Spring SciX 2026 Programme

Exeter

WELCOME

It is our pleasure to welcome you all to Exeter for the fourth Spring SciX conference in the series. Spring SciX forms part of the hugely successful based SciX Series and is backed by the Federation of Analytical Chemistry and Spectroscopy Society (FACSS). FACSS provides an international platform for representatives from academic, industrial and government institutions to confront the challenges of complex analytical problems and share knowledge.

To date Spring SciX has been exclusively a UK-based meeting, of the successful SciX series, with the plan to widen this out further European venues in due course. The conference covers a wide range of analytical chemistry and spectroscopy research, with a real focus on early career researchers. We want this to be a welcoming conference, aiming to provide a stimulating, but nurturing environment to develop your presentation skills and build networks for the future. We have a range of mixing events, scientific sessions, including plenaries from world renowned speakers, topic leading keynotes and talk slots, poster and flash posters for our future leading scientists. We are pleased to be able to welcome over 180 delegates to this year's event.

Exeter is a small city, with numerous Roman and medieval influences and sites, nestled between areas of outstanding natural beauty, including the Jurassic Coast, the only UNESCO Natural World Heritage site in the UK and the rugged National Park of Dartmoor. We hope you get to explore it further while you are here.

The conference is hosted by the Biospectroscopy Group based in the Physics Department at the University of Exeter, a research-intensive Russell Group university, based in the historic City of Exeter in Devon. Our dynamic and innovative research seeks to foster new discoveries, inspire creativity and bring people together to solve the challenges of today and tomorrow, making the world greener, healthier and fairer.

Greener: The climate emergency and ecological crisis is one of the most pressing challenges of our time. At Exeter, we are home to the UK's top five most influential climate scientists (Reuters Hot List) within a team of over 1,500 researchers and professionals working across climate change and the environment. This expertise underpins our research across a range of areas, including green futures, healthier oceans and positive tipping points.

Healthier: Our research is at the cutting-edge of innovation to transform human health and wellbeing. We partner with healthcare providers, industry and the public to ensure we can quickly translate our research into accessible treatments and care. Our research covers a range of critical areas, including antimicrobial resistance, child mental health, dementia and diabetes.

Fairer: We're driving change towards a fairer, more socially just and inclusive society. We're home to world-leading experts in Business, Economics, Law and Social Sciences who are dedicated to understanding and addressing societal challenges. Our research areas include the circular economy, evidence-based justice, social inequalities and sustainable food systems.

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Special Thanks

We would like to thank The Coblentz Society for their donation to support students at the conference.

We would like to thank The Infrared and Raman Discussion Group for their contributions to support ECRs and students at this conference.

We would like to thank The International Society of Clinical Spectroscopy for support for prizes at the conference.

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Programme Outline

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	Refreshment Break & Exhibition	Exhibition Hall
15:45	**15:45-17:15**	
	Session 1A Handheld Spectroscopy **Prof Dr Iwan Schie** Mr Joe Stradling Dr Sara Mosca Dr Sian Sloan-Dennison Dr Catherine Kendall *Chair: Dr Alex Dudgeon*	Session 1B Frontiers in IR **Prof Oxana Klementieva** Mr Krzsztof Dziuba Dr Maria Eleonora Temperini Ms Daniela Tomasetig Prof Peter Gardner *Chair: Prof Francesca Palombo*
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Wednesday 15th April 2026

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17:30	**Free Time**	
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	18:45 Arrival Drinks 19:30 Dinner 21:30 Ceilidh 23:30 END **Exeter Castle**	

Thursday 16th April 2026

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09:30	**09:30-11:00**	
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11:00	**11:00-11:30**	
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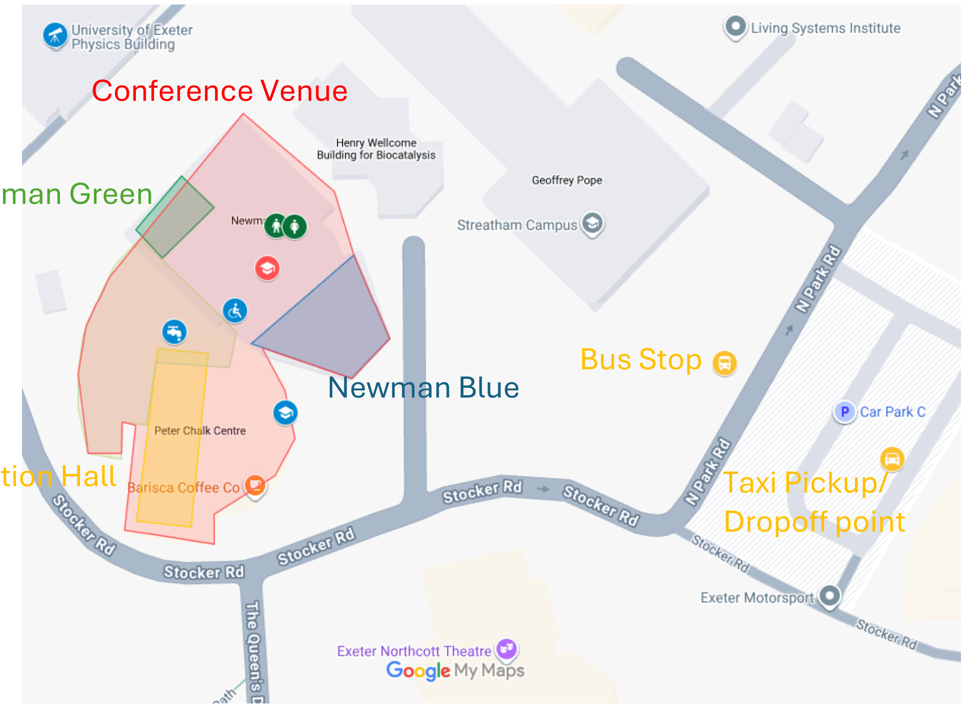
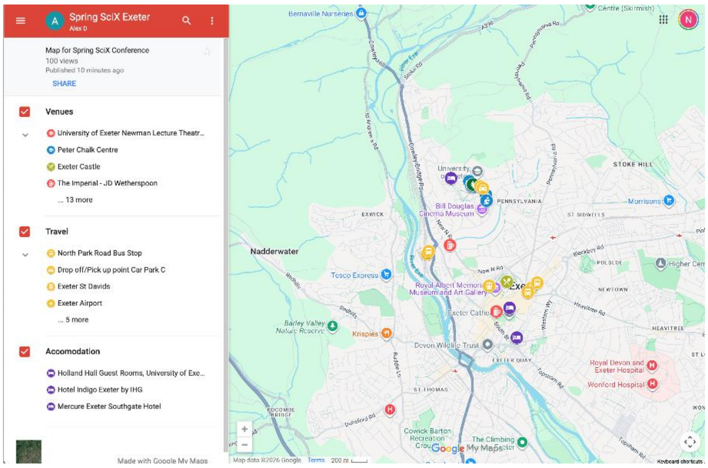
***Please note the timings in the Biomedical Raman imaging sessions differ to other sessions**

Map

Browse an interactive Google map of the conference venue and city:

Spring SciX Exeter – Google Maps





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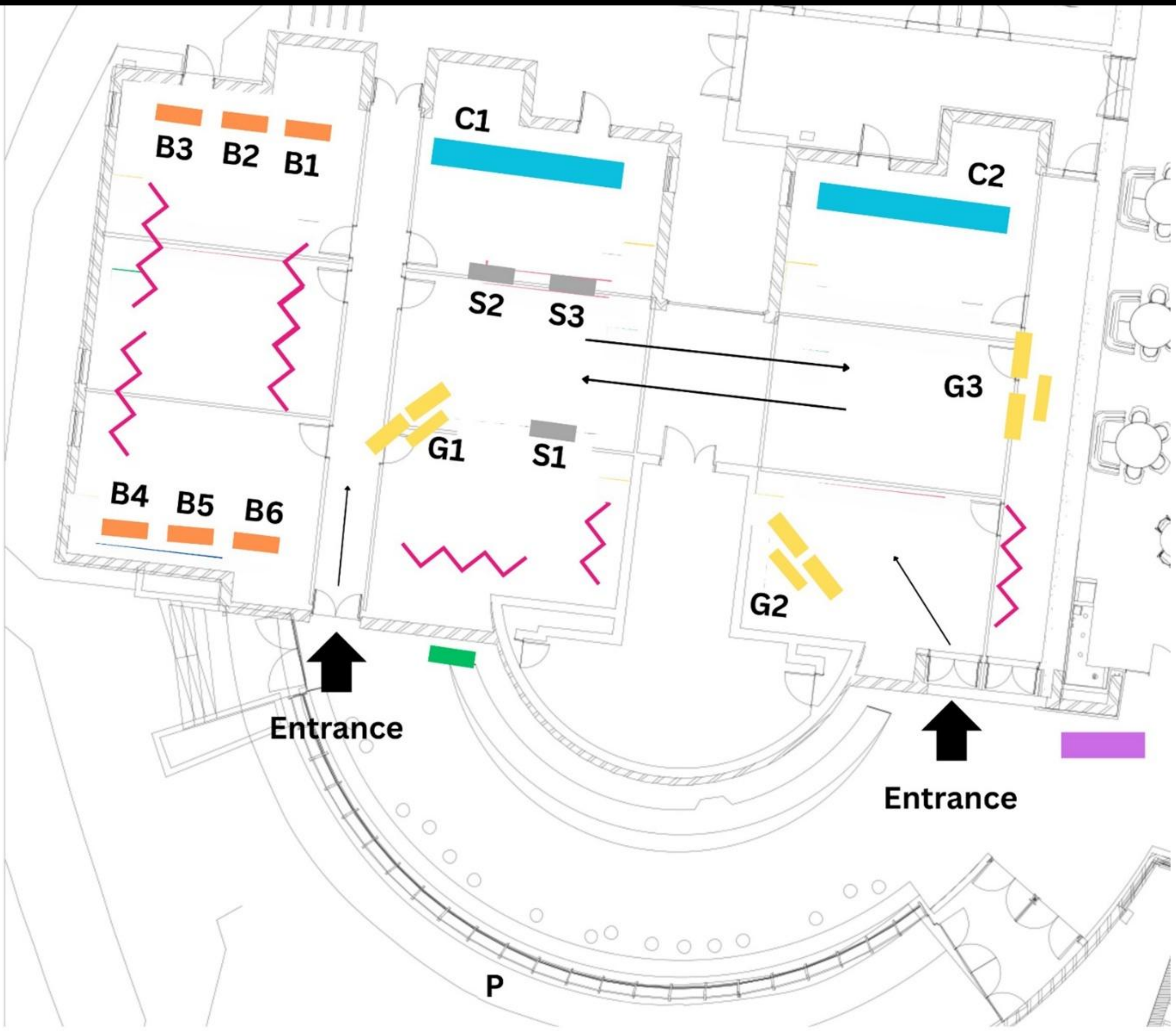
There is also a map of the whole of Streatham campus: Streatham campus map

Exhibition Hall Layout



🟦 Catering areas

🟨
G1 – Wasatch
G2 – S.T. Japan
G3 – Renishaw

⬜
S1 – Photothermal
S2 – Metrohm
S3 – Bruker

🟧
B1 – RSC
B2 – Horiba
B3 – Hubner
B4 – OptoSigma
B5 – Oxford Instruments
B6 – Edinburgh Instruments

〰 Posters

Transport

Exeter and the surrounding area has generally good public transport, you can even catch the train to the beach (Exmouth or Dawlish), if you have some spare time!

Buses

The **Number 4** (Stagecoach) bus route runs via the city centre to Streatham campus via Exeter St David's train station and back. Single journeys are capped at £3 max and can be paid for with cash or card.

For the University, catch the bus at stop 17 on Paris Street (towards the University of Exeter) and alight at the main stop on North Park Road, 2 minutes' walk from the Peter Chalk Centre.

For the city centre, catch the bus at the main stop on North Park Road (towards Cranbrook) and alight at stop 23 on Sidwell Street.

Taxis

There are taxi services available in Exeter, however, taxi availability can be limited at peak times, so advanced booking is recommended. Apple have a booking desk at the airport and St David's Station. Taxis are also normally available from outside Exeter St David's train station and the airport.

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Talk to Remember

Help us celebrate the most memorable talk of the Spring SCIX Conference!

Please vote at the end for the top two talks (using their SX___ ID number from this programme) that you found the most engaging, inspiring, or impactful.

Voting is open on Thursday 16th April between 11:00 and 13:05.

Your vote is anonymous

Upload your slides

Please upload your talk (as a PPTX) at least one hour before your session at the link below:

Upload Your Presentation Here

Day 1 – Tuesday 14th April

Registration

(11:00-13:30)

Registration in the Peter Chalk Foyer will be open from 11:00 – 13:30 to check in and collect your conference ID badge and delegate bag. It is important that you wear your ID badge whilst attending the conference, and at the Gala dinner on Wednesday 15th April. Therefore, please register as soon as you can on your arrival.

The registration desk will be open as much as possible throughout the conference and also serves as the information point. If there is no one at the desk, please call the number below, and someone will attend as soon as they can.

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(Office Hours Only)

Photothermal Workshop
(12:00-13:30) IN NEWMAN GREEN

NOTE – This will now take place in the **Newman Green Lecture Theatre**

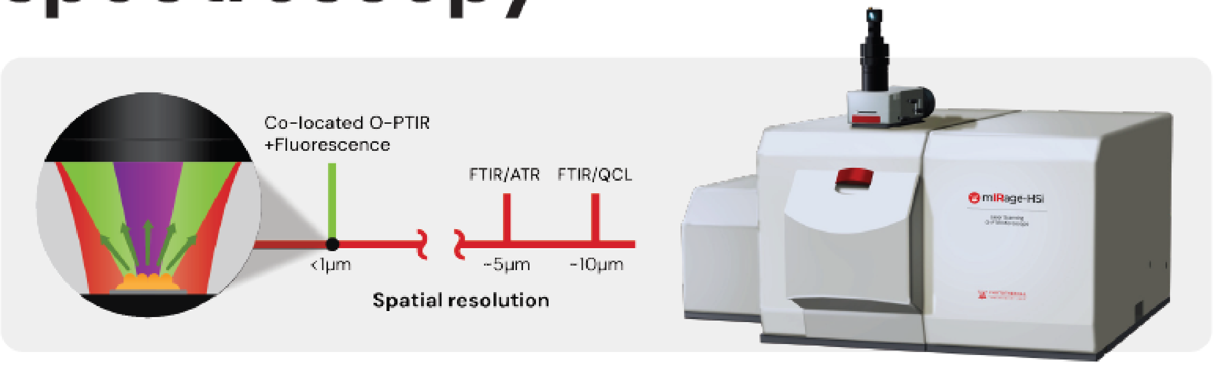
Free Lunch & Learn

Organized by Photothermal Spectroscopy Corp.

April 14th, 2026
12 - 1:30 pm

Register here:
Seats are limited

Latest advances in vibrational spectroscopy



Are you attending Spring SciX 2026 at the University of Exeter?

Join us for an exclusive Lunch & Learn workshop on Tuesday, April 14th — and discover what's possible with the latest in simultaneous submicron IR, Raman, and fluorescence imaging.

Lunch will be available for attendees and can be picked up upon entry to the event.

Location: Peter Chalk Building (main conference building), Room 2.1

Schedule

12:00 – 12:25
Latest innovations and applications in simultaneous submicron IR (O-PTIR), Raman and fluorescence imaging: Laser-Scanning O-PTIR
Dr. Mustafa Kansiz | Photothermal Spectroscopy Corp

12:25 – 12:50
Chemical imaging of amyloid polymorphs in situ
Assoc. Prof. Oxana Klementieva | Medical Microspectroscopy Laboratory, Faculty of Medicine, Lund University, Sweden

12:50 – 13:00
Online laser-scanning O-PTIR demo

13:00 – 13:25
Inside the biofilm: Mapping antibiotic response at the microscale
Dr. Howbeer Muhamad Ali | Institute of Systems, Molecular & Integrative Biology, Faculty of Health and Life Sciences, University of Liverpool, UK

Register today to secure your spot!

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Exeter Spring SciX 2026

Welcome and Plenaries
(13:30-15:15)

Plenary 1 – Prof Bernhard Lendl

Advancing mid-IR spectroscopy of liquids utilizing broadly tunable Quantum Cascade Lasers

B. Lendl*[1], A. Dabrowska[1], M. David[1], L. Lindenbauer[1], G. Ramer[1,2], D. Tomasetig[1],
J. H. Mendoza-Castro[1], Artem S. Vorobev[3], Liam O'Faolain[3]
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KEY WORDS: Liquid Sensing, Dispersion Spectroscopy, Photothermal Spectroscopy

Mid-IR quantum cascade lasers (QCLs) offer high spectral power densities, polarized and coherent radiation and allow for fast amplitude and frequency modulation. These properties enable a range of new sensing schemes which are difficult or even impossible to be realized by established FTIR spectrometers.

This presentation will introduce dispersion spectroscopy implemented in a free-space optics Mach-Zehnder Interferometer for measuring the real part of the complex refractive index of liquid samples. Dispersion spectroscopy has several advantages over absorbance spectroscopy: it is a baseline free technique, the reading is independent of power fluctuations of the laser source and the recorded signal is direct proportional to the analyte concentration, providing constant sensitivity over a large concentration range[1]. Results to be shown will include the measurement of ethanol in water and the monitoring of an enzyme-catalyzed reactions, exemplified by sucrose hydrolysis using invertase.

