Brazil

Sample preparation has applications in almost all areas in which chemical determinations are required. Unfortunately, most sample prep developments have been reduced to an appendix within the analytical chemistry niche, scattered across a large number of scientific periodicals in distinct disciplines. The recently created Task Force aims to increase the visibility of the community and promote external and internal communication of technical advances. In the current international landscape, I can envisage two avenues along which the Task Force can develop. Firstly, by including in its main efforts top international scientists and young investigators from developed countries, the network can widen its potential coverage and practical results in the sample prep arena. Secondly, the network could work with underdeveloped countries through educational programs to promote the many gains obtained by changing from the classical sample prep methods to the new technologies that allow: i) higher overall analytical efficiency and throughput, ii) a lower cost per analysis, and iii) less exposure to toxic materials.

Jared L. Anderson, Iowa State University, USA

The development of a Sample Preparation Task Force is a great way to educate the broader community about the importance of sample preparation in many interdisciplinary fields of science, ranging from molecular biology to environmental analysis. A critical role for the Task Force is to publicize the fact that sample preparation is still undergoing rapid change and that many of the advancements are in response to demands and techniques developed by the broader scientific community. I believe the initiative will bring more attention to the field and help significantly in recruiting new generations of scientists. On the global scale, I think that the efforts by the Task Force will enable more collaborative opportunities – and this will most certainly spread to other areas of study in which sample preparation procedures are still considered a major bottleneck in the workflow. It is an exciting time to be working in the field of sample preparation and I am particularly excited to see the team's efforts pay off!

"BY INTRODUCING BETTER FINANCIAL INCENTIVES, WE CAN BETTER EXPLORE THE NEXUS OF TECHNOLOGY AND SOCIETY, AND ENCOURAGE COLLABORATION WITH THE PRIVATE SECTOR."

Sample preparation is a creative science in itself, which should be practiced in both fundamental and applied arenas for the benefit of society. The EuChemS-DAC Sample Prep Task Force and Network will highlight the context within which sample prep is conducted and guide research towards areas with the greatest potential impact. A systems thinking approach will embrace green analytical chemistry, so that we are able to move towards sustainable science and meet the challenges of multiple unfolding world issues.

Just as important, EuChemS-DAC Sample Prep Task Force and Network will strengthen the interface between academia and the private sector. It will serve as the meeting point for academics and non-academics, and a hub for the exchange of information. By triggering demand-driven research, we can transform knowledge generated in universities into economic, social, and/or environmental value, bridging the gap between research and the demands of stakeholders. The EuChemS-DAC Sample Prep Task Force and Network will also work on initiatives aiming to spread the culture of entrepreneurship between academics. By introducing better financial incentives, we can better explore the nexus of technology and society, and encourage collaboration with the private sector.

Last but not least, we will strongly promote the inclusion of early-stage researchers and early-career investigators. Giving this younger generation a voice on sample preparation through active participation and networking will feed into successful future career development.

Getting involved

An open invitation for membership is extended to European and non-European professionals with an interest in sample preparation, including both senior and early-career scientists. Becoming a member is easy and free. All members of our network can increase their networking opportunities, gain visibility by sharing their work with other members, participate in our activities for dissemination of the relevance of sample preparation in many disciplines and get the latest updates in the area.

And that's not all. The Sample Preparation Task Force and Network organizes special sessions focusing on Sample Preparation in Euroanalysis and other major International Conferences running in Europe. A sample preparation course is also organized on an annual basis and serves to provide hands-on training on a variety of methods; the course moves around Europe and takes focus on different topics within sample preparation with each host.

More details on the Sample Preparation Task Force and Network and information on how to become a member are available at www.sampleprep.tuc.gr. Join us to champion the importance of sample preparation across multiple arenas!

Elia Psillakis is the Head of the EuChemS-DAC Sample Preparation Task Force and Network, Technical University of Crete, Greece.
Manuel Miró is a Core Member of the EuChemS-DAC Sample Preparation Task Force, University of the Balearic Islands, Spain.
Stig Pedersen-Bjergaard is a Core Member of the EuChemS-DAC Sample Preparation Task Force, University of Oslo, Norway.

TESTING TIMES

COVID-19 is (still) dominating news globally, and clinical chemistry labs have been thrust into the spotlight as the world's media takes takes an unprecedented interest in bioanalytical science. Here, we speak with Peter Kissinger and Rolf Halden to gain expert insight into two very distinct approaches to coronavirus monitoring.

The COVID-19 pandemic is showing no sign of letting up. As countries consider relaxing their various states of lockdown, secondary outbreaks represent a real (and, in some cases, realized) threat to those attempting to return to normality. The only way we can follow the extent of the issue is by implementing effective testing regimes. And the only way to beat it? A treatment or vaccine – both of which remain elusive.

In the world's mission to identify the virus and treat those infected, analytical scientists are a secret weapon – turning samples into answers, exploring new targets, and optimizing drug discovery efforts.

We spoke to Peter Kissinger and Rolf Halden, two scientists involved in these crucial activities, to explore the challenges we face – and what to expect in the months (and years) ahead…

TRACING INDIVIDUAL EXPOSURE

Bioanalytical guru Peter Kissinger provides an overview of the current status and future prospects of clinical COVID-19 testing

How are we testing for SARS-CoV-2?

Reverse-transcription PCR (RT-PCR) based on viral RNA sequence is the key qualitative tool for SARS-CoV-2 detection. These tests act primarily as a tool to prevent further transmission, but, being new as they are, many are yet to be validated with statistical rigor. The current situation, however, allowed for Emergency Use Authorization (EUA), meaning we have taken a shortcut, and statistical rigor will be accounted for later in time. But this must not be ignored for long.

A second approach is to detect a viral surface antigen via an antibody. Antigen tests could be conducted more simply and faster than typical PCR methods, but more data are needed to fully understand their utility. A third method then promises viral detection via CRISPR technology – developers say this can be accomplished quickly and at low cost, with the potential for home use based on nasal swabs or saliva.

Alternatively, serological antibody measurement can indicate ongoing or previous infection. These can be applied in homes and instrument-free public health settings, and one from Roche was recently approved for use in the UK, but we are still not sure if reinfection remains possible despite the presence of antibodies. If not, for how long is this the case? This would be useful to know, especially given the potential for the virus to alter and overcome immune defences over time, but – from my reading at least – we have no definitive answer yet.

