Vol. 30 No. 5 October/November 2018

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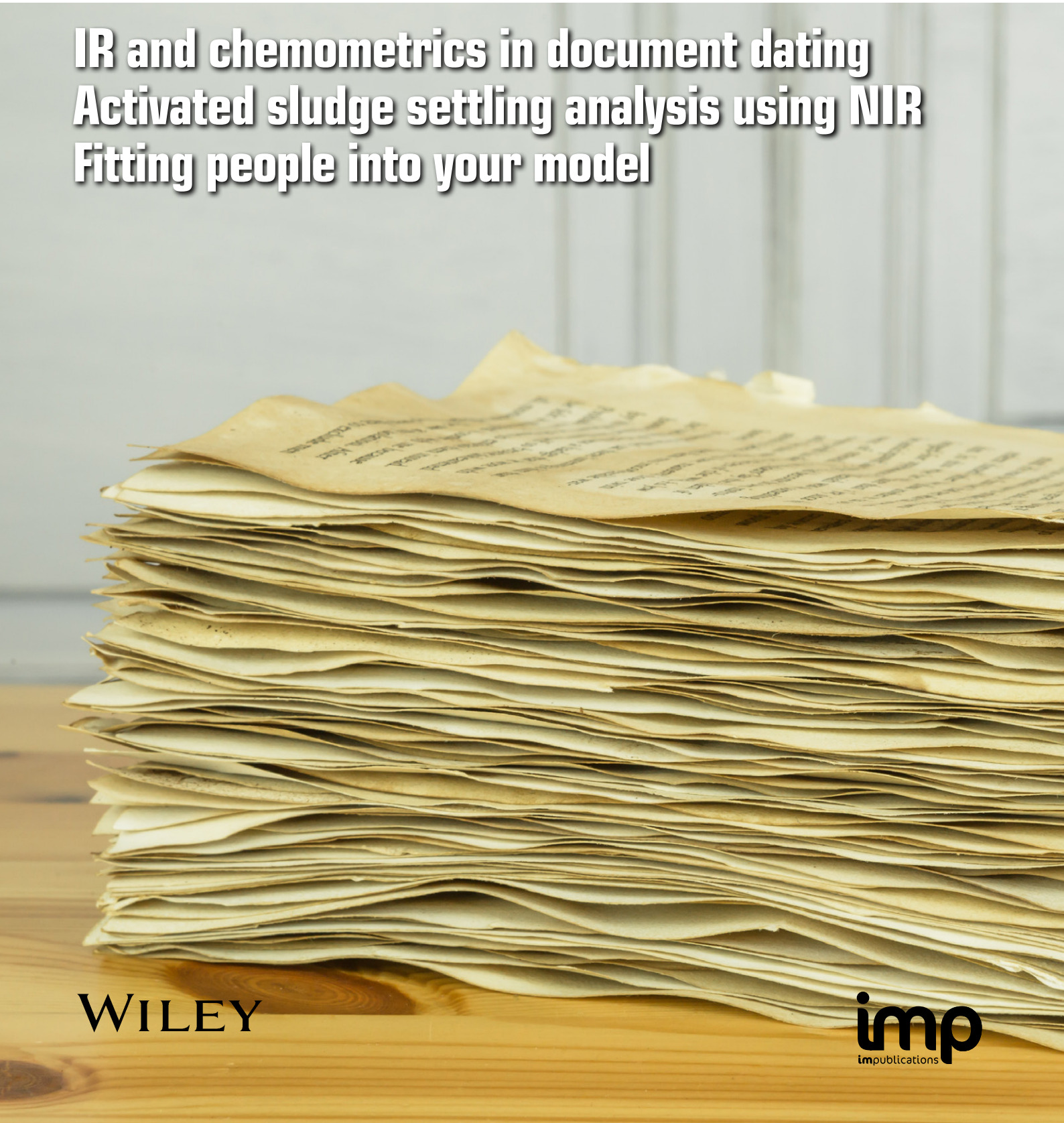
IR and chemometrics in document dating
Activated sludge settling analysis using NIR
Fitting people into your model



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EDITORIAL

And what do you think?

The world, especially the online world, is obsessed with ratings and feedback. Often, it seems to me, for all the wrong reasons: simplistic box ticking rather than genuine, thoughtful comment. However, in this issue each article and column provides opportunities for readers to provide that genuine, thoughtful comment.

Jacques Thierie's article on "Activated sludge settling analysis using a near infrared optoelectronic device: overview and application to wastewater treatment" raises a seemingly impossible observation: that in some cases, transparency can exceed 100%. The author and this publication welcome your comments and thoughts as to why this might be. You can use the commenting facility at the end of the online version of the article on spectroscopyeurope.com, or you are welcome to e-mail me direct (ian@impublications.com). I would like to have the option of publishing comments received, so please indicate if, for any reason, you would sooner I did not.

The second opportunity for comment is from the Tony Davies Column on "Fitting people into your model". Tony raises the question of whether those implementing change consider sufficiently the effects on those who need to implement it or who will be affected by it. I am sure that this has wider implications than just in industry and business.

Discussion is also one of the aims of our first article by Carolina Silva, Maria Pimentel, José Amigo, Carmen Garcia-Ruiz and Fernando Ortega-Ojeda on "Infrared spectroscopy and chemometrics to evaluate paper variability in document dating". Spectroscopy is widely used in forensics, but the determination of the age of documents was one application I had not considered. With a huge variety of papers and inks available, each with their own ageing profiles, and with such ageing depending on environmental factors, the determination of the age of a document is not straightforward. However, infrared spectroscopy and chemometrics may have the answer.

Peter Jenks makes a welcome return to the Quality Matters Column and raises the radical idea of secondary producers of certified reference materials paying for the use of the primary CRMs. How may this affect the supply and price of secondary CRMs? Your thoughts?

Finally, Kim Esbensen challenges commercial laboratories to add primary sampling to their range of responsibilities. Kim's "tale" of two fictional laboratories should certainly provoke some comment, and concludes in the next issue.

So, what do you think?

In forensics, dating documents is often required. The variety of inks and papers, combined with different storage conditions, poses a complex problem. Can infrared spectroscopy and chemometrics solve it? Find out in the article starting on page 12.

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CONTENTS

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NEWS

Hyperspectral imaging helps conservation of outdoor bronze statue by Auguste Rodin

Outdoor bronze statues make an important contribution to the culture of our cities. However, the urban atmosphere is corrosive to them, with sulfur oxides and acid rain causing the formation of the copper sulfates, brochantite and antlerite. Both compounds are green, giving the corroded bronze its typical hue, and are formed through complex electrochemical processes. Detection of these two compounds provides valuable information on the general condition of bronze sculptures and guides their preservation.

Usually, a number of samples taken from different areas of a statue are analysed in the laboratory. However, whilst sampling from a limited number of discrete spots provides detailed characterisation of corrosion products, information on their spatial distribution is limited. Further, areas of corrosion may be missed, and this is important since different corrosion mechanisms may operate on different areas due to micro-environmental conditions. For instance, hollows and other sheltered areas may have different corrosion products than more prominent features.

Scientists from Norway, Sweden and Italy have investigated the use of hyperspectral imaging (HSI) to detect the corrosion products brochantite and antlerite in two selected areas of a bronze statue, the results of which are reported in the *Journal of Spectral Imaging* (doi: 10.1255/jsi.2018.a10). The statue investigated was *The Man with the Key*. It represents Jean d'Aire and it is the first individual figure cast in bronze from the famous group *Les Bourgeois de Calais* (*The Burghers of Calais*) by Auguste Rodin. The sculpture was cast by Jacques Petermann in Brussels, Belgium. Since 1902 it has been displayed at "Solli plass", a traffic-congested area in the city centre of Oslo, Norway, which is likely to have been subjected to high levels of SO_2 pollution and acidic rain conditions. The sculpture was in a state of advanced degradation and was relocated to the courtyard of the Vigeland Museum for conservation. The HSI investigation was performed there.

Auguste Rodin "Jean d'Aire" (1901). Oslo kommunes kunstsamling (City of Oslo Art Collection).

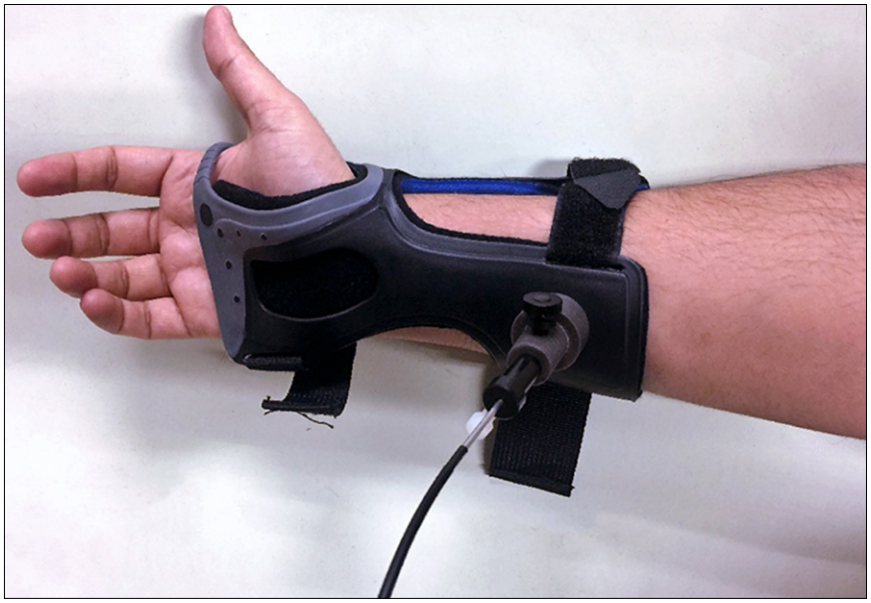
Short wavelength infrared (SWIR) HSI (960–2500 nm) was used, since both brochantite and antlerite have characteristic spectral absorbances in that wavelength region. SWIR HSI proved to be able to determine the spatial distribution of brochantite and antlerite on selected areas on the statue. None of the above compounds can be recognised by visual observation, but HSI data revealed the occurrence of each of them in certain areas. Moreover, non-uniform distribution of the above compounds was clearly shown by HSI, but it could easily be missed by an investigation of discrete spots.

Being non-destructive and allowing *in situ* analysis of large corroded areas, SWIR HSI can represent an important new tool for the investigation of bronze statuary. To the best of the authors' knowledge, this is the first *in situ* application of SWIR HSI to the assay of atmospheric corrosion of bronze statuary. Further development can be made by exploring the possibility to map other corrosion products that can be detected in this wavelength range. The technique may also find useful application in other corrosion-related fields. Devices that allow the hyperspectral camera to follow the topography of the sculpture can be developed for investigating broader monument areas.

"Hyperspectral imaging is a versatile and powerful technique. It is non-contact and non-destructive, and allows us to see the spectral fingerprint of a material in great detail. This means that we can reveal information that cannot be seen with the naked eye", said Professor Lise L. Randeberg.

Will Raman be the solution to non-invasive blood glucose testing?

For decades, researchers have tried to develop spectroscopic techniques to offer non-invasive blood glucose monitoring. Near infrared (NIR) spectroscopy has been tried but has not offered a viable solution. Now, researchers from the University of Missouri School of Medicine and the Massachusetts Institute of Technology have evaluated



the accuracy of a Raman-based technology; published in *Analytical and Bioanalytical Chemistry* (doi: 10.1007/s00216-018-1244-y). Early results show that the non-invasive technology measures blood glucose levels as effectively as a finger prick test.

The study measured the blood glucose levels of 20 healthy, non-diabetic adults prior to drinking a glucose-rich beverage. Blood glucose levels were then measured in intervals over the next 160 min using three methods: Raman spectroscopy, intravenous blood test and finger prick. The tests are designed to determine how much glucose remains in the blood and if a patient's insulin-regulating mechanisms are working effectively. The researchers found that Raman spectroscopy predicted glucose values as accurately as a finger prick test.

"This is a technology that we have been pioneering for more than 20 years", said Jeon Woong Kang, PhD, research scientist with MIT's Laser Biomedical Research Center and co-author of the study. "We know that handheld skin prick tests are not always accurate and may be uncomfortable for patients. The gold standard is intravenous blood testing, but frequent blood draws may not be an option for many patients. We were pleased to find that our initial results show Raman spectroscopy can measure glucose levels that are comparable to the finger stick devices. We hope that we can refine this method to be a non-invasive continuous glucose monitoring sensor."

With more testing, the researchers hope Raman spectroscopy can become an alternative method to test glucose levels in patients in clinical care settings who are not capable of frequent blood draws and, one day, in other settings as the technology becomes smaller and more portable. Future studies will examine the accuracy of the technology in patients with diabetes.

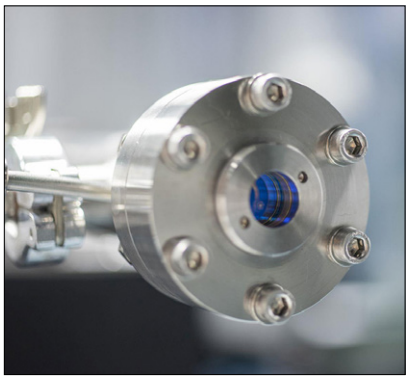
Electron spectrometer deciphers quantum mechanical effects

Electronic circuits are miniaturised to such an extent that quantum mechanical effects become noticeable. Using photoelectron spectrometers, solid-state physicists and material developers can discover more about such electron-based processes. Fraunhofer researchers have developed a new spectrometer that works in the megahertz range.

Photoelectron spectroscopy opens a window on atoms together with their energy states and their electrons. In photoelectron spectroscopy, you shoot high-energy photons onto the surface of the solid-state object to be investigated: an electronic circuit, for instance. The high-energy light knocks electrons out of the atomic bond. Depending on what energy band they are in, they reach the detector at different times. Analysing the time it takes electrons to reach the detector, material developers can draw inferences about the energy states of the electron bands and the structure of the atomic bonds in the solid. All the electrons must start at the same time, which can be achieved only by using a pulsed laser beam. Usually the lasers work in the kilohertz range.

The problem is that if you set too many electrons free simultaneously with a pulse, they repel each other—making it impossible to measure them. The answer is turn down the power of the laser. However, to be able to measure enough electrons for a reliable sample, you need to arrange for suitably long measurement times. But sometimes this is not feasible, as the samples and beam source parameters cannot be kept sufficiently stable over such a long period.

Researchers at the Fraunhofer Institutes for Applied Optics and Precision Engineering IOF and for Laser Technology ILT have worked together with their peers from the Max Planck Institute of Quantum Optics to develop the world's first photoelectron spectrometer that does not work in the kHz range, but at 18 MHz. This means that several thousand times more pulses strike the surface than with conventional spectrometers. This has a dramatic effect on measurement times. "Certain measurements used to take five hours; we can now complete them in ten seconds", says Dr Oliver de Vries, scientist at Fraunhofer IOF.



Filled with inert gas, the pressure chamber contains light-guiding hollow-core fibres. The gas and the light interact with each other. As a result, the optical spectrum widens and the pulses become shorter (30 fs). © Fraunhofer IOF, Walter Oppel

The spectrometer consists of three main components: an ultrafast laser system, an enhancement resonator and a sample chamber with the actual spectrometer itself. As the initial laser, the researchers use a phase-stable titanium-sapphire laser. They change its laser beam in the first component: by means of pre-amplifiers and amplifiers, they increase the power from 300 µW to 110 W—a million-fold increase. In addition, they shorten the pulses. To do this, they use a trick whereby the laser beam is shot umpteen times through a solid, which widens the spectrum. If you then put these newly created frequency components of the pulse back together again—that is, if you combine all frequencies in a phase-correct manner—you shorten the pulse duration. "Although this method was already known beforehand, it was not possible until now to compress the pulse energy that we need here", says Dr Peter Rußbüldt, group manager at Fraunhofer ILT.

The pulse duration of the laser light leaving the first component is already very short. However, the energy of its photons is not yet sufficient to knock electrons out of the solid. In the second component, the researchers therefore increase the photon energy and shorten the pulse duration of the laser beams once again in a resonator. Mirrors steer the laser light around in a circle several hundred times inside the resonator. Each time the light passes the starting point again, fresh laser radiation from the first component is superimposed onto it—and this is done in such a way that the power of the two beams is added together. Bottled up in the resonator, this radiation reaches such powerful intensities that high-energy attosecond XUV pulses are generated with many times the frequency of the laser beam.

