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## News: NIR can detect Zika in mosquitoes
## Infrared ion spectroscopy
## Spotlight on nuclear magnetic resonance

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# EDITORIAL

First, thank you to the thousands who have updated their registration to *Spectroscopy Europe* online as I asked if you would last issue. If you have not yet done so, please do so now by going to https://www.spectroscopyeurope.com/user, and clicking on Edit Profile. (Your e-mail address will work as the username.) If you run into any difficulty, just e-mail us at circ@spectroscopyeurope.com and we will be delighted to help.

Back to this issue. The News section demonstrates the breadth of application of spectroscopy and inspired the cover image with the story that NIR spectroscopy can determine whether a single mosquito is infected with the Zika virus. Of course, such knowledge can be used to take action before an epidemic erupts.

Our first article, by Nick Polfer, gives an excellent introduction to the recent technique of infrared ion spectroscopy. Ions held in the ion trap of a mass spectrometer can be probed with a tuneable light source, and its photodissociation studied as a function of the photon frequency. Nick believes that the technique will make an impact in small molecule analysis, such as metabolites, drugs and classes of molecules containing many isomers.

In "Spotlight on nuclear magnetic resonance: a timeless technique", Clemens Anklin gives a short history of the commercial and technical development of NMR. From the first measurement of nuclear spin in 1937 by Rabi and his 1943 Nobel Prize to recent developments in small NMR spectrometers and instrument company changes.

Tony Davies, with help from Leah McEwen, David Martinsen, Robert Lancashire and Peter Lampen, asks "Are your spectroscopic data FAIR?". FAIR, which stands for Findable, Accessible, Interoperable, Reusable, is an essential framework for the future of analytical data. Tony has taken the opportunity of a recent conference in Amsterdam to update readers on FAIR and how it affects spectroscopic data.

In the Sampling Column, Kim Esbensen's topic is "Pierre Gy (1924–2015): the key concept of sampling errors". The story of Pierre Gy, who founded the Theory of Sampling (TOS), is a remarkable one, and his work is still the basis of representative sampling today.


Near infrared spectroscopy can identify mosquitoes infected with the Zika virus. Early detection gives time to minimise the effects of outbreaks. See the News article on page 6.


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# NEWS

## Zika detection by NIR spectroscopy a potential lifesaver

Researchers from the University of Queensland, Australia, and colleagues in Brazil have found that near infrared (NIR) spectroscopy can identify mosquitoes infected with the Zika virus. NIR spectroscopy has been shown to have a 94–99 % accuracy rate in identifying infected mosquitoes under laboratory conditions in Brazil. The team, which includes researchers from Fiocruz University, Rio de Janeiro, Brazil, is testing the accuracy of the technique under field conditions in Rio de Janeiro. Dr Maggy Sikulu-Lord and Dr Jill Fernandes, at the Queensland Alliance for Agriculture and Food Innovation, together with Dr Rafael de Freitas and his team (Fiocruz, Rio de Janeiro), Dr John Beier (University of Miami) and Dr Floyd Dowell (USDA) have demonstrated that NIR spectroscopy is 18-times faster and 110-times cheaper than the current detection method.

"We can quickly identify mosquitoes that are infected with Zika virus so public health authorities can treat affected areas before disease spreads to humans", Dr Sikulu-Lord said. "This is definitely going to be a game-changer in disease surveillance, especially in the prediction of disease outbreaks. It only involves shining a beam of light onto mosquitoes and using that information to determine if the mosquito is infected."

Zika is a mosquito-borne virus that can cause abnormalities in unborn babies and is linked to the rare paralysing condition called Guillain–Barre Syndrome (GBS). Dr Sikulu-Lord hopes the World Health Organisation will use NIR spectroscopy in countries where Zika is endemic.

"We hope public health authorities can use it to predict future disease outbreaks and save lives by treating mosquito populations in time."

Further, she believes the technology has the potential to detect a number of diseases.

"We hope to have results for detecting dengue and malaria in mosquitoes in the next few months. We don't think it will eradicate diseases but it will give us the ability to detect diseases quickly so that we can stop disease outbreaks."

NIR spectroscopy being used to examine mosquitoes. Credit: Photo provided by Dr Maggy Sikulu-Lord.

The work has been published in *Science Advances* (doi: 10.1126/sciadv.aat0496).

## ICP-MS method can improve the diagnosis and monitoring of oncological diseases

Researchers at the University of Alicante Faculty of Science Analytical Atomic Spectrometry Group, Spain, in collaboration with the University of Pau et des Pays de L'Adour, France, has developed an analytical method capable of improving the diagnosis and monitoring of oncological diseases from a blood serum sample. Using size exclusion chromatography-inductively coupled plasma mass spectrometry (SEC/ICP-MS), the procedure detects several biomarkers simultaneously.

"Most of the oncological markers lack sufficient sensitivity and specificity, thus limiting their clinical usefulness. However, an analysis that includes different biomarkers whose concentration could be affected by the type of cancer that is suspected, increases diagnostic accuracy", explained Emma Pérez from the University of Alicante.

## Metrohm acquires B&W Tek

Metrohm AG and B&W Tek have announced the acquisition of B&W Tek's Spectroscopy Solution business, B&W Tek LLC, as well as several overseas subsidiaries. This acquisition contributes to Metrohm's growth plans, enhancing the company's capabilities to develop its Raman product line.

"We are pleased to strengthen our product portfolio in spectroscopy by the acquisition of B&W Tek's R&D, production and sales organisations," says Dr Christoph Fässler, CEO and president of Metrohm AG.

Dr Jack Zhou, CEO of B&W Tek LLC, says: "We are excited to see the accelerated growth potential as the result, in furthering the focus on customer-centric solutions and innovations. The addition of complementary products and technologies by B&W Tek, together with Metrohm's expertise in products and commercialisation as well as market presence will allow us to serve a much larger global customer base."

Both parties agreed to keep details about the acquisition confidential.

B&W Tek will continue to operate under their own brand with their own sales and service organisation for the time being to avoid any disruption and to continue to give B&W Tek's existing customers the best possible experience. After this transition period, the gradual integration of B&W Tek into the Metrohm organisation will then be started taking into consideration the need of all stakeholders involved.

B&W Tek was founded in 1997 and has developed Raman, LIBS, NIR and UV/vis spectrometers and solutions. B&W Tek has multiple sites in China, Taiwan and Germany, and a worldwide network of over 60 distributors and sales and service into more than 45 countries.

## Waters obtains rights to DESI mass spectrometry imaging

Waters Corp., Prosolia Inc. and the Purdue Research Foundation have announced that Waters has acquired exclusive rights to desorption electrospray ionisation (DESI) technology for all mass spectrometry applications from Prosolia and PRF.

"The acquisition of DESI technology bolsters Waters' portfolio of mass spectrometry imaging innovations, a rapidly expanding MS technique for biomedical research and related applications", said Chris O'Connell, chairman and chief executive officer of Waters Corp. "DESI mass spectrometry imaging provides complementary and actionable data when compared to classical histopathology imaging technologies with major advantages in analysing the molecular fingerprint within a sample, thus delivering deeper biological insights. Ultimately, these insights will lead to better understanding of disease and enable the development of new, more effective medical therapies."

DESI imaging technology uses a charged jet of solvent depositing micro-droplets onto a sample's surface where analytes are desorbed into a gas phase at ambient pressure and temperature. Subsequently, they are drawn in and analysed by mass spectrometry.

In connection with Waters' acquisition of DESI intellectual property from Prosolia and licensing from PRF, Waters and Purdue University, where DESI was invented by a team led by R. Graham Cooks, have also established a relationship under the terms of a new license agreement. Accordingly, Waters will provide Purdue University with a Synapt G2-Si time-of-flight mass spectrometer to continue to advance research applications of DESI technology.

"Today's announcement is an important milestone in the continued growth of DESI to the benefit of scientists around the globe. We congratulate Justin and the Prosolia team for their accomplishments and look forward to collaborating with Waters as it takes DESI into the future", Cooks said.

## Collaboration between Princeton Instruments and C-SOPS on novel pharmaceutical technology

Princeton Instruments and the Center for Structured Organic Particulate Systems (C-SOPS) have announced a six-month collaboration on a novel pharmaceutical technology that enables close monitoring and control of drug manufacturing processes. The research will be carried out by Rajesh Davé, distinguished professor of chemical engineering at the New Jersey Institute of Technology and the site-leader of C-SOPS. Dr Davé will use Raman spectroscopic measurements to monitor the formation of thin oral films, which contain medicine and dissolve in the mouth without the need for water, including in the drying process during manufacturing, in order to determine drug amount, uniformity and form. In addition, he will investigate the degradation processes of active pharmaceutical ingredients in solid-dose drugs.

"We are extremely excited about this collaboration with Dr Davé and C-SOPS. We are convinced that high performance spectrometers can provide unmatched capabilities for some of the most challenging applications in the pharmaceutical industry, like process monitoring of low dose and thin film coated drug manufacture," said Dr Peng Zou, product manager at Princeton Instruments. The primary instrument to be used in this collaboration is the FERGIE spectrometer.

"We are excited to use this technology, which allows us to better understand the manufacturing of these thin films that are loaded with drug particles and, depending on how the wet film dries, how that could potentially change the way drug particles are distributed", Dr Davé said. "Without disturbing the film, this monitoring, or 'non-destructive testing', will allow pharmaceutical companies to not only improve film product quality, but guarantee their performance without additional testing, which can involve physically destroying some of the film samples."

C-SOPS works with industry leaders and regulatory authorities to improve the way pharmaceuticals, foods and agriculture products are manufactured. The group focuses on advancing the scientific foundation for the optimal design of SOPS with advanced functionality while developing the methodologies for their active control and manufacturing. C-SOPS is based at Rutgers University, and works with partners including the New Jersey Institute of Technology, Purdue University, the University of Puerto Rico at Mayaguez and more than 40 industrial consortium member companies.

An advantage of the method lies in its sensitivity. The researchers from Alicante analysed blood serum, some of which is incubated with a mixture of antibodies labelled with lanthanide polymers. The resulting immunocomplex is separated from the remaining antibody by SEC, and the concentration of tumour markers is determined by ICP-MS from the signal of the lanthanides.

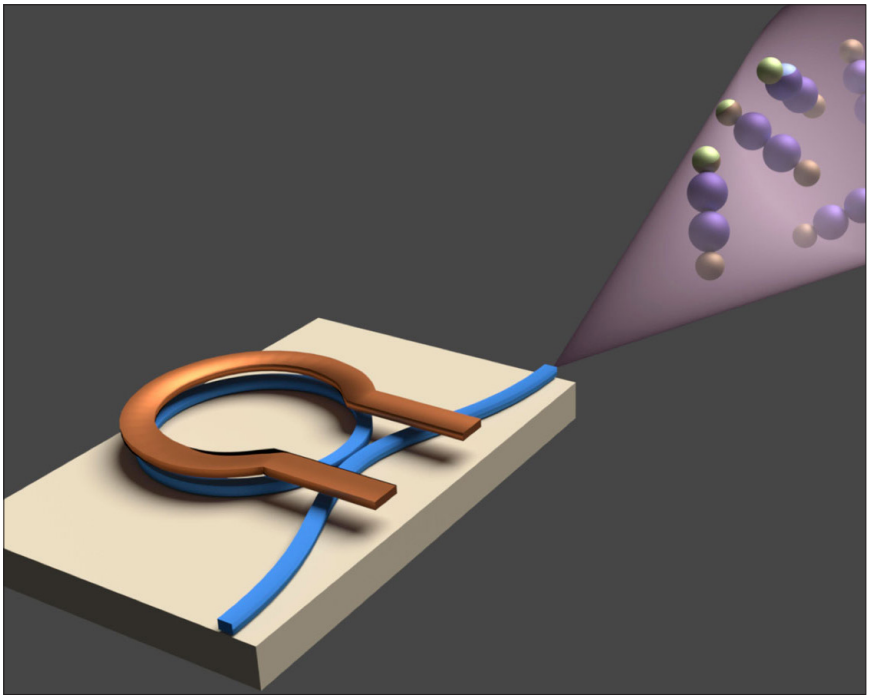
The study is part of the doctoral thesis project recently defended by Emma Pérez, which, other than being an advance in early detection and follow-up of oncological patients, also opens doors to other novel analytical methodologies based on the use of immunoassays and ICP-MS. In the food industry, for example, it could be applied to the detection of toxins at concentration levels well below those allowed by the European Union. In fact, the method could reduce the permitted levels of contamination in milk by aflatoxin M1 (AFM1) up to ten times. AFM1 represents a serious danger to consumer's health due to its carcinogenic, teratogenic and mutagenic activity, with the capacity to affect organs such as the liver, kidney or brain.

The work is reported in *Analytica Chimica Acta* (doi: 10.1016/j.aca.2018.02.056).

