NPL

Department for Business, Energy & Industrial Strategy

University of Strathclyde

University of Surrey

PGI PostGraduate Institute for measurement science

A Year in the PGI

2021 Edition

Editing Team

Tarek Haloubi	University of Edinburgh
Jennifer Blair	University of Strathclyde
Dimitri Bagkos	University of Sussex

pgi@npl.co.uk

www.npl.co.uk/pgi

@PGImetrology

@pgimetrology

https://doi.org/10.47120/npl.9325

1. Improving outcomes in healthcare
2. Meeting the digital challenge
3. Transforming technology and innovation
4. Advancing measurement science
5. Responding to climate change
6. Creating a global footprint
7. Working with industry
8. Creative development of new materials

A few words on the PGI

Richard Burguete
PGI Director

What a year 2021 was for research and showcasing how scientific advancement is relevant to us all! And what better way to finish the year than by sharing with you the impact our postgraduate researchers have had despite being in the midst of a pandemic.

Over the past year we have seen our postgraduate researchers grow in confidence and build connections with industry and other partners. This has enabled them to demonstrate how measurement science accelerates progress and is pivotal in the development of solutions that address global challenges. Some examples of how this is happening can be seen in this showcase.

The PostGraduate Institute (PGI) has been tirelessly supported by our strategic partners: the University of Strathclyde, University of Surrey and the Department for Business, Energy & Industrial Strategy. It would not have been possible to progress in the way that we have without their backing, along with the support of all our university collaborators.

I am therefore, with the whole PGI team, especially proud to be able to play a part in the journey that our postgraduate researchers are on, by helping to communicate their work, particularly as they move forward to establish careers within and beyond NPL. I hope you enjoy reflecting on some of the highlights of 2021 and that it inspires you to get in touch and become part of the PGI. We look forward with energy and enthusiasm to all that our researchers will achieve in 2022.

1 Improving outcomes in healthcare

The life sciences and healthcare landscape is transforming. Demographics, quality of life, environmental and economic shifts are all contributing to this change. As the global population is growing and aging, new areas of medical need are emerging. The COVID-19 pandemic has also shown us all that the world needs to be better prepared to respond to global health emergencies, regardless of geography, or socio-economic position. Advanced measurement science infrastructure and capability is essential to address these challenges and realise the opportunities they provide.

The role of 'disappearing' illumination in accelerating antibiotic screening

Shannan Foylan - University of Strathclyde

Antimicrobial Resistance (AMR) is a huge challenge to modern medicine, requiring a streamlining to drug discovery protocols. The chemical interactions between microbes can be examined with cutting-edge mass spectrometry while the physical interactions at microbial membranes can be visualised with novel imaging modalities.

Light microscopy has served a useful role in biological sciences for centuries but in recent years the development of new and advanced microscopy methods has transformed our knowledge. An important example is the utility of evanescence to illuminate a specimen for imaging. Evanescent light is spatially confined in one dimension such that the intensity of the light will be negligible after a few hundred nanometres, effectively creating a thin light sheet. Illuminating a sample with this sheet allows for excitation of fluorescence only within this thin sheet, thus providing detail within this region which is sharper than a normal light microscope can provide.

This technique, known as Total Internal Reflection Fluorescence (TIRF) microscopy, has been used extensively in cell biology since the 1980s.

An interesting extension to this established method is to scale it up to the mesoscale, for imaging of large cellular specimens.

At the University of Strathclyde, the custom Mesolens has been developed to image over a 36 mm lateral field of view and through a depth of 3 mm, allowing for the capture of entire colonies of bacteria, intact tissue and the full bodies of insects and mice embryos.

