Vol. 33 No. 2 March 2021

SPECTROSCOPY europe

Spectroscopy since 1975

Coating systems of historic bowed instruments
Benchtop NMR spectroscopy
TD Column: FAIR enough?
Mini series: four generations of quality
Sampling errors

IMPOpen

The varnishes that were used by the old violin makers are believed to have contributed to the exquisite sound of their instruments. The secrets of these coatings are uncovered using IR and X-ray spectroscopies in the article starting on page 19.

Publisher
Ian Michael
E-mail: ian@impopen.com

Advertising Sales
Ian Michael
IM Publications Open, 6 Charlton Mill, Charlton, Chichester, West Sussex PO18 0HY, United Kingdom. Tel: +44-1243-811334, Fax: +44-1243-811711,
E-mail: ian@impopen.com

Paid subscriptions
IM Publications Open, 6 Charlton Mill, Charlton, Chichester, West Sussex PO18 0HY, United Kingdom. Tel: +44-1243-811334, Fax: +44-1243-811711,
E-mail: katie@impopen.com

Spectroscopy Europe is published by IM Publications Open LLP, 6 Charlton Mill, Charlton, Chichester, West Sussex PO18 0HY, United Kingdom.

Vol. 33 No. 2
March 2021

ISSN: 2634-2561

CONTENTS

Spectroscopy Europe is a digital magazine, published eight times a year and available free-of-charge to qualifying individuals in Europe and the Middle East. Institutions can subscribe at the rate of €270 (Europe), £200 (UK), $360 (ROW, postage included) for the eight issues published in 2021. All paid subscription enquiries should be addressed to: Subscriptions, IM Publications Open LLP, 6 Charlton Mill, Charlton, Chichester, West Sussex PO18 0HY, United Kingdom.

IMPOpen

EDITORIAL

The first of our two articles describes a clever adaptation to benchtop NMR experiments that allows the collection of multiple scans (to produce high signal-to-noise ratios) without the time penalties involved.

Cultural heritage is a growing application area for spectroscopy, and our second article describes how infrared and X-ray spectroscopy are being used to explore the coatings used by the old Cremonese makers that produced such outstanding sound.

The Tony Davies Column offers a challenge to us all with another contribution on FAIR data, which should be Findable, Available, Interoperable and Readable. It is clearly the way we should all be going, everybody from manufacturers and software developers, through researchers to publishers needs to work together. The column has certainly given me food for thought. From this year, we have implemented the use of Creative Commons licences for all articles and columns, which clarifies and simplifies how the authors are happy for their work to be reused. We must now consider how best to deal with data.

John Hammond has contributed the first of a mini series of nine Quality Matters articles looking at the development of "Quality" in the analytical environment and concluding with some informed predictions for its future.

During the proofing of the Quality Matters column, John forwarded me a (true) story from his early days in the lab, which has sparked the idea for a new section. John's contribution will be published online in the next couple of weeks and in the next purely digital issue. Do you have a story that you would be interested in sharing? Something to do with spectroscopy and which is amusing or unusual? I would be delighted to consider something from you (ian@impopen.com).

The Sampling Column provides some easy-to-understand examples of what sampling errors are, what are the consequences of them and what can be done about them. Particular examples from pharma, PAT and NIR spectroscopy are provided.

We start the issue with a News section that truly demonstrates the breadth of application of spectroscopy. Developments that will help sufferers from Parkinson's Disease, and miniaturisation that may lead to a spectrometer in your smartphone. Whether that is a good idea or not is another question!

We conclude with our usual sections summarising new Application Notes, New Products, a Product Focus on Imaging Spectroscopy, the Diary of future events and the Directory Listing of spectroscopy suppliers.

NEWS

"Game-changing" MS-based test to diagnose Parkinson's (and COVID?)

Scientists at The University of Manchester have developed a technique which works by analysing compounds found in sebum—the oily substance that coats and protects the skin—and identifying changes in people with Parkinson's Disease. Sebum is rich in lipid-like molecules and is one of the lesser-studied biological fluids in the diagnosis of the condition. People with Parkinson's may produce more sebum than normal—a condition known as seborrhoea.

The work was sparked following an observation by Joy Milne, whose husband was diagnosed with Parkinson's at the age of 45. Working with Dr Tilo Kunath at the University of Edinburgh, Joy demonstrated an incredible ability to distinguish a distinctive Parkinson's odour in individuals using her sense of smell, even before symptoms emerge in those affected.

The team, led by Professor Perdita Barran, The University of Manchester, and the clinical lead Professor Monty Silverdale at Salford Royal Foundation Trust, recruited 500 people with and without Parkinson's. Samples of sebum were taken from their upper backs for analysis. Using different mass spectrometry (MS) methods, 10 chemical compounds in sebum were identified which are elevated or reduced in people with Parkinson's. This allows scientists to distinguish people with Parkinson's with 85% accuracy.

The team confirmed their earlier findings that the volatile compounds on skin can be used to diagnose the condition, increasing the number of people sampled and including participants from the Netherlands, as well as the UK.

Now, with high-resolution MS they are able to profile the complex chemical signature in sebum of people with Parkinson's and show subtle but fundamental changes as the condition progresses. Detailed analysis showed changes in people with Parkinson's in lipid processing and mitochondria. Problems with mitochondria are one of the hallmarks of Parkinson's.

This means this "world first" testing strategy is not only useful in diagnosing Parkinson's but also in monitoring the development of the condition. The skin swab could provide an incredibly important new tool in clinical trials helping researchers measure whether new, experimental treatments are able to slow, stop or reverse the progression of Parkinson's. The study unveiled novel diagnostic sebum-based biomarkers for Parkinson's, provides insight into understanding of how the condition develops, and links lipid dysregulation to altered mitochondrial function.

These promising results published today could lead to a definitive test to diagnose Parkinson's accurately, speedily and cost effectively. The team is now seeking funding to further develop the test, and explore the potential for using the test to "stratify" patients.

Working with the University of Manchester Innovation Factory, the team has patents filed for their diagnostic techniques and are planning to create a spin-out company to commercialise the new tests. They are also working to use this approach to develop tests for COVID-19 as shown in research published in *EClinical Medicine* (doi.org/fzwt) as well as other conditions and are actively seeking investors interested in supporting the drive to bring this technology to market.

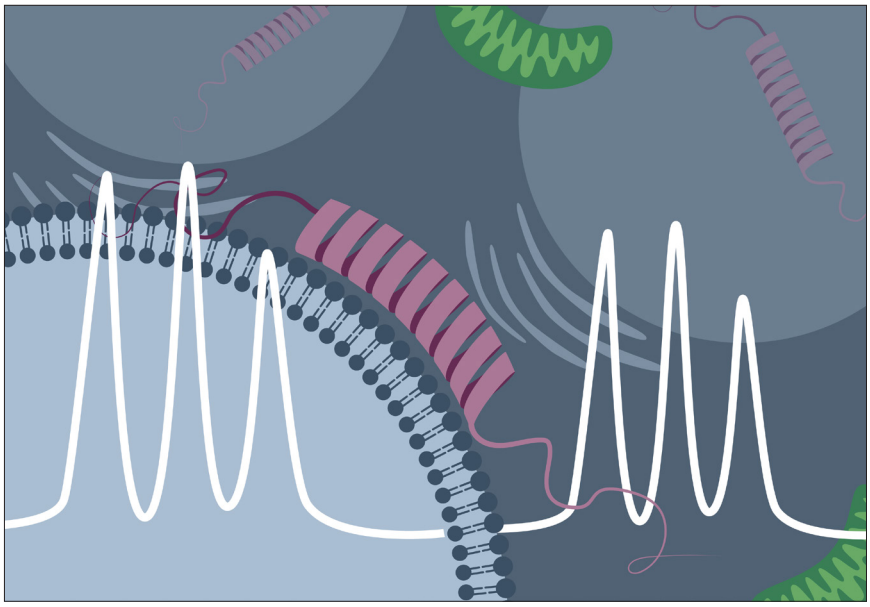
Professor Perdita Barran said: "We believe that our results are an extremely encouraging step towards tests that could be used to help diagnose and monitor Parkinson's. Not only is the test quick, simple and painless but it should also be extremely cost-effective because it uses

existing technology that is already widely available. We are now looking to take our findings forwards to refine the test to improve accuracy even further and to take steps towards making this a test that can be used in the NHS and to develop more precise diagnostics and better treatment for this debilitating condition."

Parkinson's tends to develop gradually and it may be many months, even years, before the symptoms become obvious enough for an individual to visit their GP. A DaTscan is regularly used to help specialists confirm the loss of dopamine-producing cells that cause the development of Parkinson's. However, similar loss may also occur in some other rarer neurological conditions. With no molecular test for the condition, diagnosis is made by a neurologist based on a combination of symptoms such as tremor, slowness, stiffness and balance issues. However, many of the symptoms of Parkinson's can overlap with other conditions, especially in the early stages when progression is gradual and symptoms are more subtle.

In a recent survey of more than 2000 people with Parkinson's carried out by Parkinson's UK, 26% reported they were misdiagnosed with a different condition before receiving the correct Parkinson's diagnosis.

See *ACS Central Science* (doi.org/fzws) and *Nature Communications* (doi: 10.1038/s41467-021-21669-4).



Credit: Malte Drescher Lab, University of Konstanz

EPR demystifies the "Parkinson protein"

Scientists from the University of Konstanz and the Free University of Amsterdam, in collaboration with Bruker BioSpin, have succeeded for the first time in the direct spectroscopic detection of the binding of the "Parkinson protein" α-synuclein to lipid membranes in the cell.

The protein α-synuclein is one of the most abundant proteins in the human brain. It is often referred to as the "Parkinson protein", as deposition of this protein in brain cells is a hallmark of Parkinson's disease. Despite the high interest of biomedical research in the protein, many questions concerning the function and physiology of α-synuclein in living cells still remain to be answered. For example, it was previously unclear whether and to what extent the protein binds to and interacts with internal cell components such as membranes. As such processes could play a role in the development of the disease, the team led by Konstanz-based physical chemist Professor Malte Drescher used the further development of electron paramagnetic resonance (EPR) spectroscopy to learn more about the binding properties of the "Parkinson protein". Their study furnishes proof of concept that an advanced EPR method, rapid-scan EPR spectroscopy, is fundamentally suitable for elucidating protein–lipid interactions in cells. Furthermore, this first practical test yielded direct evidence of the binding of α-synuclein to intracellular membranes.

In both methods, the conventional and the advanced, the proteins to be studied are first fitted with so-called spin probes. These chemical probes make it possible to detect changes in protein structure. Spin probes each have a free electron whose spin is excited by irradiation with microwaves. In conventional EPR spectroscopy, for each group of excited spins it is necessary to wait until this influence decays before the group can be excited again. This relatively time-consuming process must be repeated over many passes to achieve the complete measurement.

With rapid-scan EPR spectroscopy, by contrast, it is no longer necessary to wait until the influence on a spin group abates before continuing the measurement. "Instead, you rush the influence spectrally from spin group to spin group and then return to the first group at the very moment when its excitation has just subsided", says Drescher. On the one hand, this procedure shortens the required measurement time, while on the other it allows application of higher microwave power, leading to improved accuracy of the method. The researchers have made use of both of these advantages in their current study on the binding behaviour of α-synuclein.

From previous *in vitro* studies, it was already known that the "Parkinson protein" α-synuclein can attach itself to electrically negatively charged lipid membranes. In EPR spectroscopy, this binding process is accompanied by a characteristic change in the measured signal. "The initially disordered α-synuclein assumes an ordered form upon

binding to the membrane. This reduces the mobility of the spin probe, and the binding of the protein can be directly detected by the measurement method", explains Theresa Braun, doctoral student in Drescher's research team and, jointly with Juliane Stehle, lead author of the study.

Using synthetic, negatively charged membrane vesicles and purified α-synuclein, Drescher and his colleagues were able to detect the same signal change in rapid-scan EPR spectroscopy. However, they succeeded not only *in vitro*, but also inside cells of the African clawed frog (*Xenopus laevis*), into which first the artificial membrane vesicles were introduced and, a short time later, the protein was. The research team then carried out time-dependent measurements and was able to directly observe, based on the change in the measurement signal, how the proportion of the protein bound in the cell increased over time.

A comparable—albeit significantly weaker—increase in the amount of bound α-synuclein over time was also seen when no artificial membranes were introduced into the cell. Thus, according to Drescher, only one explanation remained for this crucial observation. "This is the first time that we see direct evidence that α-synuclein interacts with the endogenous, i.e. naturally existing lipid membranes as well". Due to the comparatively small size of the effect, in experiments with less precise measurement methods this had previously remained hidden.

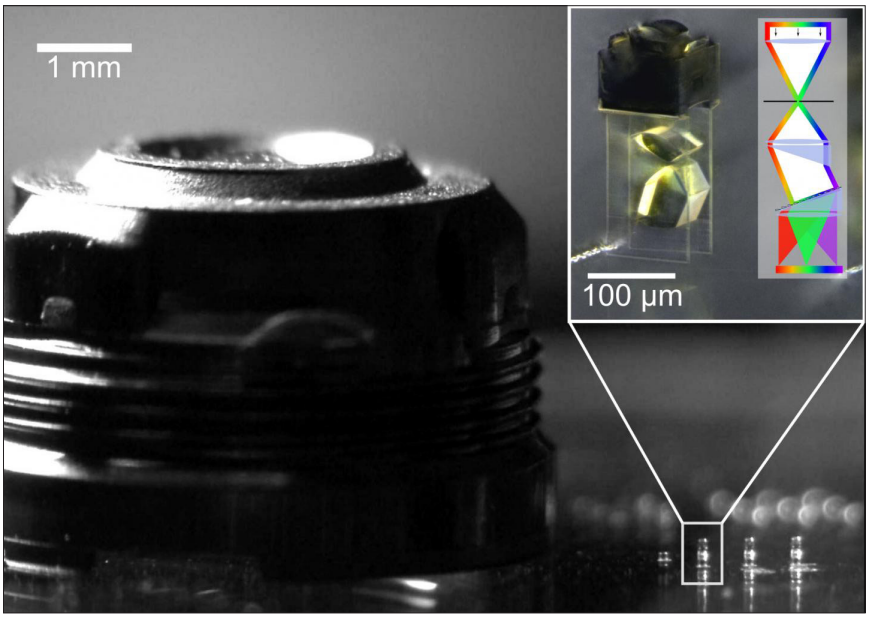
In future studies, Malte Drescher's team plans to build on this result and further elucidate the process of intracellular binding of α-synuclein to natural cell components, in order to learn more about the function of the protein. An important step in this process will be the move from frog cells as a model system to various mammalian cell types. The long-term goal is to better understand the protein–lipid interactions of the "Parkinson protein" and its role in the development of Parkinson's disease in order to be able to develop suitable therapeutic approaches.

See *The Journal of Physical Chemistry Letters* (doi.org/fz2n).

3D-printed spectrometer: how small can you go?

Femtosecond direct laser writing as a 3D printing technology has been one of the key building blocks for miniaturisation in modern times. It has transformed the field of complex microoptics since the early 2000s. Medical engineering and consumer electronics have benefitted from these developments. It is now possible to create robust, monolithic and nearly perfectly aligned freeform optical systems on almost arbitrary substrates such as image sensors or optical fibres.

Simultaneously, the miniaturisation of spectroscopic measurement devices has been advanced, for instance based on quantum dot or nanowire technology. These are based on computational approaches, which have the drawback of being calibration sensitive and require complex reconstruction algorithms. Now, a team of scientists, led by Professor Alois Herkommer and Professor Giessen from the University of Stuttgart, have demonstrated an angle-insensitive, 3D-printed miniature spectrometer with a direct separated spatial–spectral response. It has a volume of less than $100 \times 100 \times 300\,\mu m^3$.



Comparison with an iPhone 5S camera lens. The inset (white box) shows a microscope image of the fabricated spectrometer (left) and its optical design principle (right). Credit: Andrea Toulouse, Johannes Drozella, Simon Thiele, Harald Giessen, and Alois Herkommer

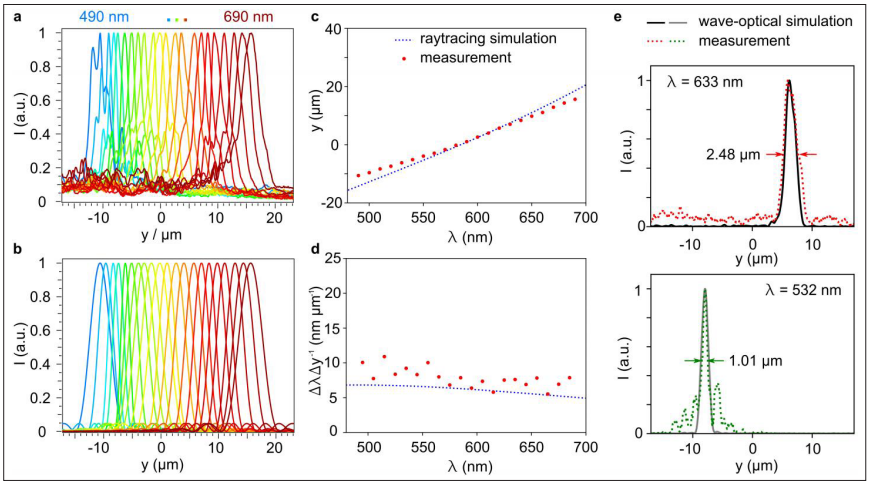
The design is based on a classical grating spectrometer and was fabricated via two-photon direct laser writing combined with a super-fine inkjet process. Its tailored and chirped high-frequency grating enables strongly dispersive behaviour. The miniature spectrometer features a wavelength range in the visible from 490 nm to 690 nm. It has a spectral resolution of 9.2 ± 1.1 nm at 532 nm and 17.8 nm ± 1.7 nm at 633 nm. First author Andrea Toulouse commented on its potential.

"With its volume of less than $100 \times 100 \times 300\,\mu m^3$ we explore a whole new size range for direct spectrometers. An order of magnitude this small could only be realised by computational approaches until now. In contrast, we translate the spectrum directly into a spatially encoded intensity signal which can be read out with a commercial monochromatic image sensor. For 3D-printed microoptics, the complexity of the optical design marks an innovation. Refractive, diffractive and

spatially filtering elements have never been combined in such a small volume to create a complex and monolithic measurement system."

"Our spectrometer could be fabricated directly on a miniature image sensor as the tip of a distal chip endoscope. This way, regions in the human body could be examined with extremely high bending radii that were not accessible before. It could also be an interesting approach for hyperspectral imaging where the spectrometer would be used as a unit cell (macro pixel). The redistribution of spectral energy instead of high-loss Fabry–Perot-filtering could thus enable highly efficient hyperspectral imaging sensors. The ever-growing world population could benefit from such a camera if it was used for spectral mapping in precision farming, for instance."

See *Light: Advanced Manufacturing* (doi.org/fzwv).



a) Measured normalised intensity profiles at the image plane of the spectrometer for illumination wavelengths ranging from 490 nm to 690 nm in 10 nm steps. b) Sinc² fits of the intensity profiles from a. c) Centre positions of the sinc² fits per wavelength. d) Wavelength shift per micrometre deduced from c. e) Linewidth simulation and measurement with a red or green laser, respectively. The measured full width at half maximum is indicated with a pair of arrows. The combination of measurements d) and e) yield a spectral resolution of 9.2 ± 1.1 nm at 532 nm and 17.8 ± 1.7 nm at 633 nm wavelength. Credit: Andrea Toulouse, Johannes Drozella, Simon Thiele, Harald Giessen, and Alois Herkommer

Laser ablation and LIBS for UK environmental research

A team of Earth scientists at the University of Portsmouth has been awarded £950,000 to buy and install an integrated femtosecond laser ablation and laser induced breakdown spectroscopy system to study and better understand environmental pollution.

Funding was awarded by the UK's leading funder of environmental science, the Natural Environment Research Council (NERC). Professor Craig Storey, in the University's School of the Environment, Geography and Geosciences, led the bid.

He said: "This instrument will provide a step change in environmental research capability. It's the only one of its kind across the UK and Europe and opens the possibility of stealing a march in the study of how the planet works. This new instrument opens a window, giving us the ability with pinpoint accuracy to analyse a vast range of materials and elements to provide high quality data critical for addressing geo-environmental problems."

The proposed facility will be housed at the University of Portsmouth and open for use by the UK scientific community.

Lockdown inspiration fuels non-linear optics advance

Forced to consider new research opportunities due to lockdown restrictions, researchers from the Physics department of the Politecnico di Milano developed an innovative connection between the field of artificial intelligence and non-linear optics.

Carlo Michele Valensise, first author of the study conducted together with Giulio Cerullo and Dario Polli of Politecnico di Milano and Alessandro Giuseppi of the Sapienza University of Rome, used the lockdown to deepen his knowledge of artificial intelligence, focusing in particular on Deep Reinforcement Learning (DRL). DRL is the branch of artificial intelligence that

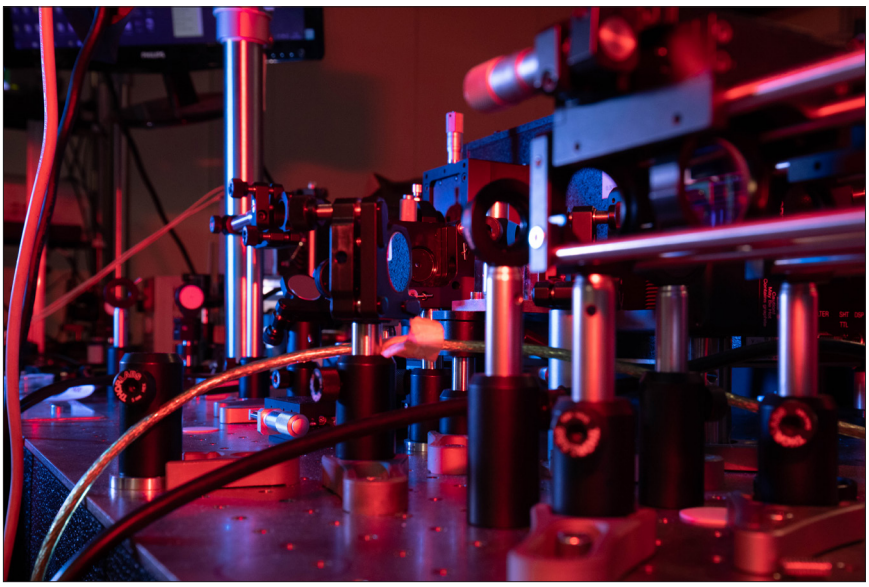


Image courtesy: Dario Polli

deals with programming agents able to learn to control automated systems.

The application of DRL on non-linear optics allows the simplification of some processes and, more generally, the speeding up of experimentation. For example, in the phenomenon of generation of white light, one of the most common in this research field, much of the time is occupied by the optimisation process through which stable and broadband optical pulses are then obtained. The work just published demonstrates, as a proof of principle, the possibility of exploiting DRL to automatically automatise this process. The artificial intelligence agent, in particular, autonomously explores the available degrees of freedom to adjust the system and, by studying their effect with respect to the set objective (i.e. the generation of broadband pulses), is able to ensure the proper functioning of the process.

"Artificial intelligence applications are touching ever more disparate areas", says Carlo Michele Valensise, "although the message often passes that automatic systems can replace human competence. In reality, with our work we are offering help to improve and speed up scientific research. But we must not forget that artificial intelligence is still developed by human intelligence: the role of the researcher therefore remains central."

Valensise added, "this study was born about a year ago, when, with the restrictions due to the pandemic, we began to explore new research perspectives. Specifically, we became interested in artificial intelligence by asking ourselves a very specific question: how can we exploit it for our research field? We then theorised the techniques at home by developing the idea and then, once the laboratories were reopened, we implemented the experiment, which was successful. The usefulness of this demonstration lies in the possibility for the researcher to delegate long optimisation processes, which are often only the beginning of more complex experiments."

See *Optica* (doi.org/fz2p).

Image by Amber Clay from Pixabay

ICP-MS shows that Gulf War illness was not caused by depleted uranium

More than a quarter of a million US, UK and other Allied nations' servicemen and women have endured Gulf War Illness since the Persian Gulf War in 1991, 30 years ago. The illness has a range of acute and chronic symptoms, including fatigue, headaches, joint pain, indigestion, insomnia, dizziness, respiratory disorders and memory problems, and appears rooted in neurological impairment.

It has long been plausibly alleged that the soldiers inhaled significant quantities of depleted uranium from allied munitions used on the battlefield and suffered from its toxic and mildly radioactive effects. For decades, medics and scientists have been looking for the elusive cause of Gulf War illness.

Research at the University of Portsmouth tested US Gulf War illness sufferers to examine levels of residual depleted uranium in their bodies using multi-collector ICP-MS. Their study proves conclusively—and, for many, surprisingly—that none of them were exposed to any significant amounts of depleted uranium.

The testing took into account the predicted decline in depleted uranium from normal metabolism over the time since potential exposure and testing, by using a highly sensitive method of testing in conjunction with metabolic modelling.

The research was carried out by Professor Randall Parrish at the University of Portsmouth and Dr Robert Haley, of the University of Texas Southwestern Medical Centre in Dallas.

See *Scientific Reports* (doi.org/fz2w)

NIR spectroscopy for real-time bitter almond detection

Almonds are a widely consumed nut around the world. However, they can sometimes suffer, or rather those who eat them can suffer, from a bitter aftertaste. This is due to amygdalin, a diglycose that, in contact with enzymes present in saliva, is broken down into glucose, benzaldehyde (responsible for the bitter taste) and hydrocyan acid. To reduce this unpleasant surprise, the research groups of Agroganadero Systems Engineering and Food Technology at the University of Córdoba, with the collaboration of the Alameda del Obispo Center of the Institute of Agricultural and Fisheries Research and Training of Andalusia (IFAPA), have developed a method capable of predicting the levels of amygdalin present in the fruits analysed with and without shells, and to correctly classify sweet and bitter almonds on an industrial scale, something that to date had only been achieved in peeled fruits, in individual or ground grains.

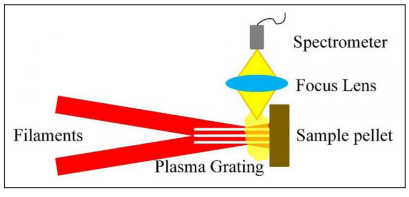
The new system uses portable near infrared (NIR) spectroscopy instrumentation capable of analysing large quantities of product onsite in real time. "It is of great interest to the agri-food sector", explains Professor Dolores Pérez Marín, because although the bitterness of almonds in nature can prevent predators from eating the seeds of certain varieties, on an industrial scale it offers no advantages and many drawbacks: an unpleasant taste, product depreciation and potential food security problems if the bitter fruit is consumed on a large scale.