Furthermore, mid-IR laser-based photothermal spectroscopy of liquids will be introduced, showcasing applications of photothermal lens and photothermal mirror techniques for determining trace water levels in organic solvents. In this context, absorption-induced heating and the resulting changes in the sample's refractive index are probed by a second visible probe laser beam. Finally, efforts will be reported on the integration of the introduced sensing principles on photonic integrated chips (PICs), employing Mach-Zehnder Interferometers, ring resonators, and nanobeams integrated on a silicon nitride on silicon-on-insulator (SiN on SoI) platform, with readout in the NIR spectral region (C-band) as a transducer for absorption-induced refractive index changes[2].

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[1] A. Dabrowska, S. Lindner, A. Schwaighofer, B. Lendl, *Spectrochim. Acta - A: Mol. Biomol. Spectrosc.*, **286** (2023) 122014.

[2] D. Tomasetig, J.H. Mendoza-Castro, S. Schobesberger, A.S. Vorobev, L. O'Faolain, B. Lendl, *ACS Meas. Sci. Au*, 2026, DOI: 10.1021/acsmeasuresciau.5c00139

Raman micro-spectroscopy reveals the spatial distribution of fumarate in cells and tissues

Sarah E. Bohndiek*[1,2]
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KEY WORDS: Raman, metabolite, live cell, tissue

Fumarate is an oncometabolite that accumulates to high levels in fumarate hydratase (FH)-deficient cancers. Raman spectroscopy (RS) detection of small metabolites is typically challenged by their concentrations being orders of magnitude weaker than dominant protein and lipid signals. In the context of oncometabolites, however, the high level of accumulation brings their Raman spectral fingerprint above the background, enabling direct detection and quantification of fumarate in biological specimens[1].

Here, we report an integrated framework combining spontaneous RS and stimulated RS (SRS) microscopy to quantitatively map endogenous fumarate in living cells and intact tissues. By leveraging approximately 100-fold concentration differences between FH-proficient and FH-deficient cells, we isolated a fumarate-specific Raman band at 1403 cm^{-1} distinct from complex biomolecular backgrounds. Hyperspectral imaging with k-means clustering achieved spatial analysis unprecedented in bulk metabolomics, resolving subcellular fumarate distributions and revealing preferential mitochondrial accumulation relative to the cytoplasm and nucleus. Longitudinal imaging from the onset of FH loss in live cells further enabled real-time tracking of early-stage fumarate dynamics.

In tissues, we applied non-negative matrix factorization to unmix overlapping Raman spectra into component spectra corresponding to protein, lipid, cytochromes, and generated spatial abundance maps for each component across FH-proficient and FH-deficient small intestine samples. Using non-negative least squares, we then extracted fumarate concentrations on a per-pixel basis from the same Raman datasets and overlaid these maps with cytochrome b, demonstrating a close spatial correspondence between fumarate-rich regions and cytochrome b hotspots. Across multiple tissue sections, Raman-derived fumarate levels correlated with liquid chromatography–mass spectrometry reference measurements.

Together, this work establishes a unified spectroscopic pipeline for tracking fumarate across biological scales, from subcellular compartments to intact tissues, and supports the development of Raman-based approaches for *in situ* metabolic phenotyping, cancer stratification, and therapeutic monitoring in fumarate-driven malignancies.

[1] M. Kamp, J. Surmacki, M. Segarra Mondejar, et al., Nat. Commun., 15 (2024) 5386.

Parallel Session 1
(15:45-17:15)
Session 1A – Handheld Spectroscopy
in NEWMAN BLUE (Chair Dr Alex Dudgeon)

Iwan Schie - Keynote

Lessons Learned from Translating Raman Spectroscopy into Clinical Diagnostics

Iwan W. Schie[1,2,*]
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[2]University of Applied Sciences Jena, Department for Medical Engineering and Biotechnology, Jena Germany
**Corresponding Author: iwan.schie@leibniz-ipht.de; https://ag-schie.org/*

KEY WORDS: Raman spectroscopy, in vivo spectroscopy, clinical translation

Raman spectroscopy has long been established as a powerful analytical tool in chemistry and materials science, providing highly specific, label-free molecular information. Despite its conceptual maturity, its impact in clinical diagnostics has remained limited for decades, largely due to practical barriers including system complexity, limited robustness, slow acquisition, workflow incompatibility, and regulatory constraints. Recent advances in fiber-optic technologies, compact spectrometer design, and system-level engineering are now enabling a transition of Raman spectroscopy from laboratory-based analysis toward integrated biomedical systems suitable for routine clinical use.

In this keynote, I present this translational shift using our Raman-based system, InvaScope, as an example of a clinically compliant, fiber-optic Raman endoscopy platform developed for real-time, in vivo tissue characterization. The system was designed under the European Medical Device Regulation (MDR 2017/745) for clinical investigative studies and enables spectroscopic measurements directly within standard surgical and endoscopic workflows. Emphasis was placed on reproducibility, sterile integration, and regulatory readiness, key factors that have historically limited clinical adoption of optical spectroscopy.

Following preclinical validation, the platform has been established across multiple clinical domains, including urology[1,], head-and-neck oncology[2], and colorectal cancer[3], demonstrating its versatility as a translational optical platform rather than a single-indication device. In addition, a multimodal extension combining Raman spectroscopy with optical coherence tomography illustrates how complementary optical contrasts can enhance diagnostic confidence beyond single-modality approaches.

Together, these studies exemplify a broader maturation of Raman spectroscopy: from an analytical technique constrained to controlled laboratory environments toward a robust clinical technology capable of supporting intraoperative decision-making. Ongoing work focuses on real-time tissue classification, expansion to additional organ systems, and the regulatory pathway toward CE-marked clinical deployment. More broadly, this transition highlights how advances in system integration and regulatory-aware design—not fundamental physics—are now the key drivers for bringing optical spectroscopy into routine clinical diagnostics.

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[1] Latka, I., Mogensen, K., Knorr, F., Kuzucu, C., Windirsch, F., Sandic, D., ... & Schie, I. W. (2024). Raman spectroscopy for instant bladder tumor diagnosis: system development and in vivo Proof-Of-Principle study in accordance with the European medical device regulation (MDR2017/745). Cancers, 16(18), 3238.Citation of a journal article: A. Pump, B. Stokes, and C. Probe, *CARS Letters*, **5** (2008) 25-27.

[2] Bali, A., Bitter, T., Kouka, M., Ballmaier, J., Latka, I., Windirsch, F., ... & Schie, I. W. (2025). Establishment of a clinical workflow for in vivo Raman spectroscopy during head and neck cancer surgery. Scientific reports, 15(1), 24230.

[3] Vasquez, D. L., Kreft, C., Latka, I., Popp, J., Mantke, R., & Schie, I. W. (2024). Colon tumor discrimination combining independent endoscopic probe-based Raman spectroscopy and optical coherence tomography modalities with Bayes rule. International journal of molecular sciences, 25(24), 13306.

Joe Stradling (SXT27)

Raman on the Palm: Portable Raman Spectroscopy and SERS for Boosted Traceability and Authentication of Palm Oil

Joe Stradling[1], Howbeer Muhamadali[1], and Royston Goodacre[1]

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Key Words

Portable, Raman, SERS

Abstract

Fraud within the palm oil industry presents significant economic, ethical, and health-related challenges. Mislabelling of geographic origin, and the illegal addition of industrial Sudan dyes compromise consumer trust and pose serious safety risks. The complexity of palm oil's global supply chain makes it particularly vulnerable to these fraudulent practices, with high demand incentivising counterfeit products and false provenance claims. As regulatory bodies tighten traceability and labelling requirements, there is growing interest in rapid, on-site analytical tools that can assist with routine screening and enforcement.

Portable Raman spectroscopy and surface-enhanced Raman scattering (SERS) offer promising solutions for in-field authentication of palm oil. Raman spectroscopy provides non-destructive, reagent-free molecular fingerprints that can differentiate oils based on variations in β-carotene levels. Portable Raman devices have become more robust and user-friendly, enabling real-time verification at ports, markets, and production facilities. Meanwhile, portable SERS allows for the detection of low concentrations of illicit additives such as Sudan dyes, which are sometimes used to fraudulently enhance the visual appeal of low-quality or diluted palm oil. These dyes are considered harmful to human health due to their teratogenicity, genotoxicity, and carcinogenicity.

This presentation explores the use of portable Raman and SERS technologies to tackle two major forms of palm oil fraud: false origin claims and the addition of Sudan dyes. By combining spectral analysis with chemometric models, we demonstrate the potential of these tools to distinguish palm oil samples from different regions in West Africa and to identify adulteration within store-bought palm oil. The findings highlight the growing role of portable spectroscopy in food authentication, offering a fast, cost-effective, and scalable approach to protecting both industry standards and consumer safety.