## New study first to demonstrate a chip-scale broadband optical system that can sense molecules in the mid-infrared

Researchers at Columbia Engineering have demonstrated, for the first time, a chip-based dual-comb spectrometer in the mid-infrared range, that requires no moving parts and can acquire spectra in less than 2µs. The system, which consists of two mutually coherent, low-noise, microresonator-based frequency combs spanning 2600–4100 nm, could lead to the development of a spectroscopy lab-on-a-chip for real-time sensing on the nanosecond time scale.

"Our results show the broadest optical bandwidth demonstrated for dual-comb spectroscopy on an integrated platform", said Alexander Gaeta, David M. Rickey Professor of Applied Physics and of Materials Science and senior author of the study, published in *Nature Communications* (doi: 10.1038/s41467-018-04350-1).



Schematic of silicon microresonator generating a frequency comb that samples molecules for chemical identification. Credit: Alexander Gaeta/Columbia Engineering

Creating a spectroscopic sensing device on a chip that can realise real-time, high-throughput detection of trace molecules has been challenging. A few months ago, teams led by Gaeta and Michal Lipson, Higgins Professor of Electrical Engineering, were the first to miniaturise dual-frequency combs by putting two frequency comb generators on a single millimetre-sized chip. They have been working on broadening the frequency span of the dual combs, and on increasing the resolution of the spectrometer by tuning the lines of the comb.

In this current study, the researchers focused on the mid-infrared (mid-IR) range, which, because its strong molecular absorption is typically 10–1000 times greater than those in the visible or near infrared, is ideal for detecting trace molecules. The team performed mid-IR dual-comb spectroscopy using two silicon nanophotonic devices as microresonators. Their integrated devices enabled the direct generation of broadband mid-infrared light and fast acquisition speeds for characterising molecular absorption.

"Our work is a critical advance for chip-based dual-comb spectroscopy for liquid/solid phase studies"' said Mengjie Yu, lead author of the paper and a PhD student in Gaeta's lab. "Our chip-scale broadband optical system, essentially a photonic lab-on-a-chip, is well-suited for identification of chemical species and could find a wide range of applications in chemistry, biomedicine, material science and industrial process control."

## New forensic DNA profiling technique on the horizon

A study recently conducted at the Circular Dichroism beamline (B23) at Diamond Light Source could lead to a new forensic DNA profiling technique. Researchers from the Ivanovo State University of Chemistry and Technology, Russia, The University of Southampton and Diamond investigated the application of specially designed DNA building blocks. The structure of DNA means it can be used as a versatile template for a variety of applications. Porphyrin-modified nucleotides in particular drew the attention of the scien-

tists of this study, as porphyrin strongly absorbs light; this molecule is derived from the natural haem and is also related to chlorophyll. They explored the properties of a zinc porphyrin 2′-deoxyuridine building block (ZnTPP-dU), but also designed a new porphyrin-derivative based on magnesium(II) 5,10,15,20-tetraaza porphine (porphyrazine, MgTAP-dU).

Both nucleosides were tested for their ability to bind to DNA, and their optical properties were analysed using spectroscopic techniques, including circular dichroism at B23. They found that the novel porphyrazine was highly fluorescent when bound to DNA, and decided to test its ability to detect forensically relevant short sections of DNA. They noted that its fluorescence was significantly increased in the presence of neighbouring adenosine nucleosides.

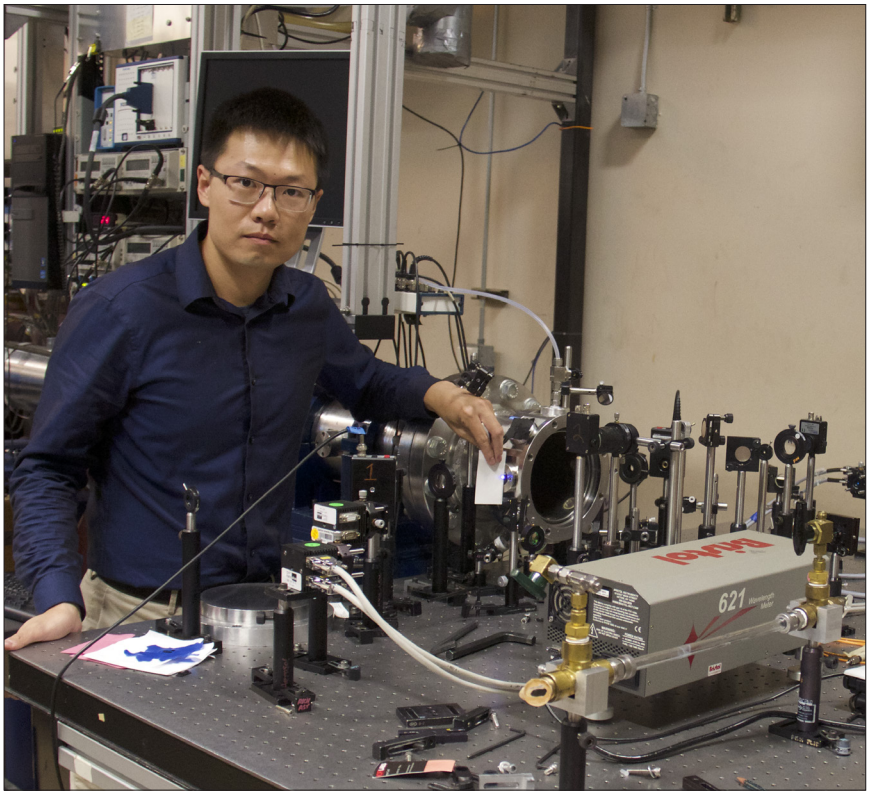
The stepwise increase in fluorescence upon increasing the number of nearby adenosines could predict the length of a section of DNA, and this makes porphyrazine highly suitable for the analysis of DNA sequences that contain multiple repeats of nucleotides. In fact, the team demonstrated that porphyrazine could quantify short tandem repeat sequences in short sections of DNA, which are used in DNA analysis of related organisms. This technique forms the basis of forensic DNA profiling to identify individuals based on their genetic material.

This new approach could see the development of other nucleosides bearing different fluorescent components to fully profile DNA.

The work has been reported in *European Journal of Organic Chemistry* (doi: 10.1002/ejoc.201800683).

## Frequency modulation spectroscopy could help development of efficient engines and fuel

Frequency modulation spectroscopy can detect hydroxyl radicals (OH) with unprecedented sensitivity. Because OH is a critical component in the combustion processes that power most vehicles, the new approach could advance the development of novel types of engines and fuels that would be more efficient and environmentally friendly.



Researchers at Stanford University have developed a novel method for measuring hydroxyl radical (OH), a critical molecule in combustion reactions, with high sensitivity. This method uses frequency modulation of ultraviolet light to eliminate noise that hindered conventional methods from accurately detecting trace amount of OH in combustion environments and paves a pathway to new regimes of combustion research that were previously not accessible. Here, Shengkai Wang is aligning the UV laser beam through the combustion reactor. Credit: courtesy of Shengkai Wang, Stanford University

"In the US, combustion produces 60% of our electricity and powers 90% of ground transportation and almost all aviation", said Shengkai Wang, a postdoctoral research fellow in mechanical engineering at Stanford University. "The ability to examine combustion processes and understand them at a more fundamental level would aid in the development of next-generation combustion strategies that can increase efficiency and reduce pollution", he said.

In *Optics Letters* (doi: 10.1364/OL.43.003518), Wang and Ronald K. Hanson, professor of mechanical engineering at Stanford, report a spectroscopy-based approach that detected levels of OH radicals at least four times lower than the previous best method used to analyse OH. Among hundreds of molecular entities involved in combustion reactions, OH is the most important because it determines whether and how fast the fuel will burn.

"OH is extremely difficult to measure, especially in the dynamic and noisy environments of fuel combustion, because it is highly reactive and present in very low concentrations", said Wang. "Our approach paves the way to practical detection of OH in the parts per billion range."

The new approach could also be useful for applications such as studying atmospheric chemistry, where OH is a key player in the formation and depletion of ozone according to Wang.

One bottleneck to commercialising new types of engines or optimised fuels is that their combustion chemistry is not fully understood due to a lack of sensitive analysis methods. To solve this problem, Wang and his

colleague developed frequency-modulation spectroscopy using ultraviolet (UV) light. Rather than using one laser wavelength, frequency modulation spectroscopy examines the differences in light absorption between multiple wavelengths, allowing any noise common among the readings to be subtracted. The method also shifts the signal coming from OH absorption to a higher frequency, thereby eliminating any low-frequency drift that challenges OH measurement.

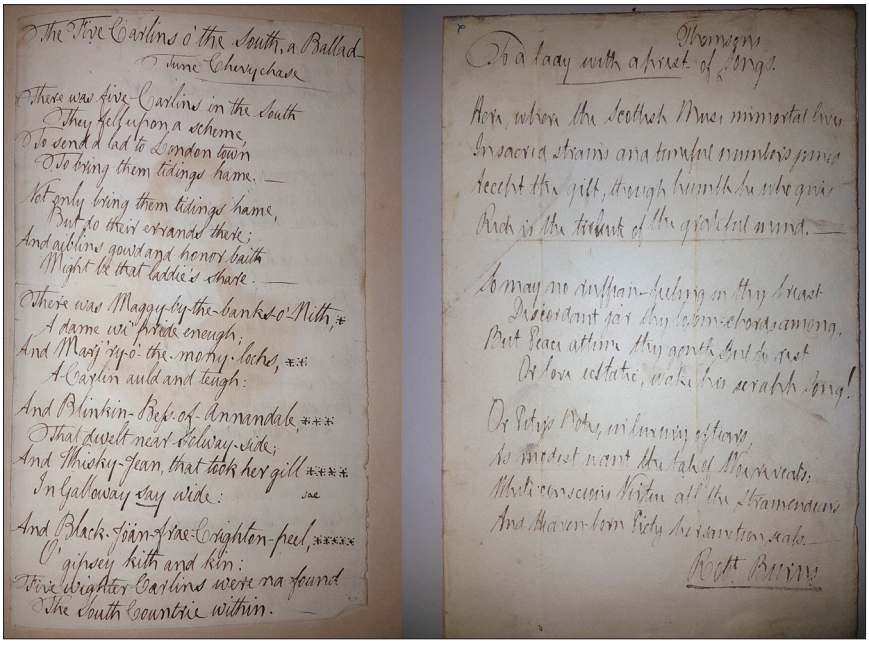
"The general idea of frequency modulation spectroscopy has existed for a while, but we are the first to demonstrate its applicability to detecting OH at this particular wavelength range", said Wang. "One reason this hasn't been done before is that the high-quality UV laser source necessary to measure OH absorption [only] became available very recently."

The researchers tested their new approach by studying the combustion reaction of a representative fuel, isooctane, in a controlled reactor. They were able to achieve a minimum detectable absorbance of $3.0 \times 10^{-4}$ at a temperature of 1330 K. This is equivalent to detecting 85 ppb of OH over 15 cm optical length and is four times better than the best record previously reported.

As a next step, the researchers plan to incorporate better optical components, which they say could improve the sensitivity by another order of magnitude. They also want to make the equipment more portable so that it could be transported on a cart to various specialised testing facilities. A portable system would also allow them to use the approach to make measurements in practical engine conditions and to eventually adapt the method for making measurements in realistic engines and combustors.

## Mass spec reveals the real Burns

Authenticating historic manuscripts can be a complicated and at times destructive process, with parts of the paper or ink damaged. However, a cross-disciplinary team of researchers from the University of Glasgow, UK, have found a novel way to accurately authenticate ancient documents in a minimally destructive way.



Left: a picture of an original Burns work, "The Five Carlins". Right: a picture of a letter, a forgery, in the hand of Burns.

The findings, published in *Scientific Reports* (doi: 10.1038/s41598-018-28810-2), use direct infusion mass spectrometry, which enables minimally destructive sample extraction directly from the paper surface. The team analysed the ink and paper of both authenticated and forged Robert Burns' manuscripts to produce a support vector machine (SVM) classifier that could accurately distinguish true Burns handwriting from the fakes. The scientists were also able to distinguish which inks Burns used to write each of his poems, whether it be ivory black, iron gall or a mixture of the two.

The project and findings are the result of collaboration between Dr Karl Burgess of the University's Glasgow Polyomics and the School of Critical Studies, led by Professor Gerard Carruthers, Francis Hutcheson Chair of Scottish Literature. With the help of Burns collector Dr William Zachs, the team were able to look at originals and fakes to ascertain the type of ink used, helped by a handwritten book owned by Dr Zachs which contained recipes for all sorts of liquids, including inks.

In total, the team tested 12 documents; three real Burns' documents selected from different periods of the bard's life and nine fakes from the 1890s by notorious forger Alexander Smith. The scientists were able to lift ink from the copies using a simple pipetting process that could be performed outside the laboratory, and that crucially did not visibly damage the original material. Tests were initially performed on one of Alexander Smith's handwritten 150-year old fakes before being performed on real Burns material.