The use of NIR spectroscopy is also useful in the early detection of potential fraud and in food authentication. For this reason, the team has launched another research project aimed at detecting batches of sweet almonds adulterated with bitter almonds and in which almost 90 % of fraudulent items have been identified. The system tested in this work, explains Professor María Teresa Sánchez Pineda de las Infantas, another of the authors of the research, "can be implemented throughout the value chain, including the reception, processing and shipping of products, and established as a fast and cost-effective anti-fraud early warning method".

See *Journal of Food Engineering* (doi.org/fz2x)

Breakthrough for laser-induced breakdown spectroscopy

In laser-induced breakdown spectroscopy (LIBS), a powerful laser pulse is focussed on a sample to create a microplasma. The elemental or molecular emission spectra from that microplasma can be used to determine the elemental composition of the sample. Compared with more traditional technology, like atomic absorption spectroscopy and inductively coupled plasma optical emission spectroscopy (ICP-OES), LIBS has some unique advantages: no sample pre-treatment, simultaneous multi-element detection and real-time non-contact measurements. These advantages make it suitable for practical analysis of solids, gases and liquids.



Experimental schematic of plasma-grating-induced breakdown spectroscopy: https://doi.org/10.1117/1.AP.2.6.065001. Credit: SPIE

Traditional LIBS systems based on a nanosecond pulse laser (ns-LIBS) have some disadvantages due to laser power intensity, long pulse duration and the plasma shielding effect. These issues adversely affect its reproducibility and signal-to-noise ratio. Femtosecond LIBS (fs-LIBS) can exclude the plasma shielding effect since the ultrashort pulse duration limits the laser–matter interaction time. The femtosecond pulse has a high power density so materials can be effectively ionised and dissociated, leading to a higher signal-to-background ratio and more precise spectral resolution.

Filament-induced breakdown spectroscopy (FIBS) combines the LIBS technique with a femtosecond laser filament. A single laser filament results from the interplay between the Kerr self-focussing and plasma defocussing mechanisms present in the propagation of an ultrashort, high-intensity beam in a transparent medium such as atmospheric air. The femtosecond laser filament produces a long and stable laser plasma channel, which guarantees the stability of the laser power density and can improve measurement stability. However, the power and electron densities saturate when the laser energy increases. This is known as laser intensity clamping effect, and it limits the detection sensitivity of FIBS.

Fortunately, the laser intensity clamping effect can be overcome through a plasma grating induced by the nonlinear interaction of multiple femtosecond filaments. The electron density in the plasma grating has been proven to be an order of magnitude higher than that in a filament.

Based on that insight, researchers under the leadership of Heping Zeng at East China Normal University in Shanghai recently demonstrated a novel technique: plasma-grating-induced breakdown spectroscopy (GIBS). GIBS can

effectively overcome the drawbacks of ns-LIBS, fs-LIBS and FIBS. With GIBS, the signal intensity is enhanced more than three times and the lifetime of plasma induced by the plasma grating is approximately double of that obtained by FIBS with the same initial pulse. Quantitative analysis is feasible because of the absence of plasma shielding effects, the high power and the electron density of femtosecond plasma grating.

Zeng notes that the GIBS technique could be a promising tool for detecting samples that are hard to melt, ionise, or dissociate, and can also serve for samples with complex matrices.

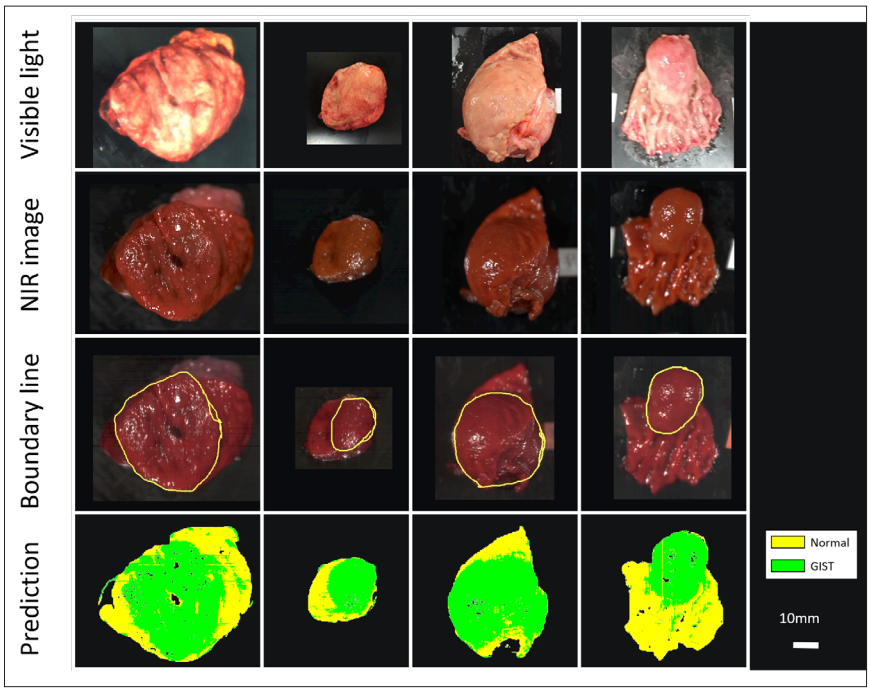
See *Advanced Photonics* (doi.org/fz23)

NIR-HSI can identify hidden GI tumours

Gastrointestinal stromal tumours grow underneath the mucous layer covering our organs. Because they are deep inside the tissue, these "submucosal tumours" are difficult to detect and diagnose, even with a biopsy. Now, researchers from Japan have developed a novel minimally invasive and accurate method using infrared imaging and machine learning to distinguish between normal tissue and tumour areas. This technique has a strong potential for widespread clinical use.

The team, led by Dr Hiroshi Takemura from Tokyo University of Science, performed imaging experiments on 12 patients with confirmed cases of GISTs, who had their tumours removed through surgery. The scientists imaged the excised tissues using NIR-HSI, and then had a pathologist examine the images to determine the border between normal and tumour tissue. These images were then used as training data for a machine-learning algorithm.

They found that even though 10 out of the 12 test tumours were completely or partly covered by a mucosal layer, the machine-learning analysis was effective in identifying GISTs, correctly classifying tumour and non-tumour sections with 86% accuracy. "This is a very exciting development", Dr Takemura explains, "being able to accurately, quickly and non-invasively diagnose different types of submucousal tumours without biopsies,



The machine learning technique developed by Dr Takemura and team could distinguish tumour tissue from healthy tissue in *ex vivo* images of resected tumours, with 86% accuracy. Photo courtesy: Hiroshi Takemura, Tokyo University of Science

a procedure that requires surgery, is much easier on both the patient and the physicians."

Dr Takemura acknowledges that there are still challenges ahead, but feels they are prepared to solve them. The researchers identified several areas that would improve on their results, such as making their training dataset much larger, adding information about how deep the tumour is for the machine-learning algorithm, and including other types of tumours in the analysis. Work is also underway to develop an NIR-HSI system that builds on top of existing endoscopy technology.

"We've already built a device that attaches an NIR-HSI camera to the end of an endoscope and hope to perform NIR-HSI analysis directly on a patient soon, instead of just on tissues that had been surgically removed", Dr Takemura says, "In the future, this will help us separate GISTs from other types of submucosal tumours that could be even more malignant and dangerous. This study is the first step towards much more ground-breaking research in the future, enabled by this interdisciplinary collaboration."

See *Scientific Reports* (doi.org/fz26)

Laser spectroscopy helps clarify biochemical cycle of greenhouse gas

Nitrous oxide (N_2O) is considered one of the major drivers of climate change, accounting for 6% of global warming. The sources of the greenhouse gas are well known and range from agriculture and the use of fertilisers, to biomass burning and natural emissions from soils and oceans. N_2O reduction remains a challenge because the gas is formed by different microorganisms and the contribution of different metabolic pathways to the overall emissions cannot be accurately determined to date. As part of her PhD thesis at Empa, Kristýna Kantnerová developed a new analytical method, based on quantum cascade laser absorption spectroscopy (QCLAS), to identify nitrous oxide molecules containing two rare isotopes of nitrogen and oxygen. In the long term, her work should contribute to a better understanding of the biochemical N_2O cycle. For her work, she received the METAS Award, worth CHF5000, which is awarded to young scientists in Switzerland who make outstanding contributions in the field of metrology in chemistry or biology.

Kristýna Kantnerová received the METAS Award by the Swiss Chemical Society for her "outstanding and timely work in the field of metrology of clumped isotopes of nitrous oxide" at Empa. Image: Empa

The isotopic composition of N_2O changes depending on the formation or decay path. Nitrogen has two stable isotopes, oxygen has three; thus, a total of twelve different N_2O isotopic compounds can be formed. The ratio of these isotopocules, or clumped isotopes, is characteristic and is considered a fingerprint for the respective formation pathway. To decipher this fingerprint, Kantnerová developed a new analytical method based on quantum cascade laser absorption spectroscopy (QCLAS) with preconcentration. QCLAS is an established technique in atmospheric chemistry to detect trace gases. However, until now, researchers have lacked spectroscopic tools to distinguish between the doubly isotopically substituted N_2O compounds.

See *Chimia* (doi.org/ggrc2z)

New microcomb design based on two microresonators

A microcomb is a photonic device capable of generating a myriad of optical frequencies on a tiny cavity known as microresonator. The frequencies are uniformly distributed, and the device can be used to measure or generate frequencies with extreme precision. Researchers from Chalmers University of Technology have described a new kind of microcomb on a chip, based on two microresonators. The new microcomb is a coherent, tuneable and reproducible device with up to ten times higher net conversion efficiency than the current state of the art.

"The reason why the results are important is that they represent a unique combination of characteristics, in terms of efficiency, low-power operation and control, that are unprecedented in the field", says Óskar Bjarki Helgason, a PhD student at the Department of Microtechnology and Nanoscience at Chalmers.

The Chalmers researchers are not the first to demonstrate a microcomb on a chip, but they have developed a method that overcomes several well-known limitations in the field. The key factor is the use of two microresonators instead of one. This arrangement results in the unique physical characteristics.

The microcombs offer a wide range of potential applications, from radically decreasing the power consumption in optical communication systems, to use in lidar for autonomous driving vehicles and in the calibration of the spectrographs used in astronomical observatories devoted to the discovery of Earth-like exoplanets.

continued

NIR spectroscopy is coming to your smartphone

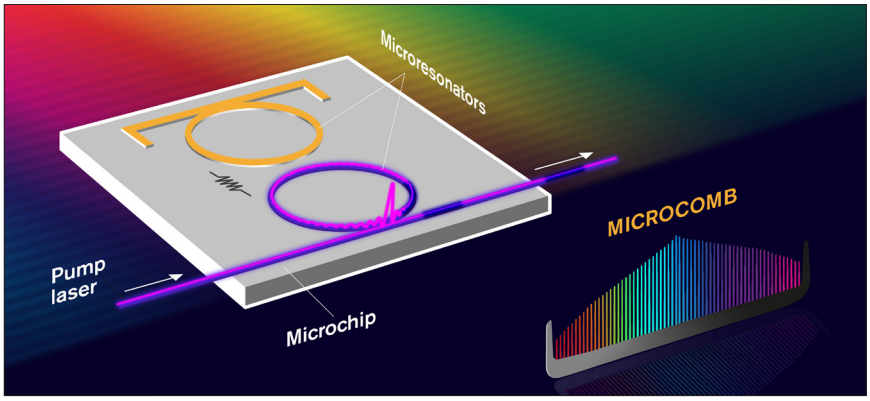
trinamiX and Viavi Solutions have announced a joint development agreement to build an near infrared (NIR) spectrometer module for integration into consumer devices. trinamiX has been miniaturising NIR spectrometer modules for smartphones, while VIAVI is an innovator in the field of optical filters with a strong track record in the consumer electronics market.

The collaboration follows trinamiX's announcement in December 2020 at Qualcomm's Snapdragon™ Tech Summit, that it plans to bring NIR spectroscopy into consumer devices.

Dr Wilfried Hermes, Director IR Sensing, trinamiX GmbH, noted: "We are very excited about VIAVI joining us as a strong partner, whose state-of-the-art optical solutions have been constantly pushing the envelope on what is technically possible within mobile handsets and other consumer electronics. This is an important milestone towards creating a first-class ecosystem around an exciting technology that will enhance our smartphone experience in the near future."

Markus Bilger, Senior Director Product Line Management, VIAVI, said: "trinamiX has broken new ground by introducing plans to bring spectroscopy to everyone. We are incredibly proud to be working with trinamiX on the next game-changing innovation that will redefine our understanding of a smartphone."

More information is available at www.trinamixsensing.com/smartphone-spectroscopy and www.viavisolutions.com/en-us/osp/technology/consumer-spectroscopy.



A new kind of microcomb based on two microresonators instead of one. It is a coherent, tuneable and reproducible device with up to ten times higher net conversion efficiency than the current state of the art. Illustration: Yen Strandqvist/Chalmers

"For the technology to be practical and find its use outside the lab, we need to co-integrate additional elements with the microresonators, such as lasers, modulators and control electronics. This is a huge challenge, that requires maybe 5–10 years and an investment in engineering research. But I am convinced that it will happen", says Victor Torres Company, who leads the research project at Chalmers. He continues:

"The most interesting advances and applications are the ones that we have not even conceived of yet. This will likely be enabled by the possibility of having multiple microcombs on the same chip. What could we achieve with tens of microcombs that we cannot do with one?"

See *Nature Photonics* (doi.org/ghxgc9)

What are frequency combs and microcombs?

A frequency comb is a special laser where the emission frequencies are evenly spaced. It functions as a ruler made of light, where the markers set the frequency scale across a portion of the electromagnetic spectrum, from the ultraviolet to the mid-infrared. The location of the markers can be linked to a known reference. This was achieved in the late 1990s, and it signified a revolution in precision metrology—an achievement recognised by the Nobel Prize in Physics in 2005.

A microcomb is a modern, alternative technology to mode-locked lasers, that can generate repetitive pulses of light at astonishing rates. They are generated by sending laser light to a tiny optical cavity called a microresonator. Thus, microcombs have two important attributes that make them extremely attractive for practical purposes: the frequency spacing between markers is very large (typically between 10 GHz and 1000 GHz), that is much higher than the spacing in mode-locked laser frequency combs, and they can be implemented with photonic integration technology. The compatibility with photonic integration brings benefits in terms of reduction of size, power consumption and the possibility to reach mass-market applications. The large spacing between teeth means that microcombs can be used for novel applications, such as light sources for fibre-optic communication systems or for the synthesis of pure microwave electromagnetic radiation.

The key to the new enhanced microcomb from Chalmers is that the researchers have used two microresonators instead of one. The microresonators interact with each other, similar to how atoms bind together when forming a diatomic molecule. This arrangement is known as a photonic molecule and has unique physical characteristics.

Fluorescence Award

HORIBA Scientific has presented Dr Luca Lanzano with the annual Young Fluorescence Investigator Award at the virtual Biophysical Society virtual event. Dr Lanzano is an Associate Professor of Applied Physics in the department of Physics and Astronomy "E. Majorana", at the University of Catania. The winner was selected by the Biological Fluorescence Subgroup of the Biophysical Society. Along with the recognition, HORIBA presented a $1000 cheque to Dr Lanzano and a crystal award.

Since March 2020, Dr Lanzano has been an Associate Professor of Applied Physics in the Department of Physics and Astronomy, University of Catania. He worked as a Post-Doctoral fellow from 2008 to 2013 at the University of California at Irvine, in the Laboratory for Fluorescence Dynamics. He developed fluorescence microscopy- and spectroscopy-based methods to measure protein dynamics and interactions in live cells. In 2013 he joined the Nanoscopy group at the Istituto Italiano di Tecnologia in Genoa, where he developed new super-resolution imaging techniques and novel image analysis tools, and was appointed a researcher in 2018.

HORIBA Scientific has been the sole sponsor of this award since 1997. The Young Fluorescence Investigator Awardee has been nominated by their peers for significant advancements and/or contributions in or using fluorescence methodologies.

"HORIBA is very proud to sponsor this prestigious award again this year, and Dr Lanzano is an excellent choice as this year's recipient for his work in super resolution fluorescence microscopy", said Cary Davies, Director of the Fluorescence group at HORIBA Scientific. "Lanzano is the 26th researcher to win the Young Investigator Award since 1997."

Luca Lanzano with his cheque.

XPS provides important insights for the solar industry

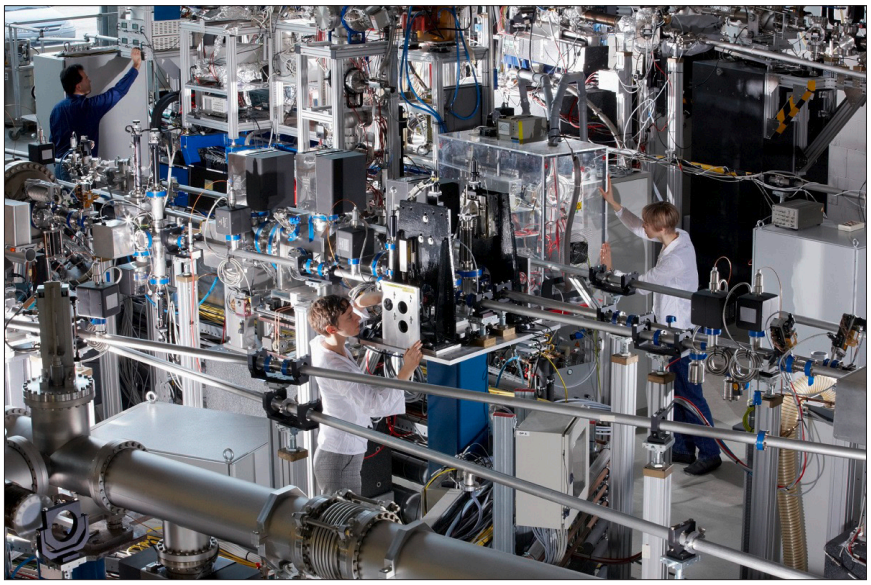
Using a new method, physicists from TU Freiberg, in cooperation with researchers from Berkeley and Hamburg, are for the first time analysing at the femtosecond scale the processes in a model system for organic solar cells. This can be used to develop high-performance and efficient solar cells.

The key are the ultra-fast flashes of light, with which the team led by Dr Friedrich Roth works at FLASH in Hamburg, the world's first free-electron laser in the X-ray region. "We took advantage of the special properties of this X-ray source and expanded them with time-resolved X-ray photoemission spectroscopy (TR-XPS). This method is based on the external photoelectric effect, for the explanation of which Albert Einstein received the Nobel Prize in Physics in 1921. "For the first time, we were able to directly analyse the specific charge separation and subsequent processes when light hits a model system such as an organic solar cell. We were also able to determine the efficiency of the charge separation in real-time", explains Dr Roth from the Institute of Experimental Physics at TU Bergakademie Freiberg.

In contrast to previous methods, the researchers were able to identify a previously unobserved channel for charge separation. "With our measurement method, we can carry out a time-resolved, atom-specific analysis. This gives us a fingerprint that can be assigned to the associated molecule. We can see when the electrons energised by the optical laser arrive at the acceptor molecule, how long they stay and when or how they disappear again", says Prof. Serguei Molodtsov. He heads the research group "Structural Research with X-ray Free Electron Lasers (XFELs) and Synchrotron Radiation" at the Freiberg Institute of Experimental Physics and is a Scientific Director at the European X-ray Free Electron Laser (EuXFEL).

Real-time analysis and the measurement of internal parameters are important aspects of basic research that the solar industry, in particular, can benefit from. "With our measurements, we draw important conclusions about the interfaces at which free charge carriers are formed or lost and thus weaken the performance of solar cells", adds Dr Roth. With the findings of the Freiberg researchers, for example, optimisation possibilities at the molecular level or in the field of materials science can be derived and quantum efficiency optimise newly emerging photovoltaic and photocatalytic systems. The quantum efficiency describes the ratio of the incident light to the photon stream (current that is generated).

See *Nature Communications* (doi.org/fz5k)



In the FLASH I experimental hall, "Albert Einstein". Photo: DESY/Heiner Müller-Elsner

ARTICLE

Sweeping Apparatus for Polarisation Enhancement (SWAPE) in benchtop nuclear magnetic resonance spectroscopy

Javier A. Romero,[a] Krzysztof Kazimierczuk[a] and Dariusz Gołowicz[a,b]
[a]Center of New Technologies, University of Warsaw, Banacha 2c, 02-097, Warsaw, Poland
[b]Faculty of Chemistry, University of Warsaw, Pasteura 1, 02-093, Warsaw, Poland

Introduction

Analytical chemists often make use of nuclear magnetic resonance (NMR) spectroscopy to identify molecules and measure their concentrations. NMR has many advantages as a technique for such an analysis: it is non-invasive and requires minimal bench time (sample preparation). Moreover, the NMR signal is linear versus concentration of nuclei of a given type and thus quantitative NMR (qNMR) is possible using reference standards different from the analyte. The technique has become a reliable tool for monitoring industrial processes in many areas. It is used, for example, to investigate the stability of oil-containing cosmetics.[1]

However, NMR suffers from relatively low sensitivity. To reach nanomolar limits of detection one has to use high magnetic fields and cryogenically cooled probes that are beyond the reach of most analytical laboratories. In recent years, a more accessible technology has started to receive much attention: benchtop NMR (BT-NMR). These compact designs are cost-effective, easy-to-operate and are becoming preferred tools for process monitoring[2] and steps in basic research. BT-NMR spectrometers use permanent magnets to operate, as opposed to the more expensive superconductive magnets (whose maintenance costs have increased significantly recently with the rising price of liquid helium). The trade-offs for compactness, however, are decreased spectral resolution and sensitivity compared to high-field spectrometers. This is because both resolution and sensitivity scale up with a magnetic field used in an NMR spectrometer.

BT-NMR has opened a way to use NMR in numerous new applications and nowadays many companies produce their own models of mini-spectrometers. New generation BT-NMR systems reach working frequencies of 80 MHz, but a loss in sensitivity remains as a major obstacle. As in many other kinds of experiments, signal-to-noise ratio (SNR) in NMR can be increased by collecting many scans (n) and adding them together. This results in an $\sqrt{n}$ improvement of SNR. However, one has to pay special attention to the longitudinal (spin-lattice) relaxation times (T_1) characterising the process of recovering the equilibrium state sample magnetisation between scans. Without an efficient recovery (too short inter-scan delays) the SNR will be reduced and relative peak intensities may be biased.

NMR measurements are performed on the active volume of the sample that fills the receiver radiofrequency (RF) coil. This volume corresponds with the most homogeneous region of the magnetic field, although the magnetic field spans a much larger region and can still adequately polarise the sample outside of the active volume. The active volume represents but a small fraction of the sample (see Figure 1), while the rest of the sample (in the vicinity of the active volume) is magnetised but typically unused in NMR.

The idea behind the technique described here is to increase the effective length of an inter-scan relaxation delay by a synchronised shifting of the sample between scans. The shifting introduces a new, polarised portion of the sample into the detection region of the spectrometer. This can serve to enhance SNR for a fixed duration of an experiment in two different ways. Either by collecting more scans (while keeping the same relaxation delay) or acquiring a fixed number of scans and taking

DOI: 10.1255/sew.2021.a7

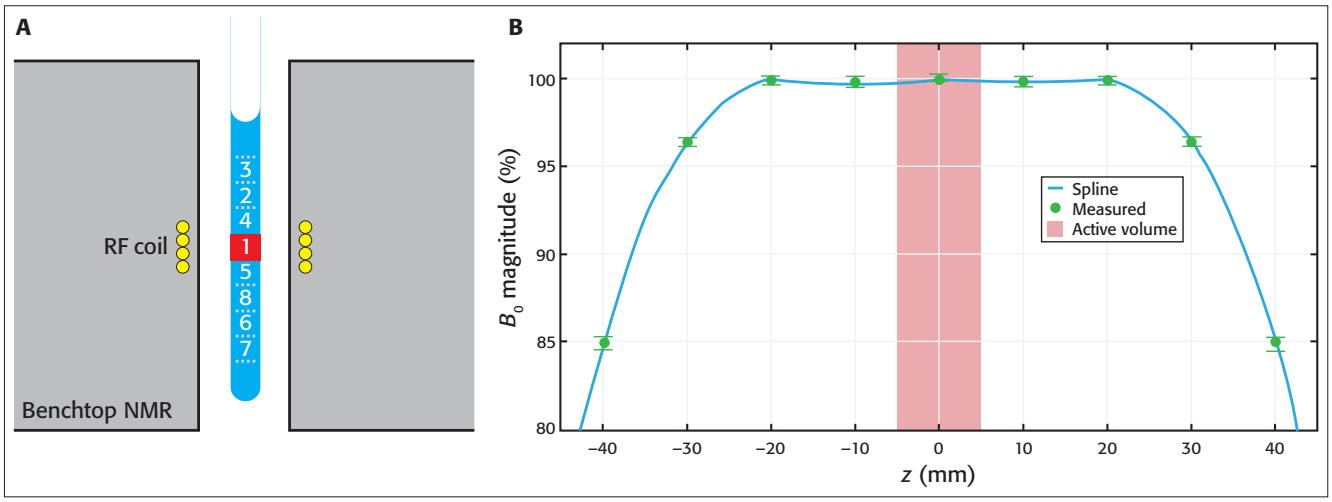


Figure 1. A) Schematic drawing of a sample inside a BT spectrometer. The "active volume" (red square) represents a small portion of the sample, but many similar portions are still strongly polarised by the magnetic field. By a synchronised, downwards shifting of the sample after the first scan the already polarised sub-sample 2 enters the active volume ready to be measured. The process is repeated with other volumes in consecutive scans. B) Profile of magnetic field magnitude along the axis of the spectrometer. Values were measured (green circles) relative to magnitude at the centre. Data were interpolated using a cubic spline (blue line) to aid visualisation. The number of sub-samples capable of being used depends on the BT-NMR model. A shows the maximum number of sub-samples used in this work (8) and the numbers represent the sequence in which the sub-samples are cycled through the active volume.