The massive bespoke optics of the Mesolens retains sub-cellular detail alongside this expansion in field of view, with a current lateral resolution of 700 nm and an axial of 7 µm. A modality for TIRF microscopy on the Mesolens would allow for resolving bacterial membranes, and any antibiotic action occurring at them, across colonies. The variability of how individual cells react to the same antimicrobial agent would provide incredibly useful qualitative and statistical information, forming a high throughput screening method for novel antimicrobials.

https://doi.org/10.7554/eLife.18659

Image: Shannan Foylan

"My research focuses on developing new imaging techniques with our custom massive field of view objective lens, the Mesolens. With an imaging field 3600 times that of a comparable resolution commercial lens, over one thousand mammalian cells can be captured simultaneously with the capability of resolving sub-cellular detail. My aim is to further improve this resolution to visualise cell membranes, which would allow us to have a high throughput screening method for antibiotic discovery."

Shannan Foylan explaining the future goals of her research

Miniaturising accurate atomic clock technology to unlock new applications

Martin James Knapp
- University of Oxford

Image: Martin James Knapp

Over the past few decades, atomic timekeeping has become a firm requirement for a myriad of critical national infrastructure applications and services such as: position and navigation, energy grid management, communication synchronisation, and timestamping for financial trades. Such precise timing is derived predominantly from atomic fountain-based clocks developed within national laboratories and research institutes around the world. These systems are state-of-the-art and provide exceptional accuracy, although these systems generally occupy an entire laboratory space.

There is a growing need for atomic clocks with high accuracy and stability, but in a compact form- factor for use in remote or local locations. Existing compact clocks operate using thermal atoms due to their simplicity; however, they are becoming limited in their capabilities as requirements increase, for example, in respect of space science, enhanced satellite navigation, mobile and high-speed communications, and autonomous vehicles. Perhaps most vital is the ability for a compact atomic clock to serve as a holdover reference during accidental or intentional global navigation satellite system (GNSS) outages, a service which many industrial and societal applications are heavily reliant on. Consequently, there is a need for compact atomic clocks based on ultra-cold atoms which will have superior accuracy and holdover performance abilities over the existing thermal atom counterparts. Such systems use novel engineering and physics adaptations that can provide performance approaching that of a laboratory sized atomic clock, but in a much smaller footprint.

This research focusses on investigating and developing a novel cold compact atomic clock that offers improved performance over existing vapour cell-based compact clock technologies. The novelty of the project is in combining existing compact cold atom source technology with well-established atom interrogation techniques.

Image: National Physical Laboratory

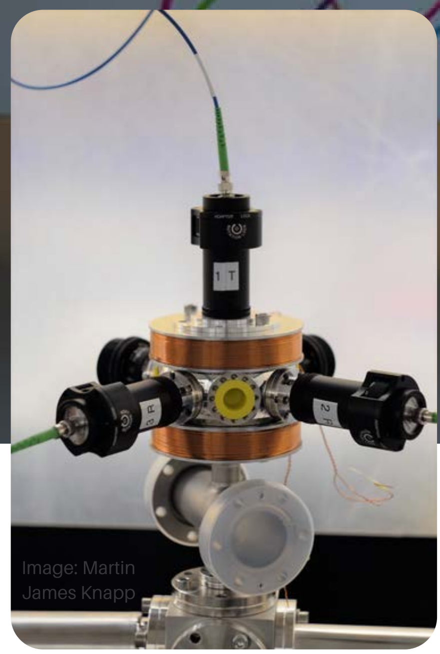


Image: Martin James Knapp

"Aside from performing exciting atomic physics, I really like that this research has close links to real-world applications and has the potential to be very impactful in industry. "

Martin James Knapp, on the perks of his PhD topic

Meeting the digital challenge

2

We are entering a period of historic universal change. The catalyst will be advances in areas such as artificial intelligence, digital pathology, super-fast intelligent communication networks, synthetic biology, distributed ledger technology, robotics, Internet of Things, additive manufacturing and autonomous systems. Secure, traceable and authenticated digital approaches and embedding measurement into our digital infrastructure is the key to meet the digital challenge.

