PostGraduate Institute
for measurement science

PGI Conference Programme

for the PGI's sixth Annual Conference:

Tackling Global Challenges through Measurement Science

19-20 October 2021 | Online

(Passcode: **metrology2021**)

Tuesday 19 October

Time (BST)	Event Description	
09:30	Arrivals and Registration	
09:45	Professor Richard Burguete | PGI Director	Introduction
09:50	Professor Sir Jim McDonald | University of Strathclyde	Welcome to the Conference
10:00	Professor Paul Monks | BEIS	Setting the Scene
	Creating a Science Based Economy	
10:15	Session Chair - Jennifer Blair | University of Strathclyde	Introduction to the Session
10:20	**Dr Alessandro Rossi | University of Strathclyde and NPL** *Understanding and exploiting quantum phenomena: towards a new technological era*	**Keynote Talk**
11:05	Rachel Clark | Cardiff University *Characterising quantum light sources*	
11:20	Break and Poster Sessions	
12:05	Shaon Debnath | University of Strathclyde *pH sensor using silver nanoparticles embedded in silica coated optical fibres*	
12:20	Tim Coveney | University of Huddersfield *NPL ULTIMUM: A new primary dimensional calibration facility for the UK*	
12:35	Jamie McMillan | University of Surrey *Traceable thermal imaging in harsh environments for nuclear material storage*	
12:50	Lunch	

Tuesday 19 October

Time (BST)	Event Description	
	Linking Research Excellence through Communities	
13:35	Session Chair - David Connolly | University of Strathclyde	Introduction to the Session
13:40	**Dr Thierry Stora | CERN** *CERN-MEDICIS - How has a collaborative project furthered nuclear medicine research?*	**Keynote Talk**
14:25	Ileana Silvestre Patallo | UCL *Harmonizing delivered dose verification among the radiobiological research community*	
14:40	Break and Poster Sessions	
15:25	Tarek Haloubi | University of Edinburgh *Machine learning techniques for evaluating disease and drugs effectiveness in fibre bundle endomicroscopy systems*	
15:40	David Fairweather | University of Edinburgh *Atomic clocks and earthquakes: seismic observation with ultrastable laser interferometry*	
15:55	Professor Richard Burguete	Wrap Up of Day One
16:05	Jamie McMillan | PGI Conference Chair	Closing Remarks
16:10	Close of Day 1	
16:10 →	**Social** *Head over to Gather.Town for fun and games at the social*	

PostGraduate Institute
for measurement science

#GrAbPGI Twitter Competition

- Submit your Graphical Abstract entry on Twitter to be in with a chance of winning the inaugural #GrAbPGI Twitter Competition.
  Email the pgiambassadors@npl.co.uk for more information

- Follow the #GrAbPGI tag throughout the day on **19 October** and like, comment and retweet other entries to help each others’ research reach a wider audience.

19 October 2021 | Twitter

Wednesday 20 October

Time (BST)	Event Description	
09:30	Arrivals and Registration	
09:45	Professor David Sampson | University of Surrey	Welcome to Day Two
	Ensuring Wellbeing for All	
09:55	Session Chair - Jamie McMillan | University of Surrey	Introduction to the Session
10:00	**Aliza Ayaz | UCL** *Sustainability is the new holistic wellbeing*	**Keynote Talk**
10:45	Hanifa Koguna | Imperial College *Brain tumour diagnosis using Laser Desorption Imaging Rapid Evaporative Ionisation Mass Spectrometry (LDI-REIMS)*	
11:00	Break and Poster Sessions	
11:45	Jessica Emily Talbott | UCL *Diffusion MRI: an early, non invasive and repeatable detection method for disease*	
12:00	Martin Metodiev | Imperial College *Measuring spatial resolution in mass spectrometry imaging*	
12:15	Dannielle Cox-Pridmore | University of Surrey *Bioelectronics and personalised disease models*	
12:30	Lunch	

Wednesday 20 October

Time (BST)	Event Description	
13:15	Introduction to Careers Session	
13:30	**Debate** Professor Scott Heath | University of Manchester Rowena Innocent | Spectris plc *How do you decide between academia or industry? Do you have to?*	
14:10	Break	
14:20	**Panel Session** PGI Alumni *An opportunity to hear from professionals in Academia and Industry and the chance to ask them your questions*	
15:00	Close of Careers Session	
15:10	**Dr Jess Wade | Imperial College**	**Motivational Talk**
15:30	Dr Jess Wade	Open Discussion
15:50	Professor Richard Burguete | PGI Director	Awards Ceremony
16:10	Jamie McMillan | PGI Conference Chair	Closing Remarks
16:15	Close of the PGI Conference 2021	

PostGraduate Institute
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Oral Presentation Abstracts

for the PGI's sixth Annual Conference:

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Professor Sir Jim McDonald, BSc, MSc, PhD, DSc, CEng

Principal and Vice-Chancellor of the University of Strathclyde

Professor Sir Jim McDonald is Principal and Vice-Chancellor of the University of Strathclyde. He Co-chairs, with the First Minister of Scotland, the Scottish Government's Energy Advisory Board. He is Co-Chair of the Independent Glasgow Economic Leadership Board. He currently holds several senior business appointments with organisations including the Weir Group plc, Scottish Power plc, the UK National Physical Laboratory and the UK Offshore Renewable Energy Catapult. Additionally, he Chairs or participates in several senior committees related to research, economic development and education. In the Queen's Jubilee Birthday Honours List 2012, Professor McDonald was awarded a Knighthood for services to education, engineering and the economy. He was elected President of the Royal Academy of Engineering in September, 2019, through which he is a member of the UK Prime Minister's Council for Science and Technology. He has held the Rolls-Royce Chair in Electrical Power Systems since 1993. He is a Fellow of the Royal Academy of Engineering, the Royal Society of Edinburgh, the Institution of Engineering and Technology, the Institute of Physics, the Energy Institute and a Foreign Fellow of the Chinese Society of Electrical Engineering.