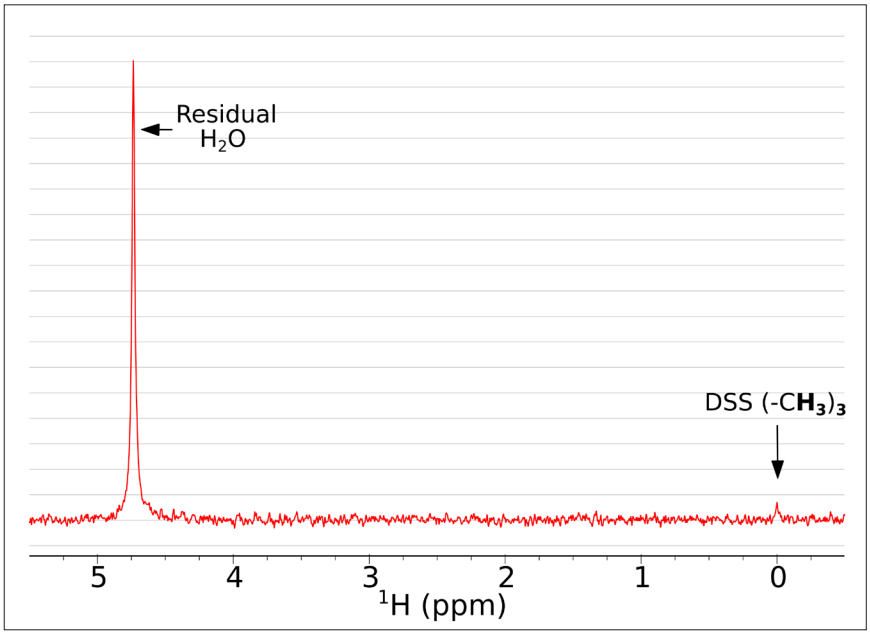


Figure 2. A single scan ^{1}H NMR spectrum of the studied sample with exponentially decaying weighting function (0.2 Hz) applied.

advantage of having the sample closer to the equilibrium state in the consecutive scans.

We built a first SWAPE prototype to test the idea on a *Spinsolve Carbon* benchtop spectrometer (Magritek, Aachen, Germany). The sample is mechanically shifted along the vertical direction by means of a stepper motor mounted on a specially designed surface. The prototype has a low fabrication cost, it does not require modification of the BT-NMR spectrometer and is easily mounted on and off. Synchronisation was achieved by writing the instructions for the stepper motor driver directly into the pulse programmer of the SpinsolveExpert software. We first used the prototype to make essential calibrations, such as measuring the magnetic field profile shown in Figure 1B. Other important calibrations are described elsewhere.[3] All measurements shown in this article were acquired using standard 9″ Norell 5 mm NMR tubes and sample volumes of approximately 2.7 mL. Sample volume is thus slightly larger than usually required, but it ensures appropriate shimming when cycling through the sub-samples.

Experimental

To demonstrate the potential of the method, we prepared the equimolar (1 mM) mixture of sodium trimethylsilyl-propanesulfonate (DSS, Armar Isotopes, 99 %) and glycine (Sigma-Aldrich, ≥99 %) in D_2O. Then, we transferred 2.7 mL of the sample to 5 mm 9″ NMR tube (Norell). We mounted the SWAPE prototype on the Magritek Carbon 43 MHz spectrometer and performed shimming using Spinsolve software. The rest of calibrations (transmitter frequency calibration and locking) and the experiments were carried out through Spinsolve Expert software. The two ^{1}H NMR experiments were performed using the same acquisition parameters, except for the fact that one was run for the static sample and the other employed SWAPE for synchronised shifting of the sample during measurement. We used 90° excitation pulse, an acquisition time of 2.458 s and a scan repetition time of 3.125 s for collection of 1600 scans per each experiment. For the SWAPE experiment, we virtually divided the sample into eight regions as shown in Figure 1. The cycling between those regions was performed following the sequence shown in Figure 1, and starting again with the region labelled as "1" after the region "8" is measured. We also acquired a single scan spectrum with the same acquisition parameters to underline a demand for a multi-scan experiment for the studied sample.

Results

Here we present how using SWAPE can improve the SNR in multi-scan ^{1}H NMR experiments. It is especially beneficial for low-concentration samples, where many scans are required to obtain sufficient SNR. A single-scan NMR spectrum of the studied sample is presented in Figure 2. The dominant signal comes from the residual H_2O, whereas the peak of DSS is barely visible and the peak of glycine is missing completely.

The collection and averaging of 1600 scans help to improve SNR, but employing SWAPE can improve SNR even more. Figure 3 shows how peaks of residual water, DSS and glycine are enhanced with SWAPE compared to the conventional (static sample) acquisition. From panels A and B one may read-out a more than three-fold signal enhancement for residual water, almost three-fold enhancement for glycine (panels C, D) and more than two-fold enhancement for DSS (panels C, D). The enhancement factor relies mainly on the T_1 relaxation time of the observed nuclei. The longer T_1 is, the better SNR enhancement is expected. At this point, it is worth mentioning a well-known method of using Ernst angle nutation for SNR enhancement in multi-scan experiments.[4] Compared to the SWAPE experiment, the main drawback of employing Ernst angle is that prior knowledge of T_1 time constants is required to calculate proper pulse length, while SWAPE usually performs best with standard 90° pulse excitation. For samples of low concentration, as in our case, measuring T_1 relaxation times would be very time consuming and hardly possible. Moreover, using an optimal nutation angle sets a compromise between overall SNR

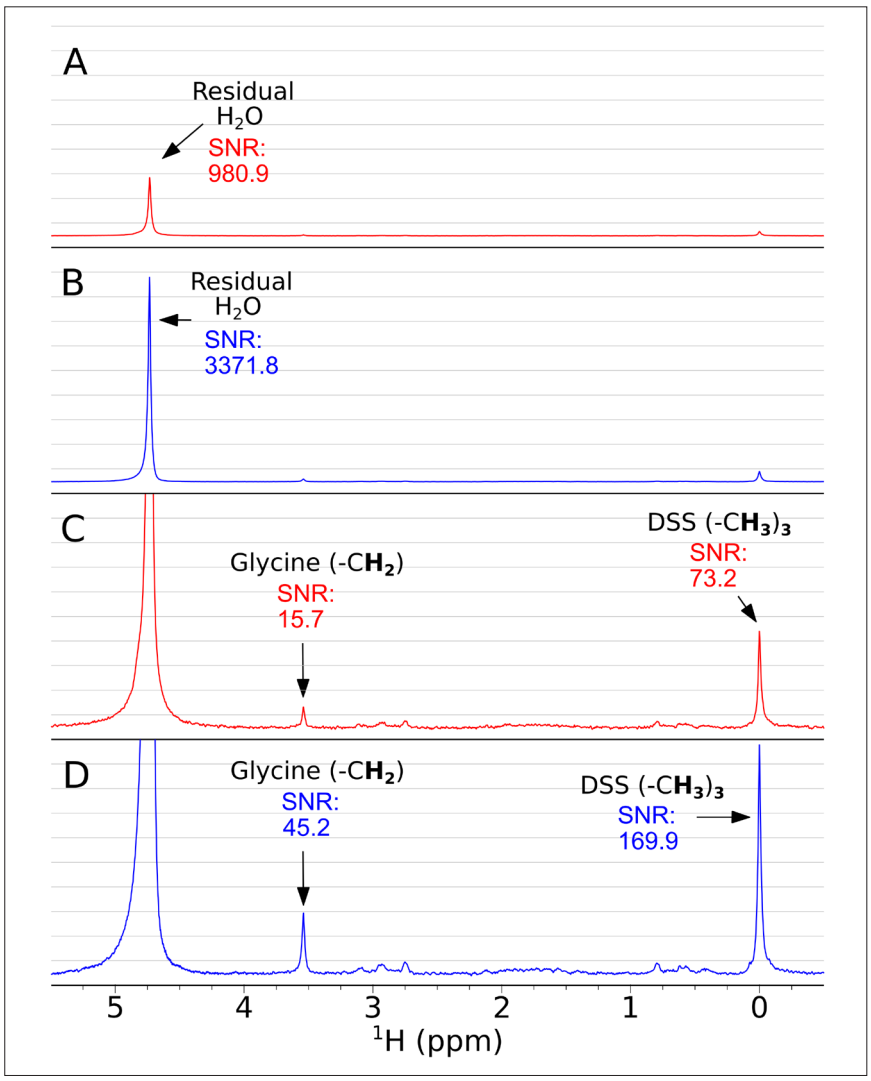


Figure 3. Accumulative ^{1}H spectra (1600 scans) acquired conventionally (red) and using SWAPE (blue). Panels A and B show spectra indicating SNR of residual water peak in conventional (A) and SWAPE (B) experiments. Panels C and D are spectra from A and B accordingly but scaled up. They indicate SNR of Glycine CH_2 peak and DSS $(CH_3)_3$ peak in conventional (C) and SWAPE experiments (D). Both spectra (red and blue) were weighted with exponentially decaying function (0.2Hz).

yield and loss of magnetisation in the consecutive scans, which means that the resulting spectra are rarely quantitative. In the SWAPE acquisition, scan repetition time may be short (3.125 s in our case), but there is a negligible suppression of the *z*-component magnetisation in the consecutive scans. In the presented case, the true relaxation delay for the excited sample volume is 25 s (8 × 3.125 s), where 8 stands for a number of different sample regions in the NMR tube exploited for a cyclic sample shifting.

Although not presented here, increasing the true relaxation delay by a factor of eight with SWAPE helps in obtaining the meaningful peak integrals (as they occur in a single scan NMR or experiments with long relaxation delays—typically 5 T_1). For the examples and discussion on the improved quantitative capabilities in BT-NMR using SWAPE and improved acquisition of ^{13}C experiments please see our previous article.[3] The examples here and in the previous work are all 1D NMR spectra, but SWAPE can also improve the collection of 2D NMR data as well.

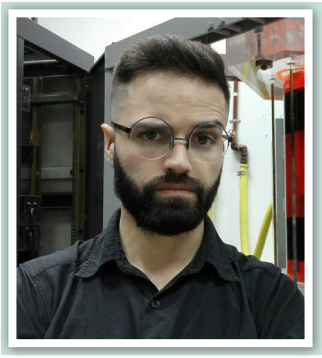
Conclusions

In this short note, we presented the general idea behind the method and the performance of the SWAPE prototype in enhancing ^{1}H NMR signals of low concentration chemical compounds. We showed that some signals may be enhanced up to several times, but the enhancement factor is specific for different chemical species and depends on T_1 relaxation times. As the method is simple to use and provides much improvement in SNR and quantitative experiments, we believe that it may help improve the general performance of the BT-NMR in many laboratories.

If you want to try out SWAPE in your lab, please contact us!

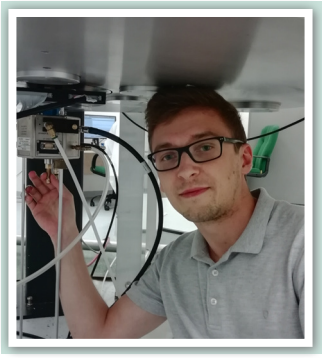
References

1. D.W. Lachenmeier, M. Gary, Y.B. Monakhova, T. Kuballa and G. Mildau "Rapid NMR screening of total aldehydes to detect oxidative rancidity in vegetable oils and decorative cosmetics", *Spectroscopy Europe* **22(6),** 11–14 (2010). https://www.spectroscopyeurope.com/article/rapid-nmr-screening-total-aldehydes-detect-oxidative-rancidity-vegetable-oils-and-decorative
2. F. Dalitz, M. Cudaj, M. Maiwald and G. Guthausen, "Process and reaction monitoring by low-field NMR spectroscopy", *Prog. Nucl. Magn. Reson. Spectrosc.* **60,** 52–70 (2012). https://doi.org/10.1016/j.pnmrs.2011.11.003
3. J.A. Romero, K. Kazimierczuk and D. Gołowicz, "Enhancing benchtop NMR spectroscopy by means of sample shifting", *Analyst* **145,** 7406–7411 (2020). https://doi.org/10.1039/D0AN01556C
4. R.R. Ernst and W.A. Anderson, "Application of Fourier transform spectroscopy to magnetic resonance", *Rev. Sci. Instrum.* **37,** 93 (1966). https://doi.org/10.1063/1.1719961



Javier A. Romero was awarded a PhD degree in Physics by the National University of Córdoba (Argentina) in 2018. His doctoral research in NMR encompassed the development of a Fast-Field-Cycling MRI prototype. Since 2019 he has worked in the laboratory of NMR spectroscopy led by dr. hab. Krzysztof Kazimierczuk on developing new tools for multidimensional spectroscopy.
https://orcid.org/0000-0001-8378-3837
j.romero@cent.uw.edu.pl

Krzysztof Kazimierczuk got his PhD degree in Chemistry from the University of Warsaw in 2009. His research interests include various novel NMR methods: sparsely sampled, time-resolved, diffusion-ordered and pure-shift spectroscopy. Prof. Kazimierczuk works at the Centre of New Technologies, University of Warsaw.
https://orcid.org/0000-0001-9585-1737
k.kazimierczuk@cent.uw.edu.pl



Dariusz Gołowicz, MSc, graduated with honours from the University of Warsaw (UW) in 2016 in Physical Chemistry. Currently, he is a PhD student in a group of professor Krzysztof Kazimierczuk at the Centre of New Technologies UW. His research focuses on the development of NMR methods with a strong emphasis on the utilisation of non-uniform sampling and non-standard signal processing strategies.
https://orcid.org/0000-0002-3602-4069
golowiczdariusz@gmail.com

ARTICLE

Surfing through the coating system of historic bowed instruments: a spectroscopic perspective

Giacomo Fiocco,[a,b] Claudia Invernizzi,[a,c] Tommaso Rovetta,[a] Michela Albano,[a,d] Marco Malagodi,[a,e] Patrizia Davit[b] and Monica Gulmini[b]

[a]Laboratorio Arvedi di Diagnostica Non Invasiva, CISRiC, Università degli Studi di Pavia, Via Bell'Aspa 3, 26100 Cremona, Italy

[b]Dipartimento di Chimica, Università di Torino, Via Pietro Giuria 7, 10125, Torino, Italy

[c]Dipartimento di Scienze Matematiche, Fisiche e Informatiche, Università degli Studi di Parma, Parco Area delle Scienze, 7/A, 43124 Parma, Italy

[d]Dipartimento di Fisica, Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133, Milano, Italy

[e]Dipartimento di Musicologia e Beni Culturali, Università degli Studi di Pavia, Corso Garibaldi 178, 26100 Cremona, Italy

Which materials did the great Cremonese violin makers use to coat their violins? Is it possible to determine the secret recipes jealously guarded by the luthiers in their workshops? Although almost three centuries have passed since his death, the myth of Antonio Stradivari still represents the epitome of violin making. Indeed, every violin maker has the ambition, more or less declared openly, to build instruments similar to those produced in the Cremonese workshops in the 17th and 18th centuries. Stradivari lived for 93 years and after his death Cremonese violin making progressively decreased in quality and quantity. This decline has inevitably led to the loss of traditions and knowledge, creating a deep gap between historical and contemporary lutherie. Since the second half of the 20th century, however, luthiers who aspired to be scientists and scientists with a passion for musical instruments proposed more or less convincing hypotheses concerning the materials used by the great masters.[1] Only in the last few decades has scientists' interest in musical instruments grown, and the increasing historic (and economic) importance of ancient violins has fuelled the scientific debate on how to approach the investigation. Technical peculiarities of these artworks have been studied,[2,3] with the main focus on the nature of the fine Cremonese varnish and of the other materials involved in the overall finishing treatment.[4]

It is known that multiple varnish layers were applied to the wood, which had been pre-treated with a sealer to prevent varnish penetration. In addition, µm-sized inorganic particles are sometimes dispersed in the coating system. The most common materials involved in the finishing processes were siccative oils, natural resins, casein or animal glues, inorganic fillers, organic and inorganic colourants.[5] Furthermore, other substances such as benzoin or shellac resin were commonly used on ancient violins—and still are in contemporary ones—as surface polishes for conservation, restoration and maintenance.[6]

Despite some similarities with other painting techniques, the finishing of wooden, bowed string instruments has peculiar purposes and characteristics. In particular, the varnish must not only be a protective layer, but it should be coloured, transparent and glossy, in order to enhance the wood features. A number of colourants (pigments, lakes or dyes), normally spread at very low concentration, or specific pre-treatments can be employed to obtain the typical shades of the varnish.

Spectroscopies based on infrared radiation and X-rays are perfect candidates for the study of these materials as they enable the identification of both organic and inorganic chemical species.

Fourier transform infrared (FT-IR) spectroscopy specifically identifies the functional groups mainly related to the organic materials and to some inorganic components (e.g. carbonates, silicates, sulphates) of the layers. As for bowed string musical instruments, where sampling is often impossible, the use of portable non-invasive reflection

DOI: 10.1255/sew.2021.a8

FT-IR spectroscopy may be necessary to collect chemical information. A tentative non-invasive stratigraphic approach—that considers spectra obtained by analysing differently preserved varnish areas—can be successful using this technique.[6] On the other hand, FT-IR micro-spectroscopy can be exploited for investigating embedded samples prepared as cross-sections. In this way, the stratigraphy can be observed and analysed layer-by-layer.[7]

As for the characterisation of the elemental composition of the inorganic materials dispersed in the coating system, X-ray-based techniques represent the first choice among the set of analytical options. X-ray fluorescence (XRF) spectroscopy characterises the elemental composition in a volume of material without the need to take samples. For this reason, XRF is one of the most widely used techniques for detecting pigments and other inorganic materials in the cultural heritage field.[8] In the investigation of musical string instruments, the entire volume of the system (coatings and wood) is involved in the analytical spot, from the external dirt deposits to the inorganic-based treatments of the wood.[9]

On the other hand, scanning electron microscopy coupled to energy-dispersive X-ray spectroscopy (SEM-EDX) enables the analyses of micrometric spots in each layer of the stratigraphy,[4] provided that a micro-sample is detached from the instrument.

Over the years, other spectroscopic techniques have been used to scrutinise the finishing layers of musical instruments: laser induced breakdown spectroscopy (LIBS) has been employed to obtain the sub-surface stratigraphy with a micro-destructive approach;[10] nuclear magnetic resonance (NMR) and Raman spectroscopy[11] provided valuable data for in-depth understanding of materials and the construction techniques of the historical Cremonese violins, although information is more difficult to obtain with these techniques. The results related to all the above-mentioned spectroscopic approaches are well described in the references cited in this article.

Here, the Bracco 1793 small violin made by Lorenzo Storioni (1744–1816) in Cremona, Italy is reported as a representative case study (Figure 1a). The instrument has been subjected to a multi-analytical procedure exploiting X-rays and IR radiation employed according to non-invasive and micro-invasive approaches.

FT-IR spectroscopy in reflection geometry

The non-invasive FT-IR data were collected with a Bruker Alpha portable spectrometer on some spots of the soundboard and backplate selected on the basis of the ultraviolet fluorescence response and the different levels of wear of the varnish. In addition, synchrotron radiation (SR)-FT-IR was performed at the SISSI beamline of Sincrotrone Elettra Trieste, with the valuable support of Dr L. Vaccari and Dr C. Stani. Here, a sample was detached from a representative area of the soundboard (Figure 1b), embedded into epoxy resin and treated to expose a polished cross-section (Figure 1c). SR brightness and lateral resolution lead to spectra with improved signal-to-noise ratios. Both the approaches, i.e. non-invasive with a portable instrument and micro-invasive at a large-scale facility, were carried out in reflection geometry.

The spectra collected through the non-invasive approach on the varnished areas mainly highlighted the signals of a resinous varnish at around 1710 cm^{-1} ($\nu C{=}O$) (Figure 2a). In order to characterise the preparation layers, often spread on the wood to avoid the penetration of the varnish into the wood pores, the analyses were also focused on some worn areas of the soundboard or backplate, where the varnish is no longer identifiable. In these areas, the spectra (Figure 2b) suggested the presence of a proteinaceous ground coat[12] as a shoulder at

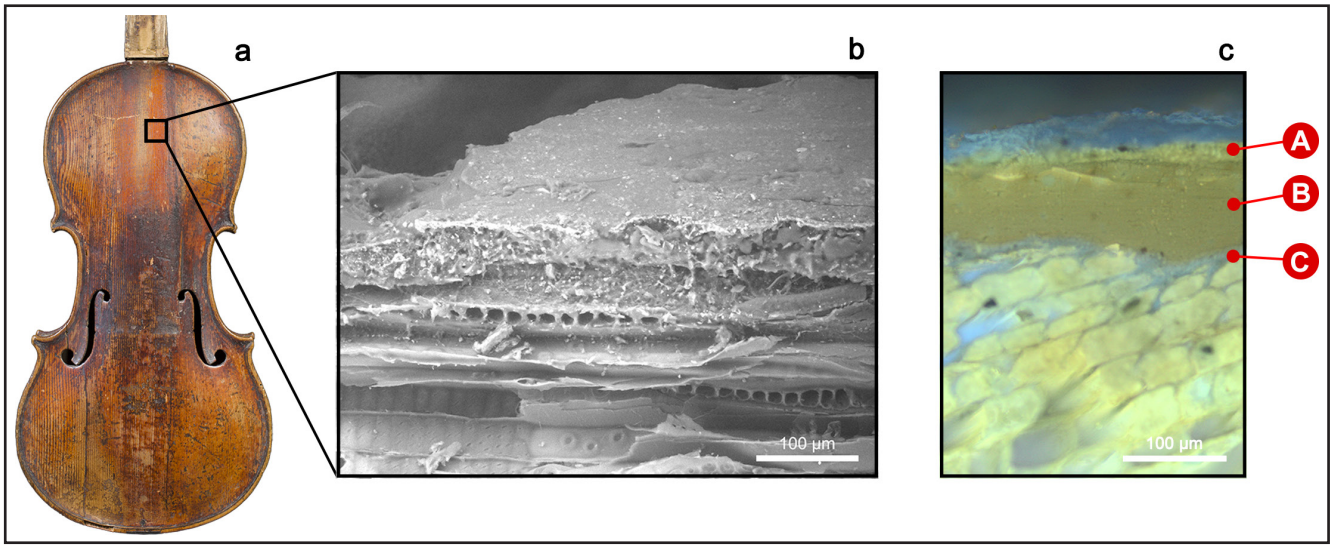


Figure 1. (a) Visible image of the soundboard of the Bracco 1793 small violin. The sampling spot is marked by the black square. The detached micro-sample observed through the (b) SEM (backscattered electron image) and (c) the optical microscope under ultraviolet (UV) light. The finishing treatments (A, B, C) are visible on the wood substrate.

1650 cm^{-1} (νC=O, amide I) and a broad band at 1550 cm^{-1} (combination of νC–N and δN–H, amide II) were present. In addition, inorganic compounds—probably dispersed in the layers or dry-filled directly in the wood pores—were also detected: the Reststrahlen bands at around 1100–1000 cm^{-1} ($\nu_{as}Si–O–Si$) can be attributed to the silicate group. Signals of the sulphate group at 1150 and 1100 cm^{-1} ($\nu_{as}SO_4$), and at 670 and 600 cm^{-1} ($\delta_{as}SO_4$) were also observed.[13]

The micro-invasive analysis carried out on the cross-section shown in Figure 1c, allowed us to deepen our knowledge of the sequence of the organic layers. SR-FTIR spectra collected on layers A and B (Figure 3a,b) clearly confirm the presence of the marker bands of natural terpenic resins[11] mainly for the intense νC=O band approximately at 1710 cm^{-1} ascribable to the carboxylic acid contribution, the δ_sCH_2 and $\delta_{as}CH_3$ at 1450 cm^{-1}, δ_sCH_3 around 1375 cm^{-1} and νC–O at 1255 and 1185 cm^{-1}.[14] Spectra collected on layer C (Figure 3c) are instead characterised by bands related to proteinaceous materials—such as animal glue or casein—at 1650 cm^{-1} and 1550 cm^{-1}.

Investigation of the inorganic phases by X-rays

For the non-invasive approach, the XRF analysis was performed with a Bruker XG Lab Elio portable spectrometer on different areas carefully selected on the basis both on the ultraviolet fluorescence response and on the different levels of wear of the varnish. SEM-EDX micro-analyses were carried out on the embedded sample detached from the soundboard with a Tescan Mira 3XMU-series equipped with an energy-dispersive X-ray spectrometer.

XRF data obtained by the non-invasive approach revealed the presence of Si, S, K, Ca and Fe both on the soundboard and the backplate. The detection of silicon in the worn areas, as well as the higher counts of calcium and sulphur, can be attributed to the presence of these inorganic phases, acting as fillers at the ground level, further supporting the information obtained through non- and micro-invasive FT-IR. The EDX micro-analysis partially confirms these results: Si- and Ca-based particles were detected in layer C, clearly identifying the presence of an inorganic dispersion in the proteinaceous layer spread on the wood. The presence of iron, identified both with XRF and EDX, was instead attributed to iron earth particles, possibly added as pigments.[6,15]

Conclusions and outlook

Techniques based on IR and X-ray spectroscopies normally allow the identification and characterisation of most of the variety of materials involved in the finishing processes of historical violins, with the Lorenzo Storioni Bracco small violin made in 1793 in Cremona discussed here as a relevant example of a comprehensive spectroscopic approach.

X-rays and IR spectroscopies revealed the presence of a natural resin-based varnish, in accordance with those identified on other historical Cremonese string instruments from the 17th and 18th century, and suggesting a remarkable consistency in the materials and procedures employed by the great masters to obtain the finishing layers over almost 150 years. A proteinaceous ground layer with a dispersion of some silicate- and sulphate-based particles, and the presence of small red earth particles were also detected in the stratigraphy.

In the future, it is expected that spectroscopic techniques will be extensively employed for the investigation of luthiers' secrets, with further stringed instruments being investigated. Radiation from X-rays to IR is leading research towards a deeper knowledge of the large variety of materials, often mixed together, employed by the luthiers.

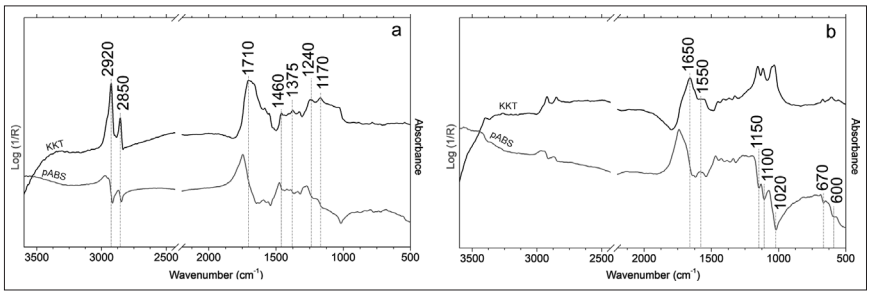


Figure 2. Reflection FT-IR spectra acquired on the varnished (a) and most worn (b) areas of the Bracco 1793 small violin in pseudo-absorbance (pABS) and after Kramers–Krönig transformation (KKT). The marker bands are reported. Reprinted with permission from Reference 7.