Transforming technology and innovation

3

Advanced manufacturing is transforming industry and productivity. Ensuring that material formulation and manufacturing technologies meet the standards and specifications that businesses demand and can be traced, are vital to control manufacturing processes and assure the quality of products. **Good measurements are vital to productivity, acceleration of product to market, and innovation.**

Developing a smart and miniaturised feeder for pharmaceuticals

Peter Hou - University of Strathclyde

Micro-factories and continuous manufacturing play an important role in allowing future manufacturing of medicine to be more flexible, resilient, and sustainable. Highly accurate powder feeding is a key element to realise micro-factories for drug products in the pharmaceutical industry. Particularly, precise dosage and hence product quality are highly dependent on the accurate feeding of raw materials.

The accuracy needed for feeding micrograms of pharmaceutical powder remains challenging with currently available feeding systems. This project focuses on developing a micro-feeding system that can feed a wide range of solid pharmaceutical materials and accurately measure micrograms. 3D printing technology was used to fabricate a modular feeder during the design stage with the advantage to optimise the design of the feeder.

The modular design provides flexibility to the feeder for handling a wide range of powder properties. A novel micro-feeder that can accurately feed a range of materials in a small quantity has been developed, i.e. 3.0 - 6.0 g/h ± 10% for poorly flowing materials and 1.5 - 15.0 g/h ± 5% for easy flowing materials.

An accurate powder micro-feeder that has the potential to act as a key element for future micro-factories to manufacture personalised medicines and the enormous potential they have to realise targeted and highly effective treatments, especially for cancer patients. Other technologies such as 3D printed medicine, direct compression and direct capsule filling require accurate powder dosing and feeding. Moreover, high-potency pharmaceutical active ingredients are growing, requiring micro-feeders that can precisely feed micrograms of the drug substance to manufacture high-quality medicines.

Image: Chung-Hsien Hou

"My project gave me access to world leading academics and scientists at the University of Strathclyde and NPL and I am excited for a future where my ground-breaking research is implemented to advance the well-being of us all"

Peter Hou's thoughts on his PhD journey

Advancing measurement science

4

Measurement solutions are critical to business and government, accelerating research and innovation, improving quality of life and enabling trade. Measurement science is always evolving and improving its methods. **The next big step forward is for superior digital measurement to become the norm in an effort to improve measurement accuracy and minimize human error.**

Uncertainty quantification for data efficient machine learning

David Fernandes - University of Bath

Organisations across all sectors are interested in employing machine learning algorithms, but can these methods be trusted? Modern deep learning is computationally powerful and scalable but is unable to offer guarantees on confidence and data efficiency. This project is addressing these issues by combining deep learning with the desirable properties (quantified uncertainty and incorporation of domain knowledge) of traditional generative probabilistic models.

Traditional (generative) data analysis methods rely on validated deterministic and statistical models of the physical system under study. These offer good predictive capabilities, importantly, with a supporting quantification of the associated uncertainty. In contrast, many recent (discriminative) black box deep learning and Artificial Intelligence approaches make inferences from training data with no underlying physical model of the system and no supporting uncertainty quantification. They employ extremely flexible, intrinsic empirical models that can match any training set, but cannot place guarantees on their predictive capability.

With a saturated set of training data, it can be expected that the trained model approximates well the true underlying physical model, at least in the region from which the training data is drawn, leading to some confidence in the inferences made by the algorithm. But for practical applications, there will be no way of knowing how well the trained response reflects real attributes of the physical system, and the uncertainties associated with their outputs are unquantifiable.

This project is investigating theoretical, algorithmic and practical issues associated with data analytics based on learning paradigms that make efficient use of the data and any prior model constraints and, support uncertainty quantification.

"My research aims to develop machine learning models that automatically incorporate uncertainty. This way, when used in real-life applications, the user can know how sure (or unsure) the model is of its predictions and act accordingly, whether that is collecting more data or changing the approach."