Sampling is also very important. Should we use a nasopharyngeal swab, a nasal swab, saliva, sputum, or blood? The first of these is closer to the action for a respiratory disease, but swabs are not without some "art" and luck. This topic has been a source of worry, and has added cost due to the need to employ experienced and (PPE) protected individuals. Home collection has recently begun, saving costly labour and travel expenses, but adding the risk of a poor collection.

The direction that disease-identifying tests are following is excellent – we just need to ensure they're accurate – and fast. Movement towards testing for specific biomarkers to track infection and treatment response will also be essential for us to account for the wide range of ways in which patients respond to the virus, and improved cytokine measurements will help us understand these responses. Labs were overwhelmed early in the outbreak due to backlogs and the lack of supplies, but we are now seeing this situation begin to stabilize.

Who conducts the tests?

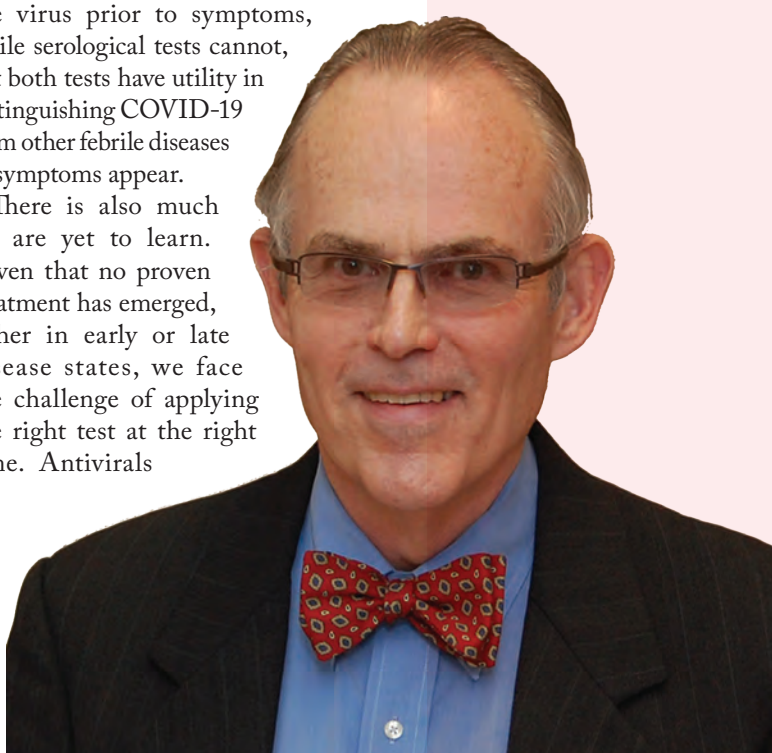
Analysts! The American Association for Clinical Chemistry (AACC) worries that the profession is generally undervalued. This is reflected in the fact that clinical measurements make up two percent of healthcare costs, while driving over 70 percent of clinical decisions. Pharma has noted for decades that a modest 10 to 12 percent of healthcare is spent on drugs – so it's strange that those working in the field are viewed as villains in wider society. This latter figure has gone up recently – most likely due to the rise of protein therapies. Enough politics…

Hospital laboratories are relatively hidden, as are commercial reference laboratories. They are appropriately certified, and personnel are licensed. Samples go in, answers come out. But there are other testing environments, such as a nursing station, physician's office, pharmacy, or even at home. In all cases, the test must be prescribed. It would be very attractive to have a reliable over-the-counter test that would reduce cost and improve speed across these settings, perhaps via a finger prick test of the blood or saliva.

What is challenging about COVID-19 testing?

Specificity with regards to both the virus and associated disease is tough. The timing of disease progression is extremely important in both cases, and so a key question is "how often should a test be performed?" PCR tests can detect the virus prior to symptoms, while serological tests cannot, but both tests have utility in distinguishing COVID-19 from other febrile diseases as symptoms appear.

There is also much we are yet to learn. Given that no proven treatment has emerged, either in early or late disease states, we face the challenge of applying the right test at the right time. Antivirals



"Every stage of our fight against this pandemic, from testing to drug development (from discovery through manufacturing), relies on analytical chemistry."

effective against HIV and Ebola are being explored, as are anti-inflammatories for malaria and arthritis. Remdesivir from Gilead has gotten the most ink thus far, but it's too early to say how useful it will be. Regeneron, Lily, Pfizer and Merck are also contributing to a great community effort. But none of the options put forward cure or prevent the disease – they show promise for reducing symptoms.

Much depends on the quality and consistency of reagents, some of which have been in short supply. Several recently announced tests appear to demonstrate good specificity, but some earlier tests were highly deficient, and gave a high percentage of false results. Reagents vary in type and source, and can also suffer differences from time to time. What's more, throwaway tests cannot be individually calibrated, and quality control can only be achieved by sampling from a manufactured batch, or periodically on a continuous production line. In other words, expect some wrong answers.

What are the limitations?

Every analytical measurement will suffer constraints at the detection limit, and that will vary with the "handle," or the label established to produce a signal. Often this is some form of fluorescence or chemiluminescence, but could alternatively utilize electrochemistry and other means of transducing a signal. And, below a certain degree of infection, a signal will not be detected. The higher we set the threshold for a positive conclusion, the more false negatives we will have and vice versa. Using instrument-free methods, the human eye becomes the detector.

We also face issues regarding selectivity and cross reactivity. Is the sequence we are targeting with RT-PCR unique to this virus? Could there be some cross reactivity with other coronaviruses? And has any of this been established? The answers to these questions, at present, are maybe, possibly, and not quite yet, respectively.

In fact, a report from South Korea described an interesting ambiguity regarding the PCR tests. Some patients were giving positive results after recovering from symptoms. Apparently, they were shedding non-infectious or dead virus particles and were not infectious. It is thus possible to have a positive test for the virus and not be required to quarantine; the same recovered patients also had a positive serological test. This nuance also reduces the worry that fully recovered patients could continue to spread the virus.

Will these tests bring us closer to helping patients?