Details of the ink and paper from the 12 documents were analysed and machine-learning algorithms were used to develop the SVM classifier, which could then be used to help predict real or fake Burns manuscripts. Sixteen significant differences were found distinguishing the Burns and Smith manuscripts. Significant differences between the inks and paper were also detected in Burns manuscripts.

## On-site analysis of precious metals in metallurgical waste spills

Precious metals come in limited supply but are in high demand. They are mainly sourced through mining, but the possi-

bility of recycling them from metallurgical waste leachates (waters that have passed through the treated materials during mineral processing and thus contain some of the compounds present in the minerals) is attracting growing attention. To this end, compact and portable instruments to perform the analysis of wastewaters in on-field rapid analysis are highly desirable to improve the efficiency of the recovery of precious metals.

Liquid-electrode plasma-optical emission spectrometry (LEP-OES) has emerged as a tool to implement on-site analysis of elements in aqueous matrices, as it is portable and much less costly than traditional methods. However, when the concentration of noble metals is very low, as is the case for precious metals in waste spills, the sensitivity of the technique become insufficient to produce accurate analysis—one of the problems being interference by several ions. In this case, analyte separation and enrichment steps have to be included in the analysis of the samples for accurate detection of the precious metals.

This is what Suman Barua, Ismail M.M. Rahman, Hiroshi Hasegawa and colleagues from Kanazawa University and Fukushima University did, reporting the first application of LEP-OES in combination with a solid-phase extraction (SPE) system (which is used as the pre-treatment step to eliminate the competing ions and to enrich the noble metals) for the rapid on-site simultaneous analysis of the precious metals gold, palladium and platinum. The SPE parameters were optimised to maximise retention and recovery of the precious metals; the LEP-OES parameters to maximise the emission peaks for the individual elements.

The method was tested both on a certified reference material for wastewater and on real aqueous waste samples, from which more than 95% of the precious metals were recovered. The high-precision on-site measurements could be performed in less than 15 min, opening the way to practical analysis of the precious metal content of wastewaters.

This work was published in *Sensors and Actuators B: Chemical* (doi: 10.1016/j.snb.2018.05.132).

## Liquid-electrode plasma-optical emission spectrometry

In liquid-electrode plasma systems, a liquid sample is inserted in a micro channel at the ends of which a high voltage is applied, generating a microplasma that acts as the excitation source for emission spectrometry. Liquid-electrode plasma-optical emission spectrometry is an analytical method that has the advantage of not requiring a nebuliser. Moreover, it can operate on batteries and is compact and portable.

## Imaging technology for nanosatellites

A project led by the University of Strathclyde, UK, is investigating the production of a multispectral imaging (MSI) device which is a fraction of the size of conventional instruments. It could be installed in nanosatellites and used to monitor climate change, observe the activity of oceans, detect forest fires or track shipping traffic.

The study has received £719,000 as one of seven successful projects to secure funding from the UK Space Agency's (UKSA) Centre for Earth Observation Instrumentation (CEOI). Researchers from Strathclyde's Department of Physics are working with partners, led by product design company Wideblue, to produce MSI technology with a compact payload. It will be designed, built and then tested by taking images during a flight attached to a drone.

A commercial MSI satellite can be up to 5.7 × 2.5 × 2.5 m and weigh 2.8 tonnes. The new device could fit on a more affordable 4 kg satellite of 10 × 10 × 30 cm size and would orbit around 500 km above Earth.

Dr Daniel Oi, a Physics Lecturer at Strathclyde and lead researcher in the project, said: "Because of the novel way it operates, this instrument could open up ways of doing Earth observation which are different from conventional operations. As nanosatellites are smaller, they don't have the capacity to take a lot of data, process it and communicate it. The technology we are developing allows us to reduce the amount of data collected, with sensitivity to specific events or targets, and will enable more efficient monitoring of Earth. Instead of a small number of very expensive MSI satellites, our instrument could be mounted on many nanosatellites to monitor the globe continuously. No satellite can be in two places at once, so operating in this way can enable the right data to be collected at the right time. The early results of our research have been highly promising, and the project is part of a significant and growing space industry in Scotland."

Traditional satellites can be replaced with nanosatellites for remote sensing, thanks to a new multispectral imaging device being developed by the University of Strathclyde.

ARTICLE

# Infrared ion spectroscopy: a bioanalytical tool for the identification of unknown small molecules

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## Introduction

As an analytical technique, mass spectrometry excels by its high sensitivity, its ability to analyse mixtures and its high throughput capabilities. Nonetheless, while knowledge of the elemental composition of an unknown analyte (by virtue of accurate mass measurement) is an important piece of information, it generally does not allow an unambiguous identification. A mass measurement lacks the chemical specificity of a spectroscopic measurement.

Infrared ion spectroscopy combines the separation capabilities of mass spectrometry with the structural information from infrared spectroscopy. Figure 1 illustrates how infrared ion spectroscopy is implemented in terms of instrumentation. Gas-phase ions $M^+$ are generated by ionisation, in this case electrospray ionisation. Electrospray ionisation is one of the softest ionisation methods that allows intact molecules to be transferred from solution to the gas phase via evaporation from droplets. Ions are then generally accumulated and stored in an ion trap, which is a highly versatile device. Here, ions can be mass isolated, so that only masses of interest are retained, while all other ions are discarded. An ion trap also conveniently focuses ions in space, so that they can be irradiated with a photon source. The purpose of irradiation is to induce photodissociation, which manifests itself as a change in mass-to-charge ($m/z$). This can be ascertained by measuring the mass spectrum after irradiation. Using a tuneable light source, the photodissociation of an ion can be probed as a function of photon frequency. This is illustrated for the non-covalent complex $M^+$•Tag, and here more specifically for PABA•$CH_3CN$ (*para*-aminobenzoic acid complexed with acetonitrile) at $m/z$ 180, which dissociates to bare PABA at $m/z$ 138. The complex dissociates at some infrared frequencies, but not at others, which is related to the vibrational modes of the complex. The photodissociation yield as a

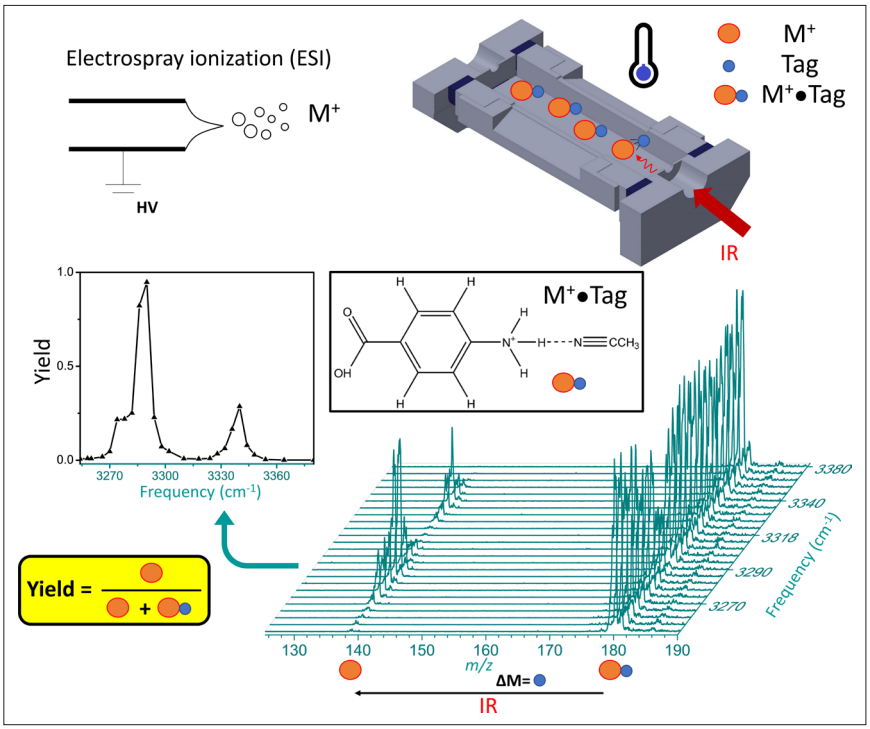


**Figure 1.** Schematic showing ionisation of analyte species $M^+$ via electrospray ionisation. Trapped tagged ions, $M^+$•Tag, are irradiated by infrared photons. In case of resonant absorption, some of the ions in the population dissociate via loss of the tag, which is verified in the mass spectrum. By monitoring the photodissociation yield as a function of infrared frequency, the infrared "action" spectrum can be obtained.

function of infrared frequency is thus an indirect measure of the inherent infrared spectrum of the ion. This is a so-called "action" spectroscopy approach, where changes in the absorbing species are measured, as opposed to an absorption approach, where changes in light intensities are measured. It should be noted that the "action" spectroscopy approach is vastly more sensitive, as the number of ions in a mass spectrometer is generally too low for absorbance measurements. It also follows that ion spectroscopy has high sensitivity, because of the high sensitivity of mass spectrometry, even if scanning the infrared frequency may take time, and thus consume more sample.

The role of the tag in Figure 1 is to report on photodissociation. Ideally, the tag does not distort the infrared spectrum of the molecule $M^+$ too much. Solvent tags, such as acetonitrile have rather strong binding, and therefore affect the infrared spectrum. More "innocent" tags, such as $N_2$, are much more weakly bound, and thus distort the infrared spectrum far less. Due to the low binding energy, ions must be cooled to low temperatures to generate $M^+ \bullet N_2$ complexes. This can be achieved in cryogenic traps, which can be cooled down below 30 K.

Infrared ion spectroscopy is well placed to address current limitations in analytical mass spectrometry of small molecules, notably in metabolomics and drug analysis. In both of these areas of research, current methodologies do not allow identification of true unknowns, as the identification is limited to mass spectral databases of known compounds. As is well known from Fourier transform infrared (FT-IR) spectral databases, molecules with similar structures also have similar infrared spectra. This correlation is the key premise for the power of infrared ion spectroscopy in the structural characterisation of unknowns.

## Cryogenic infrared spectroscopy

The chemical specificity of spectroscopic measurements depends on the spectroscopic resolution. In gas-phase spectroscopy, resolution is maximised in low-temperature experiments. In mass spectrometry-based instrumentation, it is possible to cool ions down in cryogenic traps. Figure 2 contrasts infrared "action" spectra of the amino acid tryptophan, recorded at room temperature and at cryogenic temperature. It is clear that the cryogenic spectrum is much more information rich, as there are many more spectral features that can be distinguished. The differences in the infrared spectra are not merely due to differences in the temperatures of the ions, the spectroscopic schemes also differ. In room-temperature spectroscopy, covalent bonds must be broken. This requires absorption of multiple photons, which lead to band shifting and broadening. In the cryogenic spectroscopy scheme, the van der Waals $N_2$-tagged ion dissociates upon absorption of a single photon. The fact that a single photon is sufficient to induce photodissociation has additional advantages: 1) one returns to a linear spectroscopy regime, where photodissociation yields can directly be compared to absorption cross sections and 2) the required photon fluence is lower, meaning that benchtop light sources can cover the entire spectral range (550–4000 $cm^{-1}$), as opposed to expensive free electron lasers. One caveat with cryogenic experiments is the observation of multiple conformers. In Figure 2, some of the bands are associated with two different conformers, A and B.[1,2] The relative intensities of these bands will depend on the relative presence of either conformer, which may differ based on experimental conditions in the cryogenic trap.

## Tuneable light sources

The fact that infrared spectra can now be recorded with benchtop light sources means that these measurements are accessible to individual investigator laboratories, as opposed to free electron laser user facilities. Currently, the state-of-the-art benchtop light sources for infrared "action" spectroscopy are optical parametric oscillators/amplifiers. These light sources are based on non-linear crystals (e.g. $KTiOPO_4$), where a pump photon, usually a 1064 nm Nd:YAG photon, is ultimately converted into a tuneable infrared output between 2000 $cm^{-1}$ and

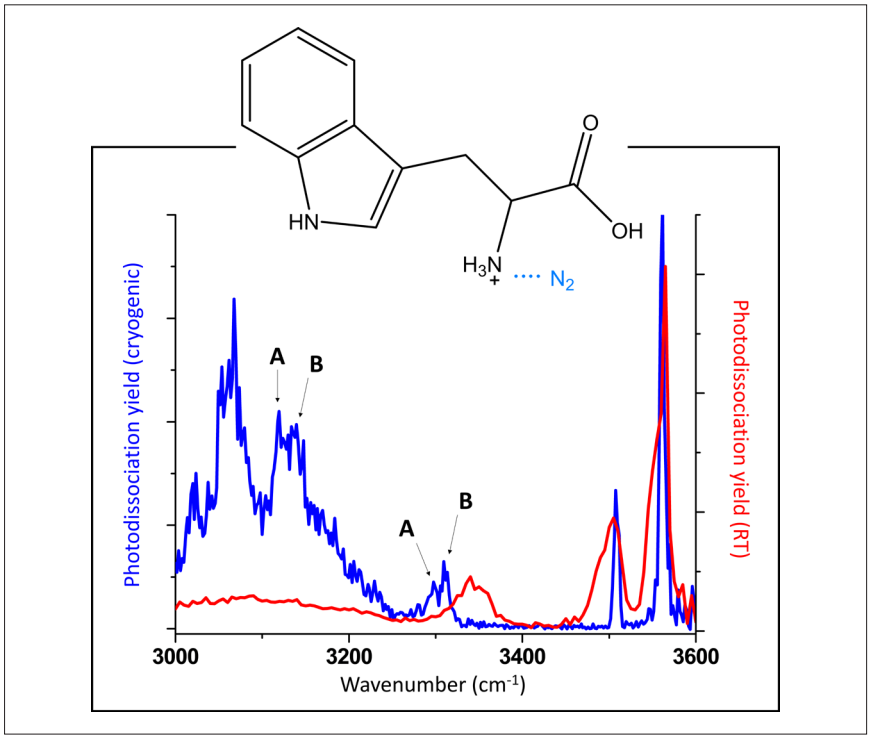


**Figure 2.** Comparison of infrared "action" spectra of protonated tryptophan recorded at room temperature and at cryogenic temperature. Some of the bands in the cryogenic infrared spectrum are tentatively assigned to different conformations (A and B).