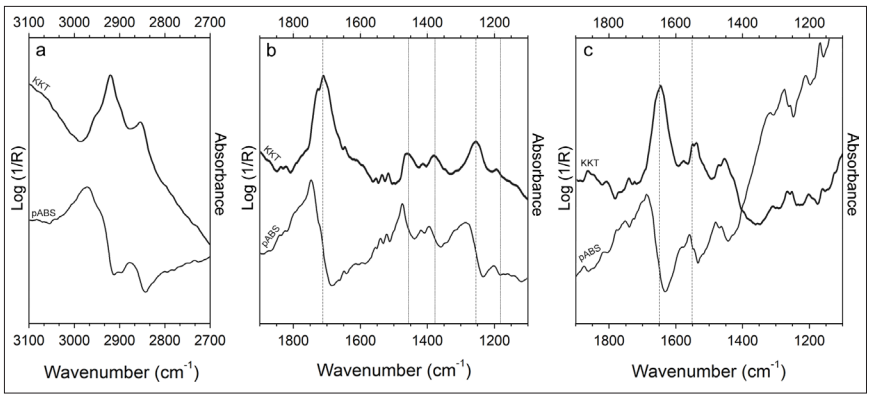


Figure 3. Reflection SR-FT-IR spectra in pseudo-absorbance (pABS) and after KKT corresponding to layer B (a,b) and C (c). Marker bands are reported. Reprinted with permission from Reference 7.

Acknowledgements

The authors acknowledge the Fondazione Arvedi-Buschini, the Fondazione Bracco and the Fondazione Museo del Violino for support. Special thanks to Dr Lisa

Vaccari and Dr Chiaramaria Stani for their assistance at the SISSI beamline.

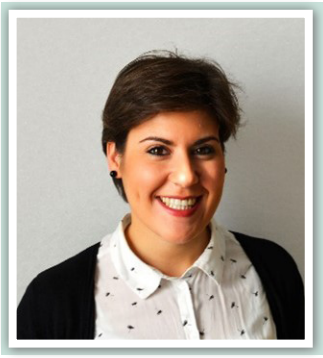
References

1. J. Michelman, *Violin Varnish: A Plausible Re-Creation of the Varnish Used by the Italian Violin Makers Between the Years 1550 and 1750*. J. Michelman (1946).
2. B.H. Tai, "Stradivari's varnish. A review of scientific findings–part I", *J. Violin. Soc. Am.* **21,** 1 (2007).
3. C. Invernizzi, A. Daveri, T. Rovetta, M. Vagnini, M. Licchelli, F. Cacciatori and M. Malagodi, "A multi-analytical non-invasive approach to violin materials: the case of Antonio Stradivari 'Hellier' (1679)", *Microchem. J.* **124,** 743–750 (2016). https://doi.org/10.1016/j.microc.2015.10.016
4. G. Fiocco, T. Rovetta, M. Gulmini, A. Piccirillo, M. Licchelli and M. Malagodi, "Spectroscopic analysis to characterize finishing treatments of ancient bowed string instruments", *Appl. Spectrosc.* **71,** 2477–2487 (2017). https://doi.org/10.1177/0003702817715622
5. V. Bucur, *Handbook of Materials for String Musical Instruments*. Springer International Publishing (2016). https://doi.org/10.1007/978-3-319-32080-9
6. C. Invernizzi, G. Fiocco, M. Iwanicka, M. Kowalska, P. Targowski, B. Blümich, C. Rehorn, V. Gabrielli, D. Bersani, M. Licchelli and M. Malagodi, "Non-invasive mobile technology to study the stratigraphy of ancient Cremonese violins: OCT, NMR-MOUSE, XRF and reflection FT-IR spectroscopy", *Microchem. J.* **155,** 104754 (2020). https://doi.org/10.1016/j.microc.2020.104754
7. G. Fiocco, C. Invernizzi, S. Grassi, P. Davit, M. Albano, T. Rovetta, C. Stani, L. Vaccari, M. Malagodi, M. Licchelli and M. Gulmini, "Reflection FTIR spectroscopy for the study of historical bowed string instruments: Invasive and non-invasive approaches", *Spectrochim. Acta A* **245,** 118926 (2021). https://doi.org/10.1016/j.saa.2020.118926
8. S. Ridolfi, "Portable X-ray fluorescence spectrometry for the analyses of cultural heritage", *IOP Conf. Ser.: Mater. Sci. Eng.* **37,** 012001 (2012). https://doi.org/10.1088/1757-899X/37/1/012001
9. F. Caruso, S. Saverwyns, M. Van Bos, D.F. Chillura Martino, A.E. Ceulemans, J. Valck and E. Caponetti, "Micro-X-Ray fluorescence and the old masters", *Appl. Phys. A* **107,** 197–202 (2011). https://doi.org/10.1007/s00339-011-6729-x
10. F. Poggialini, G. Fiocco, B. Campanella, S. Legnaioli, V. Palleschi, M. Iwanicka, P. Targowski, M. Sylwestrzak, C. Invernizzi, T. Rovetta, M. Albano and M. Malagodi, "Stratigraphic analysis of historical wooden samples from ancient bowed string instruments by laser induced breakdown spectroscopy", *J. Cult. Herit.* **44,** 275–284 (2020). https://doi.org/10.1016/j.culher.2020.01.011
11. C. Daher, C. Paris, A.S. Le Hô, L. Bellot-Gurlet and J.P. Échard, "A joint use of Raman and infrared spectroscopies for the identification of natural organic media used in ancient varnishes", *J. Raman Spectrosc.* **41,** 1494–1499 (2010). https://doi.org/10.1002/jrs.2693
12. K. Belbachir, R. Noreen, G. Gouspillou and C. Petibois, "Collagen types analysis and differentiation by FTIR spectroscopy", *Anal. Bioanal. Chem.* **395,** 829–837 (2009). https://doi.org/10.1007/s00216-009-3019-y
13. C. Miliani, F. Rosi, A. Daveri and B.G. Brunetti, "Reflection infrared spectroscopy for the non-invasive *in situ* study of artists' pigments", *Appl. Phys. A* **106,** 295–307 (2011). https://doi.org/10.1007/s00339-011-6708-2
14. C. Invernizzi, A. Daveri, M. Vagnini and M. Malagodi, "Non-invasive identification of organic materials in historical stringed musical instruments by reflection infrared spectroscopy: a methodological approach", *Anal. Bioanal. Chem.* **409,** 3281–3288 (2017). https://doi.org/10.1007/s00216-017-0296-8
15. T. Rovetta, C. Invernizzi, M. Licchelli, F. Cacciatori and M. Malagodi, "The elemental composition of Stradivari's musical instruments: new results through non-invasive EDXRF analysis", *X-Ray Spectrom.* **47,** 159–170 (2018). https://doi.org/10.1002/xrs.2825

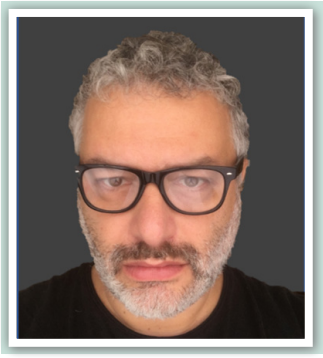
Giacomo Fiocco has been a research fellow at the Arvedi Laboratory of non-Invasive Diagnostics of the University of Pavia since 2016. In 2018 he started his PhD in Chemistry and Materials Sciences at the University of Turin with a project on the characterisation of the materials used in violin making for the colouring of stringed instruments.
https://orcid.org/0000-0002-1458-9640
giacomo.fiocco@unipv.it

Claudia Invernizzi is a research fellow at the Arvedi Laboratory of Non-Invasive Diagnostics, University of Pavia. Her PhD degree in Physics at the University of Parma focused on the study of the microscopic layered structures of musical instruments by advanced multi-analytical methods. Since 2013, she has specialised in reflection FT-IR spectroscopy (specular, diffuse, ATR, transflection).
https://orcid.org/0000-0001-5111-6589
claudia.invernizzi@unipv.it

Tommaso Rovetta is a conservation scientist and fellow of the University of Pavia in Cremona. He specialises in the analysis of the materials of ancient musical instruments through imaging techniques and X-ray fluorescence spectroscopy. Tommaso is also a violin maker and teaching coordinator of the Accademia Liuteria Piemontese San Filippo of Turin.
https://orcid.org/0000-0002-9626-8380
tommaso.rovetta@unipv.it

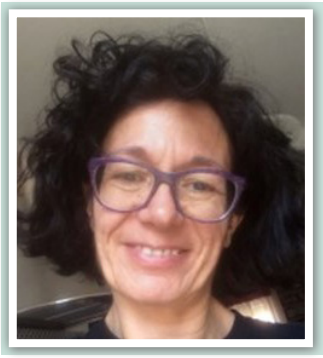


Michela Albano is a research fellow at the Arvedi Laboratory of Non-Invasive Diagnostics, University of Pavia, and a PhD student at the Polytechnic of Milan. Her research activity is focused on the characterisation of materials and procedures in the making of historical musical instruments exploiting imaging and spectroscopic techniques.
https://orcid.org/0000-0001-5129-9434
michela.albano@unipv.it



Marco Malagodi is Associate Professor of Chemistry for Cultural Heritage at University of Pavia. Malagodi is the Scientific Head of Arvedi Laboratory of non-Invasive Diagnostics for the study of historical music instruments. The research activities are focused on the characterisations of materials used during the construction procedures of musical instruments.
https://orcid.org/0000-0003-4286-6331
marco.malagodi@unipv.it

ARTICLE



Patrizia Davit is a research technician at the Chemistry Department of Torino University. Her research activities are devoted to the characterisation, evaluation of the technology of production, provenance studies and analysis of degradation phenomena of archaeological, historical and artistic materials.
https://orcid.org/0000-0002-9073-9858
patrizia.davit@unito.it

Monica Gulmini serves as a research associate in Analytical Chemistry at the Department of Chemistry (University of Torino – Italy) and leads the team ArchaeoMetry and Analytical cheMistry in Art, hiStory and Archaeology (AMAMASA). Her activity focuses on scientific investigations of archaeological finds and artworks aimed at deepen our knowledge on tangible cultural heritage.
https://orcid.org/0000-0002-0556-5401
monica.gulmini@unito.it

"…every violin maker has the ambition … to build instruments similar to those produced in the Cremonese workshops in the 17th and 18th centuries"

FAIR enough?

Robert M. Hanson,[a] Damien Jeannerat,[b] Mark Archibald,[c] Ian Bruno,[d] Stuart Chalk,[e] Antony N. Davies,[f] Robert J. Lancashire,[g] Jeffrey Lang[h] and Henry S. Rzepa[i]
[a]Department of Chemistry, St Olaf College, Northfield, Minnesota, USA
[b]NMRprocess.ch, Geneva, Switzerland
[c]Royal Society of Chemistry, Cambridge, UK
[d]Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK
[e]Department of Chemistry, University of North Florida, Jacksonville, FL, USA
[f]SERC, Sustainable Environment Research Centre, Faculty of Computing, Engineering and Science, University of South Wales, UK
[g]Prof. Emeritus, Department of Chemistry, The University of the West Indies, Kingston 7, Mona Campus, Jamaica
[h]American Chemical Society Publications Division, Rockville, Maryland, USA
[i]Department of Chemistry, Imperial College London, Molecular Sciences Research Hub, White City Campus, 82 Wood Lane, London W12 0BZ, UK

As 2021 arrives with all the promise of beating COVID-19, mixed with the realities of vaccine delays and the threatened breakdown of international consensus on tackling global pandemics, it is a strange feeling to be writing an article about the ability of all to find, access, understand and re-use spectroscopic data. However, effectively and freely sharing information needs to be at the heart of any global effort to beat a pandemic. Although nationalistic tendencies always raise their ugly heads at times of tension, it is only through strong global collaboration and free access to data that we can hope to minimise the damage to our nearest and dearest!

The International Science Council report on Opening the Record of Science

February 2021 has just seen the publication of the ISC Report on Opening the Record of Science: making scholarly publishing work for science in a digital era Figure 1.[1]

DOI: 10.1255/sew.2021.a9

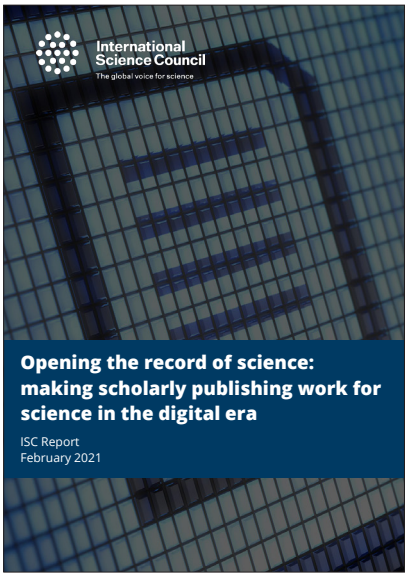


Figure 1. The ISC Report on Opening the Record of Science.

A PDF version of the report is appropriately free to download for those who want to read it in full at https://council.science/wp-content/uploads/2020/06/2020-02-19-Opening-the-record-of-science.pdf. One of the things I like about this report is that it starts with the basics, briefly explaining "Why Science Matters" including the clear statement around the communication of new experiments and new observations publicly communicated through the published record of science. The importance of the publication process is nicely summed up with *"Publication processes that achieve these ends and are adapted to the needs and priorities of the disciplines of science and interdisciplinary collaboration are essential to the function of science as a global public good".*

The ISC Report lays down seven Principles for Scientific Publishing around how modern scientific publishing needs to serve us, and which need be durable in the long term:

1) There should be universal open access to the record of science, both for authors and readers.
2) Scientific publications should carry open licenses that allow reuse and text and data mining.

Who is the ISC?

The International Science Council (ISC) is a non-governmental organisation with a global membership consisting of 40 international scientific Unions and Associations and over 140 national and regional scientific organisations including Academies and Research Councils.

3) Rigorous and ongoing peer review is essential to the integrity of the record of science.
4) The data/observations underlying a published truth claim should be concurrently published.
5) The record of science should be maintained to ensure open access by future generations.
6) Publication traditions of different disciplines should be respected.
7) Systems should adapt to new opportunities rather than embedding inflexible infrastructures.

For spectroscopists, the Principles around Open Access, Reuse of the Text and the Data and the need to concurrently publish both reinforce the position this column has taken from its inception. We do not have space to go through the whole Report, but it is well worth highlighting their approach to the importance of scientific data, including a very powerful statement that *"Publishing the data is as important, and sometimes more important, than publishing the written text"*. The ISC[2] specifically refer to the FAIR data principles which we have covered in a few articles, including reporting on the IUPAC CODATA Workshop on "Supporting FAIR Exchange of Chemical Data through Standards Development" held in Amsterdam in July 2018,[3] which led to the founding of an IUPAC project in 2019.

IUPAC Project "Development of a standard for FAIR data management of spectroscopic data"

The objective of this project is to apply FAIR data principles to spectroscopic data in the field of chemistry building on IUPAC's extensive expertise in this area. The project will develop standards for the production and dissemination of digital data objects that contain enough spectral data and metadata that they can be:
(a) findable through semantic searches on the web,
(b) available through standard interfaces,
(c) interoperable and transferable between systems and
(d) readable and reusable over time, for both humans and machines.

The IUPAC FAIRSpec Project

Following the Amsterdam workshop, a proposal was submitted to IUPAC for a project to follow up on many of the actions agreed at the workshop. The project, under the title of *Development of a Standard for FAIR Data Management of Spectroscopic Data*, was launched under the auspices of the IUPAC Committee on Publications and Cheminformatics Data Standards right at the start of the COVID epidemic on 18 March 2020 (https://iupac.org/project/2019-031-1-024). The project objectives are shown in the textbox. There has been a lot of work done this year around exactly what role IUPAC, as the standardisation body for chemistry, can play in the FAIR initiative. Clearly IUPAC's ownership and responsibility for many cheminformatics data standards, especially the JCAMP-DX series of spectroscopic data standards, places IUPAC in a special position to respond when the environment for which these standards were originally crafted changes radically. FAIR is just such a ground-breaking change, where the correct storage and accessibility with data processing opportunities means that the "minimum essential metadata" approach of the original standards needs to be brought up to date by standardising the majority of the relevant metadata with a spectroscopic data set. Indeed, this column challenged the spectroscopic community in a relatively recent article called "Are you taking your Metadata seriously?".[4]

The project team have produced a useful figure as they continue to assess the current state of available data collections. It is reproduced in Figure 2 for the example of NMR data.

One advantage of IUPAC projects being able to draw on some of the top innovators in the field is that we have people who are actively *FAIRifying* their own working environments. The

data representations	reusability level	full processing	near-full processing	allows interactive viewing and analysis	allows enhanced viewing	allows non-interactive viewing	visual comparison	machine
raw data (FID + parameters)	10	yes	yes	yes*	yes*	yes*	yes*	yes*
minimally processed data (r+i spectra)	9		yes	yes*	yes*	yes*	yes*	yes*
fully processed data (real spectrum)	8			yes	yes*	yes*	yes*	yes*
peak table with shifts, integration and splitting	7			yes*	yes*	yes*	yes	yes
PDF	6				yes	yes	yes	
journal-style description	5				yes*	yes*	yes	yes*
image (e.g. PNG)	4					yes	yes	
peak table -- shifts only	3						yes	yes#
Reuseable 'as is'		* with additional processing			# to some extent (lossiness, human error or bias)			

Figure 2. How reusable are our NMR data in scientific publications.

following sections will show a few examples of how this work is progressing.

Example of accompanying spectroscopic data from ACS Publications: submission of real data (Jeff Lang)

In February of 2020, ACS Publications began a programme to encourage authors to submit their original data for NMR, including free induction decay (FID) files, acquisition data and processing parameters in a zip file as Supporting Information with their manuscript at submission time. Two journals, *The Journal of Organic Chemistry* and *Organic Letters* joined this programme by publishing a joint editorial.[5] The goal was to utilise existing scholarly infrastructure to encourage data publication and gauge support for data publication from the chemistry community.

In the first year of the programme, these two journals published nearly 200 manuscripts with NMR primary data, demonstrating early support. These data are available during manuscript review and receive a DOI upon publication. ACS provided a tool for authors to package the primary data with metadata like structure identifiers, ORCID and funding identifiers. These would better align the resulting package with the FAIR data principles,[6] but authors have preferred to package the data themselves, often forgoing such metadata. Future efforts will focus on the incentives and workflow needed to solicit this metadata in a scalable way.

Example of accompanying spectroscopic data from the Royal Society of Chemistry: ChemSpider (Mark Archibald)

ChemSpider contains approximately 400,000 community-submitted NMR, IR, UV-vis and mass spectra (most come from existing collections or projects). Although this is a significant set of spectra, it represents a tiny percentage of >100 million total ChemSpider records. ChemSpider records can be found by searching on structure, text, experimental or calculated properties,

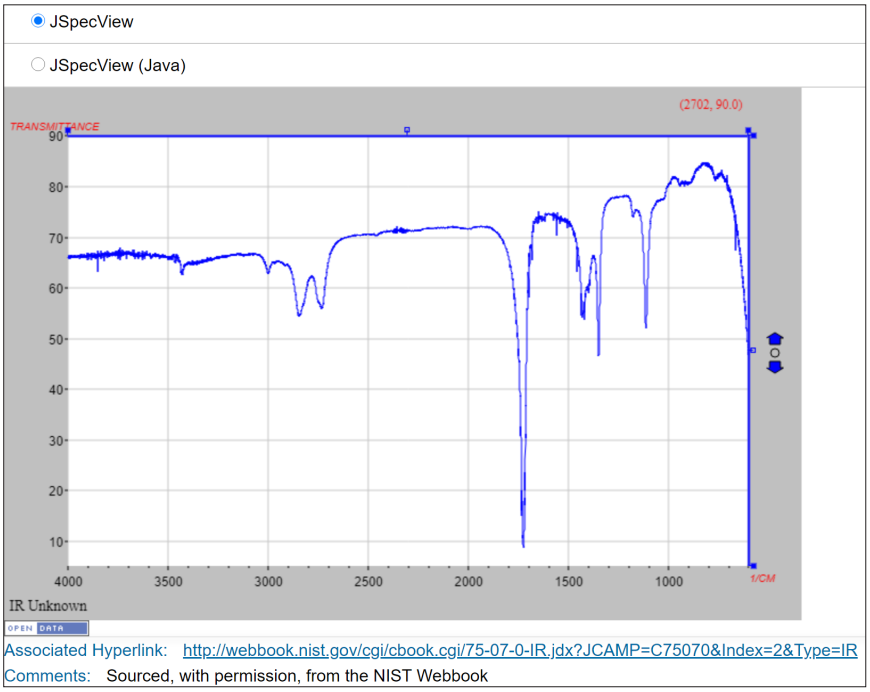


Figure 3. ChemSpider data example.

or combinations thereof. However, it is not currently possible to limit a search to only records containing spectra—the user must click through to the record to discover if a spectrum is present. Spectra within ChemSpider records are freely available to all users (Figure 3 is an example ChemSpider entry for acetaldehyde). At present, the ChemSpider APIs do not enable retrieval of spectra, limiting opportunities for machine processing. The majority (~300,000) are in JCAMP format, so they rate highly for reusability. An interactive viewer (JSpecView) allows visualisation of JCAMP spectra on the record page.

Using standardised spectroscopic metadata to facilitate cross-continent data enhancement workflows (Robert Hanson)

In discussions within the project, it has become clear that the chemical structure representation may well be one of the most important "metadata" objects associated with spectra. In an earlier column,[7] a scheme was introduced whereby an NMR spectrum could be predicted (initially ^{1}H, but now ^{13}C as well) and the input could be a name of the compound or a 2D structure drawn with JSME. This relied on the generation of sufficient information that could be forwarded to nmrdb.org at the École Polytechnique Fédérale de Lausanne (EPFL) for processing (Figure 4).[8–10]

Chemical structure metadata, such as connection tables between the atoms or simply the chemical name input, allows the processing to begin, as Table 1 shows.

NMRDB references

The following services are available, compatible with HTML5, where a SMILES string is embedded in the call.

^{1}H NMR prediction:
https://www.nmrdb.org/service.php?name=nmr-1h-prediction&smiles=c1ccccc1CC

^{13}C NMR prediction:
https://www.nmrdb.org/service.php?name=nmr-13c-prediction&smiles=c1ccccc1CC

COSY prediction:
https://www.nmrdb.org/service.php?name=cosy-prediction&smiles=c1ccccc1CC

HSQC/HMBC prediction:
https://www.nmrdb.org/

TONY DAVIES COLUMN

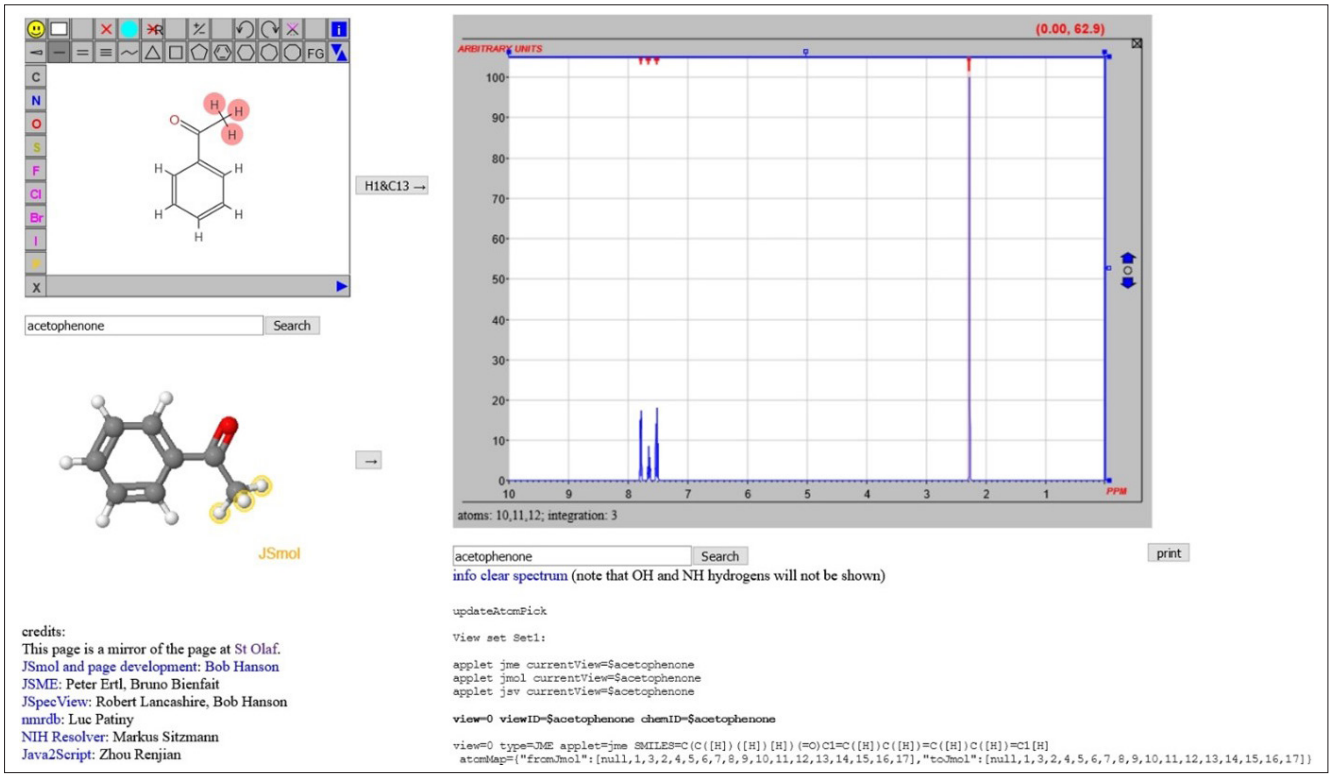


Figure 4. From structures to spectra using trans-continental data processing.

Table 1. Path of information exchange starting from a structure and from a name.