The researchers at Fraunhofer ILT use another trick to get the high-energy attosecond XUV pulses back out of the resonator. "We've developed a special mirror that not only withstands the high power, but also has a miniscule hole in the centre", explains Rußbüldt. The bundle of high-harmonic rays, as the high-energy laser beams are called, generated by the process is smaller than the other waves that are circulating. While the lower-energy light beams continue to hit the mirror and be steered around in a circle, the high-energy bundle of rays is so thin and narrow that it slips through the hole in the centre of the mirror, exits the second component and is deflected into the sample compartment inside the third component.

The prototype of the photoelectron spectrometer has been completed and is located at the Max Planck Institute in Garching, where it is used for experiments and optimised with the collaboration of Fraunhofer researchers.

Hyperspectral imaging reveals wound problems

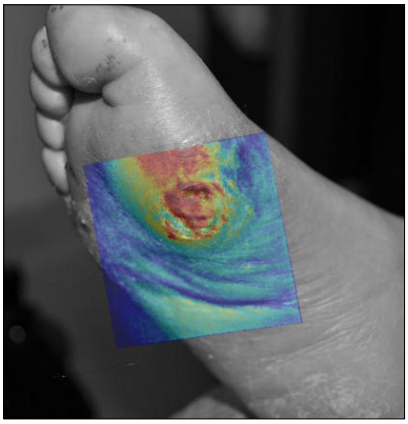
The Bolton Clarke Research Institute is working with RMIT University (Melbourne, Australia) to investigate hyperspectral imaging (HSI) as a faster way to let healthcare providers know when a leg wound is healing normally and when more treatment is needed to help heal the wound better. Their system uses up to 100 channels and reveals information that can normally only be discovered using pathology tests.

BCRI lead researcher Dr Rajna Ogrin said leg wounds happened more often in older people and could be painful, stopping people from going out and doing the things they need to do.

"They also may take a long time to heal and lead to complications like infections and needing to go to hospital," she said. "The most common type of leg wound is venous leg ulcers, which are wounds that don't heal because veins don't bring the blood back to the heart properly, and cause swelling in the legs and other problems. But a big problem in wounds is that it is hard to know which wounds won't heal as expected, and so need more help to heal better."

Previous research by RMIT has found that HSI can help better predict the healing of foot wounds in people with diabetes. The new work will build on research already done and find out if there is extra information in HSI images that will help predict how leg wounds will heal.

Trajan Scientific and Medical are funding the research work. The research project will run for 12 months and will include 80 Bolton Clarke clients with venous leg wounds in the Melbourne North region. Clients will be followed up at 12 and 24 weeks.



Example: Hyperspectral image used to show the blood oxygen level (red = high) of an ulcer with delayed healing.

Isotope ratio MS aids conservation of whale sharks

Isotope ratio mass spectrometry has shown that whale sharks, the world's largest fish, roam less than previously thought. Local and regional actions are vital for the conservation of this globally endangered species moving forward, according to a new study by researchers from the Marine Megafauna Foundation, University of Southampton and Sharkwatch Arabia.

Previously, genetic research indicated that whale sharks mixed within distinct populations in the Indo–Pacific and Atlantic Ocean, respectively. This new study used stable isotope analysis to demonstrate that whale sharks feeding at three disparate sites in the Western Indian Ocean (Mozambique and Tanzania) and the Arabian Gulf (Qatar) rarely swim more than a few hundred kilometres north or south from these areas.

"Whale sharks are amazing swimmers, often moving over 10,000 km each year, and they can dive to around 2000 m. Biochemical studies tell us more about where they go and what they do when they're out of our sight", said Dr Clare Prebble, who led the research as part

Researchers from the Marine Megafauna Foundation, University of Southampton, and Sharkwatch Arabia have used isotope ratio mass spectrometry to monitor the habits of the whale shark, Earth's largest fish. Copyright Clare Prebble, Marine Megafauna Foundation and University of Southampton.

of her PhD project at the University of Southampton.

Ratios between the heavier and lighter isotopes of nitrogen and carbon vary naturally across different habitats in the marine environment. For example, more of the heavier isotopes are found in near-shore environments than offshore. These ratios stay consistent as they are passed up through the food web and therefore provide a record of the animal's feeding and movement behaviours.

Electronic tags are commonly used with marine animals to record their movements and diving behaviours. However, the challenge of keeping them attached to a large shark, while minimising disturbance, has meant that only short-term deployments (weeks to months) have been possible. This study used tiny samples of skin tissue from wild, free-swimming whale sharks. These small pieces of skin, collected over two to three years at each location, were sufficient to reconstruct the sharks' movements and feeding preferences over the weeks and months prior to sampling.

Values of both carbon and nitrogen stable isotopes differed at each site. To complement the biochemical analysis, the researchers also took photographs of the natural markings on each whale shark to identify and track individuals over a 10-year timeframe. Every whale shark has a unique spot pattern, similar to a human fingerprint. The team recorded 4197 encounters with 1240 individual whale sharks within these three countries.

Only two sharks moved between sites, both swimming around 2000 km north from Mozambique to Tanzania. Taken together, these findings indicate that there are limited movements between these major aggregation sites over months to years. These results have implications for the conservation of this endangered species.

"The best data available suggests that more than half of the world's whale sharks have been killed since the 1980s. Although the Western Indian Ocean remains a global hotspot for the species, even the largest feeding areas only host a few hundred sharks. Our results show that we need to treat each site separately, and ensure good conservation management is in place, as the sharks may not re-populate if they're impacted by people's activities", Prebble added.

The study stresses the need to protect these filter-feeding sharks at the areas where they come together in numbers, particularly where human pressures are

also present. Whale sharks are an incidental catch in coastal gillnets, which are frequently used in Mozambique and Tanzania. The Arabian Gulf is a huge oil shipping area where vessel strikes pose a major threat to the sharks when they are feeding near the surface.

Their findings are published in *Marine Ecology Progress Series* (doi: 10.3354/meps12667).

Safety of construction materials can be assessed by hyperspectral imaging

Professor Debra Laefer from New York University's Center for Urban Science and Progress (CUSP), in collaboration with Professor Aoife Gowen and Zohreh Zahiri from University College Dublin, recently demonstrated, for the first time, the ability to use hyperspectral imaging to characterise differing strengths within a single type of construction material. With proper post-processing of the data, hyperspectral imaging can automatically and reliably detect weak from strong hardened concrete and normally fired bricks. All of this is done without any destructive testing or direct contact with the materials. The concrete results were published in *Construction and Building Materials* (doi: 10.1016/j.conbuildmat.2018.07.082) and the brick ones in the *International Journal of Architectural Heritage* (doi: 10.1080/15583058.2018.1503362).

Hyperspectral imaging has the potential to help civil engineers and developers rapidly analyse the integrity of construction materials and assist with the documentation, preservation and restoration of historical structures, as well as the asset management of our infrastructure. It can have a significant impact on architectural conservation by providing a non-destructive means for safety and serviceability assessments of existing building materials.

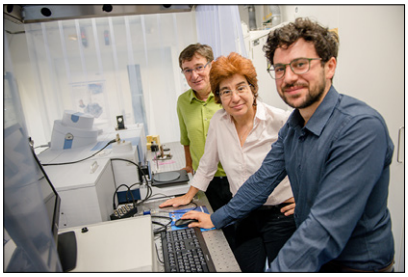
"Previous studies have shown the ability to use hyperspectral imaging to correctly distinguish between different materials, such as wood or steel. Our team was able to use the same technology to collect information that enables distinguishing the strength within a single material without touching it or destroying it", said Professor Laefer. "After further study, we believe this technology can be successfully deployed from the air or autonomous vehicles to characterise building materials at a city-scale, thereby avoiding the need for scaffolding and destructive testing during building façade inspections and other assessments."

Terahertz spectroscopy determines hydration shell size

Charged particles in aqueous solutions are always surrounded by a shell of water molecules. However, much is still unknown about the nature of this hydration shell. Using terahertz spectroscopy, chemists from Bochum have gained new insights into how an ion affects the water molecules in its environment. Professor Dr Martina Havenith, Dr Gerhard Schwaab and Dr Federico Sebastiani from the Chair of Physical Chemistry II of Ruhr-Universität Bochum (RUB) have reported an overview of the results of their experiments in *Angewandte Chemie* (doi: 10.1002/ange.201805261) and *Angewandte Chemie International Edition* (doi: 10.1002/anie.201805261).

"The hydration shell of ions is extremely important for understanding fundamental processes such as the transport of ions through membranes or batteries", says Martina Havenith, spokesperson of the Ruhr Explores Solvation Cluster of Excellence. "However, seemingly simple questions, like the size of the hydration shell or the occurrence of ion pair formation, still remain unanswered."

At the Ruhr-Universität Bochum, Martina Havenith's team approaches this question with terahertz spectroscopic methods developed in-house. The Bochum group developed special techniques using low-frequency terahertz radiation to determine the size of the hydration shell, i.e. the number of water molecules that are affected by an ion. They mathematically break down the recorded absorption pattern into its components and can thus identify the parts in the spectrum that reveal something about individual ions or pairs of ions.



The Bochum research team: Gerhard Schwaab, Martina Havenith and Federico Sebastiani (from the left). © RUB, Marquard

Hydration shells consisting of 2–21 water molecules were determined for more than 37 salts. The number depends on the size of the ion and its valency. Single-charged ions usually affect fewer water molecules than multiple-charged ions. "However, this is not entirely systematic, but also depends on the cation or anion present", explains Martina Havenith.

The researchers use their method to determine the so-called effective number of water molecules, which is the minimum number of water molecules that is affected by an ion, i.e. that cannot move as freely as the unaffected surrounding water. Due to the positive or negative charge of an ion, the water molecules with their partially positively charged hydrogen atoms or their partially negatively charged oxygen atom align themselves with the ion. "The effect of the ion on the water molecules gradually decreases with distance", Havenith explains. "Thus, there is not always a clear boundary between affected and unaffected water molecules." The team therefore specifies a minimum number for the size of the hydration shell.

However, the Bochum group dealt not only with individual ions, but also with pairs of cations and anions. The water molecules affect the formation of the ion pair. They can either form a joint hydration shell around the two partners or separate shells around cation and anion. The team is able to estimate how many water molecules these shells each consist of. "In order to know how many water molecules surround an iron chloride, it is not enough to know how many water molecules are affected by a single

chloride ion and how many by a single iron ion", explains Havenith. This is not a simple additive process.

"In general, our results clearly show that cooperative effects rather than individual ion properties are decisive", sums up the researcher. It is therefore not enough to know a single ion property in order to predict how a salt will affect the water molecules in its environment. Instead, various parameters, such as the charge density or the combination of the cation–anion will determine whether an ion pair is formed.

Mass spec uncovers dangers of world's oldest cheese

The tomb of Ptahmes, mayor of Memphis in Egypt during the 13th century BC, was initially unearthed in 1885. After being lost under drifting sands, it was rediscovered in 2010, and archaeologists found broken jars at the site a few years later. One jar contained a solidified whitish mass, as well as canvas fabric that might have covered the jar or been used to preserve its contents.

Enrico Greco from the University of Catania and colleagues used liquid chromatography-mass spectrometry to determine the identity of the contents. The peptides detected by the analysis show the sample was a dairy product made from cow's milk, and sheep's or goat's milk. The characteristics of the canvas fabric, which indicate it was suitable for containing a solid rather than a liquid, and the absence of other specific markers, support the conclusion that the dairy product was a solid cheese.

The world's oldest cheese? Credit: Enrico Greco, Università degli Studi di Catania

Other peptides in the food sample suggest it was contaminated with *Brucella melitensis*, a bacterium that causes brucellosis. This potentially deadly disease spreads from animals to people, typically from eating unpasteurised dairy products. If the team's preliminary analysis is confirmed, the sample would represent the earliest reported biomolecular evidence of the disease.

The research is reported in *Analytical Chemistry* (doi: 10.1021/acs.analchem.8b02535).

Range of spectroscopic techniques reveals evidence of life 3.4 billion years ago

Scientists have confirmed that 3.4 billion year old microfossils from Western Australia's Strelley Pool formation had chemical characteristics similar to modern bacteria. This all but confirms their biological origin and ranks them amongst the world's oldest microfossils. The work was presented at the Goldschmidt geochemistry conference in Boston, USA, with simultaneous publication in *Geochemical Perspectives Letters* (doi: 10.7185/geochemlet.1817).

The Strelley Pool formation is located about 1500 km from Perth, WA, Australia. They are probably simple prokaryote bacteria, i.e. without a cell nucleus or other sub-cellular bodies.

A team of scientists, led by Dr Julien Alleon (IMPMC, Paris, France; and MIT, Cambridge, MA, USA) have been able to show that the chemical residuals from ancient microfossils match those of younger bacterial fossils, and so are likely to have been laid down by early life forms. They compared the results of synchrotron-based X-ray absorption spectroscopy analysis of the Strelley Pool microfossils with more recent ones from the Gunflint Formation (1.9 billion years old, found on the shores of Lake Superior, Ontario, Canada) and with modern bacteria. All showed similar absorption features, indicating that the residual chemicals were made from the same building blocks, thereby supporting a biological origin (see illustration below).

The XANES spectra were collected on the 10ID-1 STXM beamline at the Canadian Light Source and on the HERMES STXM beamline at the synchrotron SOLEIL in France.

Applications invited for the Jean-Pierre Huvenne GFC Award in Chemometrics

The French Chemometrics Society (GFC) will give the GFC award in honour of the late Professor Jean-Pierre Huvenne for his early contribution to chemometrics in vibrational spectroscopy in France.

This GFC Award will be made to the best PhD thesis defended in the two years preceding the award ceremony. This will take place at the next annual GFC congress in Montpellier (France), 31 January–1 February 2019 (https://chemom2019.sciencesconf.org).

If you have just defended your thesis or if it is scheduled to take place before 1 December 2018, you can enter via the application form and detailed instructions at https://goo.gl/forms/6ZttbNu5wZKUO89P2.

- This competition is open to **PhD students worldwide** who defend their thesis between 30 November 2016 and 1 December 2018.
- The PhD thesis is expected to show significant **chemometrics results** in analytical chemistry.
- The winner of the Jean-Pierre Huvenne GFC Award in Chemometrics will be invited to present his/her work at the next annual GFC congress in Montpellier, 31 January–1 February 2019. (A complementary registration will be offered to the winner and travel expenses will be reimbursed by the GFC.)
- The deadline for applications for the Jean-Pierre Huvenne GFC Chemometrics Award must be **submitted by 1 December 2018**.

Any questions, contact the Chairman of the French Chemometric Society, Ludovic Duponchel (ludovic.duponchel@univ-lille.fr).

ARTICLE

Infrared spectroscopy and chemometrics to evaluate paper variability in document dating

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Introduction

In the forensic document examination field, document dating is one major challenge that still lacks validated methodologies. The variety of inks and papers, combined with different storage conditions, poses a complex problem when an estimation of age is needed. Although paper samples are mainly composed of cellulose, their chemical composition changes according to the manufacturing process and the raw materials. When paper samples start degrading, differences in chemical profile can be identified. However, differences in the initial composition must be considered to avoid misinterpretation.

Spectroscopic techniques such as mid-infrared are increasingly important in forensics.[1] One of the main reasons is the non-destructive and non-invasive nature of the analysis, which is able to provide chemical information whilst maintaining the integrity of the samples.

The aim of this work is to evaluate paper variability in document dating. To do this, mid-infrared spectroscopy, together with chemometric techniques, were used to estimate the document age of papers of different natures; for more detailed information, see Reference 2.

Chemometrics

Mid-infrared spectroscopy has the great advantage of providing a large amount of spectral information over a wide wavelength range. The disadvantage is that the spectral information is often redundant and affected by spectral artefacts. Therefore, multivariate techniques of analysis (a.k.a. chemometrics) are needed to extract useful chemical knowledge.

Principal component analysis (PCA) is probably the best-known chemometric technique. It is an exploratory technique of analysis that uses maximum variance to describe the dataset in a new space with reduced dimensionality. In contrast to PCA, partial least squares (PLS) is a supervised technique that aims at building a mathematical model based on spectral features to predict a parameter of interest, in this case, the age of a given document. To do this, a set of samples with a known age (Training set) is employed to establish a mathematical relationship between the spectra and the age, maximising the covariance between them. Extensions of PLS, such as sparse partial least squares (sPLS), can be employed as variable selection methods. In this case, sPLS imposes a penalty term to uninformative coefficients to have zero value, reducing noise and attenuating the influence of correlated or unrelated variables present in the spectral profile.