4400 cm$^{-1}$. Addition of another nonlinear crystal (e.g. $AgGaSe_2$) can extend this output down to 550 cm$^{-1}$.

Nonetheless, the operation of nonlinear optics-based light sources requires experience, and this imposes some challenges for making the technique widely available. The continuous development of turnkey semi-conductor light sources, such as quantum cascade lasers, could change this picture in the mid to long term.

## Mass spectrometry instrumentation

The largest impediment to making cryogenic infrared spectroscopy a routine tool in bioanalytical mass spectrometry is the unavailability of commercial cryogenic traps. All instruments to date have been custom built. Proof-of-principle experiments have shown that high-quality data can be recorded, but little emphasis has been placed on maximising sensitivity for "real" sample analysis, nor on optimising the duty cycle of the experiment. The requirement of scanning the infrared frequency makes infrared spectroscopy an inherently slow technique. It typically takes tens of minutes to record an infrared spectrum. This is further compounded by the fact that generally only one analyte is probed at a time. This makes infrared ion spectroscopy a very low throughput technique. A potential remedy to the duty cycle problem lies in the predictable photodissociation of tagged ions, involving the loss of the tag. Because tagging and detagging occurs via a known mass change (i.e., $\Delta M$ = mass of tag, see Figure 1), the infrared spectra of a number of tagged analytes can be measured in parallel in a multiplexed approach, as long as their masses do not overlap. This has already been demonstrated in proof-of-principle experiments.[1]

## Interpreting infrared spectra

Now that high-quality cryogenic infrared spectra on low-concentration samples (i.e., nM) can be recorded in a reasonable time (<30 min), the remaining question that needs to be addressed is how an infrared spectrum of an unknown can lead to identification. Figure 3 illustrates the basic strat-

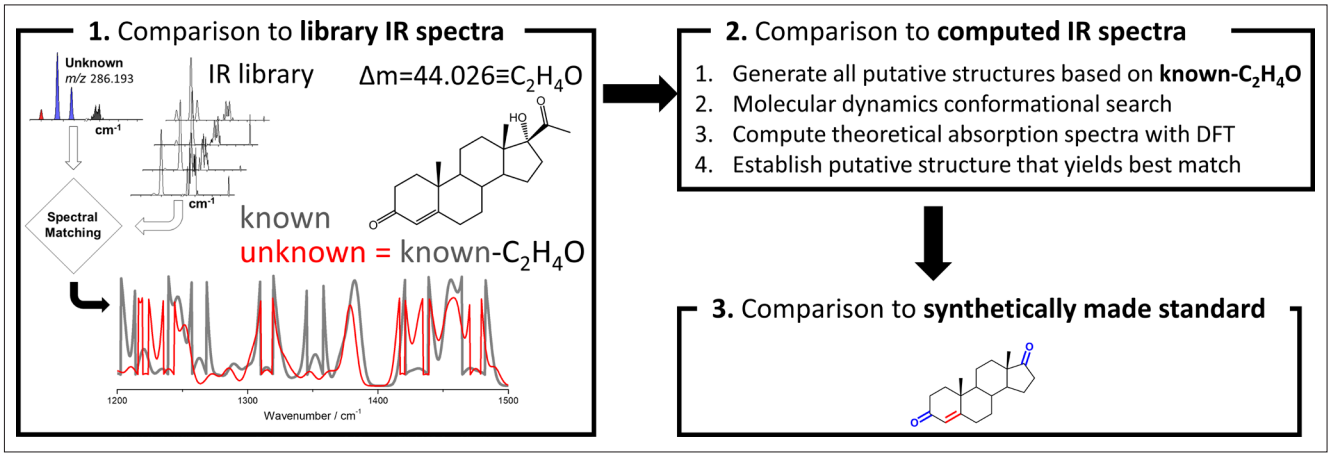


**Figure 3.** Workflow for chemical characterisation of unknown analytes based on accurate mass measurement and experimental cryogenic infrared spectrum.

# METLIN Mass Spectral Database

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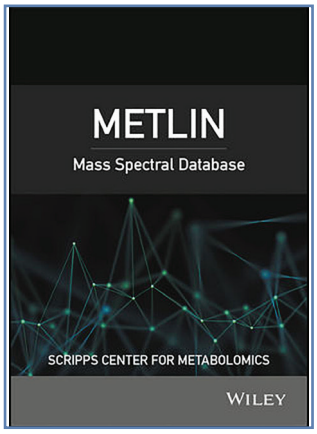


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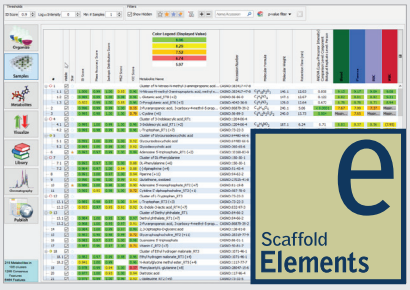


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egy for characterising analytes with unknown structures. A key component involves the comparison of the infrared spectrum of the unknown with previously catalogued infrared spectra of standards to determine which known molecule it is most similar to; this, of course, presumes that infrared spectral similarities correlate strongly with structural similarities. Especially the fingerprint region (1200–1500 $cm^{-1}$) is anticipated to be a powerful probe in this respect. The accurate mass measurement of the unknown would be expected to yield the elemental composition, which in combination with the spectral matching could then be used to generate putative candidate structures. With an infrared library that is well represented in various chemical classes of molecules, such an approach would be expected to give a good guess on what the unknown may be. Further refinements are possible via computational approaches. Computational chemistry involving molecular dynamics and density functional theory yields the theoretical infrared spectra of putative candidate molecules which can be compared to the experimental spectrum. Thus, computational approaches can be used to rank the candidate structures from most to least probable. An ultimate identification will require synthesis of the putative candidate and match with the experiment.

## Conclusions

In summary, the high information content of cryogenic infrared spectra of ions has the potential to make the technique the gold standard for molecular identification of small molecules in mass spectrometry.[3] The relatively long measurement times (i.e., minutes to an hour) would likely make this a high-end method for off-line analysis of samples where conventional approaches have failed. Over the coming years, the technique is anticipated to make an impact in small molecule analysis, such as metabolites, drugs and classes of molecules containing many isomers (e.g. saccharides), as already demonstrated in a number of proof-of-principle studies.[1,4–7]

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# Spotlight on nuclear magnetic resonance: a timeless technique

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## Introduction

Nuclear magnetic resonance (NMR) spectroscopy has evolved immensely since its early use solely in physics. Since then, chemists have come to rely on NMR for determining molecular structure, and scientists now use this method for a broad range of applications in a diverse range of fields. For example, a recent poll of methods utilised by pharma discovery scientists searching for the next new blockbuster drug highlights the dominance of NMR spectroscopy in fragment-based lead generation.[1] In addition, workers investigating food fraud used NMR to identify imitation cheese and ice cream—products in which the milk fat and/or milk protein had been replaced with cheaper, non-milk components, such as soy, starch or vegetable oil.[2]

This article looks back at the work of NMR's founding scientists and reflects on key developments that have propelled NMR to its position today—as the go-to technique for scientists looking for an information-rich and non-destructive analytical tool to reveal the structure, identity, concentration and behaviour of molecules in solid or liquid samples.

## In the beginning

The earliest NMR pioneers developed and built their own instrumentation. As the technology advanced, few chemists were prepared to invest the time and money required to build their own spectrometers, so the full impact of NMR as a new analytical technique was not realised until they could be purchased from commercial companies. Such early companies included Varian Associates (CA, USA), Japan Electron Optics Ltd, Associated Electrical Industries (UK), Perkin Elmer Corporation (UK) and Trüb Täuber (Switzerland, later Bruker-Spectrospin). These companies did not stand to make much money from NMR, as the market was so limited at the time. The definitive commercial breakthrough came with the introduction of the Varian A60, which paved the way for high-resolution NMR in organic chemistry.

Although there are small number of key players in the modern NMR market, such as JEOL, Nanalysis, Oxford Instruments and Thermo Fisher, NMR is indivisible from the early development of the two key companies that went on to establish the field—Bruker and Varian. Günther Laukien, founder of Bruker, dedicated his post-doctoral studies to NMR spectroscopy and, in 1958, published his pioneering paper on high-frequency NMR.[3] This described the theoretical aspects of what was known at the time, while also covering the practical considerations of constructing experimental systems.

Varian was established in 1948 within the Stanford Industrial Park by scientists from Stanford University. One of the early goals of the company was to commercialise the co-discovery of NMR spectroscopy by Felix Bloch in 1946. Subsequently, Edward M. Purcell and Felix Bloch were honoured with the Nobel Prize for Physics in 1952 for this work.

At around the same time that Laukien was studying, Varian had begun building the first commercial high-resolution spectrometers. They were based on continuous-wave sweep methods and electromagnets, and designed for use in analytical chemistry. When Laukien founded Bruker Physik AG in 1960, its earliest NMR spectrometer's application was restricted to physical research laboratories, rather than for routine chemistry applications like Varian's. Laukien's acquisition of the Trüb–Täuber company (to become Spectrospin AG) enabled the newly-formed Bruker-Spectrospin to extend to high-resolution NMR. This, in combination with Bruker-Spectrospin harnessing the Fourier transformation (FT) method with the first FT-NMR spectrometer, eventually set the company up to overtake Varian as market leader. A possible oversight from Varian at the time as to the significance of FT-NMR, possibly due to the original founder's replacement by sales-driven individuals without a technical background, allowed Bruker to overtake.[4]

The intense competition between these two companies drove many of the early developments and innovations in NMR for the next 20–30 years. In addition, the inputs from collaborations with several key scientists were crucial to the technological development and commercial success of these companies. For example, Dr Werner Tschopp and Dr Tony Keller contributed immensely to Bruker's success as a result of the acquisition of Spectrospin. Innovations from Keller led to the first commercial implementation of the Fourier concept at Bruker. See Table 1 for a summary of some key milestones.