From drawing a structure:	
JSME > SMILES (no H atoms)	local
SMILES > NCI > 2D SDF file (with H atoms)	USA
2D SDF file > JSME for display	
SMILES > NCI > 3D SDF file	USA
From typing a name:	
name > NCI > 2D SDF file (with H atoms)	USA
2D SDF file > JSME for display	local
name > NCI > 3D SDF file	USA
Then from either method:	
3D SDF file to JSmol and sent to EPFL	local
Generates modified 3D mol file, sends to Lisbon	Switzerland
Generates chemical shift+coupling+atom correlation matrix, sent to EPFL	Portugal
EPFL applies a second-order coupling algorithm and line broadening then sends spectral data, assignment and (modified) 3D mol file	Switzerland
2D and two 3D model atom numbering is reconciled using fully elaborated SMILES matching.* Annotated JCAMP-DX file and 3D mol displayed. Interactive atom/peak selection is enabled.	local

*see https://chemapps.stolaf.edu/jmol/jsmol/correlate.htm

https://www.nmrdb.org/service.php?name=hmbc-prediction&smiles=c1ccccc1CC

All predictions:
https://www.nmrdb.org/service.php?name=all-predictions&smiles=c1ccccc1CC

[1]H NMR prediction was possible thanks to the tool of the FCT-Universidade NOVA de Lisboa developed by Yuri Binev and Joao Aires-de-Sousa.[11]

Incorporating FAIR principles into undergraduate teaching (Henry Rzepa)

As a final example, Henry Rzepa has been developing a novel approach to capturing and disseminating NMR spectroscopic data, which incorporates the basic FAIR principles into an undergraduate student experiment illustrating the synthesis of an organic ester from carboxylic acid and phenolic components.[12]

Each student in a year class is assigned a different combination of reactants,

chosen so that the resulting synthesis produces a new-to-science molecule. Following workup, the student submits the sample for NMR analysis and the resulting instrument dataset is acquired/processed to produce a spectrum from the raw FID. The students then participate in group analysis of their individual spectra.

Finally, the student moves to publishing the primary instrumental data in a FAIRsharing data repository[13–14] in the form of both a ZIP archive and processed versions also containing an annotated spectrum (MestreNova archive + JCAMP-DX). The student adds further core metadata to the record and initiates workflows which include generating a chemical identifier (InChI string and key) and a free-to-use MestreNova dataset Access license.[15]

Publication produces a metadata record registered against a persistent identifier (DOI),[16] the latter eventually appearing in the student's ORCID researcher profile. The metadata has sufficient information to allow a variety of complex Finding searches to be undertaken[12] and includes Access information allowing potentially unsupervised machine Interoperation and Reuse of the data for e.g. further AI-based spectral analysis.[12]

Conclusions

So, we already do have some good examples of interoperability between diverse systems, but, as you can see from the examples above, they are pretty much all reliant on the developers' knowledge of the specifics of the raw spectroscopic data sets they receive, as opposed to being able to call on standardised definitions for the metadata in spectroscopy outside of the limited use in JCAMP-DX standards.

Everyone please, stay safe!

References

1. International Science Council, *Opening the Record of Science: Making Scholarly Publishing Work for Science in the Digital Era*. International Science Council, Paris, France (2021). https://doi.org/10.24948/2021.01
2. https://council.science/about-us/
3. L. McEwen, D. Martinsen, R. Lancashire, P. Lampen and A.N. Davies, "Are your spectroscopic data FAIR?", *Spectrosc. Europe* **30(4),** 21–24 (2018). https://doi.org/10.1255/sew.2018.a2
4. A.N. Davies, P. Lampen and R. Lancashire, "Are you taking your Metadata seriously", *Spectrosc. Europe* **31(2),** 17–23 (2019). https://doi.org/10.1255/sew.2019.a1
5. A.M. Hunter, E.M. Carreira and S.J. Miller, "Encouraging submission of FAIR data at *The Journal of Organic Chemistry and Organic Letters*", *Org. Lett.* **22(4),** 1231–1232 (2020). https://doi.org/10.1021/acs.orglett.0c00383; A.M. Hunter, E.M. Carreira and S.J. Miller, "Encouraging submission of FAIR data at *The Journal of Organic Chemistry and Organic Letters*", *J. Org. Chem.* **85(4),** 1773–1774 (2020). https://doi.org/10.1021/acs.joc.0c00248
6. M.D. Wilkinson, M. Dumontier, I. Aalbersberg *et al.*, "The FAIR Guiding Principles for scientific data management and stewardship", *Sci. Data* **3,** 160018 (2016). https://doi.org/10.1038/sdata.2016.18
7. A.N. Davies, M. Cashyap, R. Lancashire and R.M. Hanson, "A head in the clouds?—Part two: exploring distributed, multi-server ^{1}H NMR prediction", *Spectrosc. Europe* **26(5),** 15–17 (2014). https://doi.org/10.1255/sew.2014.a1
8. D. Banfi and L. Patiny, "www.nmrdb.org: Resurrecting and processing NMR spectra on-line, *Chimia* **62(4),** 280–281 (2008). https://doi.org/10.2533/chimia.2008.280
9. A.M. Castillo, L. Patiny and J. Wist, "Fast and accurate algorithm for the simulation of NMR spectra of large spin systems", *J. Magn. Reson.* **209(2),** 123–130 (2011). https://doi.org/10.1016/j.jmr.2010.12.008
10. J. Aires-de-Sousa, M. Hemmer and J. Gasteiger, "Prediction of ^{1}H NMR chemical shifts using neural networks", *Anal. Chem.* **74(1),** 80–90 (2002). https://doi.org/10.1021/ac010737m
11. Y. Binev, M.M. Marques, J. Aires-de-Sousa, "Prediction of ^{1}H NMR coupling constants with associative neural networks trained for chemical shifts", *J. Chem. Inform. Model.* **47(6),** 2089–2097 (2007). https://doi.org/10.1021/ci700172n
12. H.S. Rzepa and S. Kuhn, submitted for publication (2021).
13. FAIRsharing.org, *Imperial College Research Data Repository*. https://doi.org/10.25504/FAIRsharing.LEtKjT
14. A.N. Davies, D. Martinsen, H.S. Rzepa, C. Romain, A. Barba, F. Seoane, S. Dominguez and C. Cobas, "Simplifying spectroscopic supplementary data collection", *Spectrosc. Europe* **29(4),** 6–8 (2017). https://doi.org/10.1255/sew.2017.a1
15. A. Barba, S. Dominguez, C. Cobas, D.P. Martinsen, C. Romain, H.S. Rzepa and F. Seoane, "Workflows allowing creation of journal article supporting information and Findable, Accessible, Interoperable, and Reusable (FAIR)-enabled publication of spectroscopic data", *ACS Omega* **4(2),** 3280–3286 (2019). https://doi.org/10.1021/acsomega.8b03005
16. H.S. Rzepa *et al.*, "1st Year undergraduate synthesis laboratory (2019–2020)", Imperial College London data repository (2020). https://doi.org/10.14469/hpc/6215

TONY DAVIES COLUMN

Tony Davies is a long-standing *Spectroscopy Europe* column editor and recognised thought leader on standardisation and regulatory compliance with a foot in both industrial and academic camps. He spent most of his working life in Germany and the Netherlands, most recently as Lead Scientist, Strategic Research Group – Measurement and Analytical Science at AkzoNobel/ Nouryon Chemicals BV in the Netherlands. A strong advocate of the correct use of Open Innovation.
https://orcid.org/0000-0002-3119-4202
antony.n.davies@gmail.com

Henry Rzepa was trained as an experimental physical organic chemist and then spent three years learning the emerging area of computational chemistry with Michael Dewar in Austin, Texas. Upon joining the staff at Imperial College in 1977, his researches became focussed on computational mechanistic chemistry, NMR and chiroptical spectroscopies and Internet-based Chemical informatics, for which he was awarded the 2012 ACS Skolnik award.
https://orcid.org/0000-0002-8635-8390
h.rzepa@imperial.ac.uk

Prior to his retirement in 2015, Robert Lancashire was the Professor of Computational Chemistry at the Department of Chemistry, The UWI, Mona. He joined the staff there in 1979 and held the positions of Sub-Dean for Technology from 1998 to 2004 and Deputy Dean for 2007–2008. He was conferred Professor Emeritus in 2016. He served as secretary of the International Union of Pure and Applied Chemistry (IUPAC) Committee on Printed and Electronic Publications (CPEP).
https://orcid.org/0000-0002-6780-3903
rjlanc@gmail.com

Bob Hanson is a professor in the Chemistry Department at St Olaf College. He is one of the principal developers of Jmol, JSmol,and JSpecView.
https://orcid.org/0000-0001-5411-2356
hansonr@stolaf.edu

TONY DAVIES COLUMN

Jeff Lang is Assistant Director for Platform Development at The American Chemical Society Publications Division, where he supports innovation and product development that explores the untapped potential of technology to enhance scholarship. Prior to this role, Jeff worked at ProQuest in many departments, including Product Owner for RefWorks and Community Manager of GradShare.com a graduate student support community. Jeff has degrees in Computer Science and Information Management and has spent the last 20 years at the nexus of technology and academic publishing services.
https://orcid.org/0000-0003-4895-0278
J_Lang@acs.org

In nine years at the Royal Society of Chemistry, Mark Archibald has worked on the journal Organic & Biomolecular Chemistry, The Merck Index Online, the National Chemical Database Service and most recently ChemSpider. He applies his background in synthetic organic chemistry to the curation and bulk processing of chemical data in ChemSpider and is interested in cheminformatics and data management more broadly.
https://orcid.org/0000-0001-8687-7134
archibaldm@rsc.org

Dr Stuart J. Chalk is a Professor in the Department of Chemistry at the University of North Florida. Although trained as an analytical chemist, Dr Chalk's research now focuses on the areas of Chemical Informatics and Data Science. In particular, Dr Chalk has projects focused on machine accessibility of solubility online enhancement to the IUPAC Gold Book, automated extraction and annotation of chemical property data from PDF files and scientific data models. Dr Chalk's newest NSF funded grant focuses on semantic integration of heterogeneous datasets from toxicology, medicine, materials, biodiversity, and chemistry.
https://orcid.org/0000-0002-0703-7776
schalk@unf.edu

QUALITY MATTERS

Four generations of Quality: into the future

John P. Hammond
Technical and Marketing Manager, Starna Scientific Limited, 52–54 Fowler Road, Hainault, Essex IG6 3UT, UK

Introduction

Given the events of the last 12 months, if the COVID-19 pandemic has taught us anything, it is that we cannot predict the future and we all live in a changing and evolving World. Related to this, the recent enforced period of reflection has allowed us all to review our working environments in many aspects, not least the availability to work remotely from a given environment. As someone who has been involved with the science of analytical measurement and/or spectroscopy for the majority of my adult life, this period of reflection centred not only on the last 12 months, but importantly on the changes since I started in a Quality Assurance (QA) laboratory many years ago.

Those of us based in the UK will have heard our Prime Minister say, and repeat many times recently, "...we will be governed by the data, and not by the dates".

The generation of data that is Fit for Purpose is inexorably linked to its production in a Quality environment, and as a derivation of the above statement one could state that:

"…we will be governed by the quality and not by the dates".

Therefore, it seems somewhat appropriate that now is a good time to review what quality means, how it has changed with time and how it has governed some key dates in an appropriate chronological timeline.

This article introduces a series of specific reviews on associated key topics described below, but first let us expand on the title and its textual components.

DOI: 10.1255/sew.2021.a10

Definition of Quality

Use any search engine that you wish, and you'll come up with multiple definitions of the word "Quality". However, here is one generally accepted definition from Wikipedia, and which reflects its multifaceted interpretation in the English language.

"In business, engineering, and manufacturing, quality has a pragmatic interpretation as the non-inferiority or superiority of something; it's also defined as being suitable for its intended use while satisfying customer expectations. Quality is a perceptual, conditional, and somewhat subjective attribute and may be understood differently by different people. Consumers may focus on the specification quality of a product/service, or how it compares to competitors in the marketplace. Producers might measure the conformance quality, or degree to which the product/service was produced correctly. Support personnel may measure quality in the degree that a product is reliable, maintainable, or sustainable."

Let us dissect this definition further and relate the statements to our Spectroscopy World.

"In business, engineering, and manufacturing, quality has a pragmatic interpretation as the non-inferiority or superiority of something..."

In a purely commercial and decision and/or results driven environment such as a manufacturing QA laboratory, the quality of a product may be driven by and stated by its expected specification. This perceived or otherwise statement of quality will be discussed further in these series of articles.

"…defined as being suitable for its intended use while satisfying customer expectations…"

Or otherwise stated as "Fit for Purpose". This consideration is discussed alongside other the primary requirements in an article dedicated to explaining these key concepts.

"…Quality is a perceptual, conditional, and somewhat subjective attribute and may be understood differently by different people…"

This statement underpins the contractual considerations clearly defined in the ISO 9001 quality standard and will be expanded further in the appropriate article.

"…Consumers may focus on the specification quality of a product/service, or how it compares to competitors in the marketplace…"

In a laboratory environment, the comparison of instrument system specification(s) is often the essential starting point of any purchasing decision. However, sometimes "life is never straightforward" and given the importance and/or time period that the chosen system may be in use for, this fundamental decision should be given more priority than it sometimes is. A later article in the series will discuss this further and provide some additional guidance.

"…Producers might measure the conformance quality, or degree

to which the product/service was produced correctly…"

Implicit within this statement, is the measurement of quality, and as and when appropriate these articles will briefly discuss the use and application of appropriate statistical tools and concepts, as the question has to be asked "how to quantify quality"?

"*…Support personnel may measure quality in the degree that a product is reliable, maintainable, or sustainable.*"

Last, but not least, one of the ethereal considerations of quality, that one would hope is the outcome of commitment to a policy of "quality first", and which will be discussed in the final article in the series.

Why "four generations of quality"?

Having defined "quality" given the above title, an associate definition of "generation" is also in order, and again in a chronological sense, the timescale is accepted as between 20 and 35 years. It is my intention to use these generational steps as boundaries points, and reflect and review the key aspects of "quality" associated with those periods as shown below:

1st Generation: the years between 1940 and 1975,
2nd Generation: the years 1975 to 2000,
3rd Generation: the years 2000 to 2020 and
4th Generation: from 2021 forward.

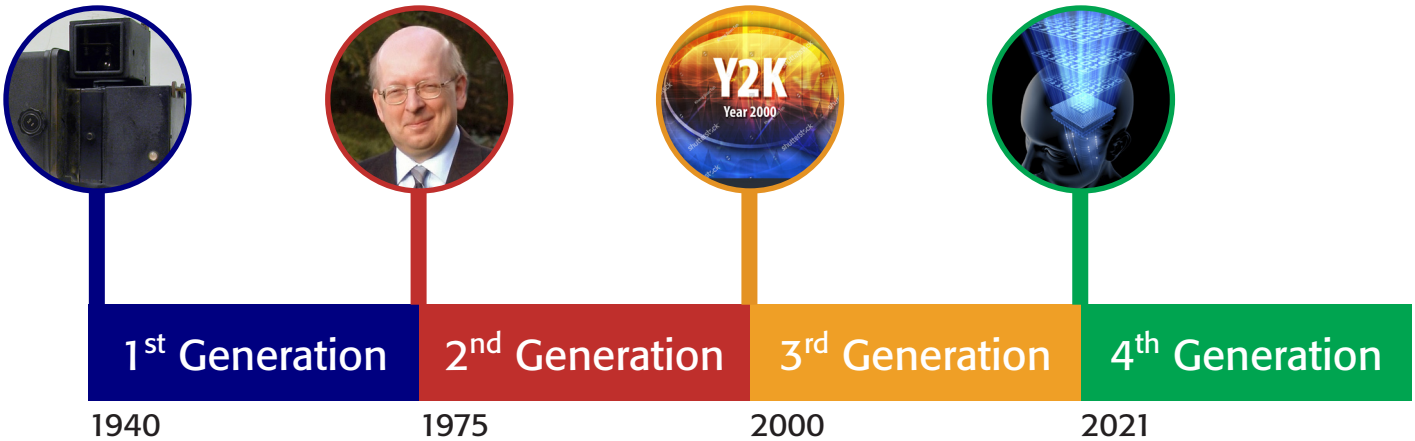
The Beckman DU spectrophotometer. Photo courtesy of the Beckman Institute for Advanced Science and Technology at the University of Illinois Urbana-Champaign

The start date of 1940 was chosen, as significantly in 1941, Beckman announced the introduction of the DU spectrophotometer, which introduced an instrumental measurement process capability to the comparison and use of visual colour science, and effectively enabled the quantitative measurement of a chemical species, by use of an associated method calibration process. Approximately 30,000 DU spectrophotometers were manufactured and sold between 1941 and 1976, and therefore, this, and other key events provides a convenient break in the chronological timeline.

From a personal perspective, my journey on the Quality path began in 1975 in a QA laboratory of a fine chemical supplier, which purely by coincidence had a DU spectrophotometer in the laboratory in which I was employed. Therefore, the non-historical review begins in earnest at the start of the 2nd Generation, and continues to this day.

Significantly, at the start of the 2nd Generation, there was an awakening in all spheres of manufacturing, driven by a consumer emphasis on quality-related issues, powered in no small part by some health-related and well-publicised issues at that time. In the laboratory sphere, this produced the inception of several key concepts that we now take for granted, and the internationally recognised organisations associated with them.

During this period, the increased importance of standards in all aspects, and the general regulatory environment in which they are used can be shown by the fact that in 1981 a reference publication describing the current standards in use with ultraviolet (UV) spectrometry



Four Generations of Quality, a chronological timeline.

was published,[1] and in 1999, this publication was reviewed and significantly updated as *Standards and Best Practice in Absorption Spectrometry*[2] and expanded to now cover the required control in a regulated environment. Along a parallel path, the development of the ubiquitous IBM PC in 1981 began the relentless shift to use of the computer system to control instrumentation, and the related software which continues to this day.

The 3rd Generation significantly starts in 2000, and if one considers the first two generations are associated principally with the development of the physical instrumentation, the Quality environment in which it is to be used and the software to control it; this generation revolves around the software associated with the instrument systems, and the increasing evidence of ensuring, and perhaps more appropriately, proving the control. Those of us involved with the process will not have forgotten the fear that the "Millennium Bug" engendered in our software engineers at the turn of the century, and the hours of coding and checking associated with it to ensure that systems did not stop working as the "clock struck twelve". Now fundamental in all aspects of "quality", a later article in the series on software will concentrate on the developments in the 21st century and the control aspects of this essential science.

Clearly, we are also at the start of what is proposed to be the 4th Generation, but already there are some key indicators to the way forward which will be discussed in the series of articles described below, using this basic chronological framework.

Mention the word quality, and immediately there is the association with "Standards", and thereby is another ambiguity of the English language, as are you referring to the control documents, or the physical reference materials used to implement them?

Take "Quality Standards" as a general term, and in addition to those described below, you could broaden the list to include for example: Environmental Quality Standards (EQS), the IATF Automotive standards, Six Sigma etc. These standards have their own position in the science of Quality, and their exclusion from this article is in no way to deride their importance, it is just an essential admission to keep this document to a reasonable size.

In fact, evolution of the metrological language associated with this science, is also another key aspect of this topic.

Regular readers of this column over the last 20 years will be familiar with the particular aspects of these standard that have been discussed, and the article which time-stamped and initiated this process is referenced.[3]

Article 1: this introductory article

A short precis/abstract of the articles to come. As described above each article will discuss the key aspects of each of the past two and current 3rd Generation, relating to the main topic area(s) of the article. Key indicators to the 4th Generation will be mentioned, but not discussed fully until the final article in the series. The number and/or sequence of the following articles is provided at this point in time, but if recent history with respect to COVID-19 has taught us anything, it is not to attempt to predict too far into the future.

Article 2: ISO 9000 and 17000 series Quality standards

This article concentrates on the stated ISO standards and their place within the Quality environment. By definition, it discusses the role of ISO in the administration and control of these standards and their evolution and harmonisation into the standards currently in existence. In relation to these standards, the role of the ISO Technical Committee, ISO/REMCO is discussed, and the reason(s) for its recent conversion to ISO/TC334 as part of this evolution.

Article 3: ISO 9000 and 17000 series Quality standards—their impact on the laboratory

A summary review of the two principal ISO 17000 series accreditation standards, namely ISO/IEC 17025[4] and ISO 17034[5] and their impact on the associated QA Testing or Calibration Laboratory. Also, how these standards have evolved and continue to be implemented. In addition, this article discusses the role(s) of the ISO 9000 series and ISO 17000 series support standards within this controlled environment.

Article 4: The GxP series Quality standards—their impact on the pharmaceutical laboratory

A summary review of the GxP standards, and their impact on the associated QA laboratories within the pharmaceutical environment. Also, how these standards have evolved and continue to be implemented. In addition, this article discusses the role(s) of the International Committee on Harmonization (ICH), and the changes in pharmacopoeial requirements within this controlled environment.

Article 5: Key quality indicators and their impact on the associated environments

Specific quality indicators are in use in both the ISO and GxP environments, and how these are defined and used are discussed. In addition, the cross-over, with respect to these specific concepts, is investigated by the use of the adoption/exchange in each environment, e.g., Qualification from GxP being implemented in ISO labs, and vice versa, the use of Expanded Uncertainty Budgets from ISO being used in updates to pharmaceutical standards etc.

Article 6: Regulatory changes, and their influence on the quality of data being produced by instrument systems

Having now defined the regulatory framework, and documentary standards associated with the environment, this article introduces the key concepts of Control Space, "Fitness for Purpose", "Proof of Control" and Data Integrity, and how this has influenced the design and manufacture of instrument systems.

Article 7: Regulatory changes, and their influence on the control software implemented on instrument systems

A software-specific article which discusses the demands and/or requirements of the key concepts discussed in the previous article, and how these requirements can be implemented. Also discussed are the "pitfalls" to avoid.

Article 8: Changes and adoption of existing and new spectroscopic techniques to meet new requirements

This article discusses the increased use or existing and/or new spectroscopic techniques, and the associated challenges that this Quality environment posses. Techniques discussed include, for example the increased use of fluorescence and/or Raman and near infrared spectroscopies in application areas. In addition, practical system hardware configurations/implementations are discussed.

Article 9: Round-up and future(s), with informed projection into the next 20 years

This final article in these series discusses the pathway into the future and uses, where possible, very recent new publications and/or changes in the discussed areas. Thereby, the final section also proposes some "blue sky" projections as we move forward into the next generation.

Ready to start?

"All the World's a stage, / And all the men and women merely players."

William Shakespeare, *As You Like It*, Act II, Scene VII, Line 139

So, "the play is written, the stage is set, ... all we need now are the players?"

Therefore, in the next article in this series, we will begin our review of this cast of players, by discussing the International Organization for Standards (ISO) and their role in establishing Quality in Spectroscopy; both from a chronological and a personal perspective.

References

1. A. Knowles and C. Knowles, *Standards in Absorption Spectrometry*. Springer (1981). ISBN: 978-0-412-22470-6
2. C. Burgess and T. Frost (Eds), *Standards and Best Practice in Absorption Spectrometry*. Blackwell Science (1999). ISBN: 0-632-05313-5
3. J.P. Hammond, "New certified reference materials for the determination of photometric accuracy in UV spectrophotometry", *Spectrosc. Europe* **13(4),** 10 (2001). https://doi.org/10.1255/sew.2001.a1
4. ISO/IEC 17025, *General Requirements for the Competence of Testing and Calibration Laboratories*. International Organization for Standardization (ISO), Geneva, Switzerland (2017). https://www.iso.org/standard/66912.html
5. ISO 17034, *General Requirements for the Competence of Reference Material Producers*. International Organization for Standardization (ISO), Geneva, Switzerland (2016). https://www.iso.org/standard/29357.html

John Hammond is an experienced analytical scientist, spectroscopist and technical marketing professional, skilled in the development, production and marketing of key analytical instrumental concepts and product into highly regulated and controlled industries. A Fellow of the Royal Society of Chemistry (FRSC), executive Working Group convenor of ISO/TC334 and an Expert Advisor to the United States Pharmacopeia, General Chapters, Chemical Analysis committee.
j.p.hammond@starna.com

SAMPLING COLUMN

WHAT are sampling errors—and WHAT can we do about them? Part 1

Rodolfo J. Romañach,[a] Aidalu Joubert Castro[a] and Kim H. Esbensen[b]
[a]Department of Chemistry, University of Puerto Rico, Mayagüez Campus, Puerto Rico
[b]Owner KHE Consulting, Copenhagen, Adjunct professor, Aalborg University (AAU), Denmark; Adjunct professor, Geological Survey of Denmark and Greenland (GEUS); Professeur associé, Université du Québec à Chicoutimi (UQAC), Quebec; Guest professor University of South-Eastern Norway (USN); Guest professor Recinto Universitario de Mayaguez, Puerto Rico

The objective of this column is to provide easy-to-understand examples of sampling errors. Prompted by recent participations and presentations at on-line conferences and meetings, we believe there is a need for a more fulfilling introduction and exemplification of the concept and real-world consequences of committing "sampling errors". WHAT is a sampling error? WHAT is the result of sampling errors? WHAT can we do about sampling errors? These are welcome topics for a series of sampling columns! The point of departure will be in the Theory of Sampling and in the near infrared spectroscopy analysis and pharma application sectors, but the focus will be developed to be more *general*, so that readers can carry-over to other scientific and application areas of interest.

Introduction: what students in analytical chemistry learn about sampling errors

It is very instructive to start with how the topic of sampling errors is seen from the point of view of where everything ends up: analysis. What is the point of view from analytical chemistry?

At the undergraduate level, students are taught that there are seven basic steps involved in an analytical chemical analysis. These are i) method selection, ii) sample acquisition, iii) sample preparation, iv) sample analysis, v) calculation and vi) interpretation of the results… and vii) preparation of a professional report. The second step in this chemical analysis pathway is known as *sampling*. Sampling is defined in a frequently adopted analytical chemistry book as "the process of collecting a small mass of a material whose composition accurately represents the bulk of the material being sampled."[1] In other words, the aliquot analysed in the lab must have the same composition as the bulk material from which it was obtained. *One notes that there is no help here as to how to acquire a representative sample and a representative analytical aliquot.*

Students are taught that all measurements in an analysis have an associated error, and for this reason the "true" or "exact" value can never be obtained. However, with knowledge of the different types of error and their sources, it is possible to reduce and estimate the magnitude of the error effects. Although there are many sources of analytical errors, they can traditionally be classified into three major types: systematic (or determinate) errors, random (or indeterminate) errors and gross errors.