University of
Strathclyde
Glasgow

Professor Paul S. Monks BSc, DPhil, FRMetS, FRSC

Chief Scientific Adviser – Department for Business, Energy and Industrial Strategy

Paul Monks is Chief Scientific Adviser of the Department for Business, Energy and Industrial Strategy. Prior to joining the department, he was Pro-Vice Chancellor and Head of College of Science and Engineering at the University of Leicester, where he remains a Professor in Atmospheric Chemistry and Earth Observation Science. His research experience covers the broad areas of air quality, atmospheric composition and climate change that has provided a platform for translation into diverse areas including forensic science, CBRN, microbiology and food safety, natural resource management and breathomics (breath analysis as a medical diagnostic). Paul was the Chair for 10 years of the Defra Air Quality Expert Group (AQEG) and Deputy-Chair of the Defra Science Advisory Council, alongside roles in the UKRI-NERC advice structures. He has worked internationally as, for example, the European representative on the Environmental Pollution and Atmospheric Chemistry Scientific Steering Committee (EPAC SSC) of the World Meteorological Organisation and ICACGP (International Commission on Atmospheric Chemistry and Global Pollution). As founding director of G-STEP (a university innovation initiative), he developed a business facing organisation with the aim of innovating using space based (EO) data to enhance the competitiveness of industry, particularly focused on SMEs.

Department for
Business, Energy
& Industrial Strategy

Dr Alessandro Rossi

Senior lecturer and a UKRI future leaders fellow at the University of Strathclyde and joint appointment at NPL

Understanding and exploiting quantum phenomena:

Towards a new technological era

Unbreakable codes, teleportation of information and ultra-fast computing will soon cease to be figments of science fiction literature thanks to the ongoing development of quantum technologies. Quantum mechanics is a branch of physics that has allowed us to understand how nature works at the atomic and sub-atomic scales. This wealth of knowledge has already enabled successful modern technologies, such as miniaturised electronics, DVD players and MRI scanners. However, even more transformative quantum-based technologies [1] are on the horizon and could lead to enhanced sensors, powerful quantum computers and un-hackable communication systems. These are considered imminent realities, so much so that governments and major ICT corporations worldwide are copiously investing to benefit from their future commercialisation.

In this talk, I will start by demystifying the popular idea that quantum science is weird and incomprehensible. To this end, I will be highlighting quantum effects that have a direct role in everyday life events, such as the flight of migratory birds and the flicking of electrical switches in our homes. Next, I will go on to discuss how some of these quantum phenomena can be exploited to build new technologies, particularly quantum computers [2] and accurate metrological tools [3-4]. As a working example, I will focus on semiconductor systems similar to those already widely deployed in today's microchip industry [5]. The development of semiconductor-based quantum devices could be advantageous with respect to more exotic material systems because one can leverage over half a century of R&D spent on optimising manufacturing processes. This could lead to swift adoption by industry and to a reduced time to market for new quantum products.

[1] https://uknqt.ukri.org
[2] Ladd, T. et al. Nature 464, 45 (2010)
[3] Piquemal, F. Nature Phys 12, 284 (2016)
[4] von Klitzing, K. Nature Phys 13, 198 (2017)
[5] Rossi, A. et al. Physics World, Focus on Computing (2019)

Rachel Clark

Postgraduate researcher at Cardiff University. Working in collaboration with the Quantum Information Processing group at NPL

Characterising quantum light sources

R. Clark[1], J. P. Hadden[2], P. Dolan[3], A. G. Sinclair[3], A. J. Bennett [1,2]
1. School of Engineering, Cardiff University, Queen's Buildings, The Parade, Cardiff, CF24 3AA
2. School of Physics and Astronomy, Cardiff University, Queen's Building, The Parade, Cardiff, Wales, UK, CF24 3AA
3. National Physical Laboratory, Teddington, TW11 0LW, UK

Quantum light sources are an enabling technology for a vast array of applications, including next generation computing and cryptography, imaging, sensing and light metrology. Particularly for quantum computing, they are a critical “building block” of its development, and efficient, easy-to-manufacture sources are necessary to ensure commercial access and widespread use in societal infrastructure. These sources can exist in a multitude of different physical systems: from nitrogen vacancy centres in diamond, to semiconductor quantum dots, to 2D materials [1].

A common way to make a like-for-like comparison of the source behaviour, regardless of its physical system, is to measure the second-order correlation-function of light, more commonly known as the autocorrelation function. This function can be determined from “time-stamped” data files recording the arrival time of every photon on each detector which, in principle, includes information on every detection-detection event. The correlation function can also be generalised to the N^{th} order, for streams of photon arrival times recorded on N detectors [2]. However, post-processing to determine the function increases the complexity of the calculation to at least a power of N, taking considerable computing resources for modest datasets.

In this talk I will discuss my work on the development of a code that calculates the function for timestamped data files, and the benefits of this method. I will also introduce the practical complexities involved in measuring and calculating this function, with an overview of the physical significance it can provide. We have used this tool to study the photon statistics of thermal light and confirm that $g^{(N)}(0, \ldots, 0) = N!$ for N=2,3.

[1] Oxborrow, M. and Sinclair, A.G., 2005. Single-photon sources. Contemporary Physics, 46(3), pp.173-206
[2] Stevens, M.J., Baek, B., Dauler, E.A., Kerman, A.J., Molnar, R.J., Hamilton, S.A., Berggren, K.K., Mirin, R.P. and Nam, S.W., 2010. High-order temporal coherences of chaotic and laser light. Optics express, 18(2), pp.1430-1437

Shaon Debnath

Postgraduate researcher at University of Strathclyde. Working in collaboration with the Electrochemistry group at NPL

pH sensor using silver nanoparticles embedded in silica-coated optical fibres

Quantifying hydrogen ion concentration in solution (or pH) has important applications in different industries. However, measurement of pH at high temperature and pressure (HTHP) remains a significant challenge, due to lack of reliable instrumentation. Recent studies on the surface plasmon resonance of gold nanoparticles coated on optical fibres exhibited sensitivity to pH in solutions at different temperatures and pressures [1,2]. Since optical fibres are stable under HTHP conditions, these findings indicate a potential way forward to develop pH sensors capable of operating in such environments.