Sara Mosca (SXT28)

Seeing Inside the Jar: In Situ, Non-Invasive Investigation of Historical Fluid-preserved collections Using Spatially Offset Raman Spectroscopy

S. Mosca[*1,2], **W. Montgomery**[3], **C. McKibbin**[3], **A. Blanco**[4], **S. Walker**[4], **P. Matousek**[1]

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[2] *Department of Physics and Astronomy, University of Exeter, Exeter EX4 4QL, U.K.*
[3] *Science Innovation Platforms, Department of Science, Natural History Museum, Cromwell Road, London SW7 5BD, U.K.*
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**sara.mosca@stfc.ac.uk, @arasfly3.bsky.social;*

KEY WORDS: SORS, Multivariate Analysis, Natural History Museum

Spatially Offset Raman Spectroscopy (SORS) has rapidly advanced as a novel and chemical specific method for non-invasive, through-barrier chemical analysis in heritage science. Our recent work demonstrated that handheld SORS can determine the dominant composition of preservation fluids[1] without opening sealed historic jar (e.g. museum fluid-preserved specimens), overcoming limitations of traditional invasive techniques and enabling safe, in situ assessment of historical collections.

In fluid-preserved natural history collections, understanding preservation fluid chemistry is crucial, as compositional changes, such as alcohol evaporation, oxidation of fixatives, and leaching of biological molecules, can signal specimen degradation.

Here we report the application of handheld SORS in combination with multivariate analysis in the characterization of both major constituents[2] and subtle residual components (e.g., lipids, protein fragments, degradation deposit)[3] directly through original glass specimen containers. We demonstrate that SORS not only identifies principal fluid types and concentrations[2] but also reveals markers of ongoing chemical changes and fluid-specimen interactions[3] that inform on conservation status. Critically, this method facilitates in situ monitoring of specimens of high historical value, including Charles Darwin's Beagle collection, without risking exposure, contamination, or loss of material integrity.

By extending from fluid identification to detection of residual degradation markers, handheld SORS offers curators actionable insights into conservation needs, enabling sustainable, preventative care of fluid-based natural history collections.

References

1 S. Mosca, W. Montgomery, C. McKibbin, R. Stokes, C. Conti and P. Matousek, *ACS Omega*, 2025, **10**, 8658–8664.

2 A. Blanco, W. Montgomery, S. Walker, C. McKibbin, R. Stokes, P. Matousek and S. Mosca, *ACS Omega*, , DOI:10.1021/acsomega.5c09045.

3 W. Montgomery, C. McKibbin, A. Blanco, S. Walker, J. Maclaine, R. Portela Miguez, P. Campbell, R. Stokes, P. Matousek and S. Mosca, *Anal. Methods*, , DOI:10.1039/D5AY01654A.

Sian Sloan-Dennison (SXT29)

Droplets to Diagnosis: Digital Microfluidic SERS Detection of microRNA-122

S. Sloan-Dennison*, R. Didio, S. Laing, K. Faulds, D. Graham
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KEY WORDS: SERS, Digital Microfluidics, Point of Care

Drug Induced Liver Injury (DILI) is liver damage caused by prescription or over-the-counter medications. In the UK, the leading cause of DILI is paracetamol overdose, which results in approximately 100,000 hospital attendances each year [1]. Rapid assessment of DILI is critical upon patient admission to Accident & Emergency to guide timely treatment. However, current diagnostic tests are limited as they produce slow time to results and rely on biomarkers that are not liver-specific and rise slowly following injury, delaying accurate assessment. To address these limitations, new biomarkers and diagnostic platforms are under investigation [2]. These aim to better stratify patients, enabling earlier intervention and more effective management of DILI.

To enable rapid detection of DILI, we have targeted the liver-specific biomarker microRNA-122 using a surface enhanced Raman scattering (SERS) based magnetic hybridisation assay. The assay format has conventionally been performed in bulk solution, however, to improve analytical sensitivity and assay reproducibility, enable high-throughput, automated processing, and minimise sample volume requirements, the assay has been transferred to a digital microfluidics (DMF) platform. DMF is a lab-on-a-chip technology that manipulates discrete nanolitre droplets via electrowetting on a patterned electrode array, enabling programmable dispensing, transport, mixing, incubation, and analysis on a single chip. It has been widely applied to biological and chemical assays and integrated with analytical readout modalities, including mass spectrometry, colorimetric detection, electrochemical sensing, electrochemiluminescence and now SERS.

By transferring the assay to a digital microfluidics (DMF) platform and integrating it with a portable Raman spectrometer, we significantly enhanced microRNA-122 detection, achieving approximately 100-fold greater sensitivity compared with the solution based assay. The assay's performance was further evaluated using human samples, yielding promising preliminary results. We envisage the DMF-SERS platform as a novel point-of-care technology capable of delivering rapid and highly sensitive responses across a range of point-of-care settings.

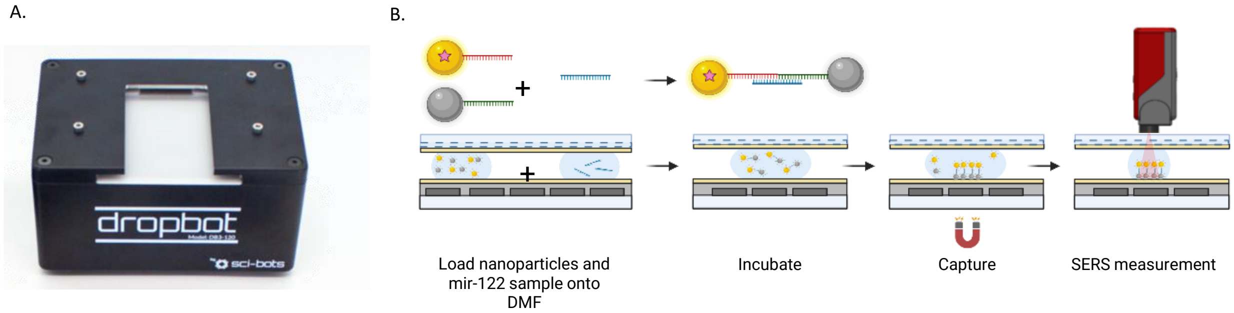

Figure 1 A. Image of Dropbot DMF B. Schematic of SERS based Magnetic hybridisation assay for the detection of mir-122 performed on DMF chip.

Catherine Kendall (SXT30)

In-vivo Raman Spectroscopic probe clinical trials: RAPIDE & DOLPHIN-VIVO

Catherine Kendall*[1], **Alex Dudgeon**[2], **Oliver Old**[3], **Charlie Hall**[3], **John Day**[4], **Nick Stone**[2]

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KEY WORDS: in-vivo, probe, cancer

Two in-vivo clinical trials, funded by the UK National Institute for Health Research Invention for Innovation programme have been undertaken at Gloucestershire Hospitals NHS Foundation Trust in collaboration with The University of Bristol and the Biomedical Spectroscopy Group at The University of Exeter. These studies have evaluated the feasibility of clinical implementation of Raman spectroscopy for cancer diagnostics.

The initial trial, RaPIDE ((RAman Probe for In vivo Diagnostics (during oesophageal) Endoscopy), developed a miniaturised probe that slides down the working channel of an endoscope, to diagnose oesophageal cancer using Raman spectroscopy without the need for an invasive, expensive and distressing biopsy. 25 patients, attending for endoscopy for surveillance of Barrett's oesophagus were recruited to the study. Routine biopsy samples were collected from the same location as where Raman spectra were measured and sent for routine processing and reporting in pathology.

DOLPHIN-VIVO (Diagnosis of LymPHoma IN VIVO) trial has evaluated the clinical implementation of a smart Raman needle probe to detect and diagnose primary and secondary cancers in lymph nodes in head and neck theatres. 14 patients, attending for surgical excision of nodes were recruited and Raman spectra measured in-vivo before fine needle aspiration samples were collected and the lymph nodes were excised for routine pathological analysis.

Both trials successfully demonstrated the aim of proving that the Raman probes could measure spectra safely from human tissue in vivo. The spectral signals measured were comparable to laboratory measurements. The pathology teams assessed the tissue where the spectra had been measured and they were unable to find any damage. The trials did not have the statistical power to develop diagnostic statistical models using cross validation, but the endoscopic probe demonstrated 84.9% training performance & the needle probe 98.4%, training performance.

Figure: Raman endoscopic probe & view from the endoscope camera

Session 1B – Frontiers in IR
in NEWMAN GREEN (Chair: Prof Francesca Palombo)

Oxana Klementieva - Keynote

Correlative photothermal infrared imaging of amyloids in cells and tissues

Oxana Klementieva
Authors' affiliation(s) & full address(es) (8-point type, centered, italicized)
**Corresponding Author e-mail address, Twitter handle (if applicable), & Personal website/Bio webpage URL (if applicable): (8-point type, centered, italicized)*

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Introduction

Understanding protein structural heterogeneity in complex biological tissues requires chemical specificity at spatial scales beyond the diffraction limit. Conventional infrared (IR) microspectroscopy provides robust information on protein secondary structure but is limited by spatial resolution. Recent advances in photothermal infrared spectromicroscopy (OPTIR) enable label-free mid-infrared spectroscopy with sub-micrometer to nanoscale resolution, offering a route to bridge this gap. However, systematic strategies for extracting biologically meaningful structural information from photothermal IR data—and validating it against established IR methodologies—remain to be explored.