As mentioned above, physical phenomena can cause variation in the dataset that is not relevant to the study (such as noise, baseline etc.) and these can mask the information of interest. Spectral preprocessing techniques can be used to correct or minimise the effect of these undesired phenomena and provide a reliable analysis. In other cases, chemical interferences can be the cause of such problems. Therefore, more dedicated methods are needed to correct those contributions. Orthogonal signal correction (OSC) and generalised least squares weighting (GLSW) are examples of these techniques.

While OSC subtracts the variability of spectral data that is orthogonal to the age, GLSW applies a filter matrix to down-weight the interferent contribution. Further information can be found elsewhere.[3,4] To evaluate model performance, validation and prediction sets were investigated, providing information about the model's ability to predict unknown samples.

Materials and methods

Reports from 15 different years between 1985 and 2012 were provided by the Spanish General Commissary of Scientific Police (Madrid, Spain). For each year, five reports containing an average of five sheets each were analysed with mid-infrared spectroscopy. Eight spectra were acquired per sheet. A Nicolet iS10 spectrometer (ThermoFisher Scientific, MA, USA) was employed for spectral acquisition with the Smart iTR diamond attenuated total reflectance accessory. The spectral range investigated was 4000–650 cm^{-1}, with resolution of 4 cm^{-1} and 32 scans per spectrum.

The samples described above were used to build two different datasets with different criteria of selection to compose the Training and the Prediction sets. The Prediction set for both datasets was, in turn, split into so-called Report Prediction and Sheet Prediction sets. In *dataset-PCA*, PCA was performed to select one whole report from each year to compose the Report Prediction set, guaranteeing that all plausible variability is included in the model and no extrapolations were made. In contrast to the statistical philosophy, but tuned for the forensic application, the *dataset-RANDOM* was built by randomly choosing a whole report from each year to compose the Report Prediction set. For both datasets, the Sheet Prediction set was built by randomly choosing one sheet from the remaining reports.

PLS models were built and compared, employing different preprocessing techniques to attenuate differences among documents from the same year. All chemometric analysis were made using the PLS_Toolbox (Eigenvector Research Inc., USA) running on Matlab (The Mathworks, MA, USA). The sPLS algorithm was used as described in Reference 5.

Results and discussion

Spectral profiles of papers (Figure 1) showed the important cellulose-related bands, such as the characteristic O–H bond vibration at 3400 cm^{-1}, absorptions at 1025 cm^{-1}, 1160 cm^{-1}, 1315 cm^{-1} and 2890 cm^{-1}, related to different C–H, C–OH, C–CH_2, C–O–C vibrations, respectively. These contributions are common to all paper samples, regardless of their age. Calcium carbonate (712 cm^{-1} and 870 cm^{-1}) and kaolinite (3690 cm^{-1} and 3620 cm^{-1}) absorptions were also found; these compounds are usually employed as inorganic fillers. These contributions are not common to all paper samples, but vary according to the manufacturing process; papers from the same year can have different compositions of these inorganic fillers.

This variability of paper composition poses a big challenge in document dating, because models to estimate paper age can be built based on the different chemical composition rather than differences due to the aging process. If the variability of samples is not considered in a proper manner, models can be optimal from a mathematical point of view but misleading as to the final aim. To reduce that variability, preprocessing techniques and variable selection were employed.

PCA shows the difference between the document types. According to Figure 1, it is possible to observe that samples

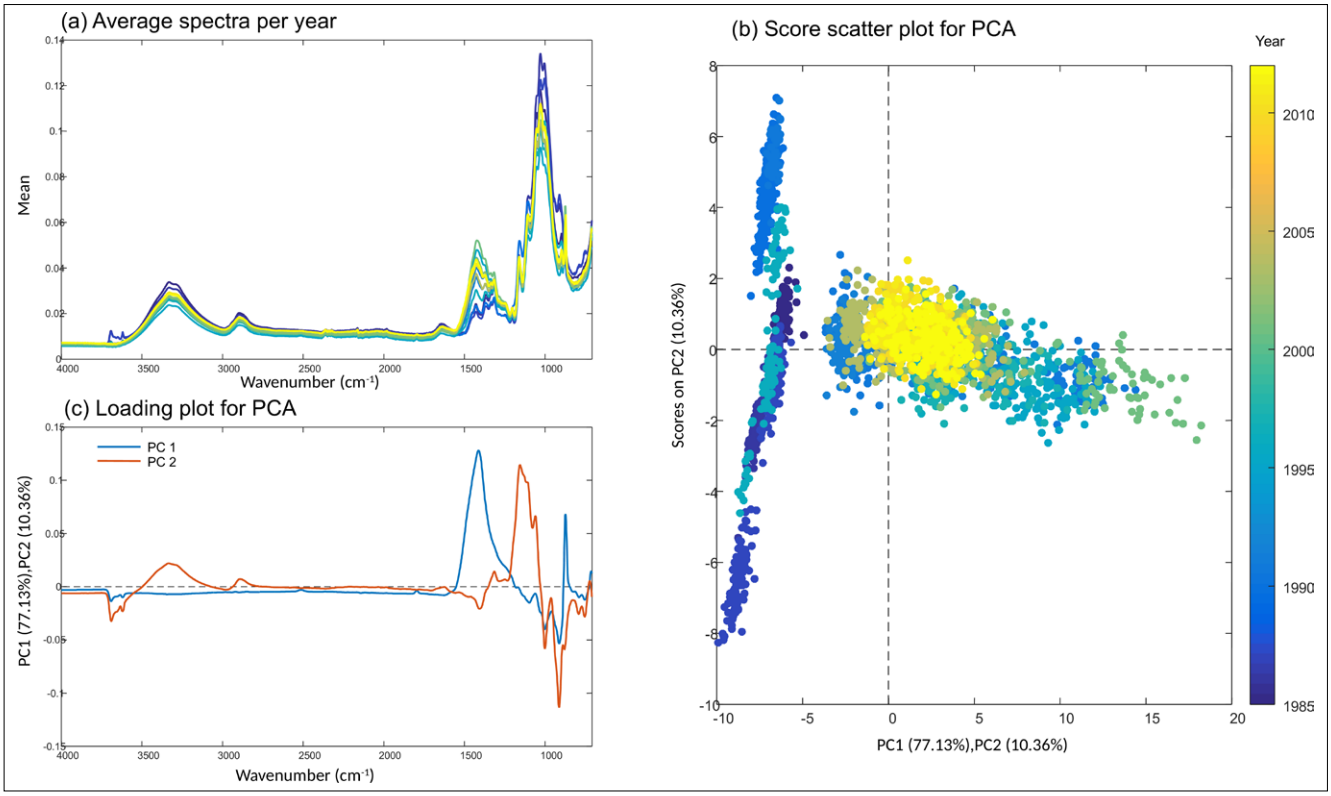

Figure 1. (a) Average spectra per year, (b) score and (c) loading plots of PCA.

Table 1. Results from the PLS models using different preprocessing techniques Model 1 [PLS model with standard normal variate (SNV), smoothing and mean-centring]; model 2 (PLS model with SNV, smoothing, OSC and mean-centring); model 3 (PLS model with SNV, smoothing GLSW and mean-centring); and model 4 (sPLS model with SNV, smoothing and mean-centring).

		Dataset-PCA				Dataset-RANDOM			
	Model	1	2	3	4	1	2	3	4
	LV	4	1	2	5	4	1	3	5
Training set	*RMSECV*	4.7	4.5	4.6	4.5	4.4	4.5	4.2	4.3
Training set	R^2_{cv}	0.83	0.85	0.86	0.88	0.74	0.74	0.76	0.73
Training set	$bias_{cv}$	0.04	0.02	0.01	–0.06	0.01	0.04	–0.00	0.87
Prediction set – Report	*RMSEP*	3.8	4.0	3.6	4.0	5.1	4.3	5.0	4.7
Prediction set – Report	R^2_{pred}	0.90	0.89	0.91	0.88	0.74	0.80	0.75	0.86
Prediction set – Report	bias	0.35	0.32	0.22	0.15	2.11	1.46	1.95	0.64
Prediction set – Sheet	*RMSEP*	4.3	3.7	4.2	4.5	4.0	3.6	3.7	4.3
Prediction set – Sheet	R^2_{pred}	0.86	0.90	0.87	0.85	0.78	0.82	0.82	0.87
Prediction set – Sheet	bias	0.05	0.24	0.07	0.00	0.44	0.22	0.34	0.97

LV: number of latent variables; *RMSECV*: root mean square error of cross validation; *RMSEP*: root mean square error of prediction

from year 1990 show more than one cluster (see score scatter plot), indicating a different chemical composition. In the loading plot it is possible to observe that these differences are explained in PC1 by the inorganic fillers' absorption bands.

After confirming the variability within samples from the same year, four PLS models with different preprocessing techniques and variable selection strategies were compared using the two datasets. Table 1 shows that results from dataset-RANDOM show higher prediction errors (root mean square error of prediction, *RMSEP*) for Report Prediction for all models, a trend that is repeated in the bias of the models. This is due the fact that some of the reports in the prediction set show high variability when compared to the training set.

From Table 1 is clear that the preprocessing filters decrease the model complexity [number of latent variables (*LV*)]. When OSC and GLSW are applied, a significant, but not relevant, amount of variance is removed from the dataset, leading to its simplification.

Comparing all strategies, OSC (model 2) showed potential in model building. With one *LV*, the model decreased the prediction error when compared to the other models and showed more stability regarding Report Prediction error for the two datasets built. In addition, the most important variables in model 2 (Figure 2) to estimate document age were 1412 cm^{-1} and 914 cm^{-1}. According to the literature, those two bands reflect

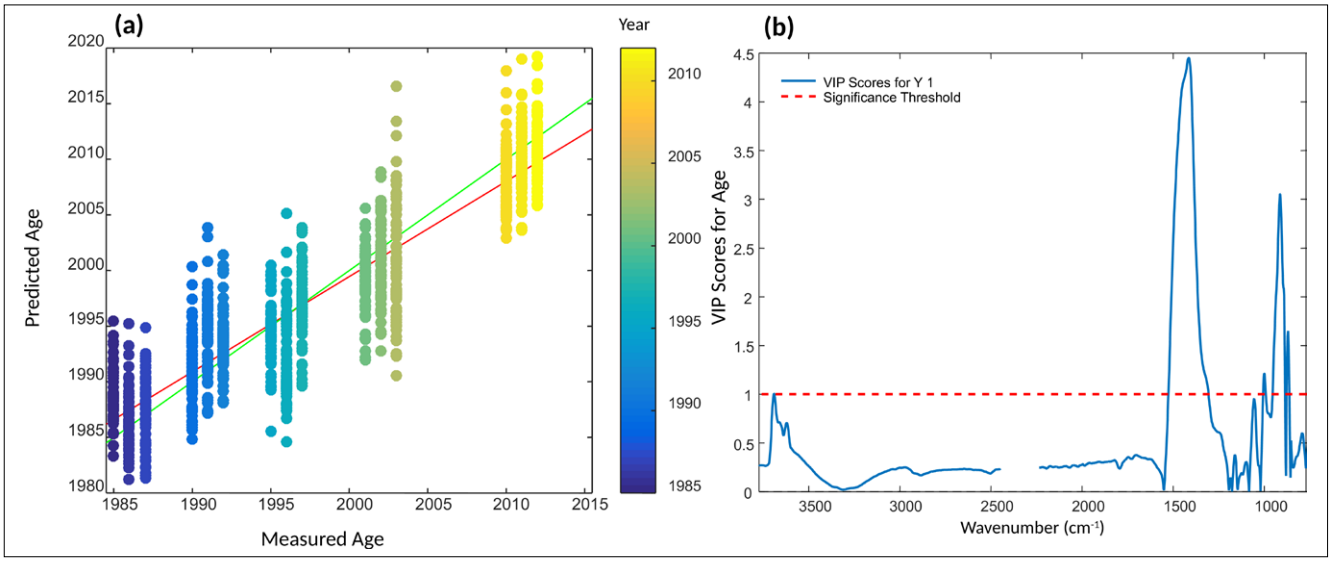

Figure 2. Results for the PLS regression model 2 (applying OSC filter with one component): (a) regression plot and (b) VIP scores for model 2.

changes in cellulose crystallinity during the degradation process, while other research has assigned the 1410 cm^{-1} absorption to the filler compounds. Although the spectral region appears to have an ambiguous interpretation, it is important to mention that the obtained values of approximately four years for *RMSECV/RMSEP* are adequate for the proposed application and the complexity of the samples.

Conclusion

The most important point of this study was to open a discussion about the implementation of spectroscopic and chemometric techniques in complex contexts such as forensics, especially regarding document aging. This is extremely important because it is not known if the degradation processes are similar for samples with different chemical compositions. Nonetheless, this study shows the potential of infrared spectroscopy and chemometrics to assess document age. It also provides the prospect of implementing advanced analytical methodologies in scientific police laboratories.

Acknowledgements

The authors would like to acknowledge the Spanish General Commissary of Scientific Police (Documentoscopy section, Spain) for providing the analysed documents. Also, the funding agencies INCTAA (Processes no.: CNPq 573894/2008-6; FAPESP 2008/57808-1), NUQAAPE – FACEPE (APQ-0346-1.06/14), Núcleo de Estudos em Química Forense – NEQUIFOR (CAPES AUXPE 3509/2014, Edital PROFORENSE 2014), CNPq (PVE/CNPq, process no: 400264/2014-5), FACEPE and CAPES (PDSE scholarship process number BEX 7712/15-4), are acknowledged.

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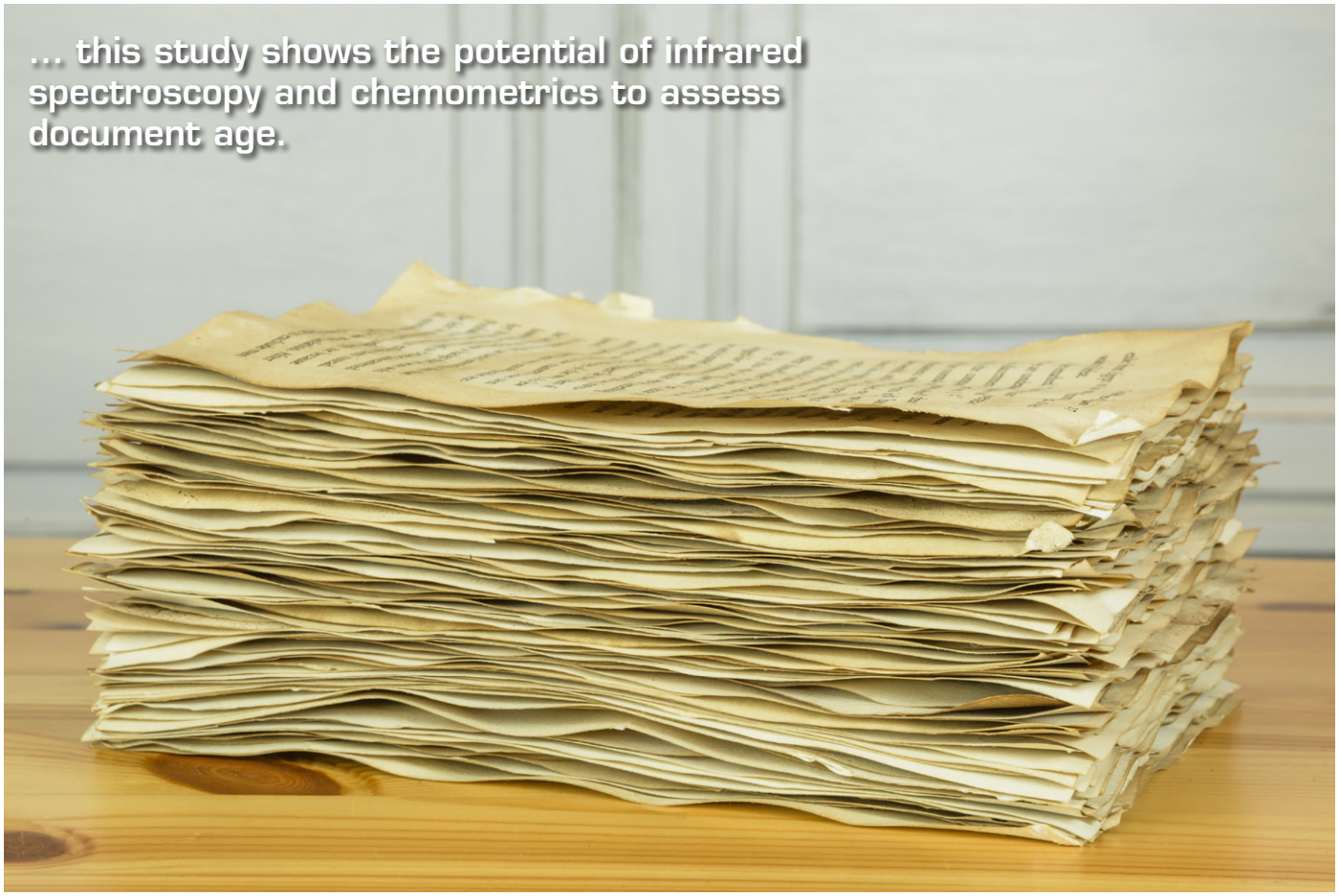

ARTICLE

Activated sludge settling analysis using a near infrared optoelectronic device: overview and application to wastewater treatment

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Unstable suspensions of microorganisms (AS, activated sludge) produced by biological treatment plants sediment in an unusual and very specific mode: hindered settling. We use an optoelectronic assembly operational at 940 nm (in the short wavelength near infrared) to study the kinetics of this settling. Amazingly, we discover that, transiently, the AS transmission can exceed 100 % compared to pure water. We hypothesise that the "optical structure" of water can be modified in this mixture, which contains numerous biological macromolecules. We locate our working wavelength on the water spectrum, close to the O–H stretching overtone. In addition, as an example, we show how this property could be used to improve the prediction and thus the management.