This work reports on the development of silver nanoparticle embedded silica coatings on optical fibres. The coatings were prepared using the sol-gel technique by adding tetraethoxysilane to ethanol, water and silver nitrate. In order to determine the optimum conditions for formation of a gel with good adhesiveness on glass, while containing sufficient silver nanoparticles for pH sensitivity, experiments were carried out by coating glass slides (Fisher Scientific, 26 mm × 76 mm × 1.2 mm) at different temperatures and reaction times.

It was observed that gel formation at 35 °C for 48 hours showed good adhesiveness with glass. After preparing the gel, glass slides were then dip-coated and dried in an oven at 200 °C for 2.5 hours, where silver ions were reduced to form silver nanoparticles. Characterization of the coating using Ultraviolet/Visible (UV-Vis) spectroscopy showed an absorbance peak at around 400 nm, which is consistent with the presence of silver nanoparticles [3].

Once the preparation method had been established, a piece of optical fibre was etched in 7 M sodium hydroxide to remove the outer coating and cladding, before being coated with the gel. The coated optical fibre was observed under a high-resolution microscope and was found to have 5-6 µm of the coating around the core of the fibre. Ongoing experiments are focused on connecting these fibres to a light source and UV-Vis spectrophotometer and measuring absorbances in solutions of different pH, which will be reported at the meeting.

[1] Wang, C. *et al.* (2015) Novel silica surface charge density mediated control of the optical properties of em-bedded optically active materials and its application for fiber optic pH sensing at elevated temperatures, Nanoscale, 7, 2527–2535
[2] Wang, C. *et al.* (2015) Novel sensing materials for harsh environment subsurface pH sensing applications, Proc. of SPIE, 9480, 1–6
[3] Agnihotri, S. *et al.* (2014) Size-controlled silver nanoparticles synthesized over the range 5–100 nm using the same protocol and their antibacterial efficacy, RSC Advances, 4(8), 3974–3983

Tim Coveney

Postgraduate researcher at the University of Huddersfield. Working in collaboration with the Dimensional Metrology group at NPL

NPL ULTIMUM: A new primary dimensional calibration facility for the UK

A world leading science-based economy requires as a foundation a world class metrology base. As the UK moves to a science based economy UK research establishments and Industry will require access to the most accurate disseminations of the SI base units available, as the accuracy of these primary calibrations are the limiting factor on the accuracy of all measurements. To meet this need, NPL is developing a new high accuracy primary 1-dimensional length calibration system. The system is specified to expand both UK and global metrology capability and to do so in a way that is usable and efficient to improve both accuracy and ease of access for users. It aims to avoid the need for highly specialised environment and skilled operators, enabling potential deployment into industry to shorten traceability chains. The system is being designed to engage with emerging digital techniques such as digital calibration certificates and digital twinning.

An uncertainty led approach is being used for the design, with a technology agnostic baseline uncertainty model designed to deliver the specified measurement uncertainty developed to specify expected contributions from each sub-system. The model will then be used as a design decision tool, with the impact of decisions being modelled and trade-offs on system specifications being made as required, while keeping the total uncertainty within specifications.

Design concepts designed to maximise throughput without compromising accuracy have been developed, including automatic artefact alignment, multiple artefact loading, a multiple carriage probing system and a thermal control enclosure designed to control temperatures along the measurement line to millikelvin stabilities. Sub-systems with the highest technical risk, interferometry, probing, motion, and thermal control, are being breadboarded to test expected technological solutions ahead of a final design phase, with design and construction planned to commence in 2022.

Jamie McMillan

Postgraduate researcher at the University of Surrey. Working in collaboration with the Temperature and Humidity group at NPL

Traceable thermal imaging in harsh environments for nuclear material storage

Temperature measurement has a storied past with many realisations of a temperature scale, but with the turn of the 20th century these were unified through an international temperature scale. The most recent of which, the International Temperature Scale of 1990 is the practical realisation of temperature that has been achievable using contact thermometers (metal in glass, thermocouples or resistance thermometers) as well as infrared radiation thermometers.

Non-contact characterisation for nuclear storage container monitoring would provide Sellafield with critical information to support container management decisions. Determination of external surface temperature provides insight to the internal thermal activity and behaviour of a container and enables targeted intervention.

This research focuses on outlining experimental considerations that have been made to enable robust surface temperature measurement using thermal imagers, traceable to an international temperature scale. Temperature measurements from an inactive nuclear container store are presented and these should highlight the current state of the art in temperature metrology, as well as provide insight to the largest sources of experimental uncertainty.

Dr Thierry Stora

Senior physicist at CERN and CERN-MEDICIS project lead

CERN-MEDICIS - How has a collaborative project furthered nuclear medicine research?

Thierry Stora has been senior physicist at CERN for more than fifteen years. Initially in charge of the developments of the techniques to produce radioactive ion beams at ISOLDE by electromagnetic mass separation, he was later involved in the very first steps of the MEDICIS project. CERN-MEDICIS (CERN MEDical Isotope Collected from ISOLDE) is a new facility that started to produce its first radionuclides for the biomedical research in 2017. With a dedicated nuclear “class A work sector” where open radioactive sources can be handled, a dedicated target remote handling system, radiochemistry laboratory, and an isotope mass separator, non-conventional radionuclides and new purity grades can be made available to the biomedical researchers.

Through his role as the CERN-MEDICIS project leader, Thierry has facilitated research into the development of nuclear medicine using novel radioactive isotopes produced within the remit of the CERN-MEDICIS collaboration. This has brought together institutes from across Europe, including, notably: CERN, the National Physical Laboratory, the Paul Scherrer Institute, and many other international nuclear research, medical and academic organisations. The aim of this highly interdisciplinary community in translational research is to further new developments in nuclear medicine to treat and more efficiently diagnose diseases, such as various cancers, through the use of novel, medically interesting, radioactive isotopes, with less side effects and better efficacy. It recently triggered a pan-European medical radionuclide program, PRISMAP.