Systematic errors

Systematic errors cause the mean of a set of analytical data to differ from the accepted value, causing **all** the results of a series of replicate measurements to be too high or too low. The presence of systematic errors will affect the *accuracy* of the analysis. Systematic errors originate from known sources or at least from sources that can be identified, and the magnitude of the systematic errors is *reproducible* from one measurement to another. Systematic errors can be classified into three types, according to their source: instrumental error, method errors and personal error.

Systematic-instrumental errors include, for example, changes of the original calibration, changes of the calibration due to the difference in the temperature for what it was intended for and/or changes of the glassware walls themselves during the drying process in an oven. Examples of glassware include pipets, volumetric flasks and burettes. These examples are illustrative, but not exhaustive.

Systematic-method errors are due to limitations of the analytical method itself.

DOI: 10.1255/sew.2021.a11

Reactions and reagents are examples of this type of error, i.e. they may be caused by an incomplete reaction and/or side reactions. Common examples would be lack of specificity or curtailed performance of a reagent to perform its full role in a reaction. This is, for example, the case when decomposition of an unknown sample fails to happen due to a reagent in the reaction. Thus, during a titration the extra titrant needed to produce a change in colour indicator after the equivalence point is an example of this type of error. Systematic-method errors are the most difficult to detect and correct because its correction will require a change of some, or all parts of the analytical method itself.

Systematic-personal errors are, for example, due to poor attention to important or critical aspects of the analysis context by the analyst. This may include poor judgement, carelessness and even lack of training of the analyst. Analytical bias, i.e. the tendency to skew estimates in the direction that favours the anticipated result, is considered an effect of systematic-personal errors in the analysis.[2]

Random errors

In analytical chemistry it is *assumed* that random errors cause analytical data to be scattered pretty much symmetrically around a mean value, and this error has the same probability of been positive or negative. The presence of random errors will affect the *precision* of the analysis. The sources of random errors are due to uncontrollable variables and because of the inability to identify their sources, they cannot be completely eliminated. A plot of relative frequency vs deviation from the mean, for a large number of individual errors, is known as a Gaussian curve or Normal Error. A Gaussian distribution assumes that only random errors are present in the analysis, i.e. that all systematic errors have been identified and corrected for. This critical assumption allows an appropriate statistical treatment of the analytical data obtained that will facilitate evaluation of the magnitude of this error—which in turn allows a bias correction to be performed.

Gross errors

Although not as common as random or systematic errors, gross errors are characterised by being "large", which can result in an analysis being either much higher or much lower than the "true" value. The sources of gross errors are typically considered to be human errors; gross errors will manifest themselves as *outliers* in a series of replicate measurements.

Through the coverage of these errors in general analytical curricula, and in the relevant analytical chemistry laboratories, the need for high accuracy and precision is constantly emphasised at the undergraduate level. However, exposure to the preceding sampling process is minimal. Students are often provided with an unknown sample, but the preceding sampling step is practically always skipped.

What has been learned about sampling errors: nothing so far

Within analytical chemistry, the *before analysis* realm is conveniently "left out"—barring gross errors, which most definitely do not equate with the realm of sampling errors in the TOS—it is for *others* to take care of whatever contributions there are to the total sampling + analysis error management. Traditionally, this responsibility falls to the entity in charge of *sampling* in the form of more-or-less trained personnel, and the difference is critically important. For untrained personnel, sampling errors do not exist, while properly TOS-trained personnel know very well that the effects from untreated sampling errors always inflate the *total* analytical error budget (sampling + analytical error budget) by up to one or two orders-of-magnitude! Neglecting the effects from sampling errors is tantamount to a breach of due diligence when seen in the light of the complete "from-lot-to-aliquot" pathway.

Implications

It is, in general, not appreciated that there is both a bias issue within the analytical domain, which **can** be brought under complete control, however, and a sampling bias, which **cannot** be addressed in a similar fashion as the analytical bias can. In fact, the sampling bias **cannot** be corrected for by any post-analysis approach (data analytical, statistical, *other*). A sampling bias can **only** be affected by expressly eliminating all so-called "Incorrect Sampling Errors (ISE)". ISE has been treated in various previous columns, and in the dedicated TOS literature, and will be revisited in this and later columns. But first WHAT are, and WHAT can be done about sampling errors?

Clearly, one must seek refuge within the TOS. Although often claimed to be complex, the TOS can be in fact be made accessible from a less in-depth theoretical level. For example, even though the TOS identifies nine sampling errors, they originate from only three **sources**: the **material** (which is always *heterogeneous*, it is only a matter of degree), the **sampling equipment** (which can be designed either to promote a representative extraction, or not) and the **sampling process** itself (even correctly designed equipment can be used in a non-representative manner).[3]

TOS basics on sampling errors

At the outset, the reader is referred to References 4–6. It is recommended that these are read together with, indeed *before*, the present column to get the best foundation for what is laid out below. Pierre Gy, founder of the TOS, took his point of departure for developing the TOS in the material phenomenon of *heterogeneity*—before even starting to solve the obvious main question "how to sample?" Thus, Gy identified all sampling errors that represent everything that *can go wrong* in sampling, sub-sampling (sample mass reduction), sample preparation and sample presentation—**due to** heterogeneity and/or inferior sampling equipment design and usage. He meticulously worked out how to *avoid* committing such practical errors in the design, manufacture, maintenance and operation of sampling equipment and elucidated how their adverse impact on the total accumulated uncertainty could be reduced as much as possible

SAMPLING COLUMN

when sampling in practice. When all this was developed into his coherent TOS, the concept of a sampling error (SE) became the key element, in as much as answering the fundamental question "how to sample?" pretty much became synonymous with "how can we *eliminate* and/or *reduce* sampling error effects on sampling performance. Being able to *identify* sampling errors is 90% of the way towards representative sampling. These sampling errors also occur in process analytical technologies (PAT) applications as discussed in depth in previous publications.[7,8]

A crucial distinction: error vs uncertainty

Two issues underlie everything regarding "representativity", the second of which is intimately connected with sampling errors—but, first, a related fundamental prerequisite in the TOS.

It is not possible to ascertain the representativity status of a specific sample or analytical aliquot from any observable feature related to the sample/aliquot itself. The sample could be representative, or it could be miles away—one will never know if the sample is removed from its origin. It is only possible to define, and document, representativity as a characteristic of the *sampling process*.[9] Everything depends on the sampling equipment, how it is designed, used and maintained. This is where representativity can be forfeited. This is all related to which sampling errors have **not** been suitably eliminated and/or reduced, i.e. how one is able to recognise and how one is able to counteract sampling error effects **in** the sampling process. This is where and why sampling errors attain key prominence. One can state that analytical results *depend* on the preceding sampling and sub-sampling processes: **only** bona fide representative sampling/sub-sampling processes lead to a representative analytical aliquot ("*the process of collecting a small mass of a material whose composition accurately represents the bulk of the material being sampled*"), while anything else will leave the aliquot affected by a significant sampling bias ... of unknown magnitude (it cannot be estimated, as it changes its magnitude with every attempt to quantify it). Accuracy w.r.t. the original material from which a primary sample was extracted will be unobtainable. Clearly, focus is critically on sampling errors ("incorrect" as well as "correct"); for a more fully developed introduction the reader is referred to Esbensen's introductory book.[3] Here, focus will be on illustrating a first set of sampling error distinctions that will start one along a path to deeper understanding.

It is necessary to speak with the outmost clarity: a crucial *distinction* needs to be made: uncertainty vs error (Gy,[10] Pitard[11]).

Error: Difference between an observed or calculated value and the corresponding "true value"; variations in measurements (e.g. analytical results), observations or calculations which are **due to** *mistakes* or to uncontrollable factors. Sampling errors are **not** called sampling uncertainties!

Uncertainty: Lack of sureness about someone or something; something that is not known beyond doubt; something not constant. Without a certain amount of relevant competence (in the TOS), one would likely first listen to statisticians, who prefer the term *uncertainty*.

> The repeatability study often performed in near infrared (NIR) spectroscopy, for example (see section further below), provides an estimate of uncertainty. The repeatability (short-term precision) of a method may be obtained by obtaining six consecutive spectra of the same sample.[12] The standard deviation of the predictions provides an estimate of an uncertainty in the predictions. This uncertainty (random error) is unavoidable, it will always be part of analytical methods.

However, Pierre Gy has the following to say: "With the exception of homogenous materials, which only exist in theory, the sampling of particulate materials is always an *aleatory*[a] operation. There is always uncertainty, regardless of how small, between the true, unknown content of a lot a_L and the true unknown content of the sample a_S. A vocabulary difficulty needs to be mentioned: tradition has established the word *error* as common practice, though it implies a mistake that *could have been prevented*, while statisticians prefer the word *uncertainty* which implies no responsibility. However, in practice, as demonstrated in the TOS, there are both sampling errors and sampling uncertainties. Sampling errors can easily be preventatively minimised, while sampling uncertainty for a preselected sampling protocol is inevitable. For the sake of simplicity, and because the word uncertainty is not strong enough, the word **error** been selected as current usage in the TOS, making it very clear it does not necessarily imply a sense of culpability."

With this error definition, here we are especially focused on the so-called ISEs, which are IDE, IEE, IPE and IWE, see Figure 1. They will receive the illustrative focus in this column.

- IDE: Increment Delineation Error
- IEE: Increment Extraction Error
- IWE: Increment Weighing Error
- IPE: Increment Preparation Error

The overarching thing to know about ISE forms the backbone of all practical sampling: if ISEs have not been appropriately eliminated/reduced, the sampling process is *biased*. All manner of bad things follow from a biased sampling process, the most important of which is that the ensuing analytical aliquot can **never** be representative of the target material, i.e. the game is lost even before one starts! What is the meaning of analysing an aliquot that cannot be proven to be representative? None—there is no meaning!

The first part on any sampling agenda is, therefore, to eliminate/reduce sufficiently all ISE, and in order to be able to do so, it is imperative to know how to correctly *identify* sampling errors a.o.

Sampling errors: WHAT are they?

For definition and full theoretical treatment of all the nine SEs, the reader is referred to the scholarly treatises by

[a]Aleatory: accidental, happening by chance, unintentional, unexpected

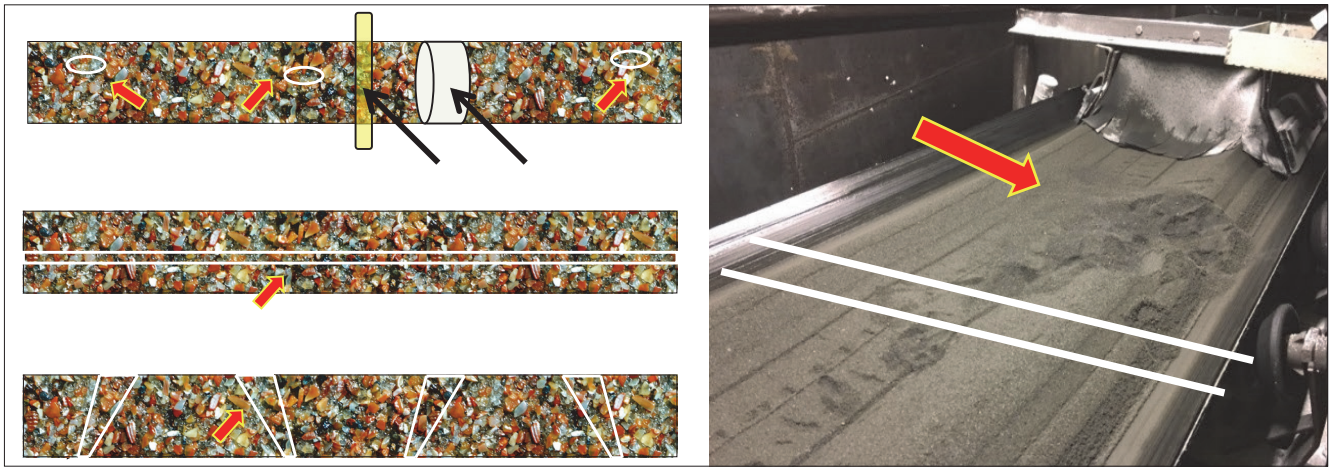


Figure 1. Left: archetypal examples of Increment Delineation Error (IDE) (also known as Incorrect Delineation Error). The TOS stipulates that the only correct (bias-free) increment delineation of a moving material is a **complete** across-stream **slice** (for example across a conveyor belt) or a complete cross-sectional volume (in the case of a moving material confined to a duct, e.g. in a pipeline or similar). Various other IDE manifestations resulting from i) grab sampling (top panel), "taking only some of the stream all of the time" (centre panel) and "unbalanced slicing" (bottom panel) are also illustrated—all contribute to a significant sampling bias. Right: real-world example of a highly unacceptable conveyor belt "sampling", resulting in a highly significant IDE, here accompanied by a concomitant IEE, in that the depth of the IDE-affected slice does not extract material all the way to the bottom of the conveyor belt either. IDE and IEE are very often bad fellow-travellers towards a significant sampling bias. Illustration copyright by KHE Consulting, reproduced with permission.

Gy[10] or Pitard.[11] Here we shall only, and simply, *illustrate* these definitions and *show their effects* in practice….[3] Many of these are particularly easy to appreciate in the process sampling realm, see Figure 1.

Examples of sampling errors in pharma

The drying of a pharmaceutical formulation provides an example of committing a sampling error[13] in a complex industrial production context, Figure 2.

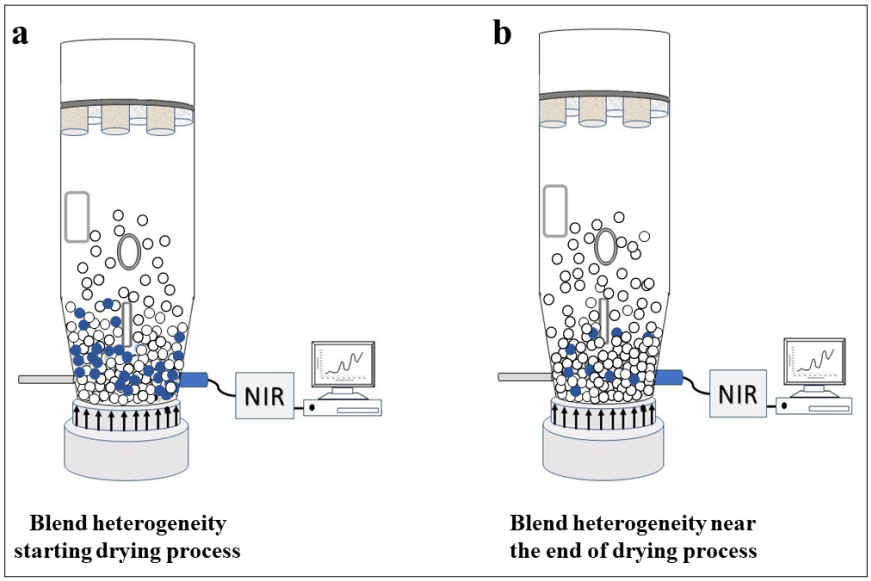


Figure 2. A fixed probe location is not necessarily always the right basis for an otherwise well-performing analytical method, e.g. a NIR probe installed close to the bottom of a drying rig. The relevance of the analytical results will vary with the compositional evolution of a drying pharmaceutical mixture. With respect to the analyte water content (moisture), segregation heterogeneity will influence the accuracy (will create a sampling bias) with respect to the full mixture volume, see text for details.

As the drying process starts, the blend is expected to have about 25% (w/w) water content. However, a NIR spectroscopic method might indicate results of 54, 31 and 27% (w/w), much higher than the expected level. Figure 2a provides a representative illustration of this situation where the material with the highest water content is located close to the bottom of the drying rig, i.e. close to where the NIR probe is installed. The higher results are related to the high heterogeneity of the blend at this drying stage. Figure 2b illustrates the blend near the end of the drying process, where the remaining water is more evenly distributed throughout the full volume of the dryer vessel. The same NIR probe installation now provides much more accurate results because the blend is very close to the target 4% (w/w) water content. The volume/mass analysed by the NIR spectrometer is now less heterogeneous and the analytical probe's GSE sampling error is reduced (GSE is a "Correct Sampling Error", see, e.g., Reference 3).

The distribution of a drug throughout a tablet can lead to a similar heterogeneity-induced sampling error. A tablet could be manufactured in a process with a target concentration of 10% (w/w). However, the top part of the tablet could have

SAMPLING COLUMN

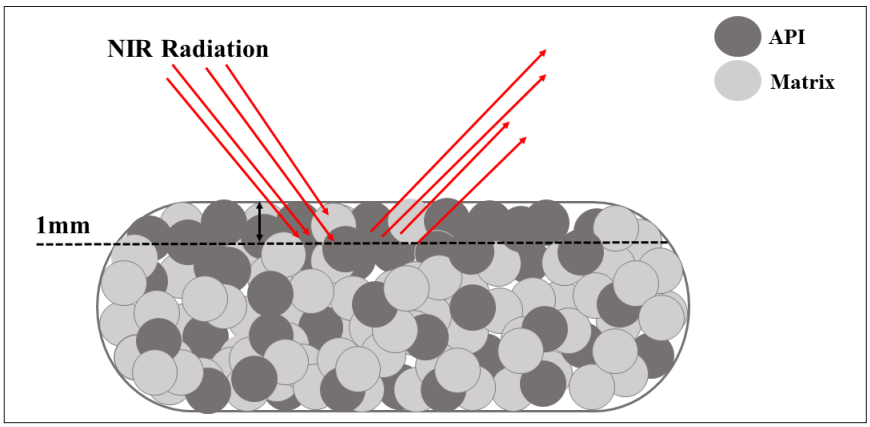


Figure 3. The inability of the diffuse NIR analytical method to penetrate more than, say, 1 mm of a single tablet, constitutes what could be called a Probe Increment Delineation Error; cf. Figure 1 for a complete slice, or a complete volume support for the signal acquisition.

more drug than the bottom part of the tablet.

Figure 3 provides an illustration of this situation. A diffuse reflectance NIR spectroscopic approach where the sensor radiation interacts mostly with the top 1 mm of the tablet could, for example, indicate a 12 % (w/w) drug concentration. However, when the tablet is reference analysed (high performance liquid chromatography, an approach where the entire tablet is dissolved and analysed), the drug concentration is found to comply with the target concentration of 10 % (w/w). This is an example of a classical IDE—but performed by the probe—in combination with heterogeneity even at the smallest scale of interest in pharma, the scale of a single tablet. Thus, many researchers and industrial monitoring engineers/technicians prefer to develop transmission NIR methods for tablets that cover the entire tablet volume, instead of diffuse reflectance methods.

For PAT analysts and chemometricians especially

A Support Mismatch Error (SME) is possible, typically when developing *calibration models* for PAT applications. As an example, Raman spectra may be obtained to characterise a mammalian cell culture in an active bioreactor, with the objective of developing a partial least squares (PLS) regression model to predict the concentration of key metabolites.[14] Raman spectra obtained from a sample would be the **X** block needed for the PLS modelling. So, this application requires extracting a sample of the cell culture from the bioreactor and using it for both **X**-data acquisition as well as reference analysing it *off-line* for the metabolites, the latter which would constitute the pertinent **Y** data. Needless to say, this sample better be representative of the whole reactor volume (the classical TOS challenge). A significant SME will be committed if the Raman spectra are not obtained for the same sample volume which is analysed by the off-line reference method, i.e. if the support volume for the **X**- and the **Y**-data acquisition are not identical, Figure 4.

The data analytical correlation between the **X** and **Y** data blocks will be negatively affected by such SMEs, which sadly cannot be improved by any spectral pre-processing—or fancy regression modelling.[15,16] The fact that bioreactors are usually forcefully mixed while the Raman spectra are obtained contributes towards *reducing* this kind of sampling error by reducing the

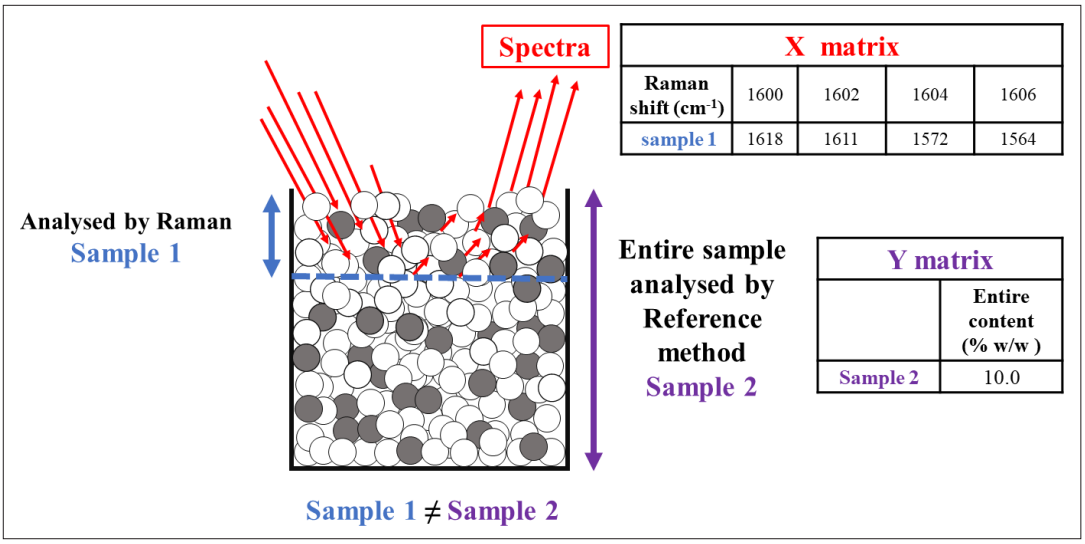


Figure 4. Focusing on the chemometric calibration modelling, may unwittingly lead to committing a SME because "sample 1", which is analysed by Raman spectroscopy, is **not** supported by the same sample volume that is analysed by the reference method "sample 2".

spatial heterogeneity of the cell culture medium in the overall reactor volume, but it cannot eliminate this entirely. Mixing or homogenisation is specified by the TOS as one of the Sampling Unit Operations that should be used to reduce sampling error effects from of heterogeneity,[3,16] and this should of course be used liberally. But the fundamental mismatch between the physical analytical volumes (masses) characterised by the two different analytical modalities is a structural condition that must be rectified in order to be able to decrease the pertinent root mean square error of prediction of the chemometric prediction model applied. The TOS insight helps us to understand why re-design of the [**X**,**Y**] data acquisition set-up can at times be less costly than carrying around an unnecessary load of ISEs. Much more on ISE, and their counterparts (the so-called "Correct Sampling Errors", CSE) in future sampling columns.

Discussion and conclusions

In the drying example, the NIR method is detecting areas of the blend that have a high water-concentration since the drying process is just starting. If the sample analysed by the NIR radiation could be pulled out and analysed by a Karl Fischer titration (the same physical sample volume), the analytical result obtained would be similar though. However, both results are not representative of the whole blend. The samples analysed do not refer to a complete slice of the drying rig, far less to the entire drying vessel volume, but refer to a small volume directly in front of the sensor probe only, a volume with excess water. The sensor is in fact performing probe *grab sampling*, a classical TOS error.[3] If the analyst does not realise that high water content heterogeneity is affecting the analytical results, a significant amount of time would be spent in *troubleshooting* an analytical method that in fact works perfectly correctly. Understanding how heterogeneity affects the manifestation of sampling errors, and what will ensue if sampling errors are not properly *counteracted*, is very helpful. The TOS is needed even *within* the analytical realm.

The NIR method s.s. also correctly determines the 12 % (w/w) drug concentration in the restricted top-most area of the tablet analysed. The spectrum obtained does indeed correspond to this concentration. The problem is not the NIR method; the problem is the heterogeneity of the tablet. The problem could be corrected, for example, by obtaining spectra of both sides of the tablet, which would detect the differences in drug concentration throughout the tablet. The problem could also be corrected by developing a NIR transmission method which would analyse the majority/all of the tablet mass, again including both sides of the tablet. The problem does not require modifying the chemometric calibration model; it only requires modifying the tablet spectral acquisition setup, or what could be called the *probe sampling* setup.

The SME related to the bioreactor example may also be corrected. This error was discussed by Mark,[17] and has been addressed in full in a recent PAT exposé.[7] The SME confusion is in fact one of the most pervasive issues in the PAT realm. This problem is not solved through any spectroscopy or chemometric approach, i.e. by trying to find a different spectral area for the calibration model, by changing spectral pre-processing or by any PLS-model mediation, e.g. trying one or two extra PLS-components might be able to compensate—all of which are completely futile. The SME is a sampling error, pure and simple, and should be addressed exclusively as such; later columns will further illustrate these issues.

Acknowledgements

The authors thank graduate student Adriluz Sánchez Paternina for preparation of figures.