David Fernandes outlining his project scope

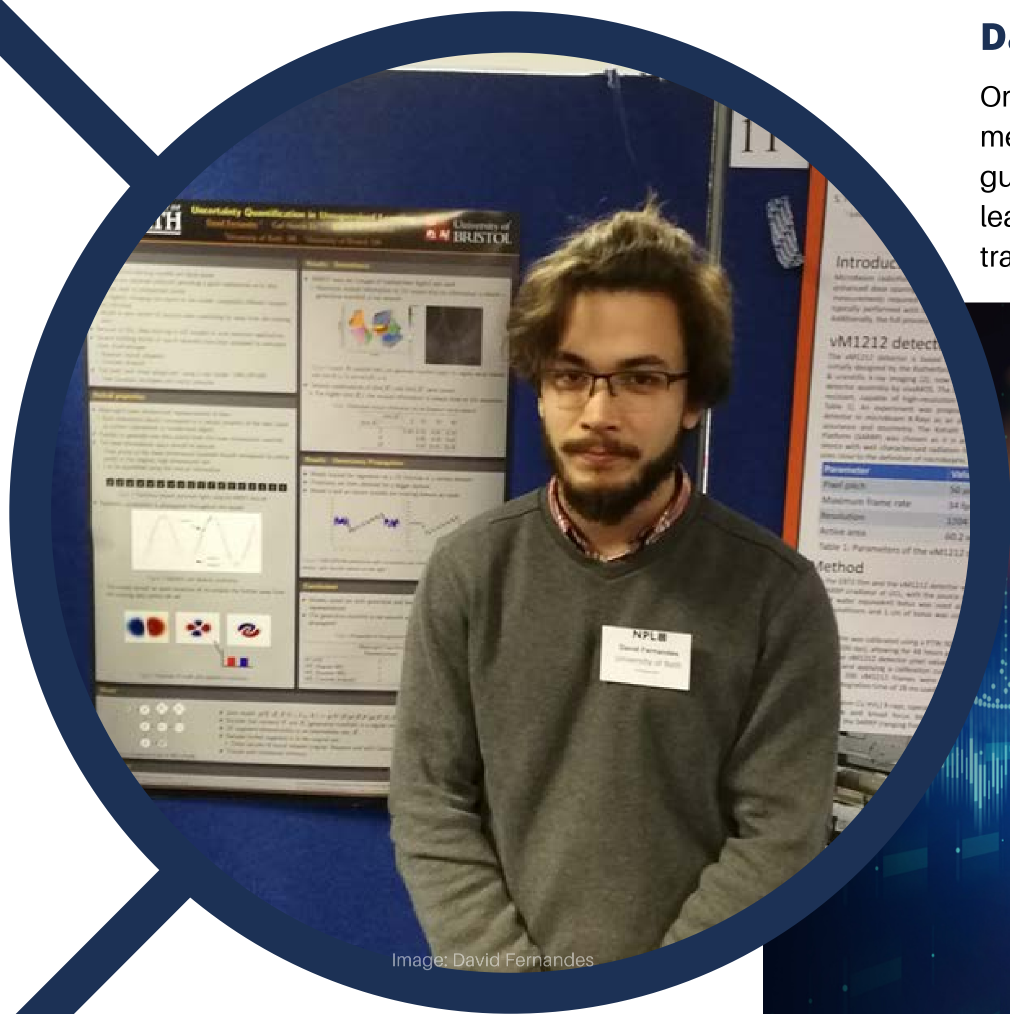


Image: David Fernandes

Image: Heather Graven

Responding to climate change

5

The need to decarbonise our economy whilst monitoring and adapting to climate change is driving huge transformation in all sectors. Managing the sometimes-conflicting needs of society and our environment is a complex challenge. It demands a whole system approach supported by a global effort, with decision making that needs to be anchored in trustworthy science and data. Measurement science is critical to identifying and quantifying this environmental impact as well as making energy generation and transport more efficient, safe and affordable.

Are London greenhouse emissions being under reported?