Ileana Silvestre Patallo

Postgraduate researcher at UCL. Working in collaboration with the Medical Radiation Physics group at NPL

Harmonizing delivered dose verification among the radiobiological research community

Preclinical studies involving irradiation of cells and small animal models have a direct impact on supporting the development of radiotherapy clinical trials, particularly those contributing to the generalization of personalized targeted therapeutic approaches. The current lack of accuracy and harmonization in dosimetry evaluations is compromising the required robustness in the comparison of radiobiological findings published by various research groups.

A dedicated system made of purposely designed zoomorphic tissue equivalent mouse phantom with insert for a detector placed in the intracranial cavity has been developed for verification of dose delivered with small animal irradiators. This system has been used in the end-to-end test employing alanine pellets as the reference detector. A set of standard planning and irradiation conditions has been used for the end-to-end test. A workflow with specific procedures was followed; these included phantom preparation, positioning, imagining, segmentation, pellet contouring, time and dose distribution calculations. The end to end test has been completed by six UK institutes using small animal radiation research platforms (SARRP).

By applying the end-to-end test, it was possible to detect problems related to the commissioning of the treatment planning system. The results for the six participating institutions give an indication of the level of accuracy that is possible to achieve while delivering the dose to targeted volumes in relevant mice irradiation conditions for the preclinical research using SARRP. This work demonstrates that alanine is a suitable detector for dosimetry tests in medium energy x-rays and that the developed procedure for an end-to-end test, in combination with a purposely designed phantom is adequate to support the efforts in improving dosimetry for preclinical irradiations.

Tarek Haloubi

Postgraduate researcher at the University of Edinburgh. Working in collaboration with the Informatics group at NPL

Machine learning techniques for evaluating disease and drugs effectiveness in fibre-bundle endomicroscopy systems

Several challenges limit the full potential of Fluorescence Lifetime Imaging Microscopy (FLIM), which is a powerful technique that uses the decay rate of fluorophore to provide a concentration-independent contrast to better visualise biological microenvironments. The emergence of miniaturised fibre-optic based endoscopes has led to the clinical widespread use of flexible and lightweight fibre-bundle endomicroscopy, making this a commonly used endomicroscopy platform. However, real-time endomicroscopy has been dominated and limited to intensity mode imaging due to existing detector technology. This limitation is now being overcome by the Kronoscan system, developed in the Queen's Medical Research Institute at the University of Edinburgh, by incorporating both intensity and lifetime imaging. This project will aim to use image processing and machine learning techniques for further developing FLIM platforms with three important contributions:

1) Improve FLIM platforms real-time applicability;
2) Improving image reconstruction; and
3) Quantification of samples for assessment, and develop clinically translatable quantification methods for monitoring of drug-target engagement.

A key ambition of the research will be to pave the way for subsequent clinical and commercial impact.

David Fairweather

Postgraduate researcher at the University of Edinburgh. Working in collaboration with the Optical Frequency Metrology group at NPL

Atomic clocks and earthquakes: seismic observation with ultrastable laser interferometry

During atomic clock comparison tests in 2017 conducted by NPL and other metrology institutes in Europe, signals were recorded that appeared to correlate with earthquakes that occurred during the testing time. Further tests revealed that not only can this laser interrogation of a fibre work across the repeaters necessary on long-range telecoms cables - it can also be utilised on live fibre. This makes the technique applicable to the global cable network and if fully implemented would open up areas previously inaccessible to consistent seismic monitoring, such as the deep ocean. This research is a collaboration between the fields of metrology and earth science.

Our aim is to classify and quantify the signals we are detecting with the ultrastable laser technology and ultimately understand the how various seismic signals register on a long-range fibre-optic cable compared to the more traditional point sensor seismometers. In doing this, we could not only expand our earthquake detection capabilities, but also aid risk management of secondary effects such as in tsunami monitoring, as well as improving tomographic images of the Earth’s interior.

Professor David D. Sampson

Pro-Vice-Chancellor, Research & Innovation, at the University of Surrey

David Sampson is the Pro-Vice-Chancellor, Research & Innovation, at the University of Surrey with portfolio responsibilities for research, innovation, and the Surrey Research Park. He is a member of the University of Surrey Executive Board, and Director of the University of Surrey Seed Fund and SETsquared Ltd. David sits on the editorial board of The Conversation (UK), and executive boards of SETsquared Partnership and SPRINT. As an active researcher, David was returned in REF 2021 and is active in the global optics & photonics community, currently as adviser to the Board of Directors of the SPIE – The International Society for Optics & Photonics and chair of the SPIE Publications Committee. David was formerly with the University of Western Australia and is a fellow of the AIMBE, IEEE, OSA, and SPIE.

UNIVERSITY OF SURREY

Aliza Ayaz

United Nations youth ambassador and Climate Action Society executive chair

Sustainability is the new holistic well-being

The private sector is interested in contributing to the United Nations SDGs; however, they lack credible objective metrics to measure progress, which hinders making a case for financial investment toward the SDGs. A set of science-based metrics could allow corporations and interested investors to meaningfully align their actions with the SDGs in locations around the world where they can make the greatest positive impact, including improving wellbeing. Using existing data on country-level electricity generation and land transportation, how can we develop a set of simple-to-implement and user-friendly metrics to evaluate the benefits of sustainable transition, be it via meteorology, investments in renewable electricity generation and improvements in land transportation to reduce CO_2 and air pollutant emissions and the health impacts of air pollution.