Introduction

Wastewater treatment is an important environmental obligation. Among the many processes used to date, biological purification remains the most common. The principle of the process is to separate the wastewater into two phases. One is "liquid" and is released into the environment (clarified water); the other is "solid" and composed mainly of microorganisms (bacteria), which have absorbed or metabolised certain pollutants. This solid phase is called "activated sludge" (AS).

It will be readily understood that the success of a biological treatment lies in the good separation of the two phases. The specific weight of AS is generally slightly higher than that of water, so the simplest and most commonly employed separation process is to allow the solid phase to settle (or sediment) under the action of gravity.

Sedimentation of AS occurs by a very specific process, rarely observed for other compounds, known as hindered settling. Hindered settling is characterised by a very flat and well-defined solid–liquid interface, almost exactly parallel to the air–water interface, as shown in Figure 1.

Given the environmental and economic importance of water purification and biological wastewater treatment plants (WWTP), we have developed a small, simple and inexpensive optoelectronic device, which we call ASAN (Activated Sludge Analyser), originally intended for study the AS sedimentation.

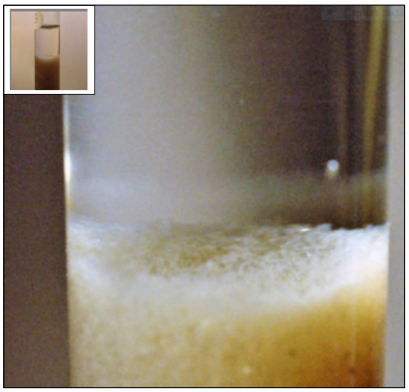

Figure 1. The box at the top-left clearly shows the sharp interface between solid (opaque) and liquid (transparent) phases characterising a hindered settling. The main picture shows the same interface surmounted by a more diffuse "ring" (which we call an "aura").

Material and methods

The ASAN device is shown in Figures 2 and 3. (Figure 4 shows the device used to hold the optical glass tube vertically.) The optical axis connects a LED emitting at 940 nm (short wavelength near infrared, SWNIR). The light beam passes through an optical glass tube ½ inch in diameter and strikes a phototransistor sensitive to this wavelength. The whole is powered by a steady DC current. The current emitted by the phototransistor is transmitted to a data logger and the data, in µA (I) and seconds (t), are sent to a PC (using a CSV file). We define transparency, $TY\%$, by

$$TY\% = \frac{I - I_b}{I_0 - I_b} \times 100 \qquad (1)$$

where I_0 is the intensity of the blank (distilled water, filtered at 0.2 µm and

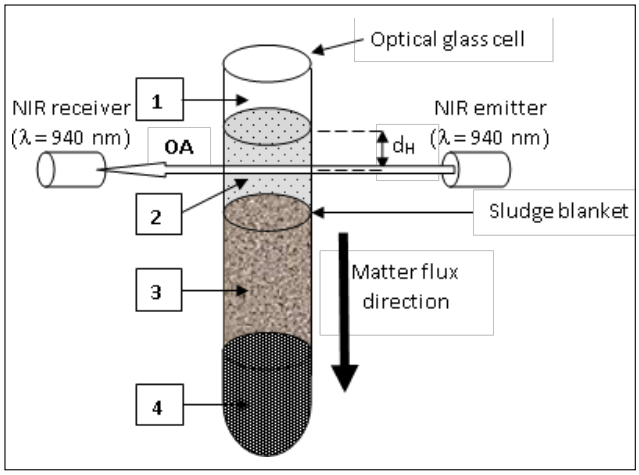

Figure 2. Sketch of the ASAN device. 1: air; 2: liquid phase; 3: settling solid phase (AS); 4: compacted AS. Reprinted by permission of SAGE Publications.

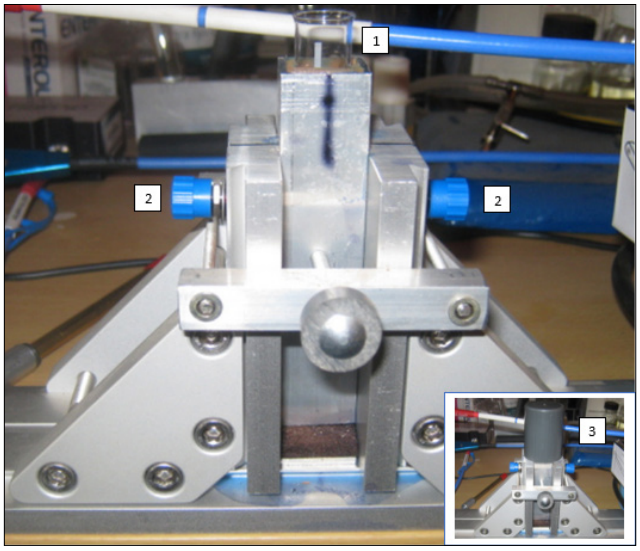

Figure 4. General view of the vertical tube holder. 1: optical glass tube ∅ ½ inch; 2: nozzle for optical fibre SMA-905 connector (with collimating lens); 3: tube covered by thick grey PVC lid.

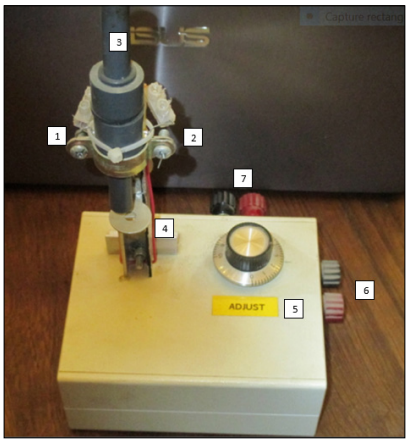

Figure 3. General view of the ASAN unit prototype. 1: phototransistor (receiver); 2: 940 nm LED (emitter); 3: optical glass tube location (here, replaced by PVC rod to protect the optoelectronics); 4: tube height adjustment system; 5: 100% adjustment potentiometer; 6: during current input (power is off to check the 0% of the unit); 7: output to datalogger.

thus made virtually sterile), I_b is the residual intensity (dark current), obtained by cutting the power supply ($I_b \ll I$; ≈ 0), I is the measured intensity. The time interval, Δt, is constant and chosen on the data logger.

Results

Figure 5 shows a set of results obtained via the ASAN device, according to various types of AS, WWTP, sampling points, concentrations etc. The study of the general profile is described in References 1–3 and we will here only consider the most striking characteristic: some maxima of transparency exceed 100% (Figure 5). Figure 6 isolates two of these curves and better highlights the phenomenon. After a noisy, but relatively constant, period [corresponding to the downward movement of the solid phase (the AS)], the transparency increases sharply and is a good indicator of the solid–liquid transition of the settling mixture interface crossing the optical axis. After this abrupt transition step, a maximum value usually occurs; in most cases, this "mini-maximum" remains less than 100%. However, in a number of situations, the transparency exceeds

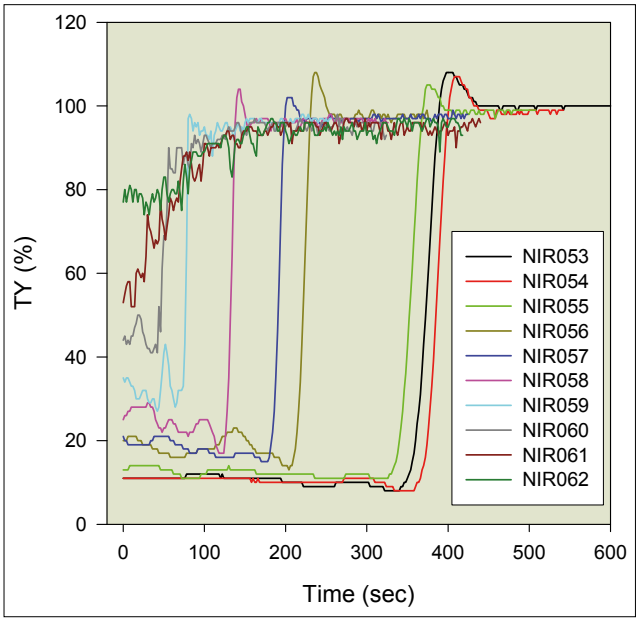

Figure 5. Various types of AS settling profiles obtained via the ASAN method. Hundreds of such curves have been studied (NIR0xx are experiment numbers).

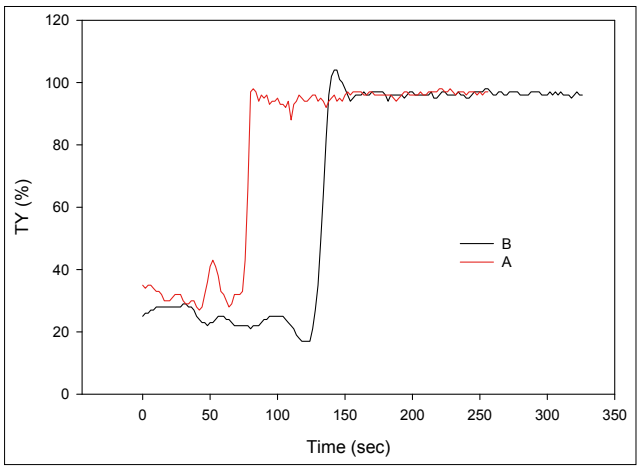

Figure 6. Two separated profiles of the Figure 5 series. Curve A shows a slight maximum just after the sudden rise in *TY%*, but it does not reach 100%; curve B, on the contrary, significantly exceeds 100%. After the maximum transient states, the two curves overlap and give an identical average value (greater than 95% transparency) of the settled water.

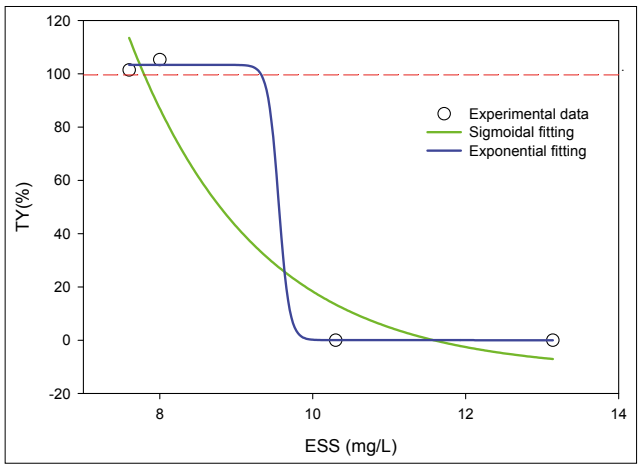

Figure 7. The figure shows a still hypothetical relation between AS with maximum transparency greater than 100% (*TY%*>100) and suspended solids in the effluent of a biological treatment plant. If the sigmoid model is confirmed, one could predict that for max(*TY%*)>100%, ESS<10 mg L^{-1}; max(*TY%*)<100%, ESS>10 mg L^{-1}. (Correlation coefficients of fittings: exponential, r=0.97, sigmoid, r=0.99.)

100%, which seems, *a priori*, impossible given the technique and relation.[1] It must be concluded that this fraction of AS is transiently more transparent than distilled water filtered at 0.2µm ("sterile", therefore). This is obviously counterintuitive and can only be explained if the solvent of the liquid phase is no longer ordinary water, and thus not comparable to the blank used to calibrate the ASAN. This observation is confirmed by the appearance of an "aura" (circular ring of matter, directly over the sedimentation mass of the AS. The phenomenon is clearly visible in Figure 1; this zone corresponds to an exclusion zone water (EZ water) according to Professor G. Pollack (personal communication) and a more crystalline form of liquid water.

These observations in the SWNIR allow us to highlight exciting and unexpected phenomena, but they are also exploitable in R&D.

The asymptotic values for $t \rightarrow \infty$ of Figures 5 and 6 (and in general), tend to *TY%*<100%, suggesting that the "clarified" water still contains suspended particles. The microorganisms forming the AS produce a significant amount of extra-polymeric substances (EPS) that can, along with other non-biodegradable pollutants, go through the treatment plant and be released into the environment. These ESS (effluent suspended solids) obviously should be avoided as much as possible (both for economic and health reasons). We have highlighted (see Figure 7) that a correlation between ESS and AS characterised by a maximum of the settling profile exceeding 100% could be established. This could provide a predictive tool to reduce ESS (via the addition of flocculants, management adjustment of the plant etc.). The data are unfortunately still insufficient to validate this correlation and the concluding form of the relationship.

Discussion

The results described above are thought-provoking and remain unexplained, from our point of view. It is obvious that more research is needed.

As discussed above, and after eliminating a possible artefact from the device through the reproduction of hundreds of experiments, our main hypothesis is the possibility of a modification of the "optical structure" of the water, observable in the SWNIR. So, we decided to locate our working position at 940 nm on the water spectrum. Figure 8 shows the result obtained via an optical fibre Vis-NIR spectrometer.

Two arguments lead us to consider that the observed value of 966.3 nm is more relevant for our study: the peak is closest to our working wavelength and its absorption is twice as high as the preceding one and therefore more likely to be more sensitive to variation in transparency. However, these are currently only hypotheses to be tested.

Let us admit, however, that we are working toward 966.3 nm ≈ 970 nm. This value would correspond to the second overtone of the stretching band of the O–H bond (probably $2\nu_1 + \nu_3$). The number of possible hypotheses then becomes considerable: from G. Pollack's liquid crystal water (associated with the aura of Figure 1, EZ zone), to more complex structures [such as "Hexamer (Cage), Liquid Surface, Liquid and Ice", which evoke "the extent of correlation between frequency and molecular environment in the liquid"].[4]

The proximity of many bio-macromolecules (EPS, cells walls and others) does not mask at all the peak at 970 nm ("these studies have reported peak absorption around 970 nm and 1180 nm in normal arterial tissue")[5] and, presumably, participate in the structuring of water.