Here, we establish a correlative photothermal infrared spectromicroscopy workflow for mapping protein secondary-structure heterogeneity in biological tissues, with specific emphasis on the combined impact of substrates and chemical fixation. We systematically evaluate commonly used support materials, including IR-transparent windows reflective metallic coatings, silicon-based substrates, and electron-microscopy-compatible supports, alongside widely applied fixatives such as paraformaldehyde, glutaraldehyde, and solvent-based fixation protocols.

Substrates and fixation strategies were assessed based on photothermal signal strength, spectral fidelity in the amide I and II regions, thermal background contributions, structural preservation, and mechanical stability during repeated imaging. Our analysis reveals clear, interdependent trade-offs between infrared sensitivity, spectral integrity, nanoscale resolution, and compatibility with optical, electron, and synchrotron-based imaging modalities. Certain substrates enhance photothermal contrast but introduce spectral distortions or elevated thermal background, while specific fixation methods alter amide band profiles or induce crosslinking-related shifts that complicate secondary-structure interpretation.

We demonstrate that both substrate choice and fixation chemistry are critical—and often limiting—parameters in photothermal infrared spectromicroscopy. No single combination is universally optimal. Instead, rational experimental design requires balancing photothermal performance, spectral accuracy, structural preservation, and multimodal compatibility. Based on these findings, we propose practical guidelines for selecting substrate–fixative combinations tailored to correlative nano-IR studies in biological tissues.

Krzysztof Dziuba (SXT24)

What is a Spectral Token? Rethinking how transformers see Infrared Spectra

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KEY WORDS: Infrared spectroscopy, Transformer, Deep learning

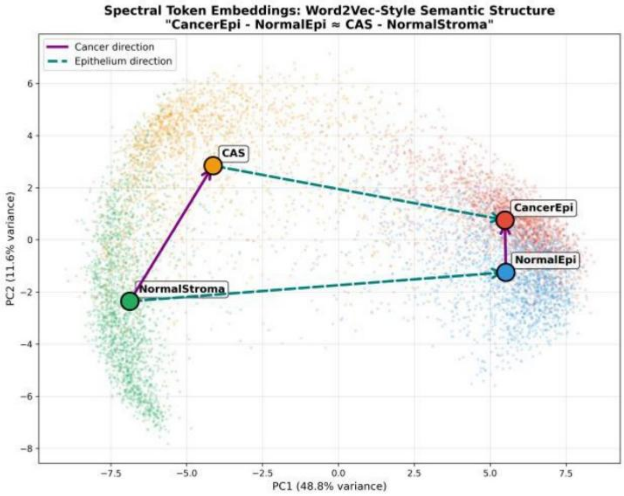
When ChatGPT reads a sentence, it first breaks text into "tokens" - meaningful units like words or subwords.[1] When Vision Transformers analyze images, they divide pictures into patch tokens.[2] But when we apply transformers to infrared spectra, we face a fundamental question that the field has largely ignored: what should a spectral token be?

Current approaches make implicit assumptions. Some treat each wavenumber as an independent token.[3] Others aggregate sliding windows.[4] Some focus only on absorption peaks.[5] Other approaches that haven't yet been extensively studied, could learn abstract representations from data.[6] Each choice encodes a different hypothesis about what constitutes meaningful information in a spectrum - yet these design decisions are rarely examined or compared.

This talk presents a systematic investigation into spectral tokenization for transformer-based tissue classification. Using Infrared Quantum Cascade Laser (QCL) based imaging data, from breast cancer sample, comprising over 700,000 spectra, we benchmark six fundamentally different tokenization philosophies under controlled conditions where only the tokenization strategy varies.

Our results challenge conventional strategies. Chemistry-guided approaches that focus on absorption peaks achieve the best accuracy with dramatic compression - but this comes at a cost. We uncover a surprising accuracy-robustness tradeoff: the strategies that perform best on clean data become most fragile under noise. We also demonstrate that the transformer encoder is not merely a classifier - it actively constructs discriminative representations from tokenizer outputs that initially show almost no class separation.

These findings reframe tokenization as a first-order design decision for spectroscopic deep learning, not an implementation detail. We offer practical guidance for practitioners navigating this design space, considering factors like instrument quality, deployment constraints, and the fundamental tradeoff between peak performance and robustness.



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Nano-IR spectroscopy of biological molecules in liquid environment with broadband synchrotron radiation

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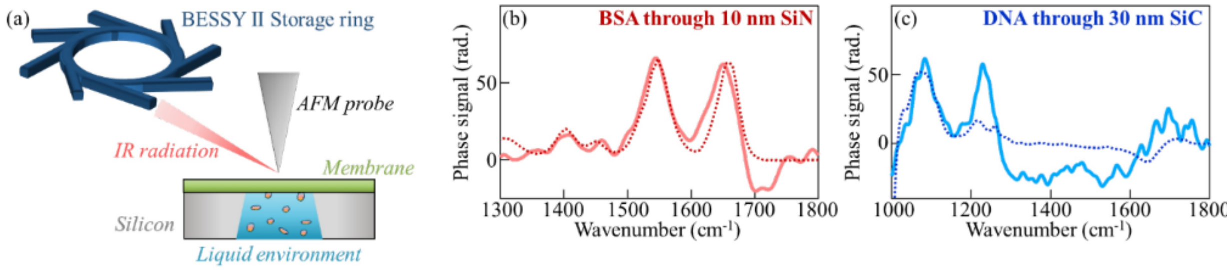
KEY WORDS: nano-IR spectroscopy, broadband synchrotron radiation, liquid environment for biological matter

Scattering-type Scanning Near-field Optical Microscopy (s-SNOM) enables the investigation of material optical properties with nanometric spatial resolution (≥ 10 nm) over a broad spectral range from visible to THz[1]. The technique is based on the access to near-field optical amplitude and phase of light scattered from a metallized AFM tip. s-SNOM in the infrared (IR) spectral region facilitates chemical imaging and spectroscopy, beyond the diffraction limit, allowing for the investigation of complex multicomponent materials at the nanoscale. Extending IR s-SNOM to aqueous environments is challenging, due to water absorption, reduced signal levels and AFM-tip contamination but of paramount importance for biological systems, whose structure and dynamic are preserved in the native aqueous environment[2].

Here, we demonstrate mid-IR s-SNOM measurements in water enabled by nanometer-thick free-standing membranes, which act as an interface between the near-field probe and the liquid phase, mitigating water absorption while preserving nanoscale sensitivity. A key element of this approach is the membrane material, which ensures stable mechanical AFM probe-sample interaction and provides transparency across the entire molecular fingerprint region[3]. By combining synchrotron-based s-SNOM with free-standing SiN and SiC membranes, we perform a comparative analysis of their near-field optical response both in dry conditions and when interfaced with liquid water. This approach enables nanoscale spectroscopic of biological matter vibrational signatures, including proteins and nucleic acids in solution. The measurements reveal membrane-dependent differences in near-field amplitude and phase, as well as spectral shifts associated with membrane material and thickness. The experimental results are supported by finite dipole model (FDM) simulations, which reproduce the observed spectral trends and allow us to disentangle the contributions of membrane properties and experimental conditions to the near-field response. Overall, our findings establish SiN and SiC membranes, in combination with synchrotron-based broadband source, as powerful approach for IR nano-spectroscopy of biological systems in liquid environments.



(a) Schematic of the experimental setup. (b)-(c) s-SNOM phase spectra of BSA protein and DNA in solution through a 10 nm thick SiN membrane and a 30 nm thick SiC membrane, respectively. Solid curves represent experimental data, while dashed curves represent modeled data.

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Daniela Tomasetig (SXT23)

Mid-IR Photothermal Spectroscopy of Liquids Based on a Photonic Integrated Mach-Zehnder Interferometer

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KEY WORDS: photothermal spectroscopy, mid-Infrared, photonic integrated circuits

Photonic integrated circuit (PIC) based on-chip structures such as ring resonators or Mach-Zehnder interferometers (MZIs) can be used to measure refractive index (RI) changes, down to 10^{-8} RIU.[1],[2] In our work we combine the RI sensing capabilities of an on-chip MZI based on a standard CMOS compatible Si_3N_4/Si material platform, together with the high output power and tunability of an external cavity quantum cascade laser (EC-QCL) as photothermal excitation source. This way we can measure photothermal mid-infrared spectra of liquid samples achieving high selectivity and sensitivity.

The MZI is interrogated using a common telecom wavelength (1550 nm) light source. At the same time, a mid-IR EC-QCL tuneable from 1725-1570 cm^{-1} is focused on the chip from the bottom side. The beam can pass through the chip and photothermally excite the sample on top of the chip. Microfluidics are placed on top for precise sample delivery (schematic see Figure 1a). By tuning and amplitude modulating the mid-IR light source PTS spectra closely resembling FTIR spectra, can be acquired.