Eric Saboya
- Imperial College London

Methane has more than 80 times the warming power of carbon dioxide (CO_2) over the first 20 years after it reaches the atmosphere. Even though CO_2 has a longer-lasting effect, methane sets the pace for warming in the near term. Collectively, urban areas form the single largest human-induced contribution to climate change. Methane, an important greenhouse gas, is emitted from a range of sources. Landfill sites, effluents, and natural gas leaks from pipes all emit methane. Forming accurate methane emission constraints of cities is vital for successful mitigation policies.

This PhD project developed different measurement and modelling techniques for improving methane emission estimates of different sources in the UK. Some of the findings will be presented in a research article; “Continuous CH_4 and $\delta^{13}CH_4$ measurements in London demonstrate under-reported natural gas leakage”. Atmospheric measurements of methane and its carbon-13 isotope from early 2018 to October 2020 were used to evaluate emission estimates of methane in central London.

Measurements indicated UK emissions reported to the United Nations were underestimating methane emissions in central London by 30-35 %. Observations suggest that many of the missing emissions can be attributed to under-reported natural gas methane emissions in London.

Having more accurate figures should increase the urgency of acting now. Cutting methane emissions is the fastest opportunity we have to immediately slow the rate of global warming and it’s an opportunity we can’t afford to miss.

"This research highlights the importance of measurements for evaluating reported greenhouse gas emissions and their use in tackling the climate crisis"

Eric Saboya (right) on his research impact

6 Creating a global footprint

Universities and businesses across the world are making the most of the possibilities by forming global partnerships and fostering relationships with other institutions. The PGI is embedding measurement solutions in PhD projects for real world problems as well as creating global partnerships that focus on interdisciplinary R&D solutions.

Fibre optic sensors for pH measurement in harsh environments

Shaon Debnath - University of Strathclyde

Currently there is no reliable instrument that is capable of accurately measuring pH at temperatures exceeding 100 °C under harsh conditions that is usually observed in oil wells. Failure to accurately determine pH under harsh conditions of high temperature and presence of aggressive chemical species could result in underestimation of the impact of reduced pH on process facilities. This could culminate in corrosion of industrial assets which could lead to accidents and fatalities as well as high cost to maintain and repair damages caused by corrosion.

Image: Shaon Debnath

This project is aimed at fabricating a pH sensor using an optical fibre suitable for measuring pH in harsh conditions of high temperature and pressure. During the project a coating consisting of silver nanoparticles embedded in silica was developed using sol-gel synthesis. This was decorated on an optical fibre and tested under different harsh conditions to observe its effectiveness to accurately measure the pH of these environments. Results indicated a change in intensity of light at different pH characteristic of each environment. Sensitivity and durability tests were carried out to investigate the suitability of the instrument in determining pH under different conditions. It was observed that the coated optical fibre gave different response in the intensity of light passing through the optical fibre at different pH. This response indicates that the coated optical fibre is a suitable sensor for the determination of pH in harsh environments. This technology is in the process of being fully developed and will be useful in the oil and gas industry.

"This idea of using coated optical fibres to measure pH under severe conditions will have significant impact in my home country, Bangladesh, as this technology is not in use at the moment. The environment in my country within the offshore is characterized by increased salinity and concentration of aggressive species as revealed by field studies within this sector. This new technology will make a great difference in developing efficient ways of monitoring the pH around these environments to ensure that adequate action is taken before failure of assets becomes imminent."