We cannot push the speculation further before continuing the experimental aspect of our research... which for a retired researcher, with little money

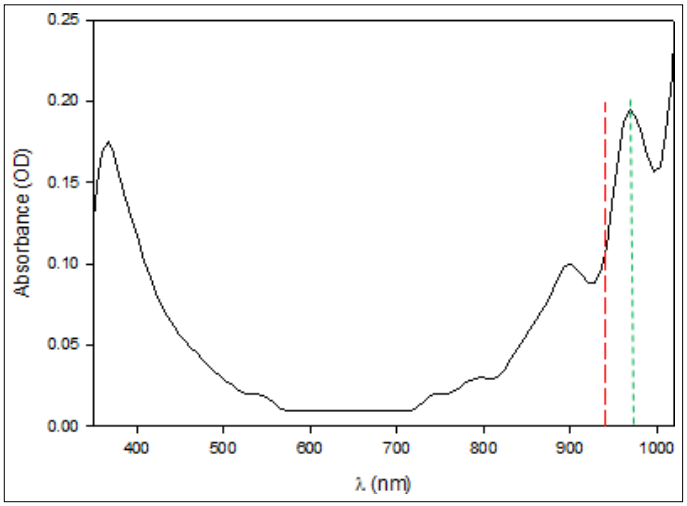

Figure 8. This shows the spectrum of liquid water between 350 nm and 1050 nm. It was obtained with a Flame NIR (Ocean Optics) fibre optic spectrometer, at ordinary temperature, on filtered distilled water and air as white (empty glass tube). The raw result was very noisy and was therefore smoothed by the bisquare method (using a degree 2 polynomial). In the SWNIR, we observe two absorption peaks at $\lambda_1 = 898.9 \pm 4.2$ nm and $\lambda_2 = 966.3 \pm 1.3$ nm (green line). Our working wavelength is represented by the red line at 940 nm.

and dropped by his academic structure requires a lot of effort and time. I would like to take this opportunity to ask readers who may be interested in collaboration or who may have ideas to explain the phenomenon described in this article to contact me.

Readers are also encouraged to use the commenting facility in the online edition to discuss any points that may arise from this article. You need to be logged in to comment, and you will find the comment form at the end of the article—Ed.

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TONY DAVIES COLUMN

Fitting people into your model

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As a community we have spent enormous amounts of time and money researching, discussing, publishing and patenting new ideas. We drive forward technology revolutions in spectroscopy, chemometric data handling, machine learning, libraries, near-line, at-line, online strategies, targeted vs non-targeted analysis—supporting the "omics" revolution—and everything that makes spectroscopy one of the most widely relevant and exciting fields in analytical science. However, are we paying enough attention to one component whose interaction in the dynamic environment is often taken for granted: are we including the human factor?

Human capital and state-of-the-art

Many articles published here over the years have focused on wonderful new discoveries. These have ranged from new hardware inventions, ways to obtain concrete, robust, validatable results where, at first glance, the data shows no initial promise, all the way to the training levels we would like to see in our future spectroscopists. But, looking at the overall picture, I am beginning to feel the glue which binds all these topics together has been rather overlooked.

We are blessed with a strong community of experts who are capable of delivering a pipeline of good ideas which result in innovation. We would clearly like to have more. Some areas of scientific endeavour bloom spectacularly, grab all the headlines only to vanish after a relatively short period in the spotlight. The field of analytical spectroscopy, however, has the very major benefit of being a vital enabler delivering long-term solutions to much of societal and industrial areas of concern. These can be as diverse as global warming, building a sustainable planet through increased use of renewables or our own biosecurity.

For the benefits of these innovations to be fully realised, I think we need to be far more aware of the environments into which they are being deployed. In the medical field, many promising developments never make it as far as the patient. This is not just due to cost, but often due to a failure, at an early stage in the development, to assess the skill sets, pressures and globally accepted working practises of the people who will need to be responsible for the deployment. Quite often you hear complaints and frustrations when an innovator's big idea does not meet with the expected acceptance and praise from those required to implement it. Terms like "they just don't get it" or "are they too stupid to see….?" bounce around meeting rooms.

When the "Broader Picture" phrase used to be used in meetings I was attending, I always knew immediately someone had run out arguments explaining why they were going to block a course of action I was trying to propose. I must admit that more recently I have developed greater sympathy for that annoyingly over-used phase and tend, if the situation demands it, to interpret it slightly differently. The older me now looks at the person bringing that argument and I ask myself—what did we miss when assessing the benefits case? Quite often we have been focussing far too much on the technical aspects of the innovation and leaving out of our models the existing status quo. All organisations, whether governmental, medical, chemical industry or academic have substantial investments in acquiring, developing and maintaining their human capital. Efficiency gains are far too often expressed in terms of reduced headcount to deliver the same output rather than better or more output with the same resources.

If you take a step back, it is often a very useful exercise to decide whether the organisation you are presenting your

ideas to requires, by its very nature, incremental improvements through sustainable technology deployments. Hopefully they are flexible enough to embrace the acquisition of more challenging disruptive technologies without risking the fundamentals of the business.

One area where this can be seen in many research papers is the descriptions of the State-of-the-Art. Almost always, these sections deal purely with the existing technical position couched in terms which shows it to be out-of-date and ripe for replacement. When have you ever seen an author use phrases like "the state-of-the-art technology benefits from years of undisturbed success across many application fields, has proven itself to be robust and is much loved by its operators as it can unreservedly be relied upon to give the correct answer on even difficult samples". Well I have never seen an example but if you have, please send them to me. If an author would think about the "bigger picture", then these issues may be addressed better in the following research and the inevitable publications promoting the results of this research would have provide some thought around its future deployment challenges and what strategies the authors propose to overcome strongly experience-based acceptance hurdles. The Humans would have entered the Model!

Emotional intelligence and change management

Right at the beginning of the process of innovation somebody has convinced someone that the work needs to be carried out. This may be through discussions with your line manager or academic superior or even an international panel of experts—but there will have been some human interaction where you are required to present arguments, written or verbally that a course of action is worth supporting.

There are two areas of Emotional Intelligence in action here:

- Empathy: the ability to understand the wants and needs of those around you… if you do not understand what the people on a funding body or simply your line manager wants, you will never be granted the funds which they control to do your work…
- Social skills: typically team players who do not need to focus exclusively on their own success, they have a reputation of helping others to develop and achieve their own advancements.

So, you have displayed that you have these skills in getting the funding for your work—so why lock them away when it comes to being able to assess and mitigate the impact your innovation will cause in the environment you are targeting for its deployment?

In an industrial setting we can often find fully mature and effective Change Management systems in place which take into consideration not only how a technological deployment will impact processes, and systems but also very strongly focus on the employees within the organisation. Good change management always includes processes for planning, testing and communicating change.

A classic example is in the area of deploying process analytical spectroscopy. As spectroscopists we have a superb array of sensor technologies covering many wavelengths and capable of being deployed in the harshest of environments. We have computers now capable of processing the most complex hyperspectral data sets with advanced algorithms. We teach this at universities and have research teams driving forward innovation. We enjoy the support of multidisciplinary teams consisting of chemists, mechanical, electrical and chemical engineers, and not forgetting the financial gurus who work out our Return of Investment calculations. Altogether we are quite capable of deploying process analytics across numerous chemical and pharmaceutical processes.

The financial benefits case of deploying process analysers is inescapable, yet to fully realise these benefits we must take into account and exploit the years of experience and investment in the human capital of our "conventional" quality control (QC) organisations. We almost always need top-quality calibrations for our analysers and these calibrations are delivered by our more conventional laboratories. The people in the QC environment have also to be won over to the new approaches. It is natural that they may be sceptical and worried that the impending changes, brought on by what is a truly disruptive technological advance, potentially could leave them out of work. It is clear that any successful deployment has to be built on their active involvement and embracing of change. Their roles may move forward, as one colleague put it, to working more to deliver product quality in the plant control room or monitor the outputs of complex sensors than living with their hands in a fume cupboard in a laboratory on the edge of the site – but their contribution will continue to be critical to the deployment of the advanced spectroscopic tools and their long-term success.

Summary

So, what do I mean to achieve with the title "Fitting people into your model", apart from the rather unsubtle chemometrics pun? Total Cost of Ownership is used frequently, for example in purchasing new pieces of hardware or changing a process. The Total Cost of Ownership calculations are commonplace and often cover not only the initial capital expenditure and deployment figures, but also long-term consumables requirements and end-life considerations. If you look for example at the Wikipedia page for Total Cost of Ownership there are some very long lists of things which need to be considered, but you will be hard pressed to find any human costs listed except for Corporate Management Time. I think we should add a few more! If properly handled, with the right amount of emotional intelligence, I strongly believe experience will show that the Total Cost of Ownership figures will probably fall! So, by adding people into your model, you will not only be increasing your chances of achieving your goals by delivering a successful project, but there is also a greater chance of delivering the project at a reduced overall long-term cost as well as retaining a happy workforce!

QUALITY MATTERS

Traceability and intellectual property

Peter J. Jenks, FRSC
The Jenks Partnership

The production of certified reference materials (CRMs) has grown rapidly since the mid-1990s, largely driven by demand created by the accreditation of testing laboratories to ISO/IEC 17025. It is now a multimillion US$ global business dominated by mixture of public sector Governmental agencies such as NIST and IRMM, public service organisations like United States Pharmacopeia, and the European Pharmacopeia and two businesses, LGC Group Ltd and Merck KgAA. These large suppliers are supported by a myriad of small, specialist commercial producers of secondary CRMs.

The public-sector producers are empowered to issue Primary CRMs. Most, but not all, commercially produced CRMs are secondary CRMs. More on the difference between primary and secondary later.

All CRM production is done by organisations that are either Accredited to ISO/IEC 17034 or work to a quality system based upon this Standard. ISO, the International Standards Organisation is an independent, non-governmental organisation made up of members from the national standards bodies of 161 countries. The Organisation works closely with two other international standards development organisations, the International Electrotechnical Commission (IEC) and International Telecommunication Union (ITU). In 2001, ISO, IEC and ITU together established the World Standards Cooperation (WSC). The WSC also promotes the adoption and implementation of international consensus-based standards worldwide.

ISO also works closely with the World Trade Organisation (WTO), seeking to reduce technical barriers to trade and with United Nations partners including the UN Economic and Social Council (ECOSOC).

In total, ISO collaborates with over 700 international, regional and national organisations. These organisations take part in the standard development process as well as sharing expertise and best practices.

ISO is funded by the national member organisations, in the UK this is the British Standards Institute (BSI) that pays a subscription towards the operational cost of the Central Secretariat. The subscription paid by each member is in proportion to the country's Gross National Income and trade figures. The sale of published ISO Standards is also a significant source of revenue. But ISO could not function without the support of countless volunteers who are supported by their employer. As an example, this author was part of the Working Group responsible for the creation of ISO/IEC 17034, but all time and travel costs were carried by my employer at the time, Sigma Aldrich Co Ltd.

An ISO/IEC 17025 accredited laboratory is required to validate analytical instruments and methods using CRMs: this is intended to prove that the analytical results produced are "traceable" back to a primary reference: in the case of analytical chemistry this is usually the Mole.

Metrological traceability is defined as a property of a measurement result, whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty.

For chemical CRMs the traceability is normally ensured by taking a primary CRM, issued by a National Metrology Institute and using this in the calibration chain, or by using a primary method, such as quantitative nuclear magnetic resonance. When a primary CRM is used the physical artefact is supplied with a comprehensive certificate of analysis (CoA). The data contained in the CoA is essential to the use of the primary CRM by the producer of the secondary CRM.

In an increasingly litigious world, it has been suggested that using a publicly funded CRM to produce secondary CRMs to be sold for commercial gain may be an infringement of the primary producers Intellectual Property (IP). It has been long believed that as primary CRMs are produced with the intention that they will be used to produce secondary CRMs, to be used by the customer, then there is an implicit licence to allow the use of the producers' IP.

But does this still apply when the customer of the primary CRM is a commercial producer that will make a very substantial profit on the sale of the secondary CRMs that are produced, often in a large quantity?

Public sector NMIs are under evermore financial pressure: would it not be reasonable for the NMIs to require the commercial producers to negotiate a formal Licence to use the IP and pay a royalty on the CRMs produced?

There is a precedent for this concept. Back in the 1990s, the US Department of Commerce, under whose authority NIST functions, established the concept of "NIST Traceable Reference Materials, or NTRMs". The NTRM producer was subject to NIST-mandated QA processes and procedures and paid a royalty fee. The process was abandoned with the accreditation of secondary CRM producers to ISO/IEC 17025 + ISO Guide 34, and now ISO/IEC 17034.

This author feels that it would be perfectly reasonable for the large, highly profitable producers of secondary CRMs to pay the NMI for the use of the IP that underpins the commercial product: let me know what you think!

SAMPLING COLUMN

A tale of two laboratories I: the challenge

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This is a tale of two fictional commercial laboratories, but all features in the story represent true events and occurrences culled from a range of real-world laboratories, here re-arranged in a more focused fashion for a purpose: "How can the Theory of Sampling (TOS) help the commercial laboratory to improve its reputation and to increase its business"? The relevance for existing laboratories is striking. The reader will have to bear with the column for mostly focusing on sampling issues in what obviously is a much more complex scientific and business context, but please indulge us for a little while—there is a sharp return to real-world realities at the end of the story. Laboratory A is in fierce market competition with Laboratory B (and indeed several others in the global market), a situation that has existed for decades. This has so far led to a healthy business-oriented science, technology and human capital drive that has served both laboratories well. Both laboratories are also keenly aware of the necessity to be in command of TOS for all relevant in-house activities involving sampling, sub-sampling, mass-reduction, sample splitting etc. But whereas Laboratory A has availed itself of the services of TOS strictly within **its regimen only (as is indeed the case for most laboratories), one fine day the manager of Laboratory B had an epiphany that made her see the potential advantages of applying TOS** in full**, which involved a distinctly "beyond-the-laboratory" scope. What happed on that fine day? And how did it help Laboratory B to do better in the market?**

Disclaimer. There is no identifiable, real-world laboratory that corresponds completely to Laboratory A; it is for the tale's convenience that individual features met with in a large swath in real world laboratories have been collected under this generic name. Thus, Laboratory A mostly exists as a collection of issues, **some** of which may happen to also characterise the reader's laboratory, while Laboratory B is of an altogether different nature. Laboratory B is an emerging entity, on the verge to become real ….

Introduction (scientific, technological)

The traditional view of the role, tasks and responsibilities of the analytical laboratory is well described by Laitinen in an Editorial in *Analytical Chemistry* in 1979.[1] Despite being written 40 years ago, this is still an apt summary of the workings, and frustrations, of *laboratory life*. The emphasis on lack of communication between stakeholders is probably still true today. The only flag-raiser is hidden in the following sentence: *"… the analyst chemist is frustrated … not being informed about the* ***full background of the sample****, its urgency, or the use to which the measurements will be put"* (**emphasis** by the current author). Based upon the body of knowledge presented in all previous Sampling Columns, it is obvious that the analytical laboratory is an important area for application of the Theory of Sampling (TOS). There is so much *essential* sub-sampling going on, and there are many aspects of sample preparation and presentation that involve elements of mass-reduction as well (which is also sampling).

Of course, analytical chemistry reigns supreme in the laboratory. Full, always updated, command of the science and technology of analytical chemistry is the *raison d'etre* for all analytical laboratories, research or commercial. However, proper sampling also plays a critical role, as has been made abundantly clear in the previous columns in their treatment of ***why?*** and ***how?*** to sample. It is indeed fully possible to make a complete mess of the internal mass-reduction pathway towards analysis with severe, often fatal, breaks with representativity **if** the elements of the ongoing sub-sampling are not in compliance with the stipulations in TOS. The problem has been, and still is, that such operations are traditionally viewed as but "trivial" mechanical parts of the analytical process, and consequently have only rarely, if at all, been viewed in a systematic fashion—enter TOS. The present tale revolves around these issues.[2]

There is analysis … and there is analysis+

As soon as *samples* have been delivered to the in-door of an analytical laboratory, sub-sampling is in fact **the** critical success factor that must be dealt with in a proper fashion in order to be able to document relevant, reliable, representative analytical results.[3,4] This is a subtlety often not fully acknowledged, or even recognised, in the flurry of busi-

SAMPLING COLUMN

ness and economic calculations taking the driver's seat in the laboratory. It is all too often *assumed* that all operations and facilities needed for proper analysis are fully known and tested in the operative realm: procedures, equipment, work-paths, training—for which reason laboratory efficiency is considered only within the narrow scope of organising and optimising the total complex workflow. Truth be told, this is far from a simple matter in practice, but this is exactly where good managers have the opportunity to shine. However, in this managerial view, the elements in all analytical workflows are **fixed** and fully optimised, so that sample *throughput* comes into focus as the key factor of interest. Such elements are sample receiving, initial sample preparation, sub-sampling, possible sending off of sub-samples to other within-company laboratories for other types of analysis, more sample preparation (this time for analytical support), e.g. grinding, milling, mixing, sieving, analyte extraction (for some types of analysis only) and many other specialised part-operations where/when needed. The key point here is that all these elements are considered as objects that can, indeed *should*, be managed *exclusively* according to a flow-path business objective with the aim of producing the necessary economic profit.