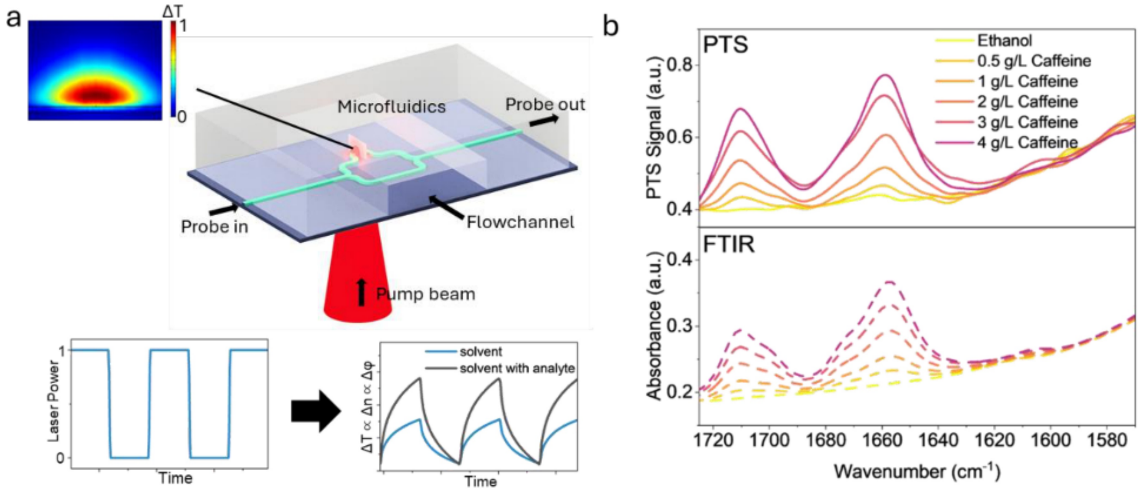

Fig. 1. a) Schematic of the photothermal setup. b) comparison of spectra of caffeine in ethanol obtained using our PTS setup and a commercial FTIR.

We demonstrate the capabilities of our system by measuring PTS spectra of caffeine dissolved in ethanol and compare our results to standard FTIR spectra (Figure 1b), providing the first measurement of its kind with a PIC transducer.

This technique offers high versatility, high potential for miniaturization and good chemical ruggedness of the sensing surface, constituting a step towards PIC-based Lab-on-a-chip type chemical sensors.

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CLIRPath-AI Reflections and Perspectives: Developing a Roadmap for Infrared Based Clinical Pathology

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KEY WORDS: CLIRPath-AI, Infrared imaging, Spectral pathology

We have known for many years that infrared spectra of tissue contain information about the biochemistry of a sample that can be of diagnostic value. Most studies have concentrated on replicating what the pathologists can already do and demonstrating that, in most instances, spectroscopic techniques can do as well or maybe in some case even a little bit better. However, infrared studies on biopsy tissue have not progressed passed this stage and have not translated into the clinic. This is, in part due to the inability for us to clearly demonstrate the “added value” of the spectroscopic imaging and in part due to the rapid development of AI tools that can significantly augment current pathology practice. The advance of digital pathology has picked the low hanging fruit of automated tissue classification meaning the spectral pathologists to tackle more complex diagnostic challenges. In order to address some of these issues we formed an EPSRC funded network (CLIRPath-AI) that links the spectral pathology, digital pathology and AI communities to stimulate and accelerate progress in using AI for the analysis of IR and Raman imaging. The aim was to access a wider range of pathology tissues, acquire large data sets and access new AI skills sets to pull out prognostic information that will demonstrate the added value of spectroscopic imaging. This culminated in a CLIRPath-AI conference (*CLIRPath-AI: A roadmap for AI-based spectral pathology)* in Coomb Abby, UK where ideas were generated on how to move the field of spectral pathology forward. In this presentation we reflect on the impact of CLIRPath-AI and discuss the roadmap for Infrared based spectral pathology.

Flash Presentations
(17:30-18:15)
in NEWMAN BLUE (Chair: Dr Ben Gardner)

Presenters have exactly 60 seconds to present their 1 slide, strictly timed! with prizes for the best ones.

Voting instructions will be provided, please bring a smartphone or laptop with you, power is available at your seat (under the table).

Fiona Smillie (SXFP02)

Development of Point of Use Bionanosensors for Liver Injury

F. Smillie[1], **B. Clark**[1], **S. Sloan-Dennison**[1], **D. Creasey**[2], **D. Bingemann**[2], **S. Laing**[1], **D. Graham**[1], **K. Faulds**[1]
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KEY WORDS: Surface Enhanced Raman Spectroscopy, Drug Induced Liver Injury, Point of Care Detection

Drug induced liver injury (DILI) is a broad term which encompasses any liver injury caused by drugs taken either for medical or recreational purposes. One of the most common causes of DILI in the UK is paracetamol overdose.[1,2] When paracetamol is taken at a high enough dose, it causes DILI which can then lead to acute liver failure. The only treatment for this is N-acetylcysteine (NAC) which, when administered within 8 hours of the overdose is extremely effective.[3] However, after this time point the effectiveness of NAC decreases drastically leading to liver damage which may require a liver transplantation or lead to death.[4] This highlights that the rapid diagnosis of DILI after paracetamol overdose is essential, especially in busy hospital admission units. Alanine aminotransaminase (ALT) is the current gold standard biomarker for diagnosing DILI, however, ALT tests currently take place in a central laboratory which can cause time delays.[3] Point of care testing for ALT, or alternative biomarkers, would be beneficial, allowing bedside diagnosis and avoiding long laboratory turnaround times. We have developed a lateral flow immunoassay (LFIA) utilising gold nanoparticles functionalised with ALT detection antibodies and a Raman reporter molecule. Surface enhanced Raman spectroscopy (SERS) was then used to detect the response at the test spot. The running conditions were optimised, calibration curves were obtained in both buffer and serum and it was confirmed that the endogenous protein could be detected by the assay. This work creates a foundation from which multiplexed lateral flow immunoassays could be developed.

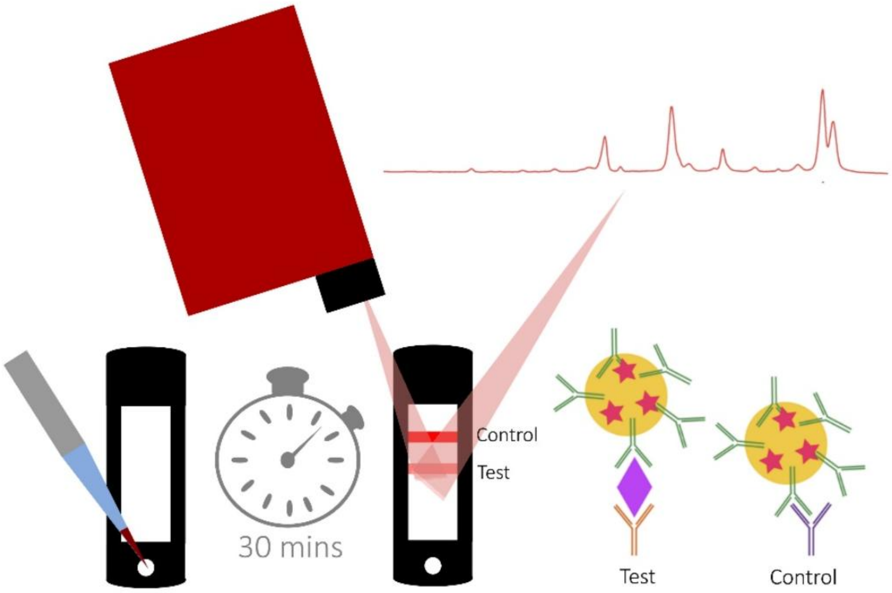

Figure 1 Schematic showing the SERS LFIA procedure of sample addition, wait time and SERS analysis, and the immunoassay complexes that form at the test and control areas

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Rocco Didio (SXFP03)

Diagnosing drug induced liver injury (DILI) faster than you can say it

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KEY WORDS: microRNA, point of care, surface-enhanced Raman scattering

Paracetamol overdose (POD) is more common than generally perceived with over 100,000 cases occurring in the UK each year.[1] It results in a drug induced liver injury (DILI) which limits the regenerative capacity of the liver tissue, damaging it faster than it can heal. This cycle continues until liver failure occurs, where the only chance of survival is a transplant. Unfortunately, the demand for a new organ outweighs the supply, resulting in one death every twenty-five patients worldwide.[1] This chain of events can only be broken with a faster diagnosis and treatment of DILI.

To rapidly diagnose DILI we have created a surface enhanced Raman scattering-lateral flow assay (SERS-LFA) to detect and quantify the biomarker miR-122, a small chain RNA sequence. miR-122 takes as little as 10 minutes to rise following POD and is specific to liver tissue, making it an ideal candidate for monitoring DILI.[2] The LFA is considered the ideal platform for this application as LFAs are widely trusted, offer fast time to results and simplicity in clinical settings, while maintaining low manufacturing costs.[3]

To detect mir-122 on the LFA, gold nanoprobes were used to capture miR-122 and anchor it onto the test line, giving rise to a red colour that varied in intensity with target concentration. Quantification was achieved by functionalising the gold nanoprobes with a Raman label, so that when the test line was analysed with a handheld Raman reader, the resulting SERS signal correlated to the concentration of miR-122. Detection and quantification of miR-122 at clinically relevant concentrations has been achieved with preliminary results indicating the potential of the assay at the point of care.