Hanifa Koguna

Postgraduate researcher at Imperial College London. Working in collaboration with the NiCE-MSI group at NPL

Brain tumour diagnosis using Laser Desorption Imaging-Rapid Evaporative Ionisation Mass Spectrometry (LDI-REIMS)

Hanifa Koguna[1,2], Daniel Simon[1,2], Chelsea Nikula[2], Teresa Murta[2], Ariadna Gonzalez[2], Alex Dexter[2], Anna Mroz[1,2], Josephine Bunch[1,2], Zoltan Takats[1]
1. Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom
2. National Centre of Excellence in Mass Spectrometry Imaging, National Physical Laboratory, Teddington, United Kingdom

INTRODUCTION/AIMS: Brain tumours have a poor prognosis with 10-year survival at 14 %. Extent of tumour excision is positively correlated with outcomes, however current neuro-navigation methods are limited. REIMS coupled with electrosurgery (Intelligent Knife (iKnife)) provides near real-time tissue characterisation comparable to histopathology. Laser Desorption Imaging–REIMS (LDI-REIMS) is a mass spectrometry imaging technique that allows for the detection of molecules in a spatially resolved manner under ambient conditions.

This study aims to build spatially resolved diagnostic ex-vivo models using LDI-REIMS that can be used for in-vivo tissue diagnosis with the iKnife, hence potentially improving extent of tumour resection by biochemically profiling cells.

METHODS: Fresh frozen brain tumours (2 low grade, 3 high grade and 1 metastatic) were obtained from patients following surgery. Tumours were sectioned (10 µm), mounted on Superfrost slides (Thermo Fisher Scientific, Waltham, USA) and stored at -80 °C. A Xevo G2-S QToF (Waters, Wimslow, UK) mass spectrometer was used in negative mode with an an Opolette HE2731 OPO laser (Opotek, Carlsbad, USA) at 2.9 µm wavelength for the LDI-REIMS to achieve a 70 µm pixel size. Post analysis, slides were sent for H&E staining. Data analysis was with multivariate analysis (MVA) including PCA and LDA. Database matching of metabolites was also conducted.

RESULTS: Preliminary results reveal distinct classification of tumours with up to 90 % accuracy on cross-validation. Additionally, insights into intra-tumour heterogeneity were gained by observing the non-uniform metabolite distribution within the tumour core and from the MVA results. Next steps include using a spectral identification algorithm based on the ex-vivo LDI-REIMS models to characterize novel samples. Co-registration with histology annotated H&E images is also planned.

CONCLUSIONS: Although sample size is limited, results are promising. LDI-REIMS has been demonstrated to be an appropriate approach to spatially resolve intra-tumour heterogeneity ex-vivo and has the potential to inform in-vivo diagnostics.

Jessica Emily Talbott

Postgraduate researcher at UCL. Working in collaboration with the Informatics group at NPL

Diffusion MRI: an early, non-invasive and repeatable detection method for disease

Jessica E Talbott[1], Nadia A S Smith[1], Chris A Clark[2] , and Matt G Hall[1]
1. National Physical Laboratory, Teddington, United Kingdom,
2. UCL GOS Institute of Child Health, London, United Kingdom

Diffusion is sensitive to very small-scale structures, thus in magnetic resonance imaging (MRI) can provide an insight into the microscopic structure of tissue via its effect on nuclear spins moving in living tissue giving an early, non-invasive and repeatable detection method [1]. Diffusion MRI follows a set equation, Bloch-Torrey, the solutions of which lead us to the generation of a synthetic signal, forming realistic biomarkers and measurements for standardization whilst bypassing obstacles such as cost and patient confidentiality.

In the presence of a magnetic field, the magnetisation vectors of atomic nuclei align either parallel or anti-parallel to the field, and they precess around the field lines at a very specific frequency, the stronger the field, the faster they precess. In diffusion imaging, additional field gradients are pulsed on and off in pairs, this encodes displacement - if the spins stay in the same place, a second pulse gradient of equal strength will re-align the spins giving a strong signal [2]. If there is diffusion, the second gradient pulse won't (quite) rephase the spins, leading to a weaker signal.

With no ground truth for diffusion MRI in biological complexity validation is key. Within the literature, various models have been presented, all aiming to numerically solve the Bloch-Torrey equation to synthetically generate MRI signal that can capture characteristics about tissue morphology. The macroscopic approaches such as finite element [3] the microscopic such as the Monte-Carlo [4] and the intermediate perspective given by Lattice-Boltzmann [5] have strengths in accuracy and computational efficiency. To date, however, there is no appropriate overall metric of comparison and so by coding the methods on an open-source platform within the same parameter and substrate space, we will be able to compare each in their suitability for different clinical scenarios which will give an insight into scan parameters required for clinical detection.

This work was funded by the UK's Department for Business, Energy and Industrial Strategy as part of the UK's National Measurement System Data Science programme.

[1] Costabile, Jamie D., *et al.* Frontiers in oncology 9 (2019): 426.
[2] Price, William S. Concepts in Magnetic Resonance: An Educational Journal 9.5 (1997): 299-336.
[3] Dang Van Nguyen, *et al.* Journal of Computational Physics, Elsevier, 2014, pp.283-302.
[4] Hall, Matt G., and Daniel C. Alexander. IEEE transactions on medical imaging 28.9 (2009): 1354-1364.
[5] Naughton, Noel M. *et al.*. Physical Review E 102.4 (2020): 043305.

Martin Metodiev

Postgraduate researcher at Imperial College London. Working in collaboration with the NiCE-MSI group at NPL

Measuring spatial resolution in mass spectrometry imaging

Mass spectrometry imaging (MSI) is a label free technique that can produce a map of the spatial distribution of metabolites, peptides, lipids, drugs and other molecules present in biological materials such as thin tissue sections. Due to its hyperspectral qualities and its ability to chemically characterise biological samples MSI sits at the forefront of cancer and pharmaceutical research and is expected to become a standard part of clinical practice in the coming years. The increasing use of MSI in biological applications means there is a need to better understand the resolution characteristics of MSI instrumentation.

Some MSI modalities like Secondary Ion Mass Spectrometry spatial resolution is limited by the size of the sampling probe. In other modalities, for example Matrix Assisted Laser Desorption/Ionisation (MALDI) features smaller than the width of the sampling probe can be imaged. In order to explain the difference between the two modalities an image formation model was developed. The model showed that the rate at which material is consumed affects image blur. It explained why commonly used methods for measuring resolution, such as measuring the blur in a sharp step edge, are not appropriate in MALDI MSI, where material consumption effects cannot be neglected. Instead, the signal to noise ratio is the limiting factor of resolution.