Yes, but it will be a long journey. As analytical chemists, we are often detached from the context of our samples, and analyze them weeks after collection and storage at -80 oC. Clearly, an ICU patient on mechanical ventilation will not benefit from these results.

Regarding treatment, each patient reacts to a drug in very different ways, and we are terrible at optimizing dosage for most drugs. This is, in part, due to "the tyranny of averages" from clinical trials. We also cannot determine drug concentrations repeatedly outside of clinical trials. We have the tools to do this, but the logistics are not currently available to support this – not even in an ICU. Our group is working on it!

Movement towards a treatment that fights the virus safely will require lots of data – acquired faster, better, and cheaper than ever before. Naturally, there are also many challenges integral to interpreting data that span the diversity of our 8 billion-strong populous. But you can't change something you can't measure, and the opportunity for analytical chemists to participate here is so much more than a supportive role – it is central.

How will analysts support the ongoing fight against COVID-19?

We can determine just about any chemical substance at any meaningful concentration given enough time and budget. But speed matters, as does context. Every stage of our fight against this pandemic, from testing to drug development (from discovery through manufacturing), relies on analytical chemistry.

Every hospital is an analytical laboratory, too. Consider a critical care nurse at 3 AM with a patient on mechanical ventilation suffering a cytokine storm. There will be a lot going on. A bunch of drugs will have already been administered. Will they interact? Will the ventilator settings be optimum? What is the right dose to be administered by infusion pump? A point-of-care device could potentially provide reliable, guiding data to help care for critically ill patients. Medicine is non-linear and intuitive, and guidance systems are always needed. Experience also guides, just as it does for a good Ferrari mechanic.

Peter Kissinger is a Professor at Brown Laboratory of Chemistry, Purdue University, and a founder of Bioanalytical Systems (BASi), Prosolia, and Phlebotics

CITY-WIDE MONITORING (VIA SEWAGE)

Rolf Halden and colleagues had just begun tracking viruses in US wastewater when the pandemic broke out. We caught up with Rolf to find out how his team is extracting population-level SARS-CoV-2 exposure information from our sewers – and how this can help us fight the virus' spread locally and globally

How did you start measuring coronavirus in wastewater?

We have been continuously monitoring hundreds of chemicals and biological markers in wastewater from around the world for years – I discussed this in "The Great Sewage Census" in The Analytical Scientist in 2019. It was in the same year that we began applying our method to viral quantification. I was fortunate to find an opportunity to collaborate with Arvind Varsani (a virologist specializing in virus discovery) and Matthew Scotch (a bioinformatician focusing on zoonotic RNA viruses), and together we discovered over 3,000 viruses – mostly by studying US wastewater (1–3).

We approached the National Institute of Health with our method, presenting it as a convenient "atlas" of viruses across the US – and as a potential early warning system to monitor infectious disease. They liked it so much that they offered us a grant of $1.5 million, and we were ready to begin real-world viral tracking by October. Two months later, the COVID-19 pandemic began, and we quickly pivoted to track population-wide exposure to the SARS-CoV-2 virus across the US by applying qPCR and metagenomic approaches to wastewater and clinical samples.

How have people responded to your work?

People have always approached our work with a degree of scepticism. When we started our viral measurements, people mocked us – they said we were wasting our time. But now it turns out that everybody is jumping on the bandwagon. Hundreds of people across the US and further afield are now playing catch-up to conduct this type of viral monitoring themselves… And that's great! Every dollar we invest in these early warning systems helps to prevent human suffering and associated costs downstream.

How can your approach help?

The beauty of public health engineering is that we can anticipate and detect a threat upon arrival, before people are exposed and made sick.

But we have to be realistic. Many people label new breakthroughs in health as "silver bullets" – people thought that sequencing the human genome would allow us to cure cancer, for example, and subsequently that proteomics and then epigenetics would provide us with all the answers required to solve pressing medical problems. I want to stress that our approach is useful but represents only one of many tools in our toolbox. We need to deploy multiple tools simultaneously in order to succeed. But wastewater analytics has immense utility in expanding our current view of viral exposure across populations, and it can do so at a very low cost.

Testing individuals is demanding, both in terms of labor and cost, and it's simply not viable to repeat these measurements as often as they are needed. Our approach can test wastewater from 2 million people over a 24-hour period for the same cost as screening one single individual. If we were to divert only one percent of the money currently spent on individual testing toward wastewater analysis, we could rapidly screen approximately 70 percent of the US population once or twice per week.

This is the main advantage we are able to provide – producing a "radar" that detects coronavirus occurrence for large populations at negligible cost. In fact, 2.1 billion people are connected to approximately 105,000 centralized wastewater treatment plants worldwide (4). Imagine the data we could extract from this sample, equivalent to around a quarter of the global population (1, 4).

"Hundreds of people across the US and further afield are now playing catch-up to conduct this type of viral monitoring themselves… Every dollar we invest in these early warning systems helps to prevent human suffering…"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Could this information help handle the spread of COVID-19?

It definitely has the potential to help contain the pandemic. Our current method can identify COVID-19 hotspots through area-specific signal intensities, and we are currently achieving this on a three-times-a-week basis in Tempe, Arizona, across different parts of the city. These data are publicly available on the world's first public dashboard, displaying information obtained by wastewater analytics without delay at https://covid19.tempe.gov – anyone can take a look!

This tracking has helped us to study the epidemic as it unfolded here in Tempe. During the first wave, uncontrolled community spread was rampant because people weren't aware that they could spread the virus while being asymptomatic and we saw it tear through communities across the United States. Then came the stay-at-home ordinance from the governor's office. Locally, we entered into a shutdown period and wastewater coronavirus concentrations soon fell to below the detection limit across all five monitored areas of Tempe. On 15th May the economy reopened – so the question now is: "at what point do we see the virus emerge again from below-the-detection limit?"

We will need to keep a watchful eye on the virus as it becomes detectable once more and monitor the delay between its detection in community wastewater and people becoming seriously sick, being hospitalized, and dying. Having this information on the relationship between changing viral levels in community wastewater and individual and healthcare events will allow us to monitor the effectiveness of social distancing measures and lockdowns, and may even inform when these measures should be put in place or lifted in order to stagger the pandemic's effects.