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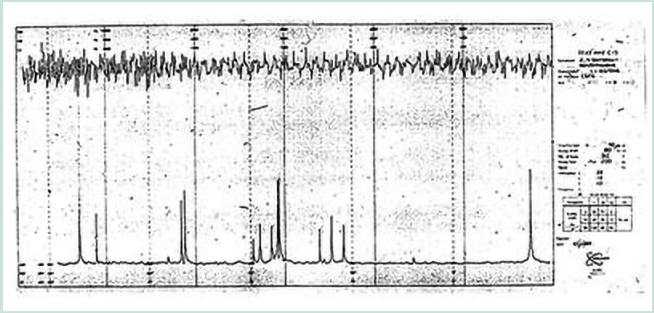
**Table 1.** Early NMR development.

| | |
|---|---|
| 1937 | Nuclear spin first measured in by Isidor Isaac Rabi in lithium isotopes and protons. |
| 1943 | Nobel Prize for Physics awarded to Rabi for this work. |
| 1946 | Discovery of nuclear magnetic resonance spectroscopy by Edward M. Purcell and Felix Bloch. |
| 1948 | Varian established in USA. |
| 1956 | Nobel Prize for Physics awarded jointly to Edward M. Purcell and Felix Bloch for their 1946 discovery. |
| 1961 | Introduction of the first high resolution NMR spectrometer—the Varian A60. |
| 1960–65 | Professor Günther Laukien founded Bruker and the development of its first NMR spectrometers began with the production of laboratory magnets and power supplies.<br>Establishment of Spectrospin AG, a company initially founded as Trüb & Täuber in Zurich before being acquired by Bruker.<br>First NMR, KIS (nuclear induction spectrometer), operated at 25 MHz using a permanent magnet.<br>KIS 2 introduced for high-resolution spectroscopy (90 MHz). |
| 1964–66 | Ground-breaking research on the use of Fourier transform algorithm by Ernst and Anderson published. FT-NMR first described. |
| 1967 | Culmination of Bruker/Spectrospin developments—introduction of first fully transistorised NMR instrument, the Bruker HFX 90.<br>  |
| 1969 | The world's first commercial FT-NMR spectrometer system introduced by Bruker.<br>  <br>Carbon FT-NMR spectrum presented by Dr Tony Keller in 1969 at the Pacific Conference on Chemistry and Spectroscopy in Anaheim. |
| 1970–75 | The work on FT-NMR by Ernst and Anderson in 1966 required minicomputers to generate tapes that could be then be processed on larger computers. The advent of smaller, cheaper, and faster computers in the early 1970s made FT-NMR all but ubiquitous. |

## From expert to everyday

After around 30 years of development, NMR was a maturing technique and was widely applied; there was hardly a paper in organic chemistry that did not report NMR data. When considering the developments from those initial NMR systems, three key areas can be identified that led to the systems today: larger magnets to improve sensitivity; improved probe technology and new designs to enhance performance; and a rapid increase in computer power to enable software to be developed that simplifies data processing and opens up the technique to non-experts. Table 2 highlights some key milestones in this "second-wave" of development. Interestingly, several of the pioneers and early adopters of NMR have published personal accounts and reviews of the development of the tech-

**Table 2.** Key developments in NMR from the 1980s to the present: decade by decade.

| | |
|---|---|
| 1980s | 2D NMR development comprised a huge step in the collection and analysis of data. Structure analysis of small and large molecules became possible and proved very useful in molecular biology and chemistry.<br><br>These systems provided a tool that an everyday chemist could use. |
| 1990s | Higher dimensional spectroscopy (3D) developed. This was made possible by rapid developments in computer technology. The Fourier transformation of three and even higher dimensional NMR data can now be performed in a matter of seconds. Much larger protein molecules can now be analysed.<br><br>Cryogenic probes first developed—significant reduction in noise from random thermal motion and this, together with tuned electronics, delivers around a five-fold enhancement in signal-to-noise ratio compared to an equivalent room temperature probe.<br><br>In 1991, Richard Ernst was honoured with the Nobel Prize for Chemistry for his contributions to the development of the methodology of high-resolution NMR spectroscopy—work that begun with his Fourier transform research in the mid-1960s. |
| 2000s | Developments in cryogenic probes further improve performance, ease of use and system automation.<br><br>In 2002, Kurt Wüthrich won the Nobel Prize in Chemistry, for his development of NMR spectroscopy for determining the three-dimensional structure of biological macromolecules in solution. |
| 2010s | Bruker introduces world's first commercially available solid-state dynamic nuclear polarisation-enhanced NMR system (DNP-NMR). Microwave irradiation is used to transfer polarisation from unpaired electron spins to nuclear spins. As a result, polarisation enhancement yields a factor of up to 200 gain in sensitivity for solid-state NMR.<br><br>Varian acquired by Agilent in 2010. Agilent exit the NMR business in 2014. |

nique through the decades from 1980 to 2010.[4–6]

## Pushing the boundaries: current trends

The reach of NMR continues outside its legacy applications. Solid-state NMR has developed rapidly in the past decade, particularly in the field of materials science. The technique can be used to solve structural questions for batteries, polymers, crystalline solids and amorphous solids, particularly in disordered materials. Battery science, for example, is the subject of growing research interest due to the focus on electric cars and renewable energy storage. Solid-state NMR can provide insights into the structure, local order, molecular mobility and chemical processes in batteries, allowing researchers to study the composition and chemical reactions during charging and discharging, as well as electrical and magnetic properties. Recent developments in high magnetic fields and probes make low gamma nuclei much more accessible with solid-state NMR, while recent developments in very fast magic angle sample spinning enable the study of highly anisotropic systems, such as the paramagnetic materials often used in batteries.

Although an extremely useful technique, NMR is not as sensitive as other methods. The sensitivity of solid-state NMR for material science, pharmaceutical and biological solids applications can be significantly enhanced, however, using a dynamic nuclear polarisation-enhanced NMR system (DNP-NMR). DNP experiments transfer polarisation from electron spins to nuclear spins, for large signal enhancements and reduced signal averaging time. There is a huge capacity for DNP-NMR to become a routine method.

Another significant change in the application of NMR spectroscopy is in metabolomics. By collecting large amounts of spectra and gathering underlying data on metabolites, statistical analysis can reveal markers for a certain disorder or disease. Once a model has been established, the measurement of a single sample allows the classification of that sample as normal or abnormal—and even allows a diagnosis as to the nature of a disease. This takes NMR and places it in the hands of clinical scientists. They can ask: is this what I expected? And answer questions with "yes" or "no".

In biopharma, researchers are now using NMR for the characterisation of the structure of monoclonal antibodies (mAbs). Another application of NMR in scale-up or production of biologics is the monitoring of the composition of growth media. Recognising the depletion of certain nutrients or the accumulation of potentially toxic metabolites can significantly improve yield as well as the efficiency of the fermentation.

The use of fluorine in the pharmaceutical industry has dramatically increased over the past few years. Today, five of the top ten selling small molecule drugs contain fluorine. $^{19}$F NMR offers a unique method in drug discovery, but also in the characterisation and quantification of fluorine-containing molecules. This has driven the launch of several cryoprobes that are capable of observing this nucleus with very high sensitivity.

## Conclusion

More than 70 years ago, a talented scientist first measured nuclear magnetic spin, work that resulted in the award of a Nobel Prize in 1943. Over the period from the mid-1950s to 2010, a small group of companies drove the development of increasingly sophisticated NMR spectrometers for a growing number of applications. Traditionally, larger instrumentation conferred higher quality results, but a new wave of benchtop NMR systems have proven their use in a range of laboratories, as well as in quality control and teaching applica-

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tions, and in clinical diagnostics. A select group of companies, including Magritek, Nanalysis and T2 Biosystems, are developing ever more compact systems (the smallest being handheld devices), separate from the manufacturers of larger instruments.

There are a number of reasons why NMR is the method of choice for a broad range of analytical laboratories: it provides a non-destructive view of molecular dynamics in the solid state or solution, leaving samples intact for further analysis. The abundance of established methods and diversity of instrument size and sensitivity enables almost any analytical laboratory to utilise NMR for characterising molecular structures, monitoring the composition of mixtures, studying molecular dynamics and interactions, and quantifying known and unknown components.

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Dr Anklin collected his first NMR spectra in 1978 as a student at ETH in Zurich, Switzerland. He started work at Bruker in 1984, in Switzerland, as an application scientist and after four years he moved to the USA. He has been directly involved in some of the milestones of NMR application development. Currently, he holds the position of VP at Bruker Biospin's facility in Massachusetts, USA.

## NMR basics

NMR relies on a property of certain atomic nuclei that causes them to absorb, then re-release, electromagnetic energy at characteristic frequencies. Shifts in the usual response frequency for a given isotope provide information about their immediate environment, including influences from nearby electrons and magnetic nuclei, making it possible to infer molecular identity, geometry and more.

Below is a high-level overview of the process.

### *Sample preparation*

NMR requires, in general, very little sample preparation. For liquids NMR the material is dissolved in a suitable solvent. Liquid samples can even be measured in the natural state. For solid samples NMR the materials are typically packed into a small diameter cylindrical rotor.

### *Sample introduction*

A thin-walled glass tube containing the sample is placed inside an NMR probe which consists of a radio frequency coil and tuning circuitry, which in turn sits inside a powerful magnet at the heart of the NMR spectrometer. The magnet causes susceptible atomic nuclei within the sample to align with its field, giving them a consistent resting alignment. NMR specifically applies to nuclei that contain an odd number of protons and/or neutrons, for example, $^{1}H$ or $^{13}C$. These nuclei exhibit a built-in magnetic moment and angular momentum that together give the nuclei a property called "spin". A strong enough magnet will cause these nuclei to align their spins with its field.

### *Data acquisition*

The radio frequency coil releases one or more radio-frequency pulses at the right frequency to perturb specific nuclei, then detects the energy released as the nuclei "relax" back to their resting alignments in a process called free-induction decay (FID). Because the FID signal can be quite small relative to background noise, multiple acquisitions are often averaged. That signal is then converted by Fourier transformation into an NMR spectrum showing the frequencies at which the nuclei responded.

### *Data interpretation*

Well-characterised differences in the response frequencies for a given isotope reveal the electromagnetic influences of neighbouring electrons ("chemical shift"). Splitting of peaks into sub-peaks indicate magnetic influences of neighbouring nuclei ("spin coupling") giving information about the number and geometry of these. The NMR signal is also directly proportional to the number of spins present in the sample, thus making NMR a primary ratio quantitative method. Customised sequences of RF pulses tease out specific details about a sample, sometimes probing multiple nuclei. Advanced software can simplify analysis and interpretation, and automate many aspects of data acquisition, analysis and reporting.

# Are your spectroscopic data FAIR?

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Let us start with a definition: FAIR stands for Findable, Accessible, Interoperable, Reusable. Surely a clear target for anyone responsible for operating academic or industrial laboratories. Let me (AND) follow up with a confession… I had previously just thought of FAIR as another offering originating from the bioinformaticians around Open Science publishing. However, I learnt very quickly that what started as a movement to improve intelligent access to Open Science and supporting data contains all the tools and methods of working to have the potential to be extremely important in all our daily work. It is equally applicable as a time-saving strategy for confidential information located and retrieved inside a company. It is perhaps worthwhile to note that FAIR does not necessarily imply free. This column has mentioned FAIR once before, in relation to Henry Rzepa's NMR data repository,[1] but had not really gone into any depth.

Why explore this topic now? Well Leah McEwen, Chemistry Librarian in the Clark Physical Sciences Library at Cornell University in the USA, with assistance from David Martinsen (30 years' experience with the American Chemical Society publishing arm) organised and ran a very successful workshop under the auspices of the International Union of Pure and Applied Chemistry (IUPAC) and the Committee on Data of the International Council for Science (CODATA). "Supporting FAIR Exchange of Chemical Data through Standards Development" was held on 16–17 July 2018, hosted by the University of Amsterdam.[2] The workshop was co-sponsored by the IUPAC Committee on Publications and Cheminformatics Data Standards (CPCDS), their Subcommittee on Cheminformatics Data Standards (SCDS), and CODATA, and was attended by some very influential people. Richard Hartshorn, the current Secretary General of IUPAC, flew in from New Zealand and had some strong words to say about the essential need to understand how our next generation of scientists will expect us to have kept up with ensuring the provision of well-curated, reliable scientific data available at a single click.

If we can regularly find out what the President of the USA is thinking in his bathroom at 7:30 am in the morning, why do I get four pages of text hits when searching for a simple fact like the name of element 113? I spoke to my mobile phone and it told me immediately the correct answer and the reason behind the naming—but sourced from Wikipedia, not IUPAC. In an age of deliberate falsehoods and alternative truths being published and widely distributed in the service of some ideology or other, it is ever more important that reputable international bodies keep abreast of the current technological advances for information distribution. Having systems which exhibit the FAIR principles promises to make it much simpler to locate peer-reviewed, real scientific data in a form that we (and our IT support systems) need.

For some thoughts from Leah on libraries in transition, see an interview recorded at the Beilstein Open Science Symposium (22–24 May 2017).[3]

## Can you call yourself FAIR?

In March 2016, Mark D. Wilkinson and a host of co-authors brought together current thinking on how we should all make sure that we improve accessibility to the data we generate.[4] An underlying assumption of FAIR is that it applies equally to human and machine interaction with scientific data. So, there is enormous emphasis on standardisation of metadata so that machines (such as my mobile phone) have far more information available to support access without the need for human interaction (like sifting through four pages of hits in text format). This approach is quite ground-breaking, as previous initiatives have almost singly focussed on improving retrieval systems for direct human consumption. Clear "false positives" are often ignored by us almost without thinking, but computer systems find that much more difficult and so need to be "fed" with much better accompanying information to provide appropriate

context. What I like about the approach in this seminal work is the fact that it is easily understandable, which is also unusual for such documents. It adds some nice detail to what is meant under the terms Findable, Accessible, Interoperable and Reusable (see below). Barend Mons and co-workers have also recently published a useful, easy-to-read paper setting FAIR in context.[5]

## FAIR principles

The seminal publication[4] proposed technical definitions of what the terms making up FAIR mean for scientific data in repositories.