References

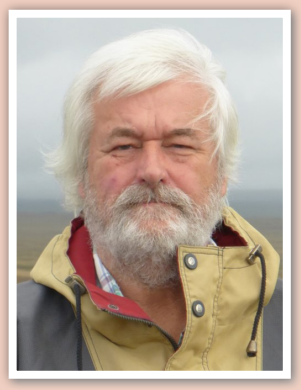
1. D.C. Harris, *Quantitative Chemical Analysis*, 9th Edn. W.H. Freeman. New York (2015).
2. D.A. Skoog, D.M. West, F.J. Holler and S.R. Crouch, *Fundamentals of Analytical Chemistry*. Nelson Education (2013).
3. K.H. Esbensen, *Introduction to the Theory and Practice of Sampling*. IMP Open, Chichester (2020). https://doi.org/10.1255/978-1-906715-29-8
4. K. Esbensen, "Pierre Gy (1924–2015): the key concept of sampling errors", *Spectrosc. Europe* **30(4),** 25–28 (2018). https://doi.org/10.1255/sew.2018.a1
5. K.H. Esbensen, "Reprint: 50 years of Pierre Gy's 'Theory of Sampling'—WCSB1: a tribute", *TOS Forum* **6(6),** 4–7 (2016).
6. P. Gy, "Sampling of discrete materials - a new introduction to the theory of sampling - I. Qualitative approach", *Chemometr. Intell. Lab. Syst.* **74(1),** 7–24 (2004). https://doi.org/10.1016/S0169-7439(04)00167-4
7. K.H. Esbensen and P. Paasch-Mortensen, "Process sampling: Theory of Sampling – the missing link in process analytical technologies (PAT)", in *Process Analytical Technology*, Ed by K. Bakeev. John Wiley & Sons, Chichester, pp. 37–80 (2010). https://doi.org/10.1002/9780470689592.ch3
8. R.J. Romañach, "Theory of Sampling - from missing link to key enabler for process analytical technology (PAT)", in *8th World Conference on Sampling and Blending*, Ed by S.C. Dominy and K.H. Esbensen. Australian Institute of Mining and Metallurgy, Perth, Australia, pp. 63–68 (2017).
9. Danish Standards Foundation, *DS 3077 Representative Sampling - Horizontal Standard*. Danish Standards Foundation (2013).
10. P. Gy, *Sampling for Analytical Purposes*, 1st Edn. Wiley, New York (1998).
11. F.F. Pitard, *Theory of Sampling and Sampling Practice*. CRC Press (2019). https://doi.org/10.1201/9781351105934
12. A. Sánchez-Paternina, N.O. Sierra-Vega, V. Cárdenas, R. Méndez, K.H. Esbensen and R.J. Romañach, "Variographic analysis: A new methodology for quality assurance of

pharmaceutical blending processes", *Comput. Chem. Eng.* **124,** 109–123 (2019). https://doi.org/10.1016/j.compchemeng.2019.02.010

13. R.L. Green, G. Thurau, N.C. Pixley, A. Mateos, R.A. Reed and J.P. Higgins, "In-line monitoring of moisture content in fluid bed dryers using near-IR spectroscopy with consideration of sampling effects on method accuracy", *Anal. Chem.* **77(14),** 4515–4522 (2005). https://doi.org/10.1021/ac050272q
14. T.E. Matthews, B.N. Berry, J. Smelko, J. Moretto, B. Moore and K. Wiltberger, "Closed loop control of lactate concentration in mammalian cell culture by Raman spectroscopy leads to improved cell density, viability, and biopharmaceutical protein production", *Biotech. Bioeng.* **113(11),** 2416–2424 (2016). https://doi.org/10.1002/bit.26018
15. K.E. Esbensen and B. Swarbrick, *Multivariate Data Analysis – In Practice. An Introduction to Multivariate Analysis, Process Analytical Technology and Quality by Design*, 6th Edn. CAMO Software AS, Oslo, Norway (2018).
16. K.H. Esbensen, R.J. Romañach and A.D. Román-Ospino, "Theory of Sampling (TOS): A necessary and sufficient guarantee for reliable multivariate data analysis in pharmaceutical manufacturing", in *Multivariate Analysis in the Pharmaceutical Industry*, Ed by A.P. Ferreira, J.C. Menezes and M. Tobyn (Eds). Academic Press, London, pp. 53–91 (2018). https://doi.org/10.1016/B978-0-12-811065-2.00005-9
17. H. Mark, *Principles and Practice of Spectroscopic Calibration*. Wiley (1991).

Dr Rodolfo Romañach is Professor of Chemistry at the University of Puerto Rico – Mayagüez Campus, and site leader for the Center for Structured Organic Particulate Systems. He worked in the pharmaceutical industry for over 12 years before joining the UPR Chemistry Department in 1999. He found his mission in training a new generation of pharmaceutical scientists capable of doing real time process measurements in the manufacturing area. He is presently continuing efforts to improve the teaching of chemometrics and further his understanding of the errors that affect real time process measurements—and what to do about all this.
https://orcid.org/0000-0001-7513-7261
rodolfoj.romanach@upr.edu

Dr Joubert is an Associate Professor of Chemistry at the University of Puerto Rico – Mayagüez Campus. She joined the Department of Chemistry after graduating from Washington State University in 1998. From 2014 to 2016, she served as Interim Department Chair, and has since then focused her efforts on teaching several undergraduate analytical chemistry courses.
https://orcid.org/0000-0003-3639-3566
aidalu.joubert@upr.edu



Kim Esbensen, PhD, Dr (hon) has had a career in research and academia for 40 years, and now is an independent researcher and consultant, founding KHE Consulting. A geologist/geochemist/data analyst by training, he first worked for 20+ years in the forefront of chemometrics, but since 2000 has devoted most of his efforts to representative sampling of heterogeneous materials, processes and systems, PAT and chemometrics. He is a member of several scientific societies and has published over 260 peer-reviewed papers and is the author of two widely used textbooks in Multivariate Data Analysis and Sampling.
https://orcid.org/0000-0001-6622-5024
khe.consult@gmail.com

Accelerate Your Publication

Letters published in 3 weeks subject to satisfactory review

JSI—Journal of Spectral Imaging is an Open Access, peer-reviewed journal dedicated to the rapid publication of leading research in spectral, hyperspectral and chemical imaging, as well as in related areas such as remote sensing, and chemometrics and data handling for spectral image data.

- *JSI* Letters offer extremely fast publication whilst retaining thorough peer review, with publication within three weeks of submission, subject to satisfactory review.
- *JSI* Letters can either express the view of the author on a particular aspect of spectral imaging that they wish to comment on, or can very briefly report an interesting aspect of the author's work: perhaps details of a chemometric routine or a sampling procedure. The conclusions should represent a significant advance in the understanding of an important issue and carry major implication for spectral imaging as a discipline.
- Authors are expected to submit revised manuscripts within 48 hours of receiving the referees' reports.
- Given the accelerated treatment accorded to Letters, it is particularly important that they are written to a standard of English to allow rapid refereeing.

impopen.com/jsi-author-centre

APPLICATIONS

Remote sensing of vegetation using SWIR cameras on a UAV

Forage Mass Monitoring analysis has been traditionally done using biomass sampling to calculate biomass yield per hectare (tha^{-1}). Research projects are now looking at reflectance spectroscopy methods using remote sensing systems on unmanned aerial vehicles (UAVs). Promising results prove the principal suitability of such systems for airborne monitoring of small- to medium-sized farmland in agricultural applications for precision agriculture, such as biomass for crops and grasslands. An imaging system in the form of a multispectral multicamera system is often used to derive well-established vegetation indices efficiently. However, due to the use of silicon-based sensors, the spectral application range of such multi-camera systems is limited to 400–1000 nm. Therefore, more robust indicators linked to biomass in the short-wave infrared (like cellulose or moisture content) cannot be considered as estimators. In a joint research project, a team from the University of Applied Science Koblenz and the Remote Sensing and GIS group at the University of Cologne developed a UAV-based multi-camera system to collect NIR/SWIR data, to prove more robust and better-performing estimators of biomass monitoring.

Quantum Design UK and Ireland

▸ Download Application Note

Testing for robusta in Arabica coffee in minutes using X-Pulse

Coffee is one of the most widely traded commodities in the world. The trade is made up of two main varieties, commonly known as Arabica and robusta, with Arabica accounting for 60–70% of the world market and robusta most of the rest. Arabica is generally considered to be of higher quality, and sells on world commodity markets for about twice the price of robusta. There is, therefore, the potential for economic fraud, with unscrupulous traders adding robusta to Arabica and still labelling the product "100% Arabica". Analytical methods are, therefore, needed to detect the presence of robusta coffee in products labelled as Arabica.

Oxford Instruments

▸ Download Application Note

Correlative Raman microscopy for 2D materials investigation

Confocal Raman imaging is an ideal method for studying 2D materials. It can be used to discern the orientation of their layers and investigate defects, strain and functionalisation as their Raman properties are determined by molecular bonds, relative orientation and number of layers. Further details can be visualised with other methods such as SEM, AFM, SNOM and photoluminescence microscopy. By correlating the information of more than one approach, 2D materials can be analysed more thoroughly. This study briefly reviews the development of 2D materials, describes Raman and correlative techniques, and provides example measurements of Graphene, MoS_2 and WS_2.

WITec

▸ Download Application Note

Gas analysis special inlet for glovebox monitoring

Gloveboxes are frequently used in a variety of research, production and quality control applications. The requirement of this equipment is to maintain a completely separate environment from the ambient conditions. Glovebox construction consists of a sealed compartment with ports fitted with gloves. A load lock ensures that the materials or inert atmosphere are contained within the compartment. Typically an impermeable, but flexible rubber or plastic glove forms part of the construction so that manipulation tasks are possible. A key aspect is for the inert atmosphere inside the glovebox to remain isolated from the ambient atmosphere. A quadrupole mass spectrometer is a convenient and powerful method of measuring and monitoring both the compartment integrity and also the chemical composition of the atmosphere. Any leaks, changes in gas from sample introduction or evolved gases from user experiments can all be tracked.

Hiden Analytical

▸ Download Application Note

Spinsolve variable sample temperature

The Spinsolve 43 MHz systems can be equipped with a unique temperature control system that allows you to measure your samples at elevated temperatures (between 26 °C and 60 °C) without requiring nitrogen or dry air supply. This is achieved by adjusting the magnet temperature instead of using a gas flow approach, which not only eliminates the need for a VT unit, it also does not require any inset in the magnet that typically reduces the available space for the sample. This solution does not compromise resolution, sensitivity or stability and is also available with Spinsolve ULTRA models.

Magritek

▸ Download Application Note

Transient absorption spectrometer diffuse reflection; measurements of benzil powder

Understanding photogenerated excited electronic states, light mediated chemical reactions and intermediates, and photo-driven energy or electron transfers is paramount to designing and developing the next generation of materials from therapeutics to solar cells. Having the ability to measure these processes in the solid state (powder, film, glass) further enables researchers to glean vital photoinduced electronic properties of their materials and devices in their real-world application uses. The Edinburgh Instruments LP980 Transient Absorption Spectrometer, equipped with the diffuse reflection accessory, is used here to measure benzil powder.

Edinburgh Instruments

▸ Download Application Note

Product Focus on Imaging Spectroscopy

Andor Technology

Tel: 02890237126
s.mulhern@andor.com
andor.oxinst.com/products/spectrographs-solutions

PRODUCT: Spectrograph Solutions from UV to SWIR
APPLICATIONS: Raman ▪ Luminescence ▪ Absorption ▪ OES and LIBS ▪ Micro-spectroscopy
KEY FEATURES: High modularity ▪ High resolution ▪ Intelligent motorisation ▪ Patented design ▪ Large simultaneous band-pass

Bruker Optik GmbH

Tel: +49 (0)7243-504 2000
info.bopt.de@bruker.com
www.bruker.com/optics

PRODUCT: FT-IR Microscope LUMOS II
APPLICATIONS: QA/QC, microspectroscopic failure analysis ▪ Microplastic analysis ▪ Plastic and polymer ▪ Particle & surface analysis ▪ Pharmaceuticals
KEY FEATURES: Plug & play ▪ No dry-air purge; Standard TE-MCT detector ▪ Optional FPA-imaging detector; Fully motorised and automated hardware

PRODUCT: Research FT-IR Microscope HYPERION
APPLICATIONS: Materials research ▪ Polymers ▪ Chemicals ▪ Forensics ▪ Art conservation ▪ Life sciences
KEY FEATURES: High-resolution FT-IR imaging ▪ High sensitivity ▪ Binoculars ▪ Sampling flexibility ▪ Multi-spectral range

DRS Daylight Solutions

Tel: +1-858-432-7500
taylor.stathopoulos@drs.com
daylightsolutions.com

PRODUCT: Spero-QT: QCL-IR Wide-field Microscope
APPLICATIONS: Biomedical imaging ▪ Pharma ▪ Material science ▪ Cancer research ▪ Forensics
KEY FEATURES: Wide-field imaging ▪ Real-time analysis ▪ Label-free ▪ Reflection and transmission ▪ No cryogenic cooling

Edinburgh Instruments

Tel: +441506425300
alison.winn@edinst.com
www.edinst.com

PRODUCT: RM5 Raman Microscope
APPLICATIONS: Bio sciences ▪ Pharmaceuticals ▪ Chemicals ▪ Polymers ▪ Nano materials
KEY FEATURES: Multiple lasers ▪ Automated calibration ▪ High performance microscope ▪ Live sample viewing ▪ Automated optical routing

Pro-Lite Technology

Tel: 01234436110
info@pro-lite.co.uk
www.pro-lite.co.uk

PRODUCT: Nireos; Hera: Ultra-Sensitive Hyperspectral Camera
APPLICATIONS: Fluorescence imaging ▪ Sorting of materials ▪ Agriculture and food quality ▪ Pharmaceuticals ▪ Art conservation ▪ Forensics
KEY FEATURES: 400–1000 nm ▪ High spatial & spectral resolution ▪ High sensitivity and throughput ▪ Compact and lightweight ▪ User friendly software ▪ Export data in ENVI format

PRODUCT: Cubert; ULTRIS 20 Plus: High resolution hyperspectral video camera with pansharpening
APPLICATIONS: The ULTRIS 20 Plus is especially designed for UAV applications ▪ Agriculture ▪ Forestry ▪ Life science ▪ Machine vision
KEY FEATURES: VNIR 450–850 nm (± 10 nm) ▪ 106 bands ▪ Panchromatic extension ▪ Spatial resolution pan: 1880 × 1880 px ▪ Spatial resolution spectral: 410 × 410 px

PRODUCT: Photon etc; Alizé™ 1.7: Cost-effective, high-end infrared camera
APPLICATIONS: Life science ▪ Material science ▪ Forensic science ▪ Food & agriculture ▪ Mining & geology ▪ Arts
KEY FEATURES: 640 × 512 pixels ▪ Low noise levels ▪ High efficiency ▪ Rapid frame rate compatible with an external trigger ▪ Four stage thermoelectric cooler

Quantum Design UK and Ireland Ltd

Tel: 01372 378822
info@qd-uki.co.uk
www.qd-uki.co.uk

PRODUCT: Specim IQ Hyperspectral Imaging Camera
APPLICATIONS: Art conservation and analysis ▪ Food fraud detection ▪ Forensics ▪ Baked goods
KEY FEATURES: Precision agriculture ▪ Food science ▪ Mineral exploration ▪ Pharmaceutics ▪ Medical science

PRODUCT: Specim FX10 Hyperspectral Imaging Camera - 400–1000 nm
APPLICATIONS: Vegetation & agriculture ▪ Phenotyping ▪ Colour & density in printing ▪ Display & light source inspection ▪ Food quality

PRODUCT: Specim FX17 Hyperspectral Imaging - 900–1700 nm
APPLICATIONS: Vegetation & agriculture ▪ Phenotyping ▪ Colour & density in printing ▪ Display & light source inspection ▪ Food quality

PRODUCT FOCUS

S.T.Japan-Europe GmbH

Tel: +49 (0)2234 956372
contact@stjapan.de
www.stjapan.de

PRODUCT: **Spectra Databases for Microplastics Analysis with ATR-FTIR and Raman Imaging Solutions**
APPLICATIONS: Microplastics analysis ▪ Environmental analysis ▪ Polymer analysis ▪ Recycling
KEY FEATURES: Efficient and reliable micro particle identification and characterisation ▪ Suitable for chemical imaging solutions but also for single-particle identification ▪ Compatible with your instruments & search

Shimadzu Europa GmbH

Tel: +49-203-76870
shimadzu@shimadzu.eu
www.shimadzu.eu

SHIMADZU Excellence in Science

PRODUCT: **MALDI-7090 TOF-TOF MS**
APPLICATIONS: Food ▪ Forensics ▪ Drug identification ▪ Proteomics and metabolomics
KEY FEATURES: Unparalleled MS/MS resolution ▪ High mass accuracy ▪ True 2kHz acquisition speed in MS and MS/MS mode ▪ Ultra-fast solid-state UV laser ▪ Untegrated 10 plate loader

PRODUCT: **iMLayer**
APPLICATIONS: Sample preparation
KEY FEATURES: Creation of finer matrix crystal grains via sublimation ▪ Good reproducibility of matrix coatings via automatic coating thickness control ▪ Simple touch pad operation

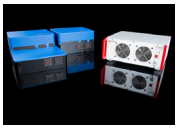
PRODUCT: **AIM-9000**
APPLICATIONS: Ultra micro FTIR analysis of polymers ▪ Food ▪ Forensics ▪ Failure analysis ▪ Contaminant analysis
KEY FEATURES: 30,000 : 1 signal-to-noise ratio ▪ Automated analysis functions ▪ Compliance with GLP/GMP ▪ FDA 21 CFR Part 11 ▪ Full support of pharmacopeia

TOPTICA Photonics AG

Tel: +49 89 85837-0
sales@toptica.com
https://www.toptica.com

TOPTICA PHOTONICS

PRODUCT: **FemtoFiber bCARS**
APPLICATIONS: Broadband CARS ▪ Standard CARS ▪ Multimodal nonlinear imaging ▪ Label-free microscopy ▪ Impulsive SRS
KEY FEATURES: Spectral resolution < 15 cm−1 ▪ Tunable CARS option covering <100–>3700 cm^{-1} ▪ Integrated time-delay and frequency modulation options ▪ Simple, turn-key and compact solution



PRODUCT: **FemtoFiber ultra 920**
APPLICATIONS: : 2-photon Microscopy ▪ Neuroscience ▪ SHG microscopy ▪ Advanced microscopy techniques
KEY FEATURES: Centre wavelength 920 nm ▪ Pulse duration <100 fs ▪ Average output power > 1.5W ▪ Repetition rate 80 MHz

Wasatch Photonics

Tel: +1-919-544-7785
ajones@wasatchphotonics.com
www.wasatchphotonics.com

Wasatch Photonics

PRODUCT: **Gratings for Spectroscopy**
APPLICATIONS: Spectroscopy ▪ Raman ▪ Fluorescence ▪ Hyperspectral imaging
KEY FEATURES: Patented broad bandwidth grating designs ▪ Exceptional 1st order diffraction efficiency ▪ Low polarisation sensitivity, uniform efficiency ▪ Near-zero scatter ▪ Robust design for easy cleaning & handling

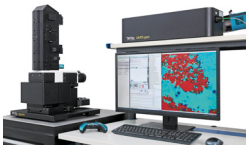
WITec GmbH

Tel: +49 (0) 731 140 700
info@witec.de
www.witec.de

WITec focus innovations

PRODUCT: **alpha300 R Confocal Raman Imaging System**
APPLICATIONS: Materials research ▪ Pharmaceutics ▪ Semiconductors & battery materials ▪ Life science ▪ Geosciences, coatings & thin films, polymer research, low-dimensional materials
KEY FEATURES: Cutting-edge 3D chemical Raman imaging while maintaining the highest measurement speed and spectral quality ▪ Confocal setup: highest spatial resolution ▪ Correlative Raman imaging

PRODUCT: **alpha300 apyron automated Raman Imaging System**
APPLICATIONS: Materials research ▪ Pharmaceutics ▪ Forensics ▪ Life science ▪ Geoscience ▪ Glove-box applications
KEY FEATURES: Push-button principle for high performance 3D Raman imaging ▪ TruePower automated absolute laser power determination ▪ Outstanding spectral and spatial resolution ▪ Accelerates the experimental workflow



PRODUCT: **alpha300 Ri inverted Raman Imaging microscope**
APPLICATIONS: Life Sciences ▪ Biomedical research ▪ Living cell analysis ▪ Aqueous samples
KEY FEATURES: Inverted beam path allows liquid samples to be placed on the stage for quick and repeatable measurements ▪ Compatible with other microscopy techniques including: fluorescence, DIC, phase-contrast

PRODUCT: **TrueSurface Microscopy**
APPLICATIONS: Large-area investigations ▪ Characterisation of rough & inclined surfaces
KEY FEATURES: Topographic confocal Raman imaging ▪ Precise tracing of the true surface while acquiring Raman imaging data in a one-pass measurement process ▪ Virtually no sample preparation of large samples

PRODUCT: **RISE Microscopy – Raman SEM Imaging**
APPLICATIONS: Materials research ▪ Pharmaceutics ▪ Nanotechnology ▪ Life science ▪ Geoscience
KEY FEATURES: Correlative Raman-SEM imaging integrated in one system ▪ Quick and convenient switching between Raman and SEM measurement on the same position ▪ Correlation of the measurement results and image overlay

ATOMIC

Handheld LIBS analyser

SciAps have introduced their new generation SciAps Z-901 handheld LIBS analyser. Similar to their new XRF platform, the Z-901 features an all-new ergonomic design, a weight reduction down to about 1.6 kg, improved heat dissipation and completely updated software and processing electronics. The Z-901 also features "dual burn" technology: users can choose either an "air burn" method or argon-purge. Air burn eliminates the need for argon canisters and offers rapid material sorting and identification. Users can also insert a small argon canister, switch to the "argon purge" app and calibration, and obtain higher precision and improved limits of detection.

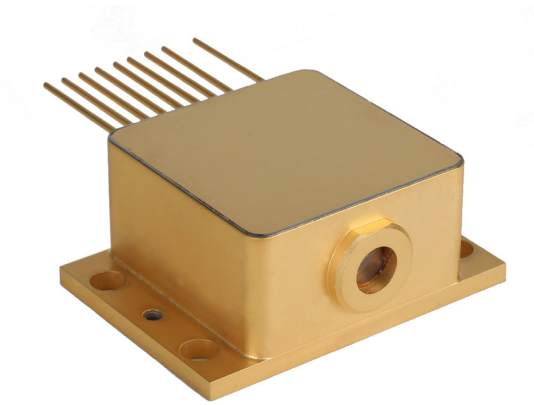
With a new form factor, the new LIBS units are better balanced, narrower, with a tapered snout for easier access to welds and hard-to-reach places, and have a rear-facing display that provides easy viewing. Initial results are displayed in one second. The Z-901 is available for alloy, mining exploration and geochemistry, forensics and other analytical applications. It also comes with desktop/tablet software allowing users to add elements and generate custom calibrations.

SciAps

https://link.spectroscopyeurope.com/1285-P1-2021

INFRARED

New QCL product line



mirSense has launched a new quantum cascade laser product line covering the 10–17 µm region enabling spectroscopic analysis of concentrations of polluting molecules like BTX and CH3i. BTX refers to the chemicals benzene, toluene and xylene which are toxic volatile organic compounds that are principally emitted by the petrochemical industry. BTX are also frequently produced and released in the atmosphere during large fires or industrial accidents. The detection of BTX is then a major issue for environmental monitoring and safety and the new mirSense lasers provide the following wavelengths: 674 cm^{-1} for benzene, 727 cm^{-1} for toluene, 746 cm^{-1}, 767 cm^{-1} and 795 cm^{-1} for xylene. CH3i refers to "methyl iodide", a radioactive toxic molecule that spreads in the gas phase and thus is a major concern for public safety in case of nuclear powerplant accidents. When a serious accident occurs at a powerplant, plant operators seek to assess the problem to avoid a long costly plant shutdown and measuring CH3i can be a way to help assess quickly the problem. This is now possible at 885 cm^{-1} with the new lasers.

mirSense

https://link.spectroscopyeurope.com/6286-P1-2021

NEW PRODUCTS

MASS SPEC

New time-of-flight mass spectrometer

The Jeol JMS-T2000GC "AccuTOF™ GC-Alpha" is the sixth generation of the AccuTOF™ GC series, with new high-performance hardware that achieves three times the mass resolving power and mass measurement accuracy of the previous "AccuTOF™ GCx-plus". This is achieved by using a new ion optics design. Additionally, the system has a wide dynamic range that is beneficial not only for quantitative analysis but also for qualitative analysis of complex mixtures. A variety of ionisation techniques—field ionisation (FI), field desorption (FD), photoionisation (PI) and chemical ionisation (CI)—are optionally available, in addition to the standard electron ionisation (EI). Two combination ion sources are also available as options: the EI/FI/FD combination ion source and the EI/PI combination ion source which allow easy switching between ionisation techniques without breaking vacuum or replacing the ion sources.

The JMS-T2000GC also features new analysis software: msFineAnalysis. This software is a new generation of automated data analysis software that provides qualitative results by combining data acquired by EI and soft ionisation (FI, CI or PI) in a simple, quick and automated way. A new two-sample comparison function provides Volcano Plots, which can visually illustrate the distinguishing components between the two samples. After determining whether there are differences, integrated analysis is performed for all components. The software also supports analysis of GC/EI data alone.

Jeol

https://link.spectroscopyeurope.com/4220-P1-2021

Sample heating for DART-MS

Direct Analysis in Real Time Mass Spectrometry (DART-MS) is a proven technique that enables rapid analysis of both solid and liquid samples under standard laboratory conditions without sample preparation. However, certain polymers, cosmetic powders and forensic materials are difficult to analyse using DART-MS due to the varying volatility of substituents in these complex samples.

To overcome these challenges, BioChromato has developed an innovative sample introduction device (ionRocket), which gradually heats a sample placed directly beneath the DART-MS gas stream. Gradient heating of the sample before ionisation creates time/temperature-resolved mass spectra, separating species both by their thermal desorption profiles and *m/z*. ionRocket generates a temperature gradient from ambient up to as high as 600 °C in just a few minutes. This allows compounds in your samples to be sublimated, vaporised or pyrolysed according to their volatility, and then introduced into the DART-MS gas stream. Because the ionRocket offers the option to weigh samples prior to analysis this results in reproducible MS intensity, allowing calibration curves of analyte amount versus peak intensity to be calculated.

Data obtained from ionRocket yields another axis of data (time/temperature) beyond that obtained from normal DART-MS analysis. Species desorb in order of their volatility along the temperature gradient, and, therefore, are separated in time. The data produced resembles that of an LC-MS or GC-MS chromatogram, consisting of temperature/time, *m/z* and intensity. This can separate rare from abundant species, making them easier to detect.

BioChromato

https://link.spectroscopyeurope.com/6290-P1-2021

Orbitrap GC-MS instrument

The Thermo Scientific Orbitrap Exploris GC mass spectrometer is a compact and easy-to-use instrument for high-resolution analysis in routine testing. It has mass resolving power up to 60,000, an analytical dynamic range across six orders, and is able to provide accurate quantitation and detection of chemical components at trace and high concentrations, for targeted and non-targeted applications. The capability to acquire accurate mass data in full scan allows for multiple compound identification points, simplifying data acquisition, facilitating retrospective data analysis and speeding up instrument set-up.

The Orbitrap Exploris GC mass spectrometer also features easy-to-use operation software and pre-defined method templates to reduce training needs, and a configurable system available with or without MS/MS capability and with flexible maximum resolving power, upgradable in the field for easier scaling.

Thermo Fisher Scientific

https://link.spectroscopyeurope.com/106-P2-2021

NIR

Microspot thin film thickness measurements

CRAIC Technologies has introduced CRAIC FilmPro™ film thickness measurement software. This software package is designed to plug into their microspectrophotometers and controlling Lambdafire™ software. CRAIC FilmPro™ allows the user to measure the thickness of thin films of many materials on both transparent and opaque substrates rapidly and non-destructively. A complete microspot film thickness solution combines a CRAIC microspectrophotometer with the FilmPro™ software. With the addition of spectral mapping from CRAIC Technologies, film thickness maps of entire devices can be created.