Call this position "Laboratory A" in this tale. It is likely a fair statement that this is the main business strategy behind most of today's commercial analytical laboratories. But under normal market conditions profit will not sky-rocket for Laboratory A as a function of even the best manager's efforts, because of the relentless market competition with (many) other commercial laboratories. For the time being, this is the same basis upon which Laboratory B is in business as well.

Thus, at the outset, Laboratories A and B are competing on what economists call a fair basis; both have competent managers and highly competent technical staff (scientists, technicians …), superior logistics and they both have access to the same external (public domain) scientific and technological facilities and developments with which to sustain their current business and, hopefully, improve their state-of-the-art capabilities, and thereby be able to drive their individual businesses forward. So how is it possible for an individual laboratory to increase its market share? Better marketing and better presence in the market are the first business-related options with which to promote its potentially better offerings. The archetypal answer in a high-tech context is either by becoming more *efficient* than competing companies and/or through being the *first mover* with respect to significant technological developments, perhaps even disruptive technological breakthroughs. Both laboratories will, in principle, have equal access to all developments which are published as a result of university R&D, but it **is** possible that the ability to spot what may *become* could be different in the two laboratories. Also, much of analytical technological development takes place **in** the laboratory regimen, and here it's everybody's game. However, the present tale is not about possible new technological drives or potential comparative advantages, far from it. The core element in this tale has been around for more than 60 years, and could thus not possibly contend with modern, disruptive technology breakthroughs—or could it?

The core issue

The core issue turned out to develop into a marked *difference*, which only Laboratory B decided to take advantage of. At its root, it is based on the in-depth understanding ("technical" understanding, if you will) that stems from TOS:

> *"The quality and relevance of an analytical result is not **only** a function of the analytical competence, analytical equipment, work-path optimisation, i.e. the traditional business understanding which is the firm position for Laboratory A. It is **equally as much a function of the specific sampling procedures** a.o. involved in producing the analytical aliquot."*[2–5]

Thus, while precision is a quality characteristic of the analytical method, and while the analytical accuracy refers to the mass that has actually been analysed only, i.e. to the mass of the aliquot, this is not in compliance with the *needs* of the users of analytical results, the clients of the laboratory. Users will invariably make important decisions (sometimes trivial decisions, at other times truly critical decisions, sometimes even life-and-death decisions in science, technology, industry and society) based on the reliability of the analytical results. In an overwhelming proportion of cases this is tantamount to the *reputation* of the analytical laboratory, be this a commercial or an in-house technical laboratory. Indeed, the specific analytical quality and performance characteristics are in the centre focus for all kinds of official or commercial auditing, accreditation and certification of laboratories (CEN, ISO, JORC etc.). The present tale focuses on the fact that all of the above demands are declared as satisfactory as long as the *analytical* accuracy and precision meet up with relevant criteria.

But the core issue of the tale constitutes a different scope. The practical user perspective is the *original lot*, **not** the analytical aliquot. Enter the critical factor of *how* the enormous gulf between lot and aliquot has been bridged. This has everything to do with the ability to comply with TOS in all stages of the pathway from-lot-to-aliquot, Figure 1.

The crux of the matter

The user who is to make critical decisions does not care one iota how accurate a specific analytical method is w.r.t. the *miniscule* analytical mass! The decision maker is **only** concerned with how accurate a particular analytical result is (say, 3.57% or 276 ppm) *with respect to the original lot*. The operative question for all users is: "how accurate is this compositional determination with respect to the original lot?". How can I be certain this is a determination that holds up w.r.t. the 1000-to-100,000 times *larger* original lot? What is the uncertainty related to the analytical result in **this** context? This focus is very real and leads to the above questions which need definite answers.

But the way clients and laboratories traditionally go about this issue lacks rele-

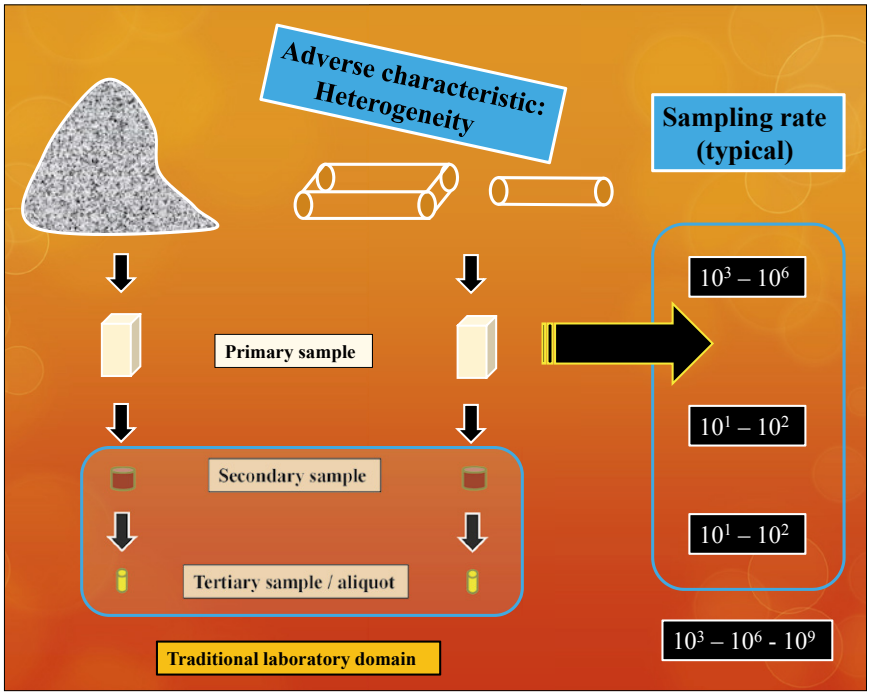

Figure 1. The common from-lot-to-aliquot pathway encompasses sampling processes which are in no way simple mass-reductions, but which require complete compliance with TOS at all sampling stages.[2–5]

vance and rigour. The tradition is to point to, and rely on, official laboratory accreditations, performance diplomas etc. But this kind of validation, verification and justification is exclusively based on the narrow analytical accuracy and precision characteristics only—which are all based on the **aliquot**.

However, the analytical aliquot mass/volume is very far away from the legitimate practical concern, the lot. The analytical aliquot is typically (on a mass/mass basis) some 10^3, 10^6 (or more) times *smaller* than the lot. The **critical success factor** of all analysis is, therefore, that the complete, multi-stage sampling process spanning a mass reduction of 1/100,000 or more, *preceding* analysis, is scrupulously **representative**. How else could the analytical result of the aliquot say anything meaningful about the composition of the entire lot? The only available **guarantee** for representativity (simultaneous accuracy and precision relevance w.r.t. the lot) is the specific sampling process used to cover these three to six (or more) orders-of-magnitude of mass reduction before analysis. From TOS it is known that it is only a specific, documentable *sampling process* that can be evaluated, assessed and declared to be representative, or not.[a]

> *"What is the nature of the accuracy and precision estimates quoted in all of this world's analytical laboratory accreditations?"*[3]

While there quite understandably may well be great pride in the analytical capabilities of a(ny) specific analytical laboratory … the *relevant* decision-making issue, relevant for the user of analytical results, is overwhelmingly *missing* from current analytical reports, diplomas and certifications.[3] This is a harsh statement, but nevertheless true.[b] Mostly, an estimate of the operative, real-world decision-making accuracy *w.r.t. the original lot* is nowhere to be found, very likely because covering this would entail that the laboratory should be involved with all sampling going on, specifically also that associated with the primary sampling from the lot.[3–5] This would require the laboratory to be(come) fully TOS competent (see all earlier columns in this series); a graphic summary of this body of knowledge is given in Figure 2. Here is the problem ….

The complete argument

There are always several *possible* different sampling methods that can be used in a particular situation, at a particular scale—first and foremost grab sampling vs composite sampling,[12,13] or composite sampling based on a significantly different number of increments vis-à-vis the lot heterogeneity addressed. In the case of, typically, three stages of sampling and sub-sampling in the laboratory, there are many possibilities for coming up with functionally different sampling pathways from-lot-to-aliquot. All will lead to an analytical aliquot, but the analytical results will per force be different because of lot heterogeneity, it is only a matter of the degree of successful heterogeneity countermeasures embedded in the actual sub-sampling processes, and the way these address the various manifestations of material heterogeneity met with at particular sampling stages. Thus, in a very real sense the specific sampling pathway will influence the analytical results—an aliquot is not just an aliquot that can be dealt with in isolation, all aliquots have a past, a provenance.

Thus, a fundamental tenet stemming from TOS is that all analytical results are but *estimates* of the composition of the original lot. Hopefully the best possible estimate of course, but "best" is not an automatic qualifier. "Best" specifically means, and should only mean, that the analytical report reflects the singular representative analytical result that directly can be used for the important societal, corporate, environmental decision-making. Which again brings forth the key understanding that the qualifier "representative" is related to the perspective of the *complete* sampling

[a]It is not possible to subject "representativeness" to grammatical declination—a sampling process either **is** representative, or it is **not**…

[b]To the reader who has already understood the point of this tale, there only remains to refer to the earlier Sampling Column which dealt with the "Replication Experiment".[11]

SAMPLING COLUMN

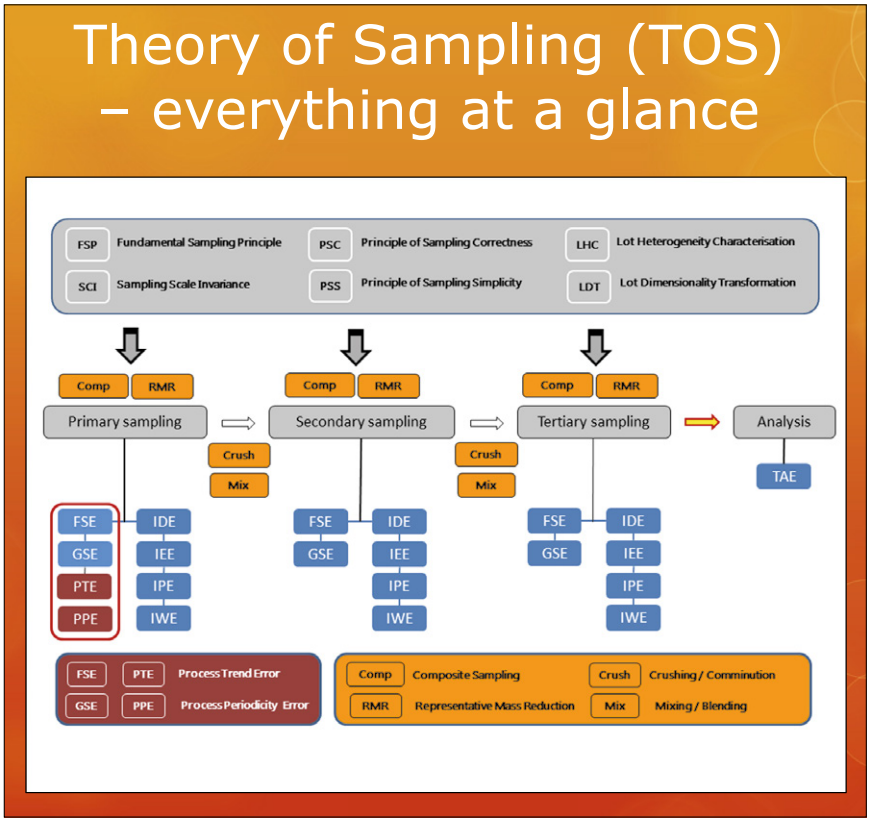

Figure 2. The most updated summary of the Theory of Sampling (TOS), the elements of which are comprised by six Governing Principles (GP, grey), four Sampling Unit Operations (SUP, yellow) and six (eight) sampling errors (blue, maroon) and their processual relationships w.r.t. the multi-staged sampling process "from-lot-to-aliquot". See TOS references below for in-depth description.[2–10] Illustration copyright KHE Consulting; reproduced with permission.

process "from-lot-to-aliquot-to-analysis", **not** to the infinitely smaller foray "from-aliquot-to analysis" only. This is an understanding that must not be subjugated the flurry of narrow economic, optimising activities … It matters, crucially, *how* the analytical aliquot was arrived at.[2–10] All laboratories must be sufficiently TOS competent.

In fact, it is fully possible to make use of *bona fide* analytical methods (likely with extremely good analytical accuracy and precision), which in the absence of a preceding representative sampling process, will have the quirky characteristic of delivering analytical results that are "precisely wrong". This surprising understanding concerns the fundamentally different nature of the analytical vs the sampling+analytical bias, an issue which has featured extensively in recent TOS literature.[3–6] Figure 3 depicts this crucial distinction graphically.

The meaning of it all

From TOS, e.g. the sampling standard DS 3077 (2013)[4] (or all earlier Sampling Columns[5]), it is well known that the uncertainty stemming from a *preceding* sampling stage is *on average* some 10× **larger**.[c] Thus, if not TOS compliant, the sampling error uncertainty stemming from the primary sampling stage operations is *on average* 10× **larger** than those originating at the secondary sampling stage (and may be even larger, depending on the material heterogeneity and the degree with which sampling errors have been adequately eliminated and/or suppressed, or not) …, which again is 10× **larger** than those pertaining to the tertiary sampling stage, the aliquot-producing stage (very often effected by a grab sampling spatula). These are but general order-of-magnitude factors. Materials will exist whose inherent heterogeneities would lead to somewhat *smaller* factors, but there just as assuredly also will exist materials with a much more troublesome heterogeneity, which would lead to larger-than factors of 10×. Finally, in general, sampling errors always greatly exceed the specific analytical uncertainty (termed the total analytical error, TAE).

What appears to be the saving grace is that all the world's laboratories can safely be assumed to have *minimised* their within-house analytical uncertainties to the highest possible standard which, alas, is but a very small fraction of TSE. Thus, the core *message* from TOS' experience is that there is a step-up, potentially up to several orders-of-magnitude, as concerns the sampling uncertainty accumulated over all effective sampling stages (the total sampling error, TSE), in the **absence** of any specific heterogeneity counteraction. This counteraction is the *raison d'etre* for TOS. Either way, TSE always *dominates* TAE, occasionally to such a degree that TAE dwindles into oblivion. The point is that a situation very rarely exists in which TAE is close to TSE in magnitude. When such is the case, this would signify a laboratory truly very much in the lead, because all sampling errors would have been completely minimised. But how would a laboratory go about proving this? A survey of reputable analytical laboratory homepages is very telling, mostly because of a certain sin-of-omission regarding estimates of the effective TSE accumulated over all sampling stages.

Inside and outside the complacent four walls of the analytical laboratory

But the real culprit, the core issue of this tale, would **still** not have been addressed, because this lies *outside* the traditional laboratory regimen. The somewhat uncomfortable summary effect of all of the above is that the *primary*

[c] The relationships between sampling—and analytical *errors* and their effects on Measurement Uncertainty (MU) is treated in a benchmark paper in great detail; interested readers are referred to Reference 3.

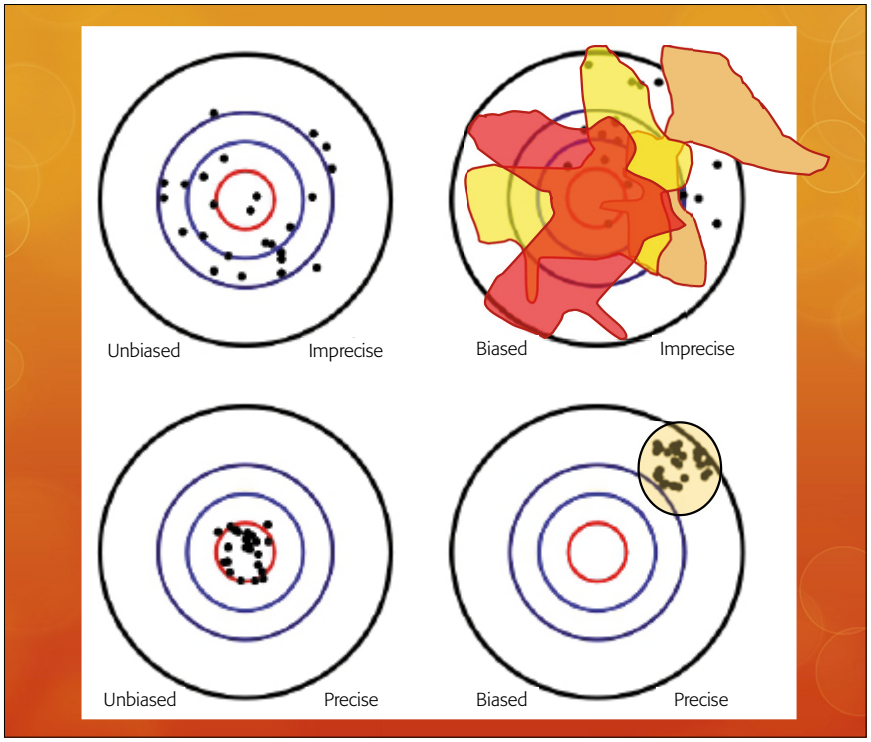

Figure 3. While an analytical bias can always be subject to a statistical bias-correction (lower panels), the nature of the sampling + analytical bias is fundamentally different (upper panels).[3] Because of the interaction between a specific material heterogeneity and a specific sampling process, which may be more-or-less removed from the qualifier "representativity", replicated sampling + analysis will always result in a **different** accuracy and precision estimate; the sampling + analysis bias is **inconstant**.[3]

sampling stage very nearly always dominates TSE all by itself. But this is almost never included in laboratory performance reports. **Why**?