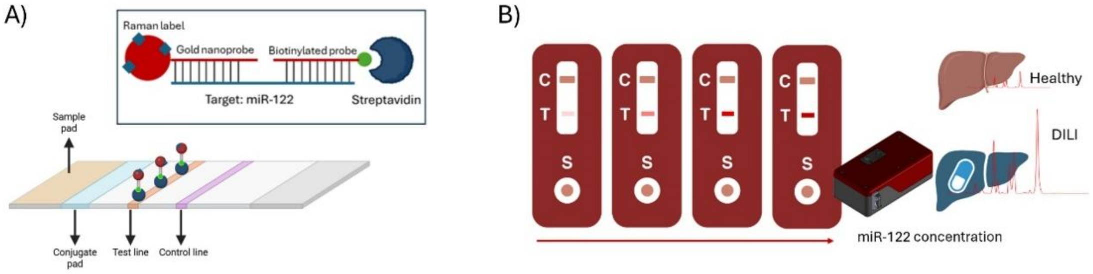

Figure 1. A) Schematic of LFA designed for the detection of mir-122. B) SERS-LFA illustrating an increase in SERS signal of the test line when DILI is present measured using the handheld Raman reader.

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Jennifer Ferguson (SXFP04)

Understanding the impact of the fabrication process on Li-ion battery anodes using chemical analysis with the Strada® Intelligent Raman microscope

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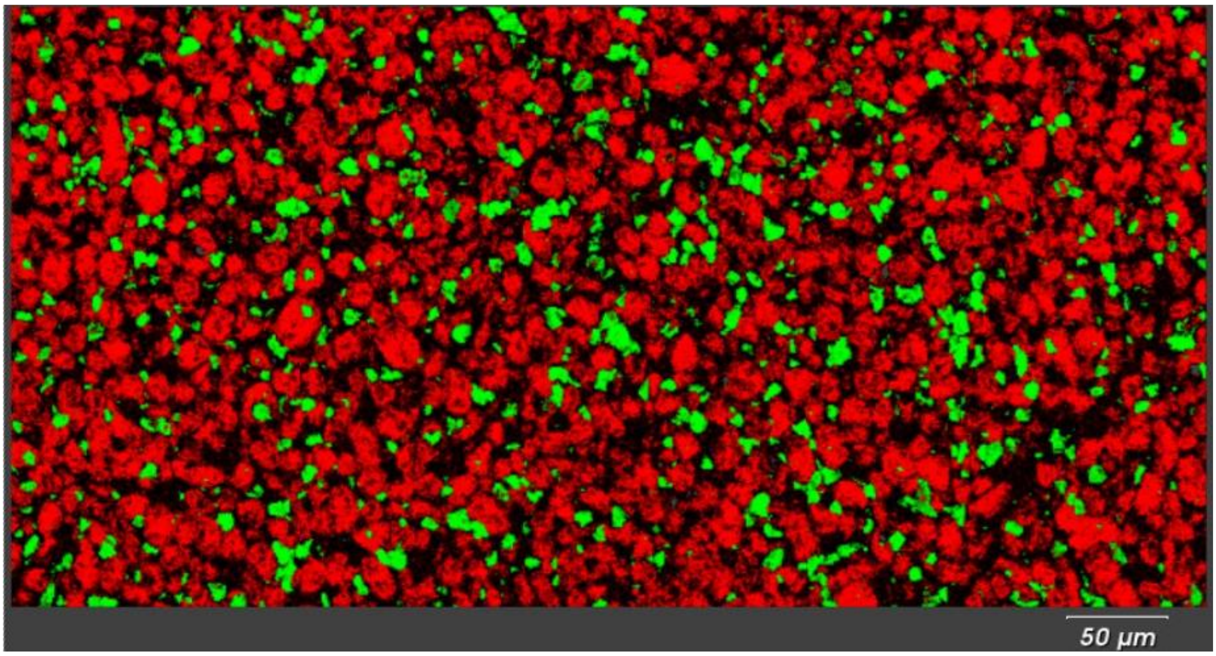
KEY WORDS: battery, carbon, anode

Li-ion battery anodes consist of a variety of components and materials, including conductive materials and binders. Different types of carbon are used in anodes to fulfil different purposes, such as participating in intercalation reactions with lithium ions, and providing conducting paths for charge carriers. The current drive to increase the lifespan and quality of batteries means that understanding chemical distribution and how this impacts the battery life and longevity is key. Raman spectroscopy is ideally suited as a tool for characterisation of anodes due to its ability to characterise different carbon forms and identify changes to the crystallinity and quality of the graphitic and amorphous material.

The Strada Intelligent Raman microscope was used for analysis of anodes fabricated using different preparation methods. Quantification of the different forms of carbon present in the anode identified relative changes in the amount of graphitic and carbon materials, as well as a reduction in the particle domain sizes, indicating a breakdown of the materials during the mixing process.



Raman image showing the chemical distribution of carbon (red) and SiOx (green) across an analysed area on an anode.

Jizhou Zhong (SXFP05)

AI-enabled FTIR phenotyping of extracellular vesicles under metabolic and inflammatory perturbations across different cell lines

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KEY WORDS: FTIR spectral analysis, Machine learning, Extracellular vesicles

Extracellular vesicles (EVs) are nanoscale lipid-bilayer particles secreted by cells that carry proteins, lipids, and nucleic acids and can report metabolic and inflammatory states. FTIR spectroscopy can acquire an EV "molecular fingerprint" within seconds and without labels, but translation to robust phenotyping is limited by spectral heterogeneity across cell types and culture conditions, and by the risk of overfitting when datasets are small.

We describe an FTIR–machine learning workflow for EV characterization across nine cell lines under three perturbation regimes: control medium, low-glucose medium (metabolic stress), and TNF-α stimulation (inflammatory signaling). EVs were isolated from conditioned media using standardized procedures and measured by FTIR to capture biochemical information in the 4000–900 cm−1 range, covering lipid CH stretching, protein amide I/II, and phosphate/carbohydrate bands. Spectra were processed with atmospheric compensation, baseline correction, and scatter-robust normalization , followed by Savitzky–Golay smoothing and derivative features; replicate-level quality control and outlier detection were used to control preparation and measurement variability.

To separate condition-driven changes from cell line effects, we benchmark classical chemometrics (PCA, PLS-DA) and modern classifiers (support vector machines and random forests). Performance is assessed with nested cross-validation and a stringent leave-one-cell-line-out protocol, providing an estimate of how well models generalize to unseen biological backgrounds. Unsupervised embeddings (PCA/t-SNE) visualize the EV spectral landscape and help compare shared versus cell line–specific responses. Feature-attribution methods (ML Feature selection) highlight discriminative wavenumber regions and relate them to vibrational assignments, yielding interpretable spectral markers of EV remodeling under glucose limitation and TNF-α exposure.

Overall, this work integrates IR spectroscopy with AI to deliver scalable, label-free EV phenotyping, supporting standardized EV quality control and providing a foundation for spectroscopic monitoring of metabolic and inflammatory perturbations in biotechnology and biomedical research.

Prasad Aradhye (SXFP07)

Adaptive Physics-Aware Raman Baseline Correction Using Machine Learning-Guided Regularization

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Key words: Raman spectroscopy; baseline correction; machine learning

Reliable baseline correction remains a fundamental bottleneck in Raman spectroscopy, particularly for low signal-to-noise, fluorescence-dominated, and high-throughput datasets. Conventional algorithms such as asymmetric least squares and its variants rely on manual tuning of regularization parameters, limiting reproducibility and scalability, while recent deep-learning approaches often lack interpretability and generalizability across experimental conditions.

Here, we present DIRAS (Dynamic Iterative Reweighted Autoregressive Spectral baseline correction), a physics-aware framework that adaptively suppresses baseline distortions while preserving true spectral features without the need for precise parameter tuning. DIRAS integrates autoregressive spectral energy estimation with residual-dependent reweighting, yielding robust baseline correction across wide variations in signal-to-noise ratio and baseline complexity. Crucially, DIRAS exhibits low sensitivity to the smoothing parameter, enabling consistent performance in batch and mapping experiments.

Building on this foundation, we introduce DIRAS+, a hybrid machine-learning extension that predicts spectrum-specific regularization parameters in real time. By combining a one-dimensional convolutional encoder with gradient-boosted regression, DIRAS+ learns a nonlinear mapping between spectral features and optimal correction parameters derived from structural similarity index (SSIM)-based optimization. This approach preserves user control while enabling fully automated, high-throughput preprocessing.