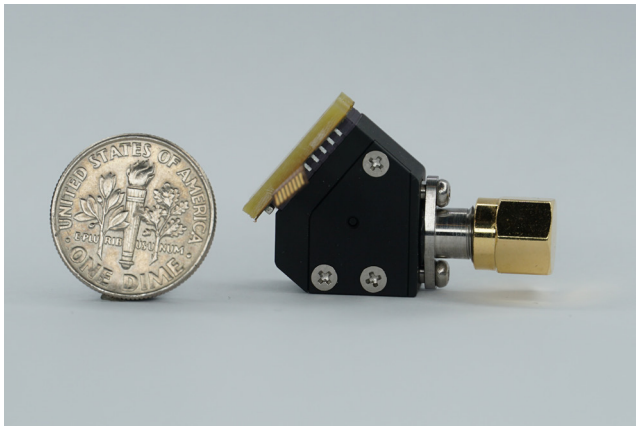
CRAIC Technologies

https://link.spectroscopyeurope.com/3247-P1-2021

Miniature Vis-NIR OEM spectrometer

Ibsen's PEBBLE VIS-NIR spectrometer is an addition to the PEBBLE platform of ultra-compact spectrometers with a form factor of only 20 × 15 × 8 mm, high resolution and sensitivity, as well as environmental ruggedness. PEBBLE VIS-NIR is based on

NEW PRODUCTS



the same diffraction grating technology used in all other Ibsen spectrometers. This ensures that PEBBLE can be manufactured in high quantities with very small unit-to-unit performance variation. The core of PEBBLE is a transmission grating manufactured in-house. Furthermore, PEBBLE utilises a fast and very sensitive CMOS detector array with 256 pixels. When combined with a large numerical aperture of 0.22 (low f-number of f/2.2) PEBBLE provides high sensitivity for such a small spectrometer.

A key benefit of using a transmission grating inside PEBBLE is a high resolution of 8 nm across the full 500–1100 nm wavelength range. Furthermore, the pure transmission-based optics inside PEBBLE ensures very good thermal stability and makes it ideal for real-time measurements in the field.

Ibsen Photonics

https://link.spectroscopyeurope.com/1142-P1-2021

RAMAN

New features for WITec ParticleScout

WITec has enhanced its ParticleScout automated particle analysis tool to offer greater speed and versatility for finding, classifying and identifying microparticles. ParticleScout now includes integration time optimisation that uses the signal-to-noise ratio to determine how long each particle is measured for identification. This not only greatly reduces overall measurement time, but also minimises the effects of fluorescence. It also has added image processing features such as vignetting correction, smart zoom that displays particle information dynamically depending on viewed area and multiple sample area targeting. These are complemented by the integration and possible combination of dark-field, bright-field, epifluorescence and transmission sample illumination.

A software routine has been introduced to accelerate measurements of round samples such as filters that contain homogeneously distributed particles. It allows a wedge section to be selected for analysis and the results can then be extrapolated to represent the whole. Another innovation is the smart separation of closely adjacent or touching particles. This is especially useful for densely packed, heterogeneous samples.

Data post-processing with WITec's TrueMatch™ Raman database management software is updated as well, including the ability to identify individual components in mixed spectra. Hit quality index (HQI) calculation is also optimised with automatic noise reduction and substrate spectra removal. Together these advances enable a new degree of precision in sample characterisation. The quantitative report that summarises the results of a ParticleScout investigation can now be formatted with pre-configured templates such as tables, bar graph histograms or pie charts for clear and effective data presentation.

WITec

https://link.spectroscopyeurope.com/702-P1

NEW PRODUCTS

Raman analyser from Anton Paar

Anton Paar have introduced the Cora 5001 Raman analyser, available in fibre and direct models. The direct model analyses samples in a closed compartment. A guided analysis procedure means Cora 5001 is suitable for operation by personnel with minimum training. Features include an autofocus to find the spot with the best Raman signal within seconds, Class 1 laser and tailored accessories for liquid and solid samples, pills, foils, microscope slides and very small samples. The small footprint and battery option make these benchtop Raman instruments versatile tools for analytical tasks in-house or in the field. The Cora 5001 can be used as a stand-alone spectrometer or combined with other Anton Paar or third-party devices, e.g. for *in situ* monitoring of chemical reactions—combined with microwave-assisted synthesis— or combined with rheometers to simultaneously monitor physical and chemical properties during a curing reaction.

Anton Paar

https://link.spectroscopyeurope.com/5078-P1-2021

Raman handheld analyser for narcotics detection

B&W Tek has introduced the TacticID® Mobile, its newest handheld 1064-nm Raman spectrometer for first responders, police and customs agents to identify illicit and hazardous substances. The TacticID Mobile has an ergonomic design with a large touchscreen display, a targeted library of pure and mixture samples and reports that can be easily generated and shared on a USB drive, or stored in a secure data management system. Relevant sample information input by the user, together with up to three photos provide sample traceability. The system is protected to IP68 and interchangeable sample adaptors give the flexibility to measure samples as they are, or in translucent packaging, bottles and disposable vials.

B&W Tek

https://link.spectroscopyeurope.com/1783-P1-2021

SAMPLING

Automated microwave digestion system

SCP Science has introduced an automated, high volume, microwave digestion system capable of digesting up to 300 samples per run with hands off operation. Coupled to automation, MultiVIEW can digest 12 samples per rack using up to 12 different methods to eliminate the need to run similar samples under the same method. Racks have a quick vessel change feature avoiding the bottleneck around preparing racks of samples.

Use of quartz vessels enables sample normalisation can be run in the calibrated transparent vessels once the sample is digested. Quartz vessels are easy to clean and do not retain metals, as do their Teflon counterparts, eliminating the need to continually replace digestion vessels. MultiVIEW with AutoLOADER systems have outer Kydex skins, triple Teflon-coated stainless-steel tunnel

NEW PRODUCTS

and Teflon coated metal parts throughout, providing protection against harsh acidic fumes. Multiple safety features are built into the instrument starting with the side-mounted door directed away from operator. Auto-venting of vessels is designed to vent away from operator. Multiple relays throughout the instrument turn off magnetrons in adverse conditions.

A 15" colour touch screen displays all operational parameters and digestion profiles simultaneously. Users can watch 12 sample digestions occurring in real time and have the ability to modify the digestion parameters of any sample on the fly.

SCP Science

https://link.spectroscopyeurope.com/6250-P1-2021

UV/VIS

Single frequency 349 nm laser

UniKLasers has launched a new ultraviolet (UV) laser, the Duetto 349. This is a single frequency DPSS CW device which emits at 349 nm with a 50 mW output; the first laser to operate with single frequency at 349 nm. The laser can be used across a wide range of scientific research and industrial engineering processes, including Raman spectroscopy, flow cytometry, confocal microscopy, high precision optics and biomedical engineering. Current UV CW laser solutions for these applications are large, either due to a need for a gas cavity, external doubling cavity or additional frequency-doubling steps. This hinders integration into existing, established measurement systems where lasers with a small footprint, low ongoing maintenance requirements and high stability are well suited.

Part of the R&D work on the Duetto 349 has been to engineer the system so the UV source replaces and improves existing sources such as HeCd or third harmonic Nd:YAG lasers: both of which can produce wavelengths close to UniKLasers' Duetto 349 in CW (continuous-wave, not pulsed). The Duetto 349 only uses one non-linear step, as opposed to two, without the need for a Nd:YAG fundamental laser at 1064 nm, making it smaller and more efficient, overall, whereas HeCd, being a large, gas-filled laser, produces an output at 325 nm. Unlike these two legacy laser sources, most lasers in the UV region are pulsed due to crystal damage/degradation so there are few sources capable of producing CW UV output at this wavelength.

UniKLasers

https://link.spectroscopyeurope.com/6253-P1-2021

X-RAY

Handheld XRF analyser

The new Thermo Scientific Niton XL5 Plus handheld XRF analyser is small and lightweight (1.3 kg). It has a 5 W X-ray tube, and enhanced software and improved detector technology. The Niton XL5 Plus features new detector protection to mitigate the risk of damage to the detector window. This enhances the durability of the XRF analyser, particularly in recycling and scrap metal settings where punctures from sharp objects is common. As a result, operators can avoid costly repairs and enjoy an extended product lifetime.

Thermo Fisher Scientific

https://link.spectroscopyeurope.com/106-P1-2021

Conferences

2021

29 March, Online. **First Italian Metabalomics Network Meeting.** http://metabonet.it

25–28 April, Oviedo, Spain. **5th International Glow Discharge Spectroscopy Symposium (IGDSS2021).** pete@masscare.co.uk, https://www.ew-gds.com/forthcoming-events/

23–26 May, Baeza (Jaen), Spain. **2nd Workshop-Symposium VitroGeowastes: Vitrification, Geopolymerization, Wastes Management and Circular Economy.** lperezvi@ujaen.es, http://vitrogeowastes.com

20–24 June, Duesseldorf, Germany. **51st International Symposium on High Performance Liquid Phase Separation and Related Techniques.** Michael Lammerhofer, michael-laemmerhofer@uni-tuebingen.de, https://www.hplc2021-duesseldorf.com/

18–23 July, Boston, MA, United States. **XXIX International Conference on Magnetic Resonance in Biological Systems (ICMRBSXXIX).** https://www.icmrbs2020.org

1–6 August, Freiberg (Sachsen), Germany. **Geoanalysis 2021.** geoanalysis2021@hzdr.de, https://geoanalysis2021.de

22–27 August, Krakow, Poland. **11th International Conference on Advanced Vibrational Spectroscopy (ICAVS 11).** icavs2021@targi.krakow.pl, http://www.icavs.org/gb/

6–10 September, Heraklion, Crete, Greece. **NanoBio Conference 2021.** info@nanobioconf.com, https://nano-bioconf.com

20–24 September, Online. **11th International Workshop on Infrared Microscopy and Spectroscopy with Accelerator Based Sources.** WIRMS2021@spring8.or.jp, http://www.spring8.or.jp/en/WIRMS2021/

18–20 October, Trondheim, Norway. **2nd Nordic Metabolomics Conference.** mila.knoff@ntnu.no, https://www.ntnu.edu/isb/nmc2021

31 October–4 November, Philadelphia, PA, United States. **69th ASMS Conference.** https://www.asms.org/conferences/annual-conference/future-annual-conferences

16–20 December, Honolulu, Hawaii, United States. **The International Chemical Congress of Pacific Basin Societies 2021.** https://pacifichem.org

2022

31 May–2 June, Kristiansand, Norway. **10th World Conference on Sampling and Blending (WCSB10).** contact@wcsb10.com, https://wcsb10.com

5–9 June, Minneapolis, Minnesota, United States. **70th ASMS Conference.** https://www.asms.org/conferences/annual-conference/future-annual-conferences

4–7 July, Skagen, Denmark. **International Association for Spectral Imaging (IASIM).** 2020@iasim.net, https://2020.iasim.net

2023

29 January–3 February, Ljubljana, Slovenia. **2023 European Winter Conference on Plasma Spectrochemistry.** Johannes T. VanElteren, http://www.ewcps2021.ki.si

Courses

2021

11–12 April, Online. **Auger Electron Spectroscopy (AES) and Data Processing Short Course.** j.grant@ieee.org, https://surfaceanalysis.org/Online_Short_Courses.html

7–9 June, Online. **X-ray Photoelectron Spectroscopy (XPS) and Data Processing Short Course.** j.grant@ieee.org, https://surfaceanalysis.org/Online_Short_Courses.html

10–11 June, Online. **Computer Aided Surface Analysis for X-ray Photoelectron Spectroscopy (CAsaXPS) Short Course.** j.grant@ieee.org, https://surfaceanalysis.org/Online_Short_Courses.html

Exhibitions

2021

24–26 March, Online. **Spectro Expo 2021.** https://www.spectroexpo.com/

23–25 September, Hyderabad, India. **analytytica Anacon India and India Lab Expo.** sheron.david@mm-india.in, https://www.analyticaindia.com/

15–17 November, Dubai, United Arab Emirates. **ARABLAB 2021.** info@arablab.com, https://www.arablab.com

2021

5–9 March, Atlanta, GA, USA. **Pittcon 2022.** https://www.pittcon.org

DIRECTORY

ATOMIC

Bruker AXS GmbH	info.BAXS@bruker.com www.bruker.com/about-us.html
Oxford Instruments NanoScience	nanoscience@oxinst.com nanoscience.oxinst.com

Atomic Emission

Bruker AXS GmbH	info.BAXS@bruker.com www.bruker.com/about-us.html

Atomic Fluorescence

Oxford Instruments NanoScience	nanoscience@oxinst.com nanoscience.oxinst.com

CHEMICALS AND RMS

Bureau of Analysed Samples Ltd	enquiries@basrid.co.uk www.basrid.co.uk
Starna Scientific Limited	sales@starna.com www.starna.com

DATA HANDLING

ACD/Labs	info@acdlabs.com www.acdlabs.com
Linkam Scientific Instruments	info@linkam.co.uk www.linkam.co.uk
Renishaw Ltd	raman@renishaw.com www.renishaw.com/raman
Sepsolve Analytical Ltd	hello@sepsolve.com www.sepsolve.com
S.T.Japan-Europe GmbH	contact@stjapan.de www.stjapan.de

GAMMA-RAY

XIA LLC	sales@xia.com www.xia.com

IMAGING

ABB Measurement & Analytics	ftir@ca.abb.com abb.com/analytical
Bruker Optik GmbH	info.bopt.de@bruker.com www.bruker.com/optics
Delta Optical Thin Film A/S	info@deltaopticalthinfilm.com www.deltaopticalthinfilm.com
IM Publications Open LLP	info@impopen.com www.impopen.com
Linkam Scientific Instruments	info@linkam.co.uk www.linkam.co.uk
Medway Optics Ltd	medwayoptics@aol.com www.medwayoptics.com
Oxford Instruments NanoScience	nanoscience@oxinst.com nanoscience.oxinst.com
Pro-Lite Technology Ltd	info@pro-lite.co.uk www.pro-lite.co.uk
Quantum Design UK and Ireland Ltd	info@qd-uki.co.uk www.qd-uki.co.uk
WITec GmbH	info@witec.de www.witec.de

INFRARED

ABB Measurement & Analytics	ftir@ca.abb.com abb.com/analytical

DIRECTORY

AP Technologies Ltd
info@aptechnologies.co.uk
www.aptechnologies.co.uk

Bruker Optik GmbH
info.bopt.de@bruker.com
www.bruker.com/optics

Edinburgh Instruments Ltd
alison.winn@edinst.com
www.edinst.com

Gigahertz Optik GmbH
info@gigahertz-optik.de
www.gigahertz-optik.de

IM Publications Open LLP
info@impopen.com
www.impopen.com

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

Medway Optics Ltd
medwayoptics@aol.com
www.medwayoptics.com

Ocean Insight
info@oceaninsight.com
oceaninsight.com

Oxford Instruments NanoScience
nanoscience@oxinst.com
nanoscience.oxinst.com

Pro-Lite Technology Ltd
info@pro-lite.co.uk
www.pro-lite.co.uk

Specac Ltd
sales@specac.co.uk
www.specac.com

Starna Scientific Limited
sales@starna.com
www.starna.com

S.T.Japan-Europe GmbH
contact@stjapan.de
www.stjapan.de

Viavi Solutions Inc.
steve.saxe@viavisolutions.com
www.micronir.com

Wasatch Photonics
info@wasatchphotonics.com
www.wasatchphotonics.com

LASER

Edinburgh Instruments Ltd
alison.winn@edinst.com
www.edinst.com

Gigahertz Optik GmbH
info@gigahertz-optik.de
www.gigahertz-optik.de

LTB Lasertechnik Berlin GmbH
info@ltb-berlin.de
www.ltb-berlin.de/en/homepage/

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

Ocean Insight
info@oceaninsight.com
oceaninsight.com

Oxford Instruments NanoScience
nanoscience@oxinst.com
nanoscience.oxinst.com

LUMINESCENCE

Applied Photophysics Ltd
info@photophysics.com
www.photophysics.com

AP Technologies Ltd
info@aptechnologies.co.uk
www.aptechnologies.co.uk

Delta Optical Thin Film A/S
info@deltaopticalthinfilm.com
www.deltaopticalthinfilm.com

Edinburgh Instruments Ltd
alison.winn@edinst.com
www.edinst.com

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

LTB Lasertechnik Berlin GmbH
info@ltb-berlin.de
www.ltb-berlin.de/en/homepage/

Medway Optics Ltd
medwayoptics@aol.com
www.medwayoptics.com

Ocean Insight
info@oceaninsight.com
oceaninsight.com

Oxford Instruments NanoScience
nanoscience@oxinst.com
nanoscience.oxinst.com

Pro-Lite Technology Ltd
info@pro-lite.co.uk
www.pro-lite.co.uk

Quantum Design UK and Ireland Ltd
info@qd-uki.co.uk
www.qd-uki.co.uk

Wasatch Photonics
info@wasatchphotonics.com
www.wasatchphotonics.com

WITec GmbH
info@witec.de
www.witec.de

XIA LLC
sales@xia.com
www.xia.com

DIRECTORY

MAGNETIC RESONANCE

IM Publications Open LLP
info@impopen.com
www.impopen.com

Magritek GmbH
sales@magritek.com
www.magritek.com

Oxford Instruments
magres@oxinst.com
www.oxinst.com/nmr

MASS SPECTROMETRY

Hiden Analytical Ltd
info@hiden.co.uk
www.hidenanalytical.com

IM Publications Open LLP
info@impopen.com
www.impopen.com

Sepsolve Analytical Ltd
hello@sepsolve.com
www.sepsolve.com

MOBILE SPECTROMETERS

AP Technologies Ltd
info@aptechnologies.co.uk
www.aptechnologies.co.uk

Bruker AXS GmbH
info.BAXS@bruker.com
www.bruker.com/about-us.html

Bruker Optik GmbH
info.bopt.de@bruker.com
www.bruker.com/optics

Gigahertz Optik GmbH
info@gigahertz-optik.de
www.gigahertz-optik.de

Magritek GmbH
sales@magritek.com
www.magritek.com

Ocean Insight
info@oceaninsight.com
oceaninsight.com

Pro-Lite Technology Ltd
info@pro-lite.co.uk
www.pro-lite.co.uk

Viavi Solutions Inc.
steve.saxe@viavisolutions.com
www.micronir.com

Wasatch Photonics
info@wasatchphotonics.com
www.wasatchphotonics.com

XIA LLC
sales@xia.com
www.xia.com

PLASMA SPECTROSCOPY

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

LTB Lasertechnik Berlin GmbH
info@ltb-berlin.de
www.ltb-berlin.de/en/homepage/

Pro-Lite Technology Ltd
info@pro-lite.co.uk
www.pro-lite.co.uk

POLARIMETRY

Applied Photophysics Ltd
info@photophysics.com
www.photophysics.com

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

Starna Scientific Limited
sales@starna.com
www.starna.com

PROCESS

ABB Measurement & Analytics
ftir@ca.abb.com
abb.com/analytical

Bruker Optik GmbH
info.bopt.de@bruker.com
www.bruker.com/optics

Hiden Analytical Ltd
info@hiden.co.uk
www.hidenanalytical.com

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

LTB Lasertechnik Berlin GmbH
info@ltb-berlin.de
www.ltb-berlin.de/en/homepage/

Magritek GmbH
sales@magritek.com
www.magritek.com

Ocean Insight
info@oceaninsight.com
oceaninsight.com

Renishaw Ltd
raman@renishaw.com
www.renishaw.com/raman

Starna Scientific Limited
sales@starna.com
www.starna.com

Viavi Solutions Inc.
steve.saxe@viavisolutions.com
www.micronir.com

PHOTONICS & OPTICS

AP Technologies Ltd
info@aptechnologies.co.uk
www.aptechnologies.co.uk

Bruker Optik GmbH
info.bopt.de@bruker.com
www.bruker.com/optics

Delta Optical Thin Film A/S
info@deltaopticalthinfilm.com
www.deltaopticalthinfilm.com

Edinburgh Instruments Ltd
alison.winn@edinst.com
www.edinst.com

Gigahertz Optik GmbH
info@gigahertz-optik.de
www.gigahertz-optik.de

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

LTB Lasertechnik Berlin GmbH
info@ltb-berlin.de
www.ltb-berlin.de/en/homepage/

Medway Optics Ltd
medwayoptics@aol.com
www.medwayoptics.com

Oxford Instruments NanoScience
nanoscience@oxinst.com
nanoscience.oxinst.com

Quantum Design UK and Ireland Ltd
info@qd-uki.co.uk
www.qd-uki.co.uk

Specac Ltd
sales@specac.co.uk
www.specac.com

Starna Scientific Limited
sales@starna.com
www.starna.com

Wasatch Photonics
info@wasatchphotonics.com
www.wasatchphotonics.com

RAMAN

Bruker Optik GmbH
info.bopt.de@bruker.com
www.bruker.com/optics

Edinburgh Instruments Ltd
alison.winn@edinst.com
www.edinst.com

IM Publications Open LLP
info@impopen.com
www.impopen.com

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

LTB Lasertechnik Berlin GmbH
info@ltb-berlin.de
www.ltb-berlin.de/en/homepage/

Ocean Insight
info@oceaninsight.com
oceaninsight.com

Oxford Instruments NanoScience
nanoscience@oxinst.com
nanoscience.oxinst.com

Pro-Lite Technology Ltd
info@pro-lite.co.uk
www.pro-lite.co.uk

Renishaw Ltd
raman@renishaw.com
www.renishaw.com/raman

Rigaku Europe SE
rese@rigaku.com
www.rigaku.com

S.T.Japan-Europe GmbH
contact@stjapan.de
www.stjapan.de

Starna Scientific Limited
sales@starna.com
www.starna.com

Wasatch Photonics
info@wasatchphotonics.com
www.wasatchphotonics.com

WITec GmbH
info@witec.de
www.witec.de

RELATED EQUIPMENT

Bruker Optik GmbH
info.bopt.de@bruker.com
www.bruker.com/optics

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

LTB Lasertechnik Berlin GmbH
info@ltb-berlin.de
www.ltb-berlin.de/en/homepage/

Magritek GmbH
sales@magritek.com
www.magritek.com

Quantum Design UK and Ireland Ltd
info@qd-uki.co.uk
www.qd-uki.co.uk

Renishaw Ltd
raman@renishaw.com
www.renishaw.com/raman

DIRECTORY

Starna Scientific Limited
sales@starna.com
www.starna.com

Viavi Solutions Inc.
steve.saxe@viavisolutions.com
www.micronir.com

XIA LLC
sales@xia.com
www.xia.com

SAMPLE PREPARATION

Medway Optics Ltd
medwayoptics@aol.com
www.medwayoptics.com

Sepsolve Analytical Ltd
hello@sepsolve.com
www.sepsolve.com

Specac Ltd
sales@specac.co.uk
www.specac.com

S.T.Japan-Europe GmbH
contact@stjapan.de
www.stjapan.de

SEPARATION SCIENCE

Sepsolve Analytical Ltd
hello@sepsolve.com
www.sepsolve.com

SPECTRORADIOMETRY

ABB Measurement & Analytics
ftir@ca.abb.com
abb.com/analytical

Gigahertz Optik GmbH
info@gigahertz-optik.de
www.gigahertz-optik.de

SURFACE ANALYSIS

Hiden Analytical Ltd
info@hiden.co.uk
www.hidenanalytical.com

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

Ocean Insight
info@oceaninsight.com
oceaninsight.com

TERAHERTZ

Edinburgh Instruments Ltd
alison.winn@edinst.com
www.edinst.com

Oxford Instruments NanoScience
nanoscience@oxinst.com
nanoscience.oxinst.com

UV AND VISIBLE

AP Technologies Ltd
info@aptechnologies.co.uk
www.aptechnologies.co.uk

Edinburgh Instruments Ltd
alison.winn@edinst.com
www.edinst.com

Gigahertz Optik GmbH
info@gigahertz-optik.de
www.gigahertz-optik.de

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

Medway Optics Ltd
medwayoptics@aol.com
www.medwayoptics.com

Ocean Insight
info@oceaninsight.com
oceaninsight.com

Oxford Instruments NanoScience
nanoscience@oxinst.com
nanoscience.oxinst.com

Pro-Lite Technology Ltd
info@pro-lite.co.uk
www.pro-lite.co.uk

Starna Scientific Limited
sales@starna.com
www.starna.com

X-RAY DIFFRACTION

Bruker AXS GmbH
info.BAXS@bruker.com
www.bruker.com/about-us.html

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

Rigaku Europe SE
rese@rigaku.com
www.rigaku.com

X-RAY SPECTROMETRY

Bruker AXS GmbH
info.BAXS@bruker.com
www.bruker.com/about-us.html

IM Publications Open LLP
info@impopen.com
www.impopen.com

Linkam Scientific Instruments
info@linkam.co.uk
www.linkam.co.uk

Quantum Design UK and Ireland Ltd
info@qd-uki.co.uk
www.qd-uki.co.uk

Rigaku Europe SE
rese@rigaku.com
www.rigaku.com

Specac Ltd
sales@specac.co.uk
www.specac.com

XIA LLC
sales@xia.com
www.xia.com

Introduction to the Theory and Practice of Sampling

Kim H. Esbensen

with contributions from Claas Wagner, Pentti Minkkinen, Claudia Paoletti, Karin Engström, Martin Lischka and Jørgen Riis Pedersen

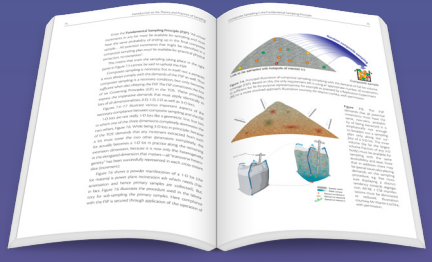
"Sampling is not gambling". Analytical results forming the basis for decision making in science, technology, industry and society must be relevant, valid and reliable. However, analytical results cannot be detached from the specific conditions under which they originated. Sampling comes to the fore as a critical success factor before analysis, which should only be made on documented representative samples. There is a complex and challenging pathway from heterogeneous materials in "lots" such as satchels, bags, drums, vessels, truck loads, railroad cars, shiploads, stockpiles (in the kg–ton range) to the miniscule laboratory aliquot (in the g–µg range), which is what is actually analysed.

This book presents the Theory and Practice of Sampling (TOS) starting from level zero in a novel didactic framework without excessive mathematics and statistics. The book covers sampling from stationary lots, from moving, dynamic lots (process sampling) and has a vital focus on sampling in the analytical laboratory.

"I recommend this book to all newcomers to TOS"

"This book may well end up being the standard introduction sourcebook for representative sampling."

"One of the book's major advantages is the lavish use of carefully designed didactic diagrams"



impopen.com/sampling

IMPublicationsOpen