Of course, we must also consider the economy when making these decisions; America has a GDP of around $21 trillion, and shutting down the entire country may cost as much as $1 trillion per month. It could be advantageous to manage economic activity and virus spread locally rather than state-wide or nationwide, using data from both the healthcare and sewer system. This should allow us to keep the nation running at a minimal capacity of at least 70 percent at all times, with rolling shutdowns implemented only where they are truly needed and beneficial.

"If we were to divert one percent of the money currently spent on individual testing toward wastewater analysis, we could rapidly screen approximately 70 percent of the US population once or twice per week."

What's the current status of your work on COVID-19?

We're currently collecting data from over 100 cities across the US, and also from South and Central America, so our team is working day and night to deal with the huge sample throughput.

We have cloned the Tempe dashboard that we originally developed for tracking the opioid epidemic (https://arcg.is/ey0Ha) to give citizens access to information on coronavirus levels in Tempe and its neighbouring cities of Guadalupe and Gilbert (https://covid19.tempe.gov). And we've received requests from hundreds more locations across the world.

At this point, I would no longer consider what we're doing to be exclusively research – we have fast-forwarded into the realm of routine monitoring. In addition to our research lab operations, paid for by tax dollars, we've also formed two additional entities to address the need for public health information. One is a non-profit called OneWaterOneHealth (https://onewateronehealth.org) that seeks to help underserved communities, and the other is Aquavitas LLC – a for-profit organization that provides not only measurements of the virus, but also helps in interpreting what those measurements mean (https://aquavitas.com/). The phone never stops ringing and

we're incredibly busy, but it's very exciting and rewarding to work on a pressing public health issue!

Are there any limitations?

Yes – there are currently a lot of unknowns surrounding our measurements. We are able to measure the viral load passing through a wastewater treatment plant, but what we don't know is exactly what this measurement means. How does our measurement correlate with the number of people who have been exposed to the virus? To what extent does each individual shed the virus in feces, and when does this occur over the course of infection? And how are the people shedding viral particles distributed throughout the region that the wastewater corresponds to? We have run simulations to gain a better insight into the potential answers to these important questions (4) and we will be able to gain a more accurate picture from our samples as the science and monitoring efforts advance.

What are the challenges in scaling up this approach?

Differences between regions, for one. For example, having 50,000 copies of viral RNA in a given amount of wastewater from the US would have a very different meaning to the same finding in wastewater from Europe, where they use approximately a third of the amount of water that we do each day. Clearly, we are dealing with different dilution factors. The overall chemistry of the samples also differs with the types and concentrations of detergents used in each region, and the presence of more industry in Europe versus the US may also have an impact, as do wastewater temperature and the average travel time of wastewater in municipal sewers.

If we were to use point-of-care tests for individuals only, it would take us a minimum of several months to test all American citizens. I equate this to of painting the Eiffel Tower – once you're finished at the top, it's time to start all over again at the bottom. But we need to test most Americans on a weekly basis to truly track the pandemic – wastewater analytics makes this an attainable and affordable goal. Associated numbers show this is feasible (4), and the approach thus promises to help prevent unnecessary human suffering, while also saving billions of dollars in individual screening costs. We said it before, both types of analyses are needed. The challenge right now is to find and implement the perfect balance between community wastewater screening to identify flare-ups and follow-up testing of individuals to isolate cases. Getting this right is a matter of life and death for both people and local economies. That's what we are working towards right now.

Rolf Halden is Founding Director of the Biodesign Center for Environmental Health Engineering at the Biodesign Institute, Professor in the Ira A. Fulton School for Sustainable Engineering and the Built Environment, Senior Sustainability Scientist in the Global Institute of Sustainability, Arizona State University, Tempe, USA, and co-founder of the non-profit project OneWaterOneHealth and the ASU start-up company AquaVitas.

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Solutions

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ASMS: A Digital Solution

The ASMS 2020 Reboot involves redesigning the entire conference program for an online format – we invited Rick Yost and Jennifer Watson to talk us through the process

By Rick Yost, President, and Jennifer Watson, Executive Director, American Society for Mass Spectrometry

As the scale of the COVID-19 pandemic became clear this spring, we quickly saw that we could not hold our annual ASMS Conference on Mass Spectrometry & Allied Topics in its usual face-to-face format. Due to take place in Houston, Texas, on June 1, we had to evaluate new options quickly: do we cancel the conference, postpone it until fall, or move it completely online?

After much discussion, the Board decided to shift our program online, reasoning that we could still share science and maintain engagement without physical meeting. ASMS is a large conference, typically with 6,000 to 7,000 attendees spanning diverse disciplines. A good number of attendees come every year, not just to present and see great science, but also to connect and engage with colleagues and friends. But how can we foster that engagement online?

It was clear that we couldn't simply move our standard conference schedule online, with eight parallel oral sessions every morning and afternoon, and around 750 poster presentations per day. Thus, we planned the ASMS 2020 Reboot (see https://www.asms.org/conferences/asms-2020-reboot), with all talks and posters to be presented in a virtual and interactive format from June 1 to June 12. Plenary lectures, tutorials, and award lectures will all be held as live webinars, as will 40 interactive workshops. These live events will be recorded and made available for three months as on-demand content (along with any other conference content), and each of the 64 oral sessions will have a "watch party" feature, including a live Q&A webinar with the speakers. The live conference program will be bookended each day with corporate events, giving attendees a look at the latest instrument developments. The week after the presentations and posters, we will hold thirteen short courses.

There are enormous challenges involved in shifting a face-to-face conference into an online format – made all the more daunting because we had only a few weeks to make it happen! It would have been much easier to cancel the conference, or postpone it, but the remarkable ASMS staff rose wonderfully to the occasion. With input from the ASMS Board, we were able to put together the online conference in record time.

A particular challenge was working out how to provide attendees with access to the online program content in a secure manner – we repurposed our mobile app and desktop planner program for this purpose since these are familiar tools for our community. We also added the option for attendees to submit questions to oral and poster authors (authors can publish the questions and provide answers), or request more info from authors. We also had to go about refunding all the

"There are enormous challenges involved in shifting a face-to-face conference into an online format – made all the more daunting because we had only a few weeks to make it happen!"

face-to-face conference registration fees, while simultaneously opening registration for the new online conference (at a quarter of the normal registration fee).