The experimental part involved producing images of a sharp silver step edge at various pixel sizes. Using a modulation transfer function (MTF) the blurring effects induced due to stage motion, beam width and material consumption were estimated. Blurring effects alone were not sufficient to determine the spatial resolution. A noise power spectrum (NPS) was then used to estimate the amount of noise corrupting the signal. Spatial resolution was then calculated by finding the point of intersection between the MTF and the NPS.

Dannielle Cox-Pridmore

Postgraduate researcher at the University of Surrey. Working in collaboration with the Electronic and Magnetic Materials group at NPL

Bioelectronics and personalised disease models

A myocardial infarction (MI), or more commonly known as a heart attack, occurs when there is a lack of blood flow and therefore oxygen to the heart. This results in tissue scarring and death during this period of hypoxia. MI is one of the leading causes of death in the world, and there are little to no effective therapies. There is a desperate need for better preclinical heart models, so that we can better understand the hypoxia process and develop novel therapeutic strategies.

Heart tissue models have the potential to be created from patient-specific human induced pluripotent stem cell-derived cardiomyocytes, a.k.a. heart muscle cells. The tissue models can then be placed in a specialised incubator chamber that mimics hypoxia (low oxygen levels) as if in the process of a heart attack.

The focus of my project is the creation and introduction of bioelectronics within these models. The field of bioelectronics is the production of devices that can provide an interface with biological systems. By introducing the flexible and biocompatible electronic mesh into the heart cell culture allows for the long-term monitoring of the cells to detect the subtle changes in cardiomyocyte excitability, contractility, and cell death rate resulting from the disease-like conditions, as well as a better understanding of peak times of drug delivery. By comparing these results to control parameters that match a physiologically healthy person could allow for a greater understanding of how to improve the survival rate of cardiac tissue experiencing hypoxia.

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Abubakr Qaasim

Postgraduate researcher at the University of Strathclyde. Working in collaboration with the Quantum Electrical Metrology group at NPL

Quantum memory with semiconductor spin defects

Quantum computing could herald a new age of calculation, whereby some problems could be solved exponentially faster than today's classical computers. Just like a classical computer requires a short-term memory to store data temporarily whilst the processor is doing a calculation, a quantum computer would benefit from a similar short-term quantum memory.

There would be three stages to implement data storage for a quantum system:

1) information would need to be transferred from the processor to a waveguide for long range photonic propagation (the equivalent of I/O bus in classical computers),
2) photons would have to be trapped into a cavity or resonator,
3) trapped photons would interact with an external two-level system (or qubit) acting as the storage system.

The coupling between the resonator and the two-level system is an important figure of merit to realise data storage, and it would depend on the specific choice of hardware implementation. In my project, I aim at realising a quantum memory by coupling semiconductor spins to superconductive resonators.

The spins of electrons trapped at crystal defect sites in silicon carbide, have been demonstrated to be an excellent host to store quantum information. Defects can be created by bombarding crystalline material with ions which displace or replace the original atoms in the semiconductor and create vacancies or substitutional defects, whose spin properties can be used as qubits.

My work explores techniques to maximise the coupling between an ensemble of such spins and a niobium resonator, and minimising loss in the transfer. How much information is lost in the information transfer can be evaluated by a metric known as the resonator quality factor, which is amenable to careful design optimisation techniques, as I will discuss. I will provide details of our cryogenic experimental set-up and present measurements for a range of resonator designs.

Binod Limbu

Postgraduate researcher at the University of Strathclyde. Working in collaboration with the Quantum Information Processing group at NPL

Frequency stabilisation of a 422 nm diode laser for doppler cooling of trapped ^{88}Sr+ ions

Trapped ions are often used for research in quantum information, quantum simulation and quantum metrology. A requirement is that the ions are Doppler cooled before applying any quantum control routines. Frequency stability of the cooling laser is necessary to maintain an efficient ion cooling rate and a constant fluorescence signal. Unlike neutral atoms, ions have no straightforward means to reference the cooling laser to a vapour of the atomic species under study.

^{88}Sr^{+} is laser cooled using the $5s^{2}\ S_{1/2}$ – $5p^{2}\ P_{1/2}$ transition at 422 nm. Conveniently, the $5s^{2}\ S_{1/2}$ (F'' = 2) – $6p^{2}\ P_{1/2}$ (F' = 3) transition in ^{85}Rb vapour, which is only 440 MHz from the ^{88}Sr+ cooling transition, can be used for stabilising the 422 nm laser. To date, we have used the frequency-doubled output of an 844 nm extended-cavity diode laser (ECDL); this is more complex and yields lower optical power than the present generation of blue ECDLs.

Frequency-modulated light from a 422 nm ECDL performs saturated absorption spectroscopy of the ^{85}Rb transition. Lock-in detection yields the first derivative of the absorption signal, which serves as the discriminant for stabilising the laser frequency. Fourier analysis of the locked discriminant was used to optimise the servo PID parameters. A wavemeter monitoring the laser frequency showed stabilisation was maintained for more than 90 hours, which is a vast improvement over the previous system. These tests demonstrate the suitability of the 422 nm ECDL for Doppler cooling of trapped ^{88}Sr+ ions.

James Murawski

Postgraduate researcher at Imperial College London. Working in collaboration with the Electrochemistry group at NPL

Stability measurement challenges for PEM water electrolysis

State of the art proton exchange membrane (PEM) electrolysers employ iridium based oxides to catalyse oxygen evolution at the anode. In order to enable scale up of PEM electrolysers to the terrawatt scale, further decreases in the iridium loading are needed, without incurring additional potential losses or reducing the device lifetime. Short term electrochemical methods alone are insufficient to predict catalyst degradation over the calendar lifetime: they can both underestimate and overestimate catalyst durability. Therefore both complimentary techniques and understanding of limitations of testing is vital for testing of new oxygen evolution catalysts that are necessary to improve both the commercial viability and scalability of this technology.