### Findable:

F1. (Meta)data are assigned a globally unique and persistent identifier
F2. Data are described with rich metadata
F3. Metadata clearly and explicitly include the identifier of the data they describe
F4. (Meta)data are registered or indexed in a searchable resource

### Accessible:

A1. (Meta)data are retrievable by their identifier using a standardised communications protocol
  A1.1. The protocol is open, free and universally implementable
  A1.2. The protocol allows for an authentication and authorisation procedure, where necessary
A2. Metadata are accessible, even when the data are no longer available

### Interoperable:

I1. (Meta)data use a formal, accessible, shared and broadly applicable language for knowledge representation
I2. (Meta)data use vocabularies that follow FAIR principles
I3. (Meta)data include qualified references to other (meta)data

### Reusable:

R1. Meta(data) are richly described with a plurality of accurate and relevant attributes
  R1.1. (Meta)data are released with a clear and accessible data usage license
  R1.2. (Meta)data are associated with detailed provenance
  R1.3. (Meta)data meet domain-relevant community standards

So, scanning through the FAIR principles it becomes clearer why the international scientific unions are becoming involved. They "own" official "domain-relevant community standards" and already have the processes in place to deliver updates etc.

After the introductory discussions, the workshop was split into two parallel streams. One stream dealt with the **GO FAIR Implementation Network for Chemistry** which is currently being created.[6,7] The network will include building a repository of FAIR resources useful to chemists. This workshop stream was tasked with the following:

Address the following themes in supporting FAIR data:

- Use cases and interoperability needs for chemical data and information across the enterprise and related disciplines
- Development of tools for researchers and other expert users to support application and use of standards for chemical data
- Mechanisms for validation and curation of standard representation of chemical data

The second stream was much closer to spectroscopists' hearts and ran under the title of **Interoperability Criteria for Spectroscopic Data Exchange**. The information distributed prior to the workshops explained the relevance of the IUPAC JCAMP-DX suite of recommendations in this context as:

*"The IUPAC JCAMP-DX data standard has become a critical piece of this FAIR data exchange for spectroscopic data. It satisfies a number of critical criteria in that JCAMP-DX file export is available in nearly all software packages for spectroscopic instruments, it is ASCII not Binary, it is non-proprietary and there has been a large amount of data already generated."*

Since the much-documented merger of the IUPAC XML in Chemistry initiative with the ASTM AnIML standardisation effort, no maintenance work on the IUPAC standards has taken place in the hope that the AnIML initiative would take up this challenge. However, work carried out by Greg Banik (Bio-Rad) surveying the use of JCAMP-DX and others has shown there is a clear and urgent need to make a decision on the future of these standards.

Again, the briefing notes clearly set the scene for some decision making…

*"IUPAC is reviewing the current status of the JCAMP-DX format, including the extent to which it is being used, what enhancements users would like to see, and the extent to which the files that are generated in 'JCAMP-DX format' adhere to the JCAMP-DX standards. Another key step towards FAIR spectroscopic data is the development of standard criteria for publishing spectroscopic data that will optimize data use, reuse, and interoperability across domain repositories."*

## Interoperability criteria for spectroscopic data axchange stream

So, with a clear remit to decide on the future of the IUPAC JCAMP-DX standards, the workstream group sat down to review the current position and make clear proposals on the requirements going forward. The first half of the workshop was set the following tasks:

### JCAMP-DX review and future requirements

- Benefits of JCAMP/agnostic data exchange
- Deficiencies of JCAMP format
- Requirements for evolving JCAMP (extensions, XML etc.)
- Community engagement
- Validation requirements

There was some very plain talking amongst the participants—contrasting the original requirements which had established the JCAMP-DX series of standards with those required for a fully FAIR compliant system. In the original standards, the aim had been to facilitate the creation of reference spectroscopic databases by providing a common

format that all instrument vendors could sign up to which had the minimum amount of metadata required to correctly identify and interpret (plot) the measured data accurately. Additional comments and structured metadata were allowed, including the introduction of "private" labels for information which was not internationally standardised but crucial for internal uses of the format within specific communities. Peter Lampen highlighted the fact that the standard also included complicated and potentially loss-less data compression schemes, which were critical to meeting the historical data file size challenges. However, these had caused enormous headaches for programmers not familiar with their unique concepts. These schemes are now less relevant with enormous improvements in network speeds and the availability of huge data storage capacity.

A brainstorm amongst the participants highlighted the following points which needed addressing:

- Clarity on IUPACs position and funding—is IUPAC committed to support maintenance of the standard?
- Standards that can be used to set up repositories
- JCAMP-DX—Yes or No?
- JCAMP-DX—Minimal vs Comprehensive. As discussed above, with a push toward data publication and with a greater demand for more detailed metadata, a more comprehensive approach might be needed.
- Practical implementation for Open Science
- Data + Publications—what are the requirements for primary research data that supports journal publications?
- Original + Processed—Should only the processed human-readable spectrum need to be defined, or does the original data also need to be included?
- Community direction, and appearance of somewhat fragmented communities—IUPAC/JCAMP, Allotrope, NMRedata, IRUG and others are creating somewhat independent solutions.
- Where is the one button? One click to go from lab to publication, with appropriate standards, identifiers etc.
- Granularity—should a data package contain multiple spectra, or multiple substances? Or should it be restricted to data for a specific molecule? Or should it be single spectra for a single molecule? What should be registered as a DOI?
- There is an urgent to update NMR, NIR, Raman
- MS is less urgent, since most vendors support netCDF rather than JCAMP-DX

Based on this assessment the focus for immediate action shifted to the NMR community needs. There had been significant developments in this field since the first IUPAC NMR standard recommendations were published. Also, at the time of the merger of efforts with the AnIML group, a multi-dimensional NMR standard, JCAMP-DX 6.0, had been almost ready for publication. It seems the vendors have adopted this in its draft form across the board, but it still needs some work to cover the majority of use cases in NMR.

## Urgent improvements, including IUPAC JCAMP-DX for NMR

Having decided the highest priority moving forward was NMR, discussions revolved around a number of technical and strategic considerations which would need to be addressed before the standard could be put forward for publication as an IUPAC Recommendation.

- XML vs traditional JCAMP (incremental extension of current format would be least disruptive; conversion to XML would be very disruptive)
- New metadata requirements (focus on JCAMP-DX as a canonical data model rather than a specific format)
- Metadata for FAIR implementation
- Newer experimental techniques, e.g. *n*-dimensional NMR, discontinuous data (some features may not be easily implemented using the current data model, for example, *n*-dimensional NMR may be simpler to implement in XML)

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- Synchronisation of JCAMP across experimental techniques
- Private label terms that need/can be made standard (where appropriate, re-use tags, definitions, look at descriptions from other communities, e.g. Allotrope, NMRedata etc.)
- An application programming interface (API) is needed to assist implementation
- Raw (FID) + spectrum: the NMR community prefers the data to be stored in the FID form and reprocessed to spectra upon opening, but this is a problem for saearchable reference databases and publications where the figures are all of spectra rarher than FIDs.

It looks as if quite a lot of urgent work is required to catch up on so many years when the hopes were that AnIML would deliver the necessary steps forward. Therefore, several projects were defined to get this moving as quickly as possible.

## Project Group 1: focus on JCAMP-DX extensions for NMR data

- The first phase will be to quickly survey the major NMR vendors to fully document their issues with the current JCAMP-DX, and their interest in supporting the effort to update JCAMP-DX.
- They are also tasked with assessing the level of effort involved in updating JCAMP-DX for NMR to include the 2D NMR specifications from the draft version 6.0 and the recommendations for standardising the private labels.
- A project proposal will be developed for the second phase, focusing on delivering the new NMR recommendation for JCAMP-DX implementing the specifications captured in the first phase.

## Project Group 2: focus on metadata for data publication and the items that could be considered important to FAIRify the data

These include such things as:

- ORCID
- Organisation ID
- InCHI
- DOI of the data
- DOI of the associated article, if there is one
- Association of structures to spectral features, as NMRedata
- Funding information
- Instrument ID
- Owner
- License information

## Project Group 3: focus on tools and workflows

- Develop a validator building on the experiences gained running the old JCAMPCHECK and DXCHECK programs. Validation should be carried out at different levels:
  - Validator level 0: check format—does it correspond to the standard?
  - Validator level 1: is the minimum required data present?
  - Validator level 2: is the content reasonable science?
- Visualisation
- Export from lab (instrument or ELN) to repository or to publisher

Project Group 3 will also need to consult on and provide recommendation on whether IUPAC develop these tools or does IUPAC give seal of approval to third party tools?

## Summary

So, we have a green light to proceed after years of stalled developments… the big challenge for us all is to deliver into this rapidly changing environment!

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SAMPLING COLUMN

# Pierre Gy (1924–2015): the key concept of sampling errors

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The founder of the Theory of Sampling (TOS), Pierre Gy (1924–2015) single-handedly developed the TOS from 1950 to 1975 and spent the following 25 years applying it in key industrial sectors (mining, minerals, cement and metals processing). In the course of his career he wrote nine books and gave more than 250 international speeches on all subjects of sampling, including the all-persuasive aspect of hidden economic losses due to neglect of salient sampling issues. In addition to developing TOS, he also carried out a significant amount of practical R&D. But he never worked at a university; he was an independent researcher and a consultant for nearly his entire career—a remarkable scientific life. Gy himself wrote a five-paper personal scientific history published in 2004.[1] We will dedicate a full Sampling Column to honour this remarkable man and his lifetime achievements later in this series. Should the reader be tempted to delve into this already now, however, a special issue of *TOS Forum* is available.[2]

## Rational understanding of heterogeneity and appropriate sampling

Gy's breakthrough was to take on the overwhelmingly complex phenomenon of *heterogeneity*. The traditional route, taken by all his contemporaries (and usually based on very dubious assumptions), was to simplify. In his quest to be rational and complete, however, Gy identified no less than eight 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 performance. Over a period of 25 years he meticulously worked out how to *avoid* committing such 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 when sampling in practice. It was a monumental job. Along the way, he studied for and was awarded two PhDs (in mineral processing and statistics) in order to be adequately equipped to solve the highly complex theoretical and practical problems identified. It is fair to say historically that Pierre Gy was the only scientist to tackle the full set of issues related to sampling of heterogeneous materials and processes.

**Figure 1.** Pierre Gy (1924–2015), founder of the Theory of Sampling (TOS), at one of his last public appearances (Porsgrunn, Norway, 2005). Photo credit: Kim H. Esbensen.

As an illustration, consider the few examples of different materials shown in Figure 2 and try to imagine what mathematical approach would be appropriate in order to describe their heterogeneity? Statistics—would very likely be the answer… But what kind, and level, of statistics? Pondering this issue, virtually everyone would likely want to get help via one, or more, type of "statistical distributions". After all, we are dealing with *heterogeneous materials*. Analytical results stemming from repeated sampling will then not be similar, far less identical, but would have to follow a distribution of a kind. It may be more-or-less easy to find the right distribution (of analytical results), or it may be difficult. Also, is there one universal distribution ruling over all the world's very different materials and their very different manifestations? This is definitely where one would like to enlist the experts, the statisticians. Surely this community will know which distribution would be appropriate, and/or will possess the knowledge and competence to find it.

Moving along, however, one would soon find oneself burdened by the necessity to state, to the statisticians, exactly what constitute the *physical basis* for all analytical results. And this would be where the headaches and severe sweating would start: the physical basis of all analytical result is the analytical aliquot (in the form of a small vial, for example). This view is tantamount to picturing the whole lot as a collection of very many, very small samples, aliquots. However, nobody in their right mind would try to sample a full lot by increments of the size of the final aliquot. On the other hand, from the approach delineated in these columns, it is clear that any aliquot is the result of a complex, multi-stage sampling, sub-sampling process. And this is the *cardinal knowledge* delineated: it is possible, indeed likely, that sampling processes can be

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**Figure 2.** The manifestations of heterogeneous materials are infinite. What would be the common approach to describing such different types of irregular "distributions"? And many intrinsic heterogeneity features are not visible to the naked eye, e.g., as illustrated by the truckload of grain shown bottom left. Pierre Gy undertook a 25-year long journey before he reached the destination: the Theory of Sampling (TOS). Photo credit: KHE Consulting (archives) and iStockphoto

carried out in ever so many and different ways, most of which are demonstrably non-representative. This would mean that it actually matters which specific sampling process was used to produce the final aliquot. Does this then mean that there are always many equally possible differing analytical results? Actually yes, **if** one is not acquainted with TOS and its distinction between representative sampling process, and worthless "specimenting". Before sinking fully into this quicksand, the last thought will be… the aliquot **must** be representative of the whole lot: but how to get this imperative demand into the statistics?

Well, the answer to this is much more complex than might be suggested by a first reflection. First of all, the statisticians do **not** know the world's very different materials and their very different heterogeneities; why should they? It is **you**, the sampler, who is the expert here. After some more reflection based on your own experiences, it will become clear that whereas statistics is addressing a population of "units", each of which are *identical* except for the differing analytical results, the "units" of a heterogeneous lot are defined by the specific nature of the material and the specific sampling procedure used, in particular by the increment, or sample, size (mass). Thus, in a very real sense, the final analytical results do indeed depend on the sampling procedure—a different sampling approach, e.g. grab sampling vs composite sampling, will assuredly give rise to different analytical results (with the composite sampling result being overwhelmingly more reliable… see all previous Sampling Columns). Go tell this to the statisticians… A direct inroad to this complexity, without all the math, can be found in Reference 3.