The response of our presenters, individual and corporate members, and attendees has been overwhelmingly positive. Even though some presenters had to modify or withdraw their presentations since they were unable to finish gathering their planned data, others submitted new presentations for the online conference – so it all worked out in the end.

Of course, there are components of the face-to-face conference that can't be moved online. How do you host

The ASMS poster presentation session in action at last year's meeting

"This year we're encouraging poster presenters to record a 3-minute 'flash talk' video to accompany their online poster."

an opening mixer for thousands of online attendees, for example? And the planned finale event in the Houston Museum of Natural Science doesn't translate well to an online format – at least in part because of the inevitable lack of food, wine, and beer to share… But we've done our best to move most of our conference and engagement activities into the digital realm.

Everyone is looking forward to a return to face-to-face conferences (ASMS 2021 will be in Philadelphia next June), but some of the features developed for the ASMS 2020 Reboot may be preserved for future events – online or otherwise. We've offered attendees the opportunity to watch the recorded oral presentations and look over the posters online for months after the conference for a number of years. This year we're encouraging poster presenters to record a 3-minute "flash talk" video to accompany their online poster – perhaps we can offer that option at face-to-face poster presentations, too. We'd love to hear your feedback during and after the event (send this to info@asms.org) – what worked seamlessly, what fell flat, and what you would like to see become a regular fixture.

It's always stimulating to think about how we can best showcase brilliant science and provide opportunities to network and engage. The COVID-19 pandemic has thrown obstacles in our path, but we encourage others who are planning (or re-planning) conferences to be creative in their approach. We hope to see you (virtually) there from June 1!

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What to Look Out For…

Tutorial: "Glycoprotein Analysis for Understanding Human Disease"

Fields like proteomics and genomics have been hailed as breakthrough fields for medical application, but glycoproteins remain less frequently discussed. Their complex structures require specific analytical considerations to open the doors to sweet success, but analysts are making swift progress. Here, Heather Desaire explores the shifting landscape of this booming topic, sharing expertise garnered from her research into how analysis of glycoproteins can improve the diagnosis and treatment of a number of human diseases. With a focus on future applications, as well as the challenges that must be overcome, this is a must-see talk for anyone dabbling in the area.

Special Keynote Lecture: "Is There Still Gender Bias in Academic Science (and Does It Matter)? What the Scientific Studies Say"

We are all well aware of the gender disparity in academic science and the need to increase female participation in the field – yet the issue persists. In this live webinar, Corinne Moss-Racusin (Skidmore College) will explore how gender stereotypes throughout the STEM fields can contribute to inequality in academia. Not only has her work been extensively covered by the media and published in leading journals, such as Nature and Science, but she has also presented her findings at the White House.

Opening plenary lecture "Mars 2020"

Launching in late July, the Mars 2020 mission will not only search for signs of ancient life on the Red Planet, but also gather rock and soil samples for future analysis back on Earth. In a truly out-of-this-world lecture, Patricia Beauchamp, Chief Technologist, Engineering and Science Directorate at the Jet Propulsion Laboratory, California Institute of Technology, will discuss the objectives of the mission, including the testing of new technology that could benefit future human and robotic exploration of Mars.

Award Session: "Presentation of Al Yergey MS Scientist Award and John B. Fenn Award for a Distinguished Contribution in Mass Spectrometry"

In this live webinar session, Rick Yost will present two prestigious awards for contributions in MS. The Al Yergey MS Scientist Award, recognizing the "unsung heroes" of MS, will be awarded to Rachel Ogorzalek Loo for her contributions to our understanding of electrospray ionization, charging, and protein structure. The second award, in honor of John B Fenn – recipient of the 2002 Nobel Prize for the development of electrospray Ionization – will be awarded to Michael L Gross for innovative and integrative MS-based footprinting for structural proteomics.

Closing plenary lecture: New Dinosaur Discoveries

In this lecture, attendees will delve into the world of paleontology with Steve Brusatte – author of the popular science book "The Rise and Fall of the Dinosaurs, a New History of a Lost World." Steve has spent his career exploring the anatomy, genealogy and evolution of dinosaurs and other fossil vertebrates. His work has been covered by prominent journals such as Nature and Science, and he's also become a mainstay of TV and radio programs on the topic; he was the "resident palaeontologist" on the BBC program "Walking with Dinosaurs," for one! All things considered, it's an opportunity not to be missed!

… And much more.

There will also be a number of "Watch Party" sessions covering a number of topics, each followed by live Q&A sessions with the speakers. Just some of the topics to be covered include: Microorganisms and the Microbiome; Exposomics, Toxicology, and Health Outcomes; Therapeutic Proteins, Antibodies, and Antibody/Drug Conjugates; Art, Archaeology, and Paleontology; and Cannabis Testing. And make sure to get your quizzing caps on for the "Lunchtime Trivia Breaks," too – participants can take part in a live quiz with 2,000 other attendees – all competing for real prizes!

Spotlight on... Technology

IONICON PTR-TOF 1000 Ultra X2 for Extremely Sensitive VOC Monitoring

The "gold standard" products for real-time VOC and trace gas analysis got more sensitive in 2020. The X2 performance boost for many of our analyzers enables extremely low detection limits for VOCs in real-time. The PTR-TOF 1000 ultra X2 instrument now even sets the new industry-benchmark in PTR-MS sensitivity.
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CAMAG® Derivatizer

The CAMAG® Derivatizer is used for automated reagent transfer in the derivatization of thin-layer chromatograms and allows for reproducible and user-independent results by employing the patented "micro droplet" spraying technology. Suitable for all common reagents, the device ensures homogeneity and convenience in applying derivatization reagents.
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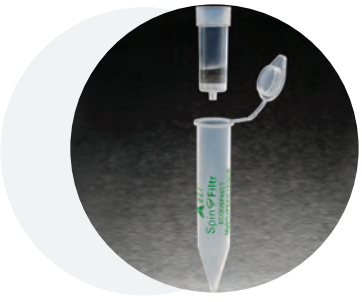
PAL Closed-System Dynamic Headspace Module