Emily Webster

Postgraduate researcher at the University of Southampton. Working in collaboration with the Mass Metrology group at NPL

µKibble balance: towards the realisation of the milligram on the production floor

Mass measurement touches all parts of our lives. Everything from ensuring governments are paid the correct amount of tax on commodities traded to delivering a safe amount of active ingredient in medicine currently relies upon an unbroken chain of traceably calibrated ‘mass standards’ or weights.

Historically the definition of mass has always been a special object. The last kilogram artefact was the International Prototype Kilogram (IPK) stored at the Bureau of International Weights and Measures (BIPM). In 2019 the SI kilogram was redefined in terms of the Planck constant *h* a fundamental constant of nature. This paradigm shift has heralded the beginning of a new chapter.

National Measurement Institutes (NMIs) are now able to realise the unit of mass independently and at any point on the mass scale with direct traceability. This opens up the possibility of improved measurement capability at small scales and in particular for sub-milligram mass applications where traceability is limited by high relative uncertainty due to the process of sub-division.

One of the routes to realising the new kilogram is via a Kibble balance which compares a mechanical force (the weight of a mass) with an electrical force generated, for example, by a coil in a magnetic field. Traceability to the definition is established through quantum electrical standards. Instruments and sensors based on the Kibble principle have the capability to make mass standards redundant by delivering directly traceable measurement at the point of use.

I will present a concept microelectromechanical Kibble balance aimed at providing traceable milligram and sub-milligram measurement on the production floor.

Lillian Koppensteiner

Postgraduate researcher at the University of Edinburgh. Working in collaboration with the Optical Frequency Metrology group at NPL

Development of a surface-biomarker signature to identify tumour-relevant T cells in non-small cell lung cancer (NSCLC)

The presence of functionally efficient cytotoxic T lymphocytes (CTL) in the tumour nest is crucial in mediating a successful immune response to cancer. However, the detection and elimination of cancer cells by CTL can be impaired by cancer mediated immune evasion. Immunotherapies such as checkpoint inhibition aim to revive the CTL response but remain ineffective in a large proportion and current methods for stratifying patients are limited.

In this project, we aim to develop and validate a surface biomarker signature to identify tumour relevant CTL in NSCLC, which could allow us to predict and monitor responsiveness to treatment. To gain a better understanding of the most biologically relevant biomarkers, we investigate tumour tissue from early NSCLC patients, which we receive from an onsite hospital, through collaboration with NHS research nurses. As part of a 3-student cohort, in collaboration with Glaxo-Smith Kline, the University of Edinburgh and NPL, we have the fantastic opportunity to widen the impact of our research and work together towards translational approaches to apply our findings for clinical, in patient use. In the spirit of bench to bedside research, we aim to develop novel chemical probes for relevant biomarkers and test their validity in ex-vivo lung models. In the University of Edinburgh's Healthcare Technology Accelerator Facility, we have the unique chance to work closely with an exceptionally interdisciplinary team of scientists from a broad range of fields including chemistry, physics, machine learning, clinical sciences and more. In this scope, we have access to novel technologies being developed in house for in situ visualisation of targets of interest. This project strongly benefits from the collaborative approach within academia and with our partners at GSK and NPL, as this has allowed me to broaden my perspectives and drive this project towards exciting, clinically relevant and statistically robust medical research.

Patrick Hunter

Postgraduate researcher at the University of York. Working in collaboration with the Biometrology group at NPL

Collaborative development of next generation bioimaging tools to dissect the immunological synapse in single cells, one molecule at a time

The adaptive immune response relies on the ability of cells to recognise pathogens as well as to communicate with surrounding cells. This is carried out in part by the presentation of antigens on the cell surface and the transfer of cytokines between cells. However, transfer of information between mobile lymphocytes and their target cells requires spatial organisation, substantial timescales and relies on binding reactions with a relatively low binding affinity. Therefore, immune cell communication requires the formation of a stable immunological synapse (IS) interface capable of colocalising cells long enough for sustained signalling to take place.

Upon the formation of the IS, cell signalling components and surface receptors are recruited to the IS interface forming micro-scale domains. C-C chemokine receptor type 5 (CCR5), a known coreceptor of the human immunodeficiency virus (HIV-1), is one such receptor theorised to be involved in the promotion of the IS formed between T cells and antigen presenting cells and its investigation in the context of the IS forms the basis of this study.

To provide a thorough study of the architecture of CCR5 complexes and their involvement in the regulation and function of the IS, investigations must be made using high-resolution high-speed methods capable of determining receptor dynamics and stoichiometry on a single molecule level in situ. This characterisation of localised receptor distributions and cell surface dynamics will be achieved using a suite of complementary techniques, including super-resolution structured illumination microscopy and high-speed total internal reflection fluorescence microscopy, made accessible through collaborations between NPL and the University of York. Through the shared use of state of the art interdisciplinary imaging facilities at both NPL and York this project aims to provide unprecedented insight into the microstructures and chemokine behaviour that underpin the regulation of the IS.

Ruan Mayworm

Postgraduate researcher with the National Institute of Metrology, Quality and Technology (INMETRO). Working in collaboration with the Mass Metrology group at NPL

Development of a Kibble balance for ultrasound applications

The International System of Units (SI) has been evolving and changing with new technologies. In May 2019, the SI was revised. One of its consequences was the redefinition of the kilogram, one of the seven base units of the SI, in which, as of May 20, 2019, it is now based on the Planck constant and no longer related to a physical artifact, the international prototype of the kilogram (IPK). The SI revision process highlighted the Kibble balance, which is one of the experiments that will be used to realise the redefined kilogram and relates mass to fundamental electrical standards. During this process, several National Metrology Institutes (NMI) developed their models of Kibble balances to assist in the redefinition of the kilogram. One of these balances was the bench Kibble balance, which, despite not showing the accuracy and precision of a NMIs Kibble balance, uses the same physical principle in its measurements.