At the outset, then, we are not in a position to simply take over conventional statistical notions, populations, units. We are left to fend for ourselves: and this was exactly what Pierre Gy realised. Upon which he set himself the goal of developing the "appropriate statistics" with which to be able to describe the real-world of heterogeneous materials (and processes, see later) which is infinitely more complex than a world conceptualised as conventional vectors, matrices and arrays of data, which lend themselves to simple descriptions by statistical moments: averages, standard deviations, variances etc. For the interested reader, there are several, carefully

**Figure 3.** There is no end to the many ways heterogeneity appears. Here a pronounced grain size segregation sometimes expresses itself dramatically (left), at other times completely "embedded" (top-right). It takes a radically different approach to be able to include such features in standard statistical distribution models, in fact Pierre Gy had to invent a new kind of "unit" in order to accomplish this goal, the "heterogeneity contribution". Photo credit: KHE Consulting (archives).

crafted next-level introductions to this journey.[4–7]

## There is hope, however

Although complex, TOS can in fact be made easily accessible. There are many systematic elements of the TOS, which makes mastering it possible, also from a decidedly less in-depth theoretical and mathematical level.

For example, the eight sampling errors originate from only three sources: the *material* (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* (even correctly designed equipment can be used in a non-representative manner). In general, sampling is also defined by whether the lot is *stationary* or *moving* when sampling takes place, a distinction that is well-known within many application fields, in the realm of powders for example: "sample only when the powder is moving".

And, the breakthrough: as it turned out, *some* sampling errors were found to be able to be *eliminated* completely, which simplifies the sampling agenda considerably. But it is, of course, necessary to know exactly how to identify these errors and exactly how to eliminate them. These are the so-called Incorrect Sampling Errors (ISE), a concept that was to be instrumental in order to be able to give a distinct definition of both a "correct" as well as a "representative" sampling process.

Following this rational simplification route, recently TOS has been presented in a fully axiomatic framework.[8–10] Figure 4 shows the systematics of the complete framework of TOS' General Principles (GP), Sampling Unit Operations (SUO) and all eight sampling errors, distinguished as ISE and Correct Sampling Errors (CSE). The value of this overview stems from the fact that all principal elements needed for a guarantee for a guaranteed representative pathway "from-lot-to-aliquot" are outlined here. This framework should be viewed as a master enabler for delving into the TOS literature in full.

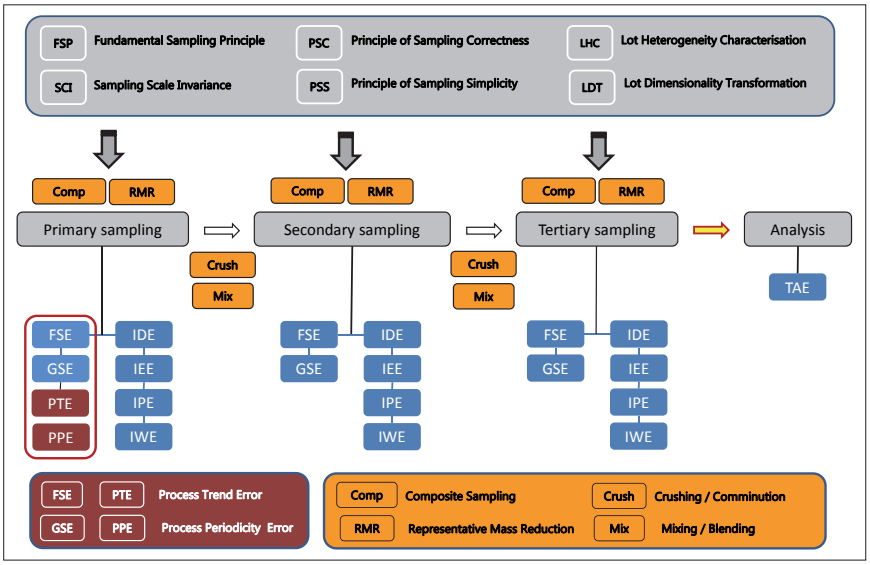


**Figure 4.** Theory of Sampling (TOS) synoptic overview, shown here for three sampling stages. TOS is comprised by six Governing Principles (GP) (top grey panel), four Sampling Unit Operations (bottom yellow panel) and eight sampling errors (blue/maroon). The basic differentiation between the ISEs (IDE, IEE, IPE, IWE) and the CSEs (FSE, GSE) will be covered in a future column. For details, see References 11–13 and other authoritative references therein. Illustration copyright KHE Consulting; reproduced with permission.

## How to sample representatively: TOS

The first task on **any** sampling agenda is to eliminate the ISEs, mainly an issue regarding the design, installation, operation and maintenance of the sampling equipment. Subsequently, what remains, are the CSEs which can be dealt with by standard means, i.e. by increasing the number of composite sampling increments, *Q*, with respect to the empirical heterogeneity encountered (always honouring the Fundamental Sampling Principle, FSP) and always involving the pertinent GPs and other SUOs. Recent introductions to TOS, in general, are References 8, 9, 13, 14. In relation to the specific disciplines of chemometrics and multivariate data analysis in general, as well as in relation to pharmaceutical production, dedicated introductions can be found in References 5 and 15.

Figure 4 depicts a generic, multi-stage sampling process outline, the singular purpose of which is to deliver a representative analytical aliquot (yellow arrow). Sampling of stationary lots makes use of six basic sampling errors (blue), while process sampling (sampling of dynamic lots) needs two more errors to be tackled in full (maroon).

TOS logically demands that all pre-aliquot steps are supervised and governed by a *unified* sampling responsibility. This is a legal person, either in the form of a single individual (a "sampling czar") or by a committee representing all departments in which sampling is performed. The latter situation is typical of very many organisational solutions in big companies and corporations; but is unfortunately also the reason behind a considerable proportion of the sampling problems met with in real life. Experience with many big corporations, companies and organisations unfortunately points to considerable difficulties expressly related to inter-departmental collaboration, or rather, to the lack thereof. Many are the cases where traditional rivalries between departments, individuals or just historical traditions make effective sampling across the entire "lot-to-analysis" pathway impossible. Even though such issues often are the main culprits behind what appear to be "impossible-to-solve" sampling problems, solutions rather come from the realm of organisational psychology. However, there also exist disruptive solution possibilities within the realm of TOS: it is most certainly not only the front-line sampler who need proper education with respect to TOS, because they

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collect the samples upon which analytical results are produced and upon which ultimately important decisions are made. Indeed, all individuals who are responsible for optimising sampling and process performance should feel a responsibility to become conversant with TOS. Thus, whether presidents, vice presidents, operations managers, process technicians, laboratory supervisors, quality assurance and quality control managers (see, for example, Reference 16) and indeed also concerned investors and company shareholders need a succinct understanding of TOS to be fully competent in their respective roles and capacities.

And it is all about how be able to identify and eliminate, or reduce, a small group of sampling errors—the legacy of Pierre Gy.

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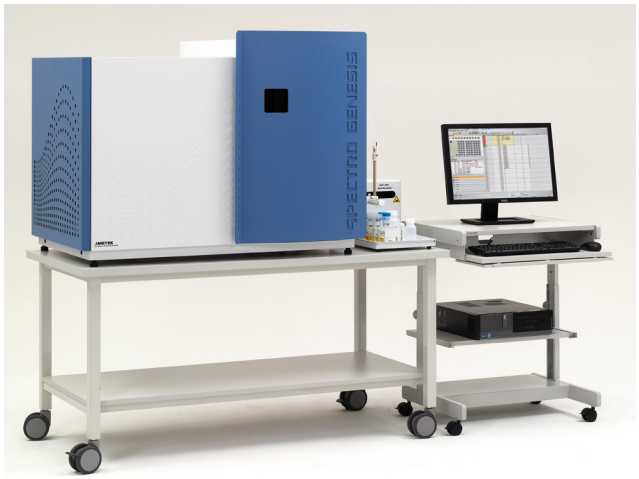
# ATOMIC

## Homogenising autosampler for oils applications

Teledyne CETAC has introduced a new homogenising autosampler for oils, wear oils and coolants for sample introduction for inductively coupled plasma-optical emission spectroscopy (ICP-OES). The Oils 7400 Homogenising Autosampler is built on the Teledyne CETAC ASX-7000 automation platform, and is designed to meet the needs of the evolving wear metals market, which means a quick and easy way to convert it for use in coolant analysis. The dual pump/dual rinse station design allows for a fast and easy transition between the two different matrices. When used with the Teledyne CETAC ASXpress® Plus Rapid Sample Introduction system, two samples can be introduced to ICP-OES instrumentation per minute for analysis in accordance with ASTM 5185 (oils) and ASTM 6130 (coolants).

*Teledyne CETAC*

http://link.spectroscopyeurope.com/30-W-089




## New generator for SPECTRO Genesis ICP-OES spectrometer

SPECTRO Analytical Instruments has introduced the latest version of the SPECTRO Genesis inductively coupled plasma optical emission spectrometer, which has been updated with a powerful new generator. It provides factory calibrated method packages for industrial applications, including waste water, sludge, soil, fuels and wear metals/additives in oil. The new laterally diffused metal oxide semiconductor (LDMOS) generator delivers up to 1700 W. Benefits include faster warmup time for high productivity, excellent matrix compatibility and longer lifetime. SPECTRO Genesis offers fully simultaneous analysis, achieving sample cycle times of 90 s or less—independent of how many elements are analysed.

*SPECTRO Analytical Instruments*

http://link.spectroscopyeurope.com/30-W-090

## LA-ICP-MS imaging software

Teledyne CETAC has released HDIP Software for HDF-based image processing for laser ablation systems. HDIP software was developed in close collaboration with Professor Vanhaecke and Dr Van Malderen at the University of Ghent and is now exclusively available through Teledyne CETAC. The HDIP image processing software offers fully automated image optimisation for highest resolution; several "autopilot" functions that automate data reduction and building of publication-ready 2D and 3D multi-element images; automated optimisation function to suggest optimum analytical parameters (spot size, rep rate, dwell times etc.) based on the user's analytical needs; and it allows data manipulation including full quantitation, drift correction, interrogation of datasets acquired to output region of interest data.

*Teledyne CETAC*

http://link.spectroscopyeurope.com/30-W-086

# INFRARED

## FT-IR accessory for analysis of large objects

A new accessory compatible with Thermo Scientific FT-IR spectrometers is designed to enable art conservationists to verify the authenticity of paintings, sculptures, textiles and other large artworks. The Thermo Scientific ConservatIR FT-IR external reflection accessory lets users analyse objects that do not fit inside the sample compartment. The external accessory directs an infrared

# NEW PRODUCTS

beam to an opto–mechanical arm that articulates in a range of motion from –5° to 95°, enabling samples to be measured in multiple orientations. Users can also measure samples in two modes: specular/diffuse reflection, for non-contact analysis, or attenuated total reflection (ATR), using an optional diamond ATR sampling interface. An integrated video camera on the accessory enables users to magnify the sample image to facilitate higher confidence in the measurement location. The ConservatIR accessory is also designed to enable analysis of other large objects, including automotive parts, toys, fixtures and castings.

*Thermo Fisher Scientific*

http://link.spectroscopyeurope.com/30-W-079

## RAMAN

### Trace analysis capabilities added to Progeny ResQ 1064 nm Raman analyser

Rigaku Analytical Devices have added QuickDetect™ mode, that provides automated colorimetrics for trace or non-visible amounts, to its existing Progeny ResQ 1064 nm handheld Raman analyser. This new feature removes the human-error and subjectivity of traditional colour reagent kits. QuickDetect is optional on Progeny ResQ and Progeny ResQ FLX product lines and is compatible with Detectachem's MobileDetect pouches, used for trace amounts, residues or non-visible substances.

*Rigaku Analytical Devices*

http://link.spectroscopyeurope.com/30-W-082

### Handheld 1064 nm Raman analyser

B&W Tek has announced the TacticID®-1064, a handheld Raman analyser for real-time identification of suspicious and unknown substances in the field. It is based on third-generation 1064 nm technology, which improves fluorescence elimination, detection limits and response time. It also allows for safe and direct measurement of darker substances. The TacticID-1064 has a large on-board library, and allows users to create and import customised libraries. It can be operated via a touch screen or using hardware buttons. The system comes equipped with an on-board camera to capture evidence photos at the scene that are included in the test report, which can be exported directly onto a USB drive. The TacticID-1064 displays both GHS and NFPA704 chemical safety information, giving additional actionable data.