The PAL Dynamic Headspace module is a plug and play option for CDS 7000C concentrator. This module adds dynamic headspace capability to PAL RTC/RSI rail in a closed system that is compliant to USP 467, EPA 5035A and 8260C soil methods with max temperature at 300 °C.
https://www.cdsanalytical.com/purge-trap-7000c



UCT's Novel SpinFiltr® Column

Summary: UCT's SpinFiltr® is a new take on traditional QuEChERS Dispersive SPE (dSPE). It allows for enhanced extract purification via its built-in 0.2 µm filtration device. Simply discard the dSPE clean-up chamber containing unwanted matrix and sorbent following centrifugation. Users can recover additional sample volume without worrying about the disruption of intricate centrifugation layers. Try a sample today!
https://www.unitedchem.com/product/spinfiltr/

High Throughput LC-MS Proteomics Using Micro Pillar Array Columns

µPAC™ capLC for enhanced robustness and reproducibility for high sample turnover MS-based applications

By Robert van Ling

Many proteomics laboratories show a keen interest to apply nanoflow MS-based methods to diagnostic and clinical questions. However, such methods can be vulnerable to technical difficulties, such as instable nano-spray, nanocolumn reproducibility and clogging.

This has resulted in increasing interest towards capillary and microflow LC-MS for large quantitative proteomics studies, combining increased throughput, excellent robustness, reproducibility and sensitivity. We have used a µPAC™ capLC column to provide the required chromatographic robustness and reproducibility. Micro Pillar Array Columns use nano-meter precision 2D designs transferred onto silicon wafers and transformed into highly uniform arrays of superficially porous silicon pillars. This eliminates virtually any column to column variability, and the precise positioning of the silicon pillars creates a stationary phase support that minimizes dispersion. µPAC™ columns are operated at significantly lower backpressures than needed to operate current sub-2 µm particle packed-bed columns, positively affecting their lifetime.

To demonstrate the flow flexibility of the µPAC™ capLC column, figure 1 shows the column operated at 2 µL/min (a), 5 µL/min (b) and 10 µL/min (c), with direct injection of 4 µL sample onto the column.

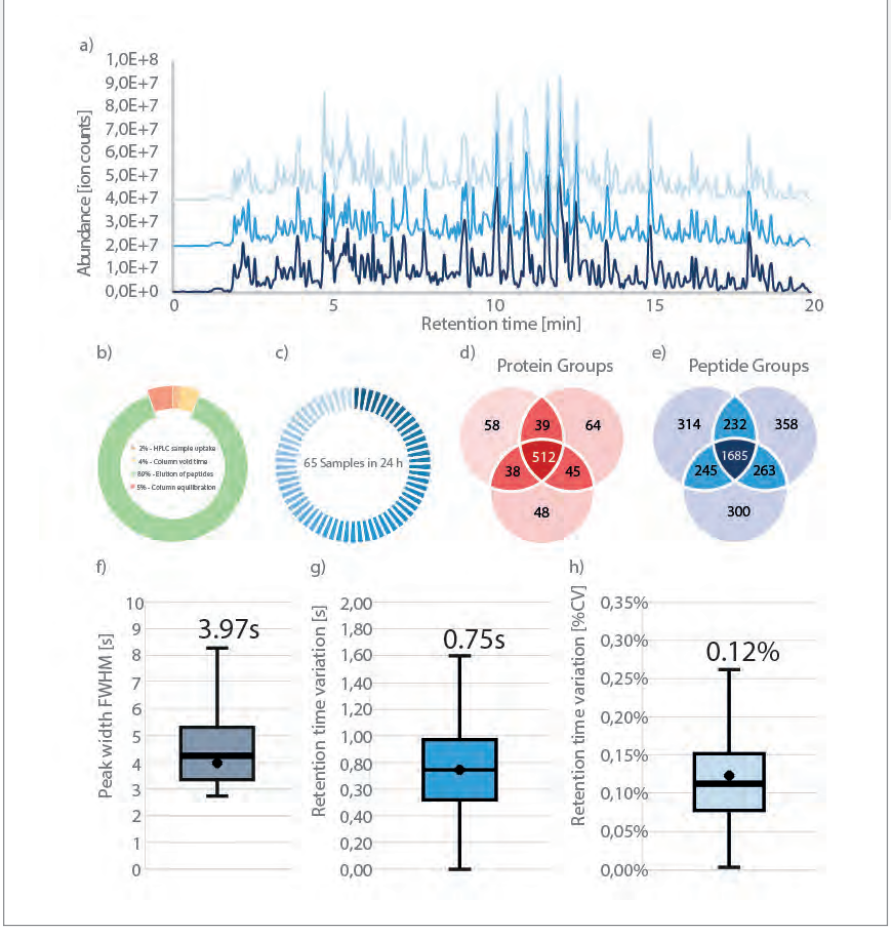


Figure 1. High throughput proteome analysis with a µPAC™ capLC column. 2 µg of HeLa cell digest was injected using a direct injection mode. a) Basepeak chromatograms obtained for triplicate analysis. b) Relative time use of the instrument. c) Sample turnover rate. d) Number of identified protein groups. e) Number of identified peptide groups. f) Average peak widths (FWHM) for all PSM's. g) Retention time variation (absolute - s) observed for all peptides shared in triplicate runs. h) Retention time variation (relative - %CV) observed for all peptides shared in triplicate runs.

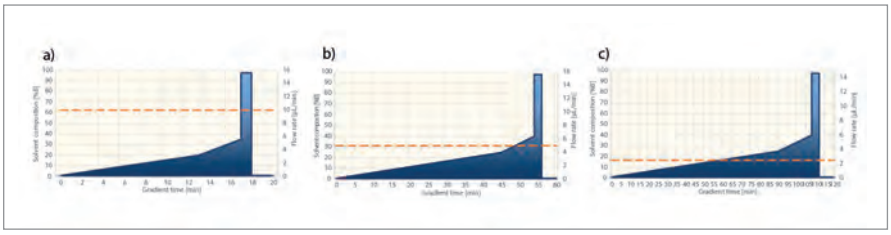


Figure 2. Optimal LC solvent gradient profiles for 3 defined needs in LC-MS proteome research a) High throughput method, 10 µL/min, total run time (with sample pick-up) 20.68 min. b) Routine method, 5 µL/min, total run time (with sample pick-up) 60.68 min. c) Comprehensive method, 2 µL/min, total run time (with sample pick-up) 120.68 min. Solvents A: Water (100%) with 0,1% (v/v) Formic Acid B: Water/acetonitrile (20/80) with 0,1% (v/v) Formic Acid.