And, **where** did primary sampling arise from all of a sudden? **Why** is this critical?

For two reasons:

i) Due to market competition, the responsible analytical laboratory will always tend to have the smallest possible residual uncertainty from all the operative steps involved in its many different analytical offerings to its clients. For *fully* responsible laboratories this includes a genuine focus on minimising the tertiary and often also secondary in-house sampling (in reality *sub-sampling* in relation to the not-yet-included primary sampling from the lot). This aspect is what will differentiate between individual real-world laboratories, which *may* decide differently as to what degree to also venture outside the laboratory when **full** TOS optimisation is wanted.

ii) The second reason why TSE very nearly always dominates the *total* uncertainty budget [TSE + TAE] is that Laboratory A deliberately declares: "Primary sampling is **outside** our responsibility". This is the hidden elephant in the room. Analytical laboratories may, or may not, deliberately consider that all ex-laboratory issues per definition are irrelevant—while the reality for users of the analytical results is completely dominated by the contribution from this "missing link". This issue is actually the **only** discriminating issue between the generic Laboratory A and Laboratory B.

What happened to generate this potential difference?

"One fine day" …

"One fine day" the manager of Laboratory B called in at work consumed with a completely new attitude, based on an epiphany she had had in her dreams the night before. Barely in the door, calling an immediate board and section chiefs meeting, the manager declared (eyes shining with newfound *righteousness*):

"There is a completely unrecognised business opportunity that no other laboratory has tapped into … yet. Laboratory B must be the first mover, Laboratory B must be the first to reap this competitive advantage! It has dawned upon me that despite Laboratory B's most stringent efforts to curtail all total in-house errors, we have erred, believing that this was well summarised by TAE … We have erred grossly! It is in reality [TSE + TAE] that is accountable for all the real-world's 'analytical variance'. It has dawned upon me that we are at least a factor 10× too low in our declarations in our analytical certificates—and depending upon the heterogeneity of lot materials and the ability to follow TOS, this factor could be higher!' (the manager shuddered visibly). 'What's more—today we have absolutely no, or only very little, possibility to influence this issue since this problem originates with/at the primary sampling from the original lot, which this laboratory so far has declared to be exclusively the responsibility of the client. How often does our Laboratory B, which we like to call 'the leading laboratory in the world', insist that it is in fact also **our responsibility** *to explain to clients that this is a problem of significantly larger impact with respect to the interpretability of the analytical results* **in context** *than any other? A factor of 10+ or larger."*

Taking a step back, the writer of this column, who has visited, audited and consulted with scores of analytical laboratories during a long professional career, offers a quantitative comment on the side: laboratories that do not care about the issue surrounding primary sampling errors and their inflationary impact on the total uncertainty budget, the proverbial Laboratory A, unfortunately dominates the field. Hardly one Laboratory B exists today—but there ***could*** very well be one tomorrow!

SAMPLING COLUMN

The above account, actually not a tale **at all**, has gone to great efforts to explain the "technical" TOS-based evidence for the situation revealed: as long as virtually no-one still does not take primary sampling sufficiently serious (neither clients, nor laboratories), this should rightly be called the primary sampling disaster! As long as this has not happened, what are the consequences?

They are numerous, and they concern both company bottom lines and laboratory efficiency, i.e. direct economic negative outcomes. They also concern the possibilities for necessary and efficient societal and public regulation and control (e.g. food, feed, pharmaceutical drugs, public health), and here with likely much larger negative economic impacts, although often *hidden* at first sight.[14] And they concern the reputation of the analytical science, technology and trade—which in the end reflects on the reputation of each individual analytical laboratory (commercial or not).

The really important aspect: costs or gains

Could there really be direct economic and business advantages in taking on the primary sampling issue—an issue so long considered as **not** our laboratory's responsibility? The most often heard "justification" used in this context (remember that every single feature in this constructed tale is **true** …) is:

> *"This laboratory need not concern itself with primary sampling …. This will cost us additional work, man hours, expenditures. This will break up our established work paths—all of which will impact negatively on our bottom line. And we will especially not be involved in this matter, since none of our competitors take this up either—we would simply be losing money in-house, and to no business advantage!"*

The world's laboratories, clan A, have spoken!

This is the *status quo* in a large segment of the commercial analytical laboratory realm.

Nevertheless, Laboratory B decided to be the *first mover* and to proceed down this new road.

What in the world?

What was the *epiphany* experienced by the manager of what became: Laboratory A → Laboratory B?

- **What** was the *business argument* that negated the above justification for doing nothing, for continuing exactly as before—for continuing exactly as all the other, competing laboratories?
- **What** will it take to seize the day?
- **Will** your laboratory become Laboratory B tomorrow?

The following proverb is attributed to the founder of the Theory of Sampling (TOS) Pierre Gy.[15] Think of this in relation to the dominating primary sampling error/uncertainty!

> *"SAMPLING – is not gambling!"*
> *Pierre Gy (1924–2015)*

One may also factor in a well-known contradiction regarding human capital management:

> *"CFO asks CEO: 'What happens if we invest in developing our people and then they all leave us?' CEO: 'What happens if we don't, and they stay?'"—Anon*

What was the epiphany all about? Find out in the next issue!

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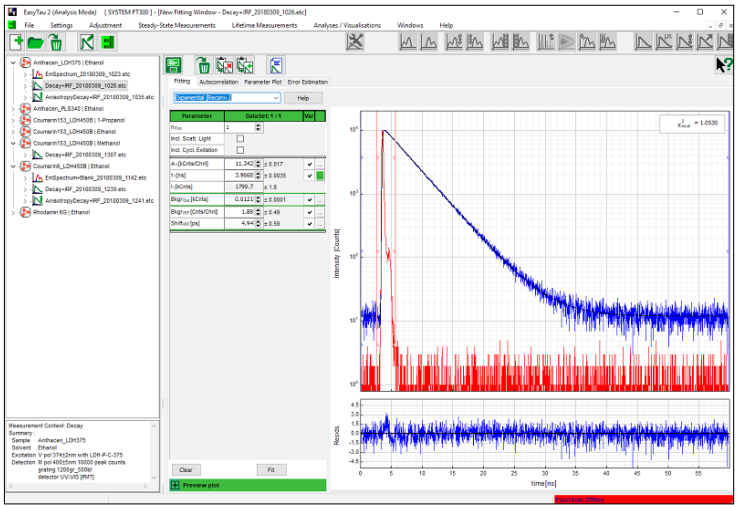
15. K.H. Esbensen, "Pierre Gy (1924–2015): the key concept of sampling errors", *Spectrosc. Europe* **30(4),** 25–28 (2018). https://www.spectroscopyeurope.com/sampling/pierre-gy-1924%E2%80%932015-key-concept-sampling-errors

LUMINESCENCE

EasyTau 2 fluorescence software package



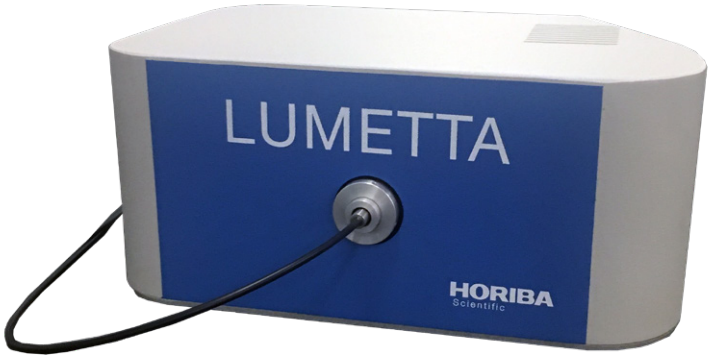
The EasyTau 2 software package now provides a fully integrated, comprehensive suite of fitting and analytical tools for time-resolved fluorescence spectroscopy applications. With this upgrade, EasyTau 2 becomes a one-stop solution for both acquiring and analysing data with PicoQuant's FluoTime 300 spectrometer. In addition to providing full control over all hardware components of the FluoTime 300, the new fitting module includes all functions that were previously offered by the standalone FluoFit Pro program. Both measurement and analysis of the results can be performed in a single graphical environment with efficient data management.

Steady-state and time-resolved data can be subjected to basic arithmetic functions (such as addition, normalisation and integration) and fitted to determine fluorescence lifetimes or anisotropy. The module offers global decay analysis, tail and iterative reconvolution fitting with non-linear error minimisation as well as using various exponential decay (up to fifth order) or rate constant distribution models. The software also allows for rigorous error analysis (bootstrap) as well as generating presentation-ready numerical and graphical output.

PicoQuant

http://link.spectroscopyeurope.com/30-W-093

Horiba introduces the Lumetta fixed grating spectrograph



Horiba Scientific has introduced the Lumetta fixed grating F/2 spectrograph. It is designed to optimally gather light from most fibres and high-angle scattering phenomena. Being an imaging spectrograph, it also enables such techniques as multitrack spectroscopy and fast hyperspectral imaging. With multitrack spectroscopy, multiple independent spectroscopy channels can be measured, either improving sample measurement throughput for similar measurements on different samples or simultaneous measurement of different but complementary spectra, such as photoluminescence and absorbance, from the same sample. It has a scientific Grade 1 CCD deep cooled to –50 °C together with low-noise, 16-bit electronics and signal-to-noise ratio of 1200 : 1. Lumetta also has a flexible signal input interface, accommodating free-space as well as FC, SMA and ferrule fibre interfaces. Furthermore, spectral resolution can be controlled from a selection of interchangeable slits.

HORIBA Scientific

http://link.spectroscopyeurope.com/30-W-102

MASS SPECTROMETRY

TSQ Fortis triple quadrupole mass spectrometer

The Thermo Scientific TSQ Fortis triple quadrupole mass spectrometer has Active Ion Management Plus, which enables high precision for every molecule type in complex matrices. Selected reaction monitoring capability with ion transmission efficiency is designed for simultaneous, reliable quantitation of all components in a complex matrix for high instrument throughput. It also has a novel ion optics design, which provides simple, tool-free maintenance. The Matrix Separator Ion Guide provides maximum robustness while minimising ion loss. Easy-to-use workflows offer efficiency without compromising data quality from sample injection to report generation. Intuitive drag-and-drop method

NEW PRODUCTS

editor software provides simple method development and operation through application-based templates.

Thermo Fisher Scientific

http://link.spectroscopyeurope.com/30-W-095

LCMS-9030 Q-TOF from Shimadzu

Shimadzu has released the LCMS-9030 quadrupole time-of-flight liquid chromatograph mass spectrometer. It is a research-grade mass spectrometer designed for high-resolution, accurate mass detection with fast data acquisition rates. It utilises the same engineering as Shimadzu's proven, rugged, high-performance triple quadrupole (LC-MS/MS) platform and integrates this with TOF architecture. In the LCMS-9030, core ion beam technologies have a new approach in ion gating using UFaccumulation™ to create a precise pulse of ions in the flight tube optimised for high sensitivity and high resolution using iRefTOF™ reflectron technology. The iRefTOF™ generates an ideal reflectron field, delivering the highest resolution for the flight path with highly stable mass accuracy.

Shimadzu

http://link.spectroscopyeurope.com/30-W-100

MS-based dried blood spot screening system

Waters Corporation has introduced the RenataDX™ Screening System, a flow-injection tandem mass spectrometry (FIA-MS/MS) system for rapid high-throughput analysis of extracted dried blood spots and other human biological matrices. The need for dried blood spot analysis in clinical laboratories is growing annually, so scientists need more sample throughput capabilities to meet the demand.

The RenataDX Screening System also offers laboratories the flexibility to run any suitable FIA-MS/MS laboratory developed test or ready to use reagent kit. It incorporates the high-performance combination of the Xevo™ TQD IVD Mass Spectrometer, the ACQUITY™ UPLC™ I-Class IVD Binary Solvent Manager and the 3777C IVD Sample Manager.

The system runs the combination of MassLynx (IVD) and IonLynx™ Application Manager Software, seamlessly integrates data into laboratory workflows. The IonLynx Application Manager processes FIA-MS/MS data, to present clinical scientists with a familiar, yet robust and reliable diagnostically-proven informatics tool.

The RenataDX Screening System is manufactured as an US FDA Class I medical device and is CE Marked to the European Directive 98/79/EC (IVDD).

Waters

http://link.spectroscopyeurope.com/30-W-104

FAIMS Pro differential ion mobility interface

Thermo Fisher Scientific has introduced a differential ion mobility device that integrates with high-resolution mass spectrometers. The Thermo Scientific FAIMS Pro interface is designed to increase the range of proteins scientists can identify while reducing the time taken in sample preparation steps. Its new design further enhances instrument selectivity and detection limits through gas-phase fractionation and reduced matrix interference. Menu-driven software can be used to design methods using pre-configured parameters, increasing productivity and simplifying use. Sample fractionation steps are reduced, which can help save time, long-term costs and maintenance through increased productivity. The FAIMS Pro device's interface has been designed

to improve nano, capillary and microflow applications, producing high data quality on sample-limited studies.

Thermo Fisher Scientific

http://link.spectroscopyeurope.com/30-W-096

RAMAN

New handheld Raman analyser from Rigaku for chemical threat identification

Rigaku Analytical Devices has announced its next generation 1064 nm handheld Raman analyser, the Rigaku ResQ CQL. It has improved ergonomics, analytical performance and sample presentation for analysis of powders, liquids, gels and mixtures—even in non-visible amounts. Its standard library contains over 13,000 chemicals, including explosives, chemical warfare agents (CWAs), precursors, hazardous chemicals, narcotics, cutting agents, pesticides and steroids. There are also the added capabilities to upgrade, transfer and translate entries. By utilising 1064 nm Raman excitation, users are able to reduce sample fluorescence and identify coloured substances or scan through coloured packaging.

Additional features include an on-board 5 MP camera for imaging, colorimetrics analysis or barcode scanning; an LED flashlight for optimal sample visibility; a Quick Scan button for faster scans; 4C Technology for precursor monitoring; optional QuickDetect automated colorimetric for non-visible detection; periscope adaptor for sampling flexibility; connectivity via WiFi, peer-to-peer or USB; tamper-proof reports; and Li-PO rechargeable or CR123 disposable batteries.

Rigaku Analytical Devices

http://link.spectroscopyeurope.com/30-W-098

532-nm Raman spectroscopy accessories

Princeton Instruments has introduced 532-nm Raman accessories for its FERGIE spectrometer product line. Raman measurements at 532 nm offer better sensitivity with a higher Raman cross-section [$\sigma \propto (1/\lambda^4)$] compared to Raman measurements at 785 nm or longer wavelengths. The 532 nm excitation wavelength also delivers higher spatial resolution for Raman microscopy measurements, making it ideal for carbon materials (e.g., graphene and carbon nanotubes) and other thin film material characterisation. In contrast, the 785-nm excitation wavelength is preferred for organic and biological samples that have fluorescence background.

Princeton Instruments

http://link.spectroscopyeurope.com/30-W-099

X-RAY

New X-MET 8000 analyser from Hitachi High-Tech Analytical Science

Hitachi High-Tech Analytical Science has introduced a new entry-level handheld X-ray fluorescence (XRF) X-MET8000 Smart model to offer users a more competitively priced package for the X-MET brand. A large area silicon drift detector (SDD) detector allows users to pick up to three calibrations: Alloy FP, Aluminium FP and Precious FP. The instrument has a shield window as standard to protect the instrument from sharp objects, one battery that allows a full day's operation (10–12 hours) and a power supply. Users can purchase additional accessories as needed. The X-MET8000 Smart has over 1600 grades in the built-in library and a comprehensive metals database as an option post purchase. It is robust in design, and IP54 and MIL-STD-810G standard compliant. Users also get access to advanced data management with ExTOPE Connect including mobile phone app, cloud service for instant data sharing and secure storage.