The present work is developing a bench Kibble balance to perform ultrasonic power measurement. Ultrasonic power measurement is typically based on a measurement system with the aid of a conventional balance. Knowing the emission of ultrasonic power is extremely important, considering that ultrasound is widely used in medical instruments for therapeutic and diagnostic purposes. Due to its operating principle, the use of a Kibble balance will provide advantages for the measurement of ultrasonic power, such as the non-influence of the acceleration of gravity in measurements. That issue will allow the mobility of the measurement system and, in addition, it may provide a higher level of metrological reliability than the current system.

Kanokrat Charoenpornpukdee

Postgraduate researcher at the University of Bristol. Working in collaboration with the Gas Metrology group at NPL

Development of synthetic nitrous oxide (N_2O) reference standard for atmospheric observation

Nitrous oxide (N_2O) is the third most potent greenhouse gas with a global warming potential over a 100-year time horizon (GWP100) of 296 higher than CO_2. It is also defined as the most significant indirect ozone depleted substance. The primary emission of N_2O is from natural sources, with 40 % from anthropogenic sources. Atmospheric N_2O concentrations have increased from 270 nmol/mol in the pre-industrial era to 332.0 ± 0.1 nmol/mol in 2019 (WMO, 2020). The significant change in N_2O concentration is from the modified land to agricultural area. To better understand N_2O emissions in the UK, it is vital to use atmospheric measurements at various locations to constrain the emission sources. The World Metrology Organisation (WMO) establish the compatibility goal of atmospheric N_2O measuring is 0.1 nmol/mol (extended to 0.3 nmol/mol). To achieve this we report the deployment of an in-situ, high frequency, high precision, advanced laser spectrometer combined with the development of calibration standards with a quoted small uncertainty which is traceable to internationally accepted scale. Developing the N_2O synthetic standard would avoid the inaccuracy of impurities in whole air and reduce the standard uncertainty. Synthetic N_2O primary reference materials prepared gravimetrically showed that one of the significant uncertainty contributions is from the purity assessment of trace N_2O in the matrix gases such as nitrogen and oxygen (Hill-Pearce et al., 2021). In this study, the determination of trace N_2O in pure gases has been developed using the Boreas system – an inline sample preconcentration system coupled with a laser spectrometer (Rennick et al., 2021). This system allows the preconcentration up to 250 times, with a limit of detection of N_2O is up to 40 pmol/mol.

Sam Flynn

Postgraduate researcher at the University of Birmingham. Working in collaboration with the Medical Radiation Science group at NPL

Development of an adjustable collimator for microbeam irradiations in proton beams for radiobiological and dosimetric studies

Spatial fractionation in radiotherapy is an emerging technique which is indicated to have preferential normal tissue sparing relative to conventional radiotherapy. Preclinical studies have indicated that this dose pattern has a greater efficacy than that of a single uniform field but a substantial amount of research is still required before translation into routine clinical practices. Spatial fractionation in protons is theorised to have additional benefits as multiple Coulomb scattering can be exploited to maintain a uniform dose distribution in the tumour volume.

This project is developing an adjustable microbeam collimator for low energy proton microbeam irradiations with an ambition of establishing a test facility for cellular irradiations and the development of novel dosimetry techniques. Using the University of Birmingham's MC40 cyclotron and a Monte Carlo optimised tantalum collimator with 100 μm slits we present a novel system capable of delivering a variety of peak-to-valley dose ratio configurations.

Melina Kyriazi

Postgraduate researcher at Imperial College London. Working in collaboration with the NiCE-MSI group at NPL

Interlaboratory evaluation of MALDI and DESI MSI in the CRUK Grand Challenge Programme

Melina Kyriazi[1,2], Chelsea Nikula[1], Alex Dexter[1], Adam Taylor[1], Zoltan Takats[2], Josephine Bunch[1,2]

1. National Centre of Excellence in Mass Spectrometry Imaging, National Physical Laboratory, Teddington, UK;
2. Department of Metabolism, Digestion and Reproduction, Imperial College London, London, UK

Mass Spectrometry Imaging (MSI) allows the investigation of the spatial distribution of molecules at complex surfaces. Interlaboratory studies are collaborative exercises by laboratories to assess or improve the quality of their measurements. They are important in cancer research to evaluate if methods are effective, fit for purpose and transferable between sites. Reproducibility across multiple research centres is the largest obstacle in moving MSI towards routine clinical use. Developing suitable reference standards is important for ensuring quality control in MSI.

Metabolites of interest were selected, dissolved in chemicals in known concentrations and spotted on glass slide. They were also spiked in serum and spotted on a glass slide obtaining up to 600 spots in one glass slide. The same metabolites were also spotted on top of tissue mounted on glass slide. The spotting in all above preparations was done using the Biofluidix Biospot which is an automated nanolitre dispenser which offers high precision and accuracy in sampling. Ion suppression and ion enhancement effects were compared between different reference standard preparations when using the same concentration of metabolites of interest. Limit of detection of metabolites when using different reference standard preparations and analysing by MALDI and DESI MSI was assessed.

Tissue homogenates were prepared and a hypothesis that metabolites of interest will undergo further metabolism after being spiked on tissue homogenates was proven using a colorimetric assay method. Alanine transaminase (ALT), which catalyzes the conversion of alanine and a-ketoglutarate to form pyruvate and glutamate, was used as an indicator of the liver activity. Quantitation of the pyruvate in liver tissue homogenate was preformed from the pyruvate calibration curve and the ALT activity was determined in the liver tissue homogenate. Initial experiments show that fresh frozen liver tissues remain metabolically active according to this assay.

Future work will involve more work towards developing reference standards for quality control purpose and improving reproducibility. This includes investigating different fixation methods to assess their ability to prevent further metabolic activity. More work will also be done towards the evaluation and optimisation of selected imaging parameters and their effect on metabolites detected. A multi-technique, multi-site comparison will be performed to assess repeatability and reproducibility of results.