Figure 2 summarizes the results obtained for a tryptic HeLa cell digest, using the 10 µL/min method with 21 min total runtime. Base peak chromatograms obtained for triplicate injections of 2 µg HeLa cell digest clearly indicate the high level of chromatographic repeatability that can be achieved.

To minimizing overhead time, a direct injection method was configured. Up to 83% of the total time was effectively used to identify peptides at a sample turnover rate of 65 samples per day. Combining the output of all 3 runs resulted in a total number of peptide and protein groups of respectively 3397 and 804, using an UltiMate 3000/ Orbitrap Elite (Thermo Fisher Scientific) LC-MS instrument set-up.

Determination of Epoxy to Hardener Ratios in a Cycloaliphatic Epoxy

Epoxy resin is a type of synthetic resin that could be used in a wide range of applications such as adhesives, coatings and fluxes, which require varieties of engineered curing kinetics and glass transition temperatures. The versatility of these epoxy resin systems arises from combining the epoxy resin with a co-reactant, called hardener, into a two-component epoxy. To make the precision control of the epoxy to hardener ratio, modern delivery systems package each component separately at a pre-defined volume. However, it is always a challenge in R&D and QA/QC to measure the epoxy to hardener ratio from cured epoxy to certify the optimized ratio. This application note presents a novel method to quantify the epoxy to hardener ratio from cured two component epoxy by using a pyrolyzer coupled to a GC/MS system.

Experimental Setup

In this example, 3,4-Epoxycyclohexylmethyl 3,4- epoxy cyclohexane carboxylate is picked as the epoxy resin, and methylhexahydrophthalic anhydride (MHHPA) is used as the hardener. Standards of epoxy to hardener were prepared in ratios of 0.50, 0.66, and 1.00. These standards were pyrolyzed using a CDS 6150 Pyroprobe. Peaks representing epoxy and hardener were chosen to calculate area ratios for a calibration curve.

Pyroprobe Setpoints:

Pyrolysis:	700°C 15 seconds
Interface:	300°C
Transfer Line:	*325°C*
Valve oven:	325°C
Transfer Line:	300°C
Valve Oven:	300°C

GC-MS

Column:	5% phenyl (30m x 0.25mm)
Carrier:	Helium, 1.00mL/min 75:1 split
Injector:	300°C
Oven:	40°C for 2 minutes 10°C/min to 325°C
Ion Source:	*230°C*
Mass Range:	35-600 amu

Results and Discussion

When pyrolyzed, the cured epoxy produces a pyrogram in which most of the components elute around 14 minutes (Figure 1).

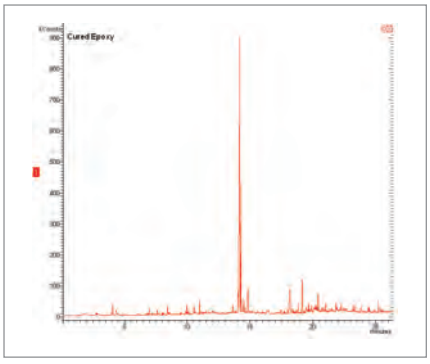


Figure 1. Pyrogram of epoxy at 700°C.

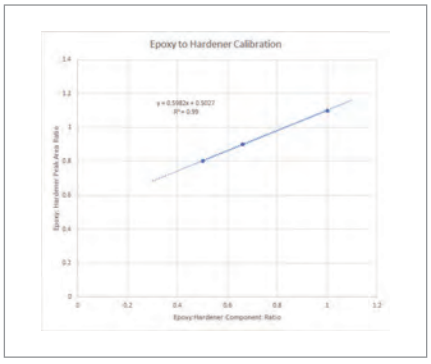


Figure 3. Epoxy: Hardener Calibration Curve.

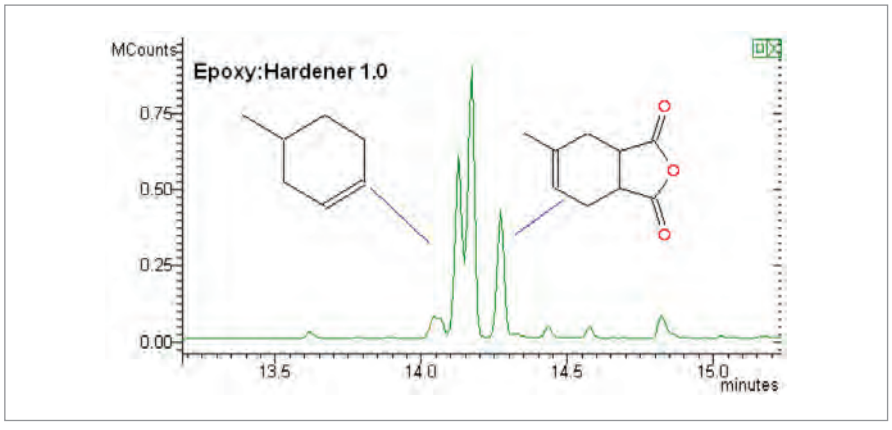


Figure 2. Expanded View of epoxy standards. Labeled peaks represent contributions from resin (left) and hardener (right).

Peaks in this epoxy could be ascribed to either epoxy or hardener. Figure 2 shows an expanded view of one epoxy sample with epoxy to hardener ratios at 1.0.

Matching the first peak to epoxy resin, and the third peak to hardener, peak area ratios were plotted against the relative amounts of the constituents. This generated a linear calibration curve which could be used to ascertain mix ratios of unknown resins as shown in Figure 3.

From the data fitting, the coefficient of determination was observed at 0.99. This linearity demonstrated that the Pyroprobe can provide quantitative analysis to determine epoxy to hardener component ratios.