Shaon Debnath discussing his research motivation

7 Working with industry

Industry needs support from science and technology communities to meet challenges of the fourth industrial revolution and the advancing digital transformation. Without this, there is a risk that the UK falls behind on the international stage, fails to meet climate change targets, and businesses struggle to survive. **Good measurement creates certainty in the quality and safety of new and existing products and processes, and boosts productivity by reducing waste, increasing efficiency and enabling confidence.**

Machine learning techniques for evaluating disease and drug effectiveness in fibre-bundle endo-microscopy systems

Tarek Haloubi - University of Edinburgh

Modern pharmaceutical R&D demands sensitive and specific measurement technologies to understand disease and interrogate drug response. Progress continues to be made using radiological and nuclear medicine methods, e.g., positron emission tomography (PET) radiotracers for specific targets of interest or functional magnetic resonance imaging (MRI) of tissues. However, concerns regarding radiation exposure and the long-term toxicity of MRI contrast agents are likely to reduce future development opportunities and ease of translation. In addition, particularly for immunological targets, measurements and analysis methods that can study specific cell populations in vivo together with the tissue matrix are more important than ever, and this demands greater performance than the traditional whole-body imaging techniques can offer.

Optical methods have potential to complement whole body measurements if tissue access is possible. A three-way collaboration between the GlaxoSmithKline (GSK), the University of Edinburgh and the National Physical Laboratory (NPL) is developing novel optical imaging methods.

This project is an addition to enhance the body of work to be conducted under the recently awarded EPSRC Health Innovation Partnership (HIP) award, by addressing unknowns and bottlenecks in the Fluorescence Lifetime Imaging Microscopy (FLIM) platform (including aspects of quantification, reproducibility, and validation), and it is aiming to address the challenges associated with image processing and machine learning.

To date, real-time endomicroscopy has been dominated and limited to intensity mode imaging due to existing detector technology. The systems in development are poised for disruptive healthcare impact, and a key ambition of the research will be to pave the way for subsequent clinical and commercial impact.

The project will also, in parallel, explore application of the platform in cancer and drug-target engagement, which are of key interest to the GSK. This will focus on imaging the relevant biology, including through optical life-time analysis. This three way collaboration provides an end-to-end capability from basic science to clinical application, thus enhancing the depth of research and enabling quicker translation of research ideas to improve health outcomes and treatment.

" My project has been truly inspirational. The sense of community and purpose, resources and networking opportunities provided by the university and those supported by NPL and GSK are second to none"

Tarek Haloubi describing the impact of his PhD project

Physicochemical characterisation of graphene based 2D materials for industrial applications