Hitachi High-Tech Analytical Science

http://link.spectroscopyeurope.com/30-W-103

DIARY

Conferences
2018

2–6 November, Pacific Grove, California, United States. **34th Asilomar Conference on Mass Spectrometry: Quantitative Analysis of Posttranslational Modifications by Mass Spectrometry.** info@asms.org, http://www.asms.org/conferences/asilomar-conference/asilomar-conference-homepage.

4–7 November, Washington, DC, United States. **American Association of Pharmaceutical Scientists (AAPS) 2018 Annual Meeting.** aaps@aaps.org, https://www.aaps.org/aaps/pharmsci/annual-meeting.

4–8 November, Sacramento, CA, United States. **SETAC North American 39th Annual Meeting.** setac@setac.org, http://www.setac.org/.

4–8 November, Indianapolis, Indiana, United States. **2018 Geological Society of America (GSA) Annual Meeting.** meetings@geosociety.org, http://www.geosociety.org/meetings/.

4–7 November, Washington, DC, United States. **American Association of Pharmaceutical Scientists (AAPS) Annual Meeting and Exposition (AAPS PharmSci 360).** https://www.aaps.org/annual-meeting-and-conferences/annual-meeting.

5–6 November, Madrid, Spain. **18th Annual Pharmaceutical and Chemical Analysis Congress.** https://analysis.pharmaceuticalconferences.com/exhibition.php.

6–8 November, Nantes, France. **32nd EFFoST International Conference.** http://www.effostconference.com/.

6 November, Wageningen, Netherlands. **Global Future Farming Summit.** https://www.globalfuturefarming.nl/summit/.

7 November, Stuttgart, Germany. **European Photonics Industry Consortium (EPIC) Meeting on Hyperspectral Imaging at VISION.** http://www.epic-assoc.com/epic-meeting-on-hyperspectral-imaging-at-vision/.

8–9 November, Montpellier, France. **19th HelioSPIR 2018.** president@heliospir.net, http://www.heliospir.net/actualites/article/119.

11–14 November, Charleston, United States. **IMSS II & OURCON VI.** https://www.imagingmssociety.org/event-2825357.

12–14 November, Princeton, New Jersey, United States. **Eastern Analytical Symposium and Exposition (EAS 2018).** askEAS@eas.org, http://easinc.org/wordpress/.

12–15 November, La Serena, Chile. **XIII Latin American Symposium on Environmental Analytical Chemistry (LASEAC).** dragana@eventotal.cl, https://cpqcol.gov.co/eventos/xiii-laseac/.

19–20 November, London, United Kingdom. **20th International Conference on Biomedical Engineering (ICBE 2018).** https://waset.org/conference/2018/12/london/ICBE.

22–23 November, Koblenz, Germany. **6th Workshop on Field-Flow Fractionation-Mass Spectrometry (FFF-MS).** meermann@bafg.de, https://www.bafg.de/DE/05_Wissen/02_Veranst/2018_11_22.html.

25–30 November, Boston, MA, United States. **2018 Materials Research Society Fall Meeting and Exhibition.** info@mrs.org, http://www.mrs.org/fall2018.

29–30 November, San Francisco, CA, United States. **ASMS Fall Workshop, Metabolomics Informatics.** https://www.asms.org/conferences/fall-workshop/fall-workshop-homepage.

2–6 December, Awaji, Hyogo, Japan. **The 3rd Aquaphotomics International Symposium.** conference@aquaphotomics.com, http://conference.aquaphotomics.com/.

3–6 December, Caparica, Portugal. **3rd Caparica Christmas Conference on Sample Treatment 2018.** Dr Carlos Lodiero Espino, jlcapelom.sampletreatment2018@bioscopegroup.org, http://www.sampletreatment2018.com.

8–12 December, Rio de Janeiro, Brazil. **7th Brazilian Conference on Mass Spectrometry (BrMASS 2018).** contato@brmass.com, http://congresso2018.brmass.com/.

2019

24–28 January, San Diego, CA, United States. **Pacific Conference on Spectroscopy and Dynamics (PCSD 2019).** https://www.westernspectroscopy.org/.

24–27 January, Fort Myers, FL, United States. **Sanibel Conference on Mass Spectrometry, Chemical Cross-linking and Covalent Labeling: from Proteins to Cellular Networks.** http://www.asms.org/conferences/sanibel-conference.

30 January–3 February, Auckland, New Zealand. **Australian and New Zealand Society for Mass Spectrometry Conference (ANZSMS27).** president@anzsms.org, https://aomevents.eventsair.com/QuickEventWebsitePortal/anzsms-27/2019.

30 January, Huddersfield, United Kingdom. **5th Ambient Ionisation SIG Meeting.** Andrew Ray, andrew.ray@astrazeneca.com, http://www.bmss.org.uk/SIG_ambient-ion.shtml.

30 January–1 February, Montpellier, France. **Chimiométrie 2019.** chemom2019@sciencesconf.org, https://chemom2019.sciencesconf.org/.

2–7 February, San Francisco, United States. **Photonics West 2019.** http://spie.org/conferences-and-exhibitions/photonics-west?SSO=1.

2–6 February, Washington, United States. **Society for Laboratory Automation and Screening (SLAS) 2019.** http://www.slas2019.org/.

DIARY

3–8 February, Pau, France. **European Winter Conference on Plasma Spectrochemistry (EWCPS-2019).** Ryszard Lobinski, ewcps2019-chair@winterplasma2019.com, http://www.winterplasma2019.com.

18–23 February, Baltimore, United States. **American Academy of Forensic Sciences (AAFS) 71st Annual Scientific Meeting.** https://www.aafs.org/home-page/meetings/aafs-71st-annual-scientific-meeting-baltimore-maryland-2019/.

19–20 February, Prague, Czech Republic. **European Congress on Pharmaceutics & Pharmaceutical Technology.** pharmaceutics@pharmaeuroscicon.com, https://pharmaceutics.euroscicon.com/.

25–27 February, Prague, Caech Republic. **PHOTOPTICS 2019: 7th International Conference on Photonics, Optics and Laser Technology.** photoptics.secretariat@insticc.org, http://www.photoptics.org/.

3–7 March, Hilton Head Island, SC, United States. **7th Annual Practical Applications of NMR in Industry Conference (PANIC-2019).** https://www.panicnmr.com/.

3–6 March, Bethesda, United States. **International Foundation Process Analytical Chemistry (IFPAC-2019) Annual Meeting.** http://www.ifpac-global.org/.

18–20 March, Edinburgh, United Kingdom. **17th International Conference and Exhibition on Pharmaceutics & Novel Drug Delivery Systems (Pharmaceutica 2019).** pharmaceutica@pharmaceuticalconferences.org, https://novel-drugdelivery-systems.pharmaceuticalconferences.com/.

25–26 March, Budapest, Hungary. **EuroSciCon Conference on Biosimilars 2019.** kennedypeyton001@gmail.com, https://biosimilars.euroscicon.com.

25–28 March, Berlin, Germany. **2nd International Plant Spectroscopy Conference (IPSC-2019).** https://ipsc2019.julius-kuehn.de/.

31 March–4 April, Orlando, FL, United States. **257th American Chemical Society (ACS) National Meeting & Exposition: Chemistry for New Frontiers.** NationalMeetings@acs.org, https://www.acs.org/content/acs/en/meetings.html.

6–10 April, Orlando, United States. **Experimental Biology 2019.** http://experimentalbiology.org/2017/About-EB/Future-Meetings.aspx.

22–26 April, Phoenix, Arizona, United States. **2019 Materials Research Society (MRS) Spring Meeting & Exhibition.** https://www.mrs.org/spring2019.

30 April–2 May, Chester, United Kingdom. **APACT19.** https://apact.co.uk/.

5–10 May, San Jose, United States. **Conference on Lasers and Electro-Optics (CLEO).** confserv@osa.org, https://www.cleoconference.org/home/.

6–9 May, Beijing, China. **The 9th World Conference on Sampling and Blending (WCSB9).** http://www.wcsb9.com/.

13–15 May, Edinburgh, United Kingdom. **Challenges in Analysis of Complex Natural Mixtures: Faraday Discussion.** http://www.rsc.org/events/detail/29574/challenges-in-analysis-of-complex-natural-mixtures-faraday-discussion.

20–21 May, Zurich, Switzerland. **21st Annual European Pharma Congress.** pharmaeurope@pharmaceuticalconferences.org, https://europe.pharmaceuticalconferences.com/.

21–25 May, Toronto, Canada. **7th Georgian Bay International Conference on Bioinorganic Chemistry (CANBIC-7).** Martin Stillman, canbic@uwo.ca, http://canbic.ca/index.html.

2–5 June, Nara, Japan. **15th International Symposium on Applied Bioinorganic Chemistry (ISABC 15).** http://web.apollon.nta.co.jp/isabc15/.

2–6 June, Atlanta, United States. **67th ASMS Conference on Mass Spectrometry.** office@asms.org, http://www.asms.org/conferences/annual-conference/future-annual-conferences.

9–14 June, Mexico City, Mexico. **Latin American Meeting on Laser-Induced Breakdown Spectroscopy (LAMLIBS).** mayo.villagran@icat.unam.mx, http://www.csi2019mexico.com/index.php/lamlibs.

9–14 June, Mexico City, Mexico. **Colloquium Spectroscopicum Internationale XLI (CSI XLI).** http://www.csi2019mexico.com/.

11–12 June, Münster, Germany. **5th International Workshop on Electrochemistry/Mass Spectrometry (ElCheMS 2019).** martin.vogel@uni-muenster.de, https://www.uni-muenster.de/Chemie.ac/en/karst/workshops/elchems.html.

16–20 June, Split, Croatia. **5th International Sclerochronology Conference (ISC2019).** Melita Peharda, isc2019@izor.hr, http://jadran.izor.hr/isc2019/index.html.

17–20 June, Oslo, Norway. **16th Scandinavian Symposium on Chemometrics (SSC16).** ssc16@nofima.no, http://ssc16.org/.

27–29 June, Amsterdam, Netherlands. **18th Annual Congress on Pharmaceutics & Drug Delivery Systems.** clarajane567@gmail.com, https://pharmaceutics.annualcongress.com/.

30 June–3 July, Warsaw, Poland. **7th International Symposium on Metallomics.** Ryszard Lobinski, sekretariat@metallomics2019.pl, http://metallomics2019.pl/.

8–12 July, Auckland, New Zealand. **International Conference on Advanced Vibrational Spectroscopy (ICAVS10).**

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ICAVS Secretariat, Podium Conference Specialists, 2661 Queenswood Drive, Victoria, BC, Canada, V8N 1X6. http://www.icavs.org/2019-conference/.

15–18 July, Honolulu, Hawaii, United States. **15th International Congress of Toxicology (ICTXV).** sothq@toxicology.org, http://toxicology.org/events/ict/meeting-highlights.asp.

5–9 August, Lombard, IL, United States. **68th Annual Denver X-ray Conference (DXC 2019).** http://www.dxcicdd.com.

18–23 August, Barcelona, Spain. **GOLDSCHMIDT2019.** https://goldschmidt.info/2019/.

25–30 August, Berlin, Germany. **21st International Society of Magnetic Resonance (ISMAR) Conference joint with EUROMAR 2019.** https://www.weizmann.ac.il/ISMAR/.

3–5 September, Manchester, United Kingdom. **40th BMSS Annual Meeting 2019.** bmssadmin@btinternet.com, http://www.bmss.org.uk/bmss2019/bmss2019.shtml.

8–13 September, Maui, Hawaii, United States. **15th International Conference on Laser Ablation.** Vassila Zorba, vzorba@lbl.gov, https://cola2017.sciencesconf.org/resource/page/id/11.

8–11 September, Denver, United States. **133rd AOAC International Annual Meeting and Exposition.** meetings@aoac.org, http://www.aoac.org.

15–20 September, Gold Coast, Australia. **NIR-2019.** nir2019@yrd.com.au, http://www.nir2019.com.

23–26 September, Freiberg, Germany. **Colloquium Analytical Atomic Spectroscopy 2019: CANAS 2019.** canas@chemie.tu-freiberg.de, http://www.canas.eu.

24–26 September, Sao Paulo, Brazil. **6th Analitica Latin American Congress.** analitica@nm-brasil.com.br, http://www.analiticanet.com.br.

29 September–3 October, Portland, United States. **2019 Materials Science and Technology Conference (MS&T19).** metsoc@cim.org, http://www.matscitech.org/.

13–18 October, Palm Springs, United States. **2019 SciX Conference (formerly FACSS): Annual National Meeting of Society for Applied Spectroscopy (SAS)/The 46th Annual North American Meeting of the Federation of Analytical Chemistry and Spectroscopy Societies..** scix@scixconference.org, http://www.scixconference.org.

5–8 November, Prague, Czech Republic. **9th International Symposium on Recent Advances in Food Analysis (RAFA 2019).** jana.hajslova@vscht.cz, http://www.rafa2019.eu.

2020

12–18 January, Tucson, Arizona, United States. **2020 Winter Conference on Plasma Spectrochemistry.** Ramon Barnes, wc2020@chem.umass.edu, http://icpinformation.org.

1–4 June, Houston, Texas, United States. **68th ASMS Conference.** https://www.asms.org/conferences/annual-conference/future-annual-conferences.

23–28 August, Boston, MA, United States. **XXIX International Conference on Magnetic Resonance in Biological Systems (ICMRBSXXIX).** John Markley, jmarkley@wisc.edu, http://www.icmrbs.org/.

9–17 September, Reno, NV, United States. **47th Annual Conference of Federation of Analytical Chemistry and Spectroscopy Societies (SciX2020).** scix@scixconference.org, https://www.scixconference.org/index.php/scix-home/future-conferences.

Courses

2018

5–8 November, Berlin, Germany. **16th European Short Course on Time-Resolved Fluorescence Spectroscopy.** Nicola Kasse, trfcourse@picoquant.com, https://www.picoquant.com/news/item/16.-european-short-course-on-time-resolved-fluorescence-spectroscopy.

2019

19–21 February, Berlin, Germany. **11th Annual Short Course on Time-Resolved Microscopy and Correlation Spectroscopy.** https://www.picoquant.com/events/workshops-and-courses.

11–15 March, Gembloux, Belgium. **Training on Vibrational Spectroscopy and Chemometrics.** Juan Antonio Fernández, j.fernandez@cra.wallonie.be.

29 April, Chester, United Kingdom. **APACT19 Pre-Conference Courses.** https://apact.co.uk/pre-conference-courses.

Exhibitions

2018

21–22 November, Telford, United Kingdom. **WWEM 2018: The 8th International Conference and Exhibition on Water, Wastewater & Environmental Monitoring.** info@ilmexhibitions.com, https://www.ilmexhibitions.com/wwem/.

2019

12–14 March, Dubai, United Arab Emirates. **ARABLAB 2019.** info@arablab.com, https://www.arablab.com/.

17–21 March, Philadelphia, United States. **Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy—Pittcon 2019.** pittconinfo@pittcon.org, http://www.pittcon.org.

2020

1–5 March, Chicago, United States. **Pittcon 2020.** pittconinfo@pittcon.org, http://www.pittcon.org.

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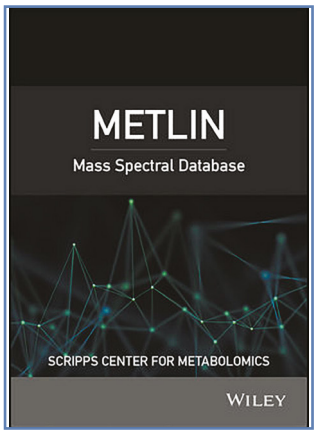

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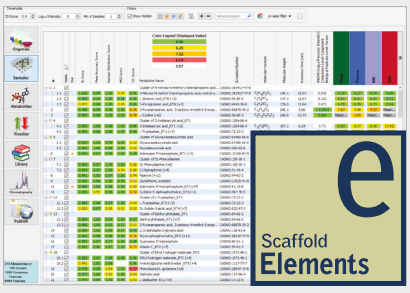

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