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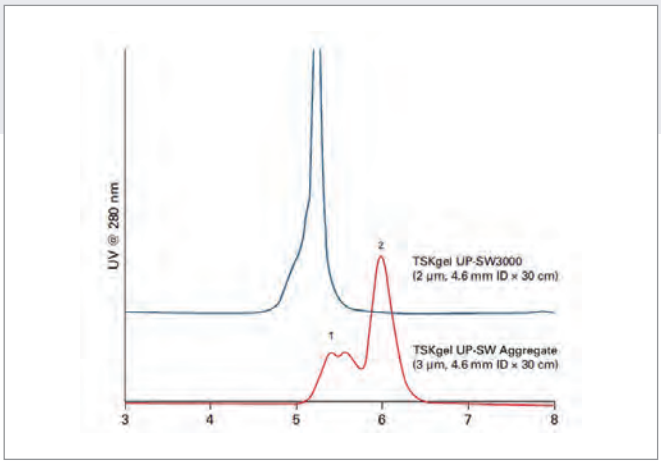
Contact Phone Number: (610) 932-3636

Analysis of Large Immunoglobulins by UHPSEC

Antibody therapeutics are still enjoying high growth rates. Today new antibody formats are entering clinical phases some of which are larger than conventional mAbs. The characterization of these complex molecules with regard to high molecular weight (HMW) and low molecular weight (LMW) impurities is needed in R & D, process monitoring and quality control.

A new application note describes the advantages of using a new size exclusion UHPLC column for the determination of higher order mAb aggregates or larger immunoglobulin classes, such as IgM. This SEC column is featuring the largest pore size within the renowned TSKgel UP-SW series and was designed to meet the requirements of users analyzing biomolecules with higher molecular weight than standard IgG.



Analysis of human IgM on SEC columns with different pore sizes (1: IgM Aggregates, 2: IgM Monomer).

While TSKgel UP-SW3000 (25 nm average pore size) does not resolve monomer and aggregates, TSKgel UP-SW Aggregate (30 nm average pore size) allows determination of the aggregate content.

Read the full application note at https://bit.ly/UP-SWAggregate

Critical Calling

Sitting Down With… Isabelle François,
Independent Consultant,
Sint-Lievens-Houtem, Belgium

What's your drive for conducting research?

I've worked within an instrument manufacturer and as an academic researcher, and obviously the motivation is dependent on the role. As a vendor, it's interesting to lend a hand in supporting the research of your customers while generating business revenue – I thoroughly enjoyed the many collaborations with customers across industries in this space.

My overall drive, though, is the impact that our field has on developing understanding across disciplines. It's not simply about the chromatography or the MS, but mostly about the information these techniques present to us. In biopharmaceuticals, for example, analytical approaches facilitate drug development and quality, and – further afield – they also ensure the quality of the food we eat and the water we drink. Many are unaware of this link between analytical science and our day-to-day lives, but it's highly motivating to know that we support crucial areas of society.

What's your career highlight?

Obtaining my PhD. That one achievement lies at the base of everything I have done since. Moreover, I was fortunate to complete this under Pat Sandra, focusing mostly on two-dimensional separation approaches. Pat mentored me incredibly well – he didn't always dictate what the next concrete steps in my research had to be. Instead, he made me think thoroughly about potential solutions, resulting in many fresh and independent ideas. Not only did it give me the skills needed to be an analytical scientist, but it also opened the door to job opportunities at ExxonMobil and Waters.

There are other highlights, of course. Attending a conference where your presentation attracts great interest is always fantastic, and being able to look back on my accomplishments after long stints in vendor roles leading to major business successes also fills me with pride. At Waters, I managed niche techniques such as 2D-LC and supercritical fluid chromatography (SFC), and being able to contribute to more widespread adoption of such technologies – within and outside of Waters - felt greatly rewarding.

How would you describe the uptake of 2D-LC?

This approach is becoming increasingly accepted, but there's still some hesitation – particularly in industry. Wider acceptance will come as a result of education, partly regarding the distinction as to when we should be using 2D-LC versus increasing the power of a single-dimensional method. The reality is that single-dimension LC does not have enough separation power to deal with highly complex samples, such as those handled in the emerging biopharma applications. 2D-LC can fill this void (and in biopharma, is already doing so). What is needed, however, are advances in the user knowledge, the available software and data interpretation – this gap is still daunting for many users, especially those lacking specialist training.

What drove your decision to work for an instrument manufacturer?

To be honest, it wasn't my first choice after my PhD. My first job after obtaining my PhD was in the petrochemical industry at Exxon Mobil, where chromatography and MS were only tools to support the overall business. It quickly became clear that job rotation away from my role as chromatography lab manager would have been appreciated, which would have rapidly moved me away from my beloved analytical science. I was not willing to make that change so soon after my research.

I decided to return to a topic closer to my PhD, which led me to working with state-of-the-art instruments with an instrument manufacturer. At Waters, I worked in roles from lab manager to sales, business development, marketing, internal consultancy, business analysis, and so on. My technical knowledge supported me in all of these roles, while also learning from exposure to different areas of the business.

A major part of my role entailed sharing my expertise to contribute to product customization – essentially designing configurations to address customers' analytical challenges. Following my dismissal from Waters, I've started my own consultancy business. Various former customers and vendors have approached me to ask for support via consultancy, training and overall advice – so I thought why not make a business of it while searching for other job opportunities! I'm also interested in the medicinal cannabis arena, which was one of the topics I worked on at Waters.

Where do you predict analytical science is heading?

The combination of separation science with MS will prove to be increasingly key – and increasingly powerful, too, with innovation in ion mobility. Current issues with storing and processing data will also be addressed. As is the case in industry now, I anticipate continued trends towards simplified approaches with high robustness, and easy-to-use instrumentation.

As an example, Shimadzu recently introduced a new system that uses analytical intelligence, and I strongly believe that we will see continued movement towards this type of approach. In such cases, troubleshooting is completed more or less by the system itself, and operational staff can look into how specific problems can be solved without necessarily needing the knowledge to address such issues. This will significantly reduce system downtime and service costs. Finally, sample preparation still represents a bottleneck in many labs today – it's an important step but it's time-consuming and labor-intensive. I hope the future delivers automated solutions in this area – there is much work that needs to be done.

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