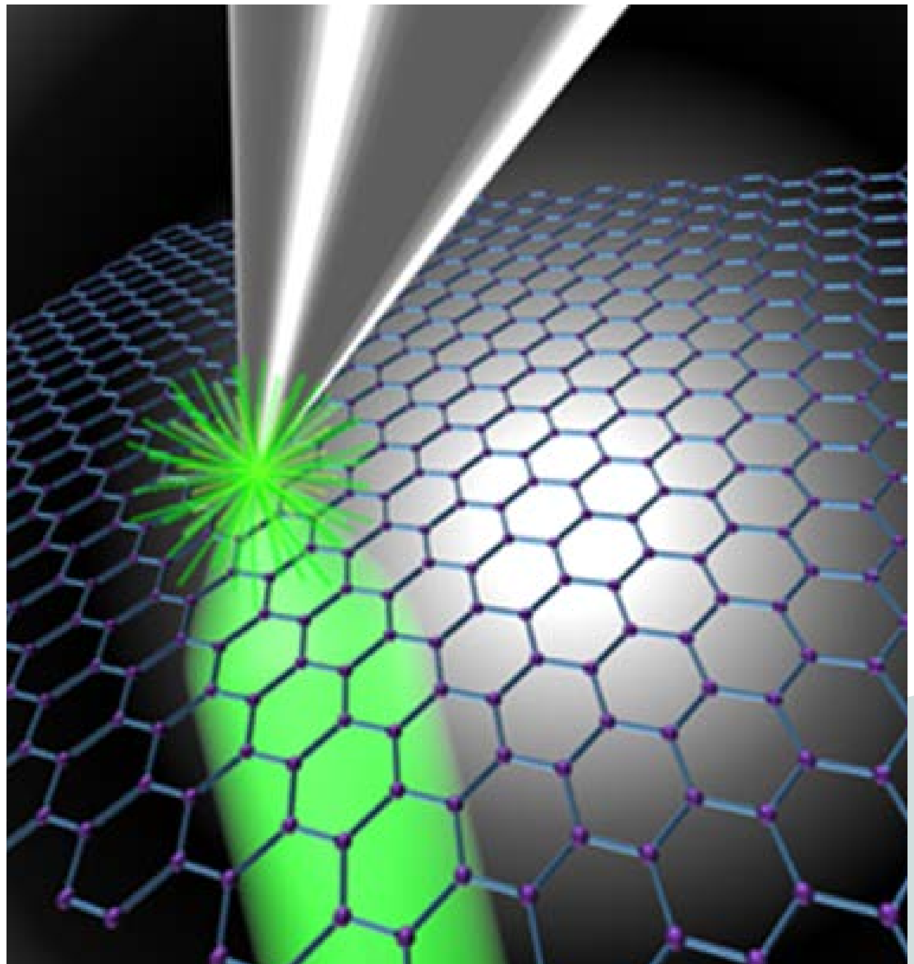
Liz Legge - University of Surrey

Harder than diamond yet more elastic than rubber; tougher than steel yet lighter than aluminium. Graphene is the strongest known material. However, it wasn't until 2004 when the isolation of graphene uncovered a new area of research into 2D materials, which is now transitioning into industry.

For successful commercialisation of this material, we still need to improve our understanding of the properties of modified graphene for specific applications, and how those modifications will affect the final product. We also need measurement standards and methods in place for this transition to be successful. In collaboration with other universities and companies, this project aimed to address some of these aspects.

This project explored the structural characterisation of graphene and contributed to the NPL Good Practice Guide (GPG, No. 145). Two international standards will be formed from this GPG, one for flakes (ISO TS 21356-1) and one for CVD-grown sheets (ISO PWI 21356-2). The GPG has been downloaded and used by academics and companies across the world, and the standards will ensure repeatable and reliable measurements across different companies and institutions.

In addition, the chemical characterisation of various types of graphene was explored for their suitability in conductive thin films, nanocomposites and biosensors. Due to the high conductivity of graphene, it is suitable for conductive thin films, which are important for touch sensors and future electronics applications. Graphene is also the strongest material measured, therefore it can significantly increase the strength of a product when small quantities are combined with another material, for example in nanocomposites. The project team have successfully produced conductive thin films at lower temperatures than previously required, using vitamin C as a more environmentally friendly chemical than hydrazine: https://doi.org/10.1039/C8RA08849G .



Artistic visualisation of the use of tip-enhanced Raman spectroscopy (TERS) to measure nanoscale variations in graphene. Courtesy: Liz Legge

They also performed tip-enhanced Raman spectroscopy (TERS) measurements for the first time on a commercially available product containing few-layer graphene. The TERS measurements show nanoscale variations in the location of functionalisation (edge vs basal plane) and the resulting effect on the strength of the final nanocomposite https://pubs.acs.org/doi/abs/10.1021/acsami.9b22144.

This project also investigated the bonding mechanisms of organic molecules deposited on graphene for biosensing applications: https://doi.org/10.1063/5.0064136

8 Creative development of new materials

Materials that can endure, the harshest conditions, are needed to allow us to dig at the bottom of the ocean and to transport the fuels of tomorrow. Learning to manufacture these materials at scale and incorporating safety and sustainability into their design and innovation is as important as their discovery and development. **This effort is essential to unlocking innovation across all major industrial sectors which could not be achieved without measurement science.**

Image: Liz Legge

"The collaboration between NPL and University of Surrey has significantly increased the impact of my work, allowing access to the world class facilities at both institutions and invaluable discussions with experts in their areas. I have had a very enjoyable experience and would definitely recommend future students to do a PhD with NPL."

Liz Legge reflecting on her PhD experience