*B&W Tek*

http://link.spectroscopyeurope.com/30-W-083

## MASS SPECTROMETRY

### scimaX magnetic resonance mass spectrometer

Bruker introduced the scimaX™ magnetic resonance mass spectrometer, which has mass resolution exceeding twenty million ($R > 20{,}000{,}000$), in a smaller footprint and without the need for any liquid cryogens. Bruker's novel conduction-cooled Maxwell™ magnet technology essentially makes the magnet "invisible", and allows the use of high-performance magnetic resonance mass spectrometry (MRMS) in standard MS laboratories. This MRMS resolution allows isotopic fine structure (IFS) analysis to easily determine exact elemental formulae in complex mixtures, without any chromatography. Using this capability, the scimaX enables the novel workflow of flow injection analysis (FIA-MRMS) for large cohort, high-throughput phenomics studies

with up to 200 samples per day. Biopharma users can perform advanced native protein and fragment-based drug discovery studies using MRMS, which has recently been called a "bona-fide" platform for native protein analysis in the scientific literature. With an optional MALDI source, pharma customers have demonstrated the capabilities of MRMS for label-free MS imaging for PK/PD studies in drug development.

*Bruker*

http://link.spectroscopyeurope.com/30-W-081

# X-RAY

## Handheld XRF spectrometer with graphene window SDD

Bruker has introduced the TRACER 5g handheld x-ray fluorescence (XRF) elemental analyser, incorporating a silicon drift detector (SDD) with a graphene entrance window. The graphene window has higher transmission of x-rays throughout the energy spectrum and improves the transmission for light elements such as sodium (Na), magnesium (Mg), silicon (Si) and aluminium (Al). This improved light element sensitivity enables new applications for handheld XRF in the fields of geology, agriculture and material science. The TRACER 5g can achieve detection limits as low as 275 ppm for Na and 100 ppm for Mg when the operated with helium purge. The TRACER 5g retains all the features from the TRACER 5i, including integrated software with complete user control of the excitation, a choice of excitation collimators and filters, the ability to operate in air, vacuum or helium atmosphere, as well as the suite of powerful PC software, including Artax™ and EasyCal™, that is supplied with the instrument.

*Bruker*

http://link.spectroscopyeurope.com/30-W-080

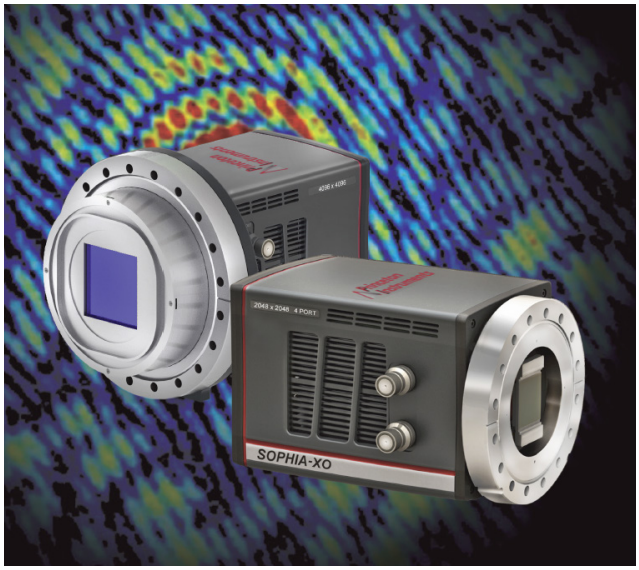

## Cameras for soft x-ray applications

Princeton Instruments has introduced several new, high-speed, ultra-low-noise cameras engineered for vacuum ultraviolet (VUV) and soft x-ray direct-detection applications. The SOPHIA-XO camera platform is specially designed for scientific applications such as VUV/EUV/XUV imaging, x-ray diffraction, x-ray microscopy, x-ray holography, x-ray spectroscopy and x-ray plasma.

The new SOPHIA-XO cameras utilise back-illuminated CCDs for direct detection of a wide range of VUV and x-rays (~5 eV to 30 keV). These new "XO" camera models, which are extensions of Princeton Instruments' popular SOPHIA® product line, feature 2048×2048 and 4096×4096 formats with 100% fill factor, up to 150,000 $e^-$ full well, >95% peak QE and read noise as low as 3.5 $e^-$ rms. A 4-port, 16 MHz readout architecture allows the new cameras to deliver more than three full frames per second: 7–10× faster than previous 2-port cameras.

The SOPHIA-XO is available either with UV-enhanced coating for VUV applications or with no AR coating for soft x-ray applications. All SOPHIA-XO cameras have Princeton Instruments' ArcTec™, a proprietary technology that uses air or liquid to thermoelectrically cool to –90 °C.

The SOPHIA-XO cameras suitable for myriad large field-of-view x-ray applications in laboratory, synchrotron and OEM systems. Interfacing with UHV instrumentation is easy and convenient via a rotatable industry-standard CF flange with a high-vacuum seal design.




SOPHIA-XO cameras are supported by Princeton Instruments' 64-bit LightField® imaging and spectroscopy software, available as a system option.

*Princeton Instruments*

http://link.spectroscopyeurope.com/30-W-091

# DIARY



## Conferences 2018

19–24 August, Coimbra, Portugal. **XXXIV European Congress on Molecular Spectroscopy (EUCMOS 2018).** Rui Fausto, rfausto@ci.uc.pt, http://www.qui.uc.pt/eucmos2018/.

21–24 August, Budapest, Hungary. **International Conference on Many Particle Spectroscopy of Atoms, Molecules, Clusters and Surfaces (MPS 18).** mps2018@atomki.mta.hu, http://ekho94.hu/en.

26–29 August, Toronto, Ontario, Canada. **132nd Association of Official Agricultural Chemists (AOAC) International Annual Meeting and Exposition.** meetings@aoac.org, www.aoac.org.

26–30 August, Liverpool, United Kingdom. **7th EuCheMS Chemistry Congress.** www.euchems2018.org.

26–31 August, Jeju, South Korea. **The 26th International Conference on Raman Spectroscopy (XXVI ICORS).** icors2018@icors2018.org, http://www.icors2018.org/.

26–31 August, Florence, Italy. **XXII International Mass Spectrometry Conference (IMSC 2018).** Secretariat, info@imsc2018.it, www.imsc2018.it.

31 August–1 September, Toronto, Canada. **18th International Conference on Pure & Applied Chemistry (IPAC 2018).** appliedchemistry@conferencescanada.org, https://pureapplied-chemistry.conferenceseries.com/.

2–7 September, Aveiro, Portugal. **56th European High Pressure Research Group Meeting: High Pressure Science and Technology (EHPRG 2018).** Secretariat, tania.rodrigues@abreu.pt, http://ehprg2018.org/.

3–7 September, Portsmouth, United Kingdom. **8th International Conference on Synchrotron Radiation and Neutrons in Art and Archaeology—SR2A-2018.** Emma Clarke, events@diamond.ac.uk, http://www.diamond.ac.uk/Conference/SR2A-2018.html.

3–7 September, Bilbao, Spain. **25th International Conference on High Resolution Molecular Spectroscopy (BILBAO2018).** http://www.chem.uni-wuppertal.de/conference/.

9–13 September, Brescia, Italy. **6th International Conference on Vibrational Optical Activity (VOA-6).** www.voa6.org.

9–13 September, Berlin, Germany. **1st International Conference on Ion Analysis (ICIA 2018).** Dr Wolfgang Frenzel, https://www.icia-conference.net/.

10–13 September, Cambridge, United Kingdom. **39th BMSS Annual Meeting 2018.** Lisa Sage, bmssadmin@btinternet.com, http://www.bmss.org.uk/bmss2018/bmss2018.shtml.

11–12 September, Stockholm, Sweden. **8th World Congress on Spectroscopy & Analytical Techniques.** olivi-aspecter801@gmail.com, https://

analyticaltechniques.annualcongress.com/.

12–14 September, Perugia, Italy. **International Thematic Workshop: Advances in Brillouin Light Scattering.** Prof. Giovanni Carlotti, giovanni.carlotti@unipg.it, https://sites.google.com/view/advances-in-bls-2018.

16–19 September, Philadelphia, United States. **Small Molecule NMR Conference (SMASH 2018).** https://www.smashnmr.org/.

17–21 September, Rennes, France. **14th International Conference on the Applications of Magnetic Resonance in Food Science.** mrfood2018@irstea.fr, https://www.foodmr.org/.

23–26 September, Amsterdam, Netherlands. **9th Workshop on Hyperspectral Image and Signal Processing: Evolution in Remote Sensing (WHISPERS).** http://ieee-whispers.com.

24–26 September, Ulm, Germany. **15th WITec Confocal Raman Imaging Symposium.** https://witec.de/resources-and-education/events.

24–28 September, Brisbane, Australia. **3rd Joint Conference of the Asia–Pacific EPR/ESR Society and the International EPR (ESR) Society (IES) Symposium.** apes_ies2018@uq.edu.au, www.apes-ies2018.org.

24–28 September, Kazan, Russia. **Modern Development of Magnetic Resonance.** Secretariat, mdmr.kazan@yandex.ru, www.kfti.knc.ru/mdmr/2018.

29 September–1 October, London, Ontario, Canada. **30th Annual Moot NMR Conference.** mootnmr@gmail.com, http://www.mootnmr.org/.

30 September–3 October, Orlando, FL, United States. **17th Human Proteome Organization World Congress–HUPO 2018.** Secretariat, office@ushupo.org, http://hupo2018.org/.

5–8 October, Tokyo, Japan. **Functional Near-Infrared Spectroscopy (fNIRS 2018).** http://fnirs2018.org/.

10–11 October, Coventry, United Kingdom. **Hyperspectral Imaging and Applications Conference (HSI2018).** Brenda Hargreaves, brenda@xmark-media.com, https://www.hsi2018.com/.

16–17 October, Galveston, TX, United States. **Gulf Coast Conference 2018.** https://www.gulfcoastconference.com/.

21–26 October, Atlanta, GA, United States. **45th Annual Conference of Federation of Analytical Chemistry and Spectroscopy Societies (SciX2018).** facss@facss.org, https://www.scix-conference.org/.

21–26 October, Long Beach, CA, United States. **AVS 65th International Symposium and Exhibition.** https://www.avs.org/symposium.

31 October–1 November, Columbus, Ohio, United States. **International Conference on Analytical and Bioanalytical Techniques–Analytica Acta 2018.** https://analytical-bioanalytical.pharmaceuticalconferences.com/.

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

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

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

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

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

3–6 December, Caparica, Portugal. **3rd Caparica Christmas Conference on Sample Treatment 2018.** Dr Carlos Lodiero Espino, jlcapelom.sample-treatment2018@bioscopegroup.org, http://www.sampletreatment2018.com.

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

## 2019

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

3–8 February, Pau, France. European Winter **Conference on Plasma Spectrochemistry.** Ryszard Lobinski, ewcps2019-chair@winterplasma2019.com, www.winterplasma2019.com.

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

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

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

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# DIARY

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

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

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

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

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

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

8–12 July, Auckland, New Zealand. **International Conference on Advanced Vibrational Spectroscopy (ICAVS10).** ICAVS Secretariat, Podium Conference Specialists, 2661 Queenswood Drive, Victoria, BC, Canada, V8N 1X6. http://www.icavs.org/2019-conference/.

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

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

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

15–20 September, Gold Coast, Australia. **NIR-2019.** www.nir2019.com.

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

13–18 October, Palm Springs, United States. **46th Annual Conference of Federation of Analytical Chemistry and Spectroscopy Societies (SciX2019).** facss@facss.org, http://www.scixconference.org.

5–8 November, Prague, Czech Republic. **9th International Symposium on Recent Advances in Food Analysis.** rafa2019@vscht.cz, www.rafa2019.eu.

## Courses

### 2018

19–23 August, Joensuu, Finland. **1st Summer School of The European Network of Fourier-Transform Ion-Cyclotron-Resonance Mass Spectrometry Centers.** janne.janis@uef.fi, www.eu-fticr-ms.eu.

1 November, Córdoba, Spain. **2nd Edition of Fundamentals and Applications of Near Infrared Technology.** Prof. Ana Garrido Varo, pa1gavaa@uco.es.

## Exhibitions

### 2019

23–26 September, Amsterdam, Netherlands. **Spectro Expo: Science. Technology. Applications.** http://www.spectroexpo.com/.

31 October–1 November, Birmingham, United Kingdom. **Lab Innovations 2018.** Aleiya Lonsdale, Aleiya.Lonsdale@easyfairs.com, www.lab-innovations.com.

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

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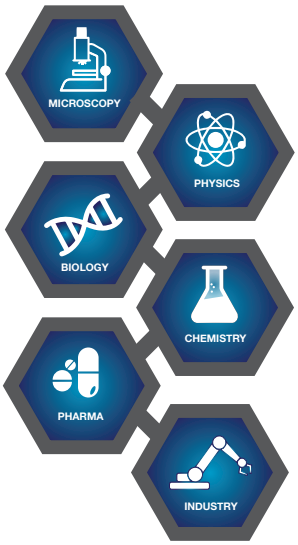


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