Benchmarking on synthetic Raman spectra and experimental SERS datasets demonstrates that DIRAS and DIRAS+ outperform established methods in baseline fidelity, peak preservation, and batch consistency. Importantly, improved preprocessing directly enhances downstream chemometric performance, yielding lower prediction errors in intensity-based sensing tasks. Together, DIRAS and DIRAS+ provide an interpretable, scalable, and parameter-robust solution for Raman baseline correction, bridging physics-based modeling with machine learning automation for modern spectroscopic workflows.[1]

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Optimising AI for chemical imaging: benchmarking performance against foundation models for task-specific applications in histopathology

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KEY WORDS: Indicate up to 3 key words, for example: CARS, four-wave mixing, spectral analysis, phase retrieval, imaging, live cells, ….

The integration of chemical imaging with artificial intelligence presents a compelling route toward fully digital, label-free histopathology, yet it also introduces notable challenges. While deep learning models from domains like machine vision, digital pathology, and remote sensing are readily accessible, they frequently struggle to generalize effectively to chemical imaging data, as highlighted in recent research[1] . Additionally, although foundational pathological models show potential for advancing AI-based chemical imaging, our recent assessments suggest they may fall short in addressing the broad spectrum of classification tasks encountered in clinical settings.

In this work, we highlight some recent published work from our research towards developing AI for diagnostics and prognostics with chemical imaging data, and benchmark these against various foundation pathological models for task-specific applications in breast cancer. We identify and analyze critical limitations, and provide a focus on both architectural and data-centric options to improve performance and achieve the full potential of this approach in histopathological workflows.

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Low-Cost Electrochemical Biosensor for Cancer Cell Surface N-Glycan Detection and Drug Response Monitoring

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KEY WORDS: Electrochemical biosensor, Electrochemical Impedance Spectroscopy, Cancer Detection

Accurate detection of cancer, along with the effective monitoring of treatment response, remain a critical challenge in oncology. Conventional diagnostic and drug-screening methods are often time-consuming, expensive, and reliant on complex instrumentation which limits their accessibility in resource-limited settings. Electrochemical biosensors offer an attractive alternative to traditional diagnostic techniques owing to their rapid detection, high sensitivity, low cost, and ease-of-use[1]. Further, the potential for translation of electrochemical biosensors into point-of-care diagnostic devices provides an exciting opportunity for rapid and accessible screening applications. However, designing sensing interfaces capable of reliably detecting whole cancer cells and distinguishing between subtle phenotypic changes remains difficult.

Altered N-glycosylation, including changes in the structure and expression levels, is strongly associated with cancer progression and has been widely reported[2]. As an integral building block of the N-glycan structure, mannose is a potential target analyte. Here, we report the development of an easily fabricated, simple, and cost-effective electrochemical biosensor for the detection of N-glycans present on the surface of cancer cells. Based on a gold screen-printed electrode, a biocompatible chitosan layer immobilises concanavalin A (a mannose-specific lectin), enabling selective binding[3].

In this work, label-free detection is achieved using electrochemical impedance spectroscopy, and distinct impedance responses are obtained for different cancer cell lines based on variations in their surface glycosylation profiles. The simple interface fabrication process does not require expensive reagents yet demonstrates a detection limit which rivals more complex electrochemical biosensors reported in literature. Furthermore, the sensor can detect drug-induced changes in cancer cells upon treatment with N-glycan inhibitors, highlighting its potential for non-destructive monitoring of therapeutic response.

The biosensor's label-free, real-time monitoring of cancer cell glycosylation and drug treatment response addresses critical limitations in current diagnostic and screening techniques and shows promise for the future development of accessible electrochemical biosensors used in cancer research.

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Thomas Hibbard (SXFP10)

Fourier Transform Infrared Quantification of Skin Permeation to Expedite Pharmaceutical Development

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KEYWORDS: FTIR-Microscopy, Quantification, Permeation.

Transdermal formulations are optimised by quantifying drug permeation through surgically excised human skin[1]. Although this reduces the need for *in vivo* animal testing, the number of experiments performed is limited by the time required for liquid chromatography analysis. Each permeation study may produce ~10 time points, and each study is repeated 5-8 times; this equates to hours of analysis time using liquid chromatography[2]. In this study, Fourier transform infrared microscopy (FTIR) was explored as an alternative quantification method for rapid, low-cost analysis of skin permeability. This method will reduce the constraints on formulation optimisation, thereby expediting the pharmaceutical development of dermatology products.

FTIR was used to quantify diclofenac diethylamine content in a dried 1 μL droplet. One spectrum per droplet was obtained by averaging the 100 x 100 μm pixel spectral map. Transmission acquisition mode provided a signal-to-noise ratio (SNR) of ~100 and offered much higher sensitivity than an attenuated transmission reflectance (ATR) approach (SNR < 10).

A two-component partial least squares regression model for diclofenac was optimised. The limit of detection (LOD) and model parameters for this compound were calculated as 0.58 μg/mL ($r^2 = 0.9915$), corresponding to a detection limit of 0.58 ng. These detection limits are similar to high-performance liquid chromatography (HPLC) analysis. The FTIR method has the advantage of being quicker (5 min vs. 40 min per sample) and using less solvent (1 μL vs. 400mL) than the traditional liquid chromatography method for diclofenac analysis.

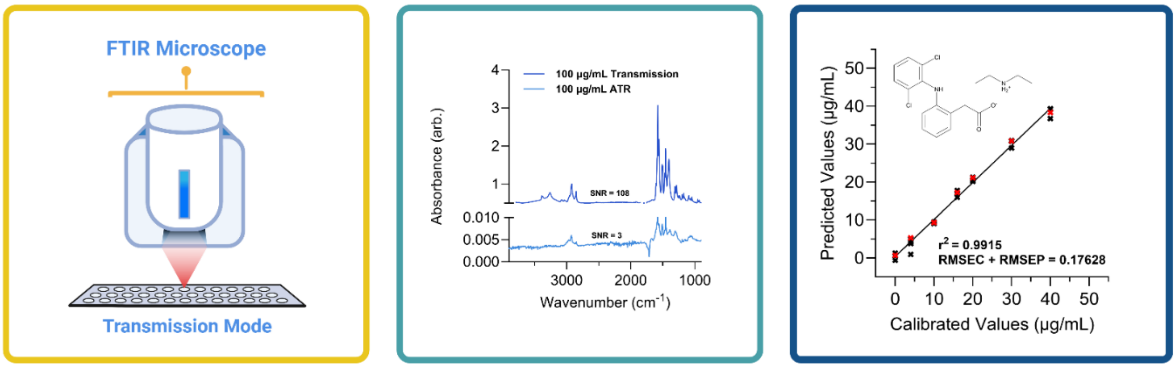

Figure 1: Graphical abstract with transmission data compared to ATR data and optimised PLS regression model for Diclofenac Diethylamine in skin permeation relevant solvent. Validation points marked in red.

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Ruairi Carland (SXFP14)

Separation and Characterisation of Ultrabright Nanotags for Surface-Enhanced-Raman-Spectroscopy (SERS)

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KEY WORDS: *SERS, Field-Flow-Fractionation (FFF), Plasmonics.*

Surface-enhanced Raman scattering (SERS) is a powerful spectroscopic technique which harnesses the optical properties of plasmonic nanostructures to amplify Raman scattering. Indirect detection by SERS involves the preparation of a plasmonic nanostructure functionalised with Raman reporter molecules, a 'SERS nanotag' to act as a spectroscopic label for the analyte of interest. Often, this 'nanotag' is encapsulated in an outer shell, which can support the conjugation of targeting moieties. For many applications an intense SERS signal is crucial, such as the detection of these 'nanotags' in complex biological environments. Understanding the relationship between structure and SERS response therefore represents an important fundamental aspect in the preparation of ultrabright SERS nanotags.

SERS response can be increased by 3-4 orders of magnitude through aggregation of the plasmonic nanoparticle substrate. However, aggregation is an uncontrolled process that yields a wide range of structures. In this work, we discuss our recent endeavours in the separation, characterisation and optimisation of gold nanoparticle aggregates, with the aim of better understanding the relationship between aggregate structure and optical response. Specifically, to determine a combination of structural features that will maximise the SERS response and batch-to-batch reproducibility of spectroscopic tags.

This work involves the separative characterisation of aggregated AuNP-based SERS nanotags, primarily by Field-Flow-Fractionation (FFF). FFF facilitates the comprehensive characterisation of specific nanotag morphologies by subjecting polydisperse samples to a high-resolution separation under flow, prior to on-line structural and optical characterisation. The modularity of FFF detector suites is a strength of the method, allowing an analyst to tailor their chosen characterisations to the sample of interest; in this work we detail efforts towards the hyphenation of Raman with FFF for the first time, greatly improving the utility of this method for the study of colloidal SERS substrates.

Connor Wilson (SXFP15)

Advancing Near-Infrared Surface Enhanced Raman: Towards Improved Depths and Resolutions

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KEY WORDS: Surface Enhanced Spatially Offset Raman Scattering, Shell-Isolated Nanoparticles, Photothermal Therapy

Surface enhanced spatially offset Raman spectroscopy (SESORS) is a specialised technique that provides signals at depths that are not possible using conventional Raman spectroscopy.[1] Typically conducted with laser excitation wavelengths in the visible to near-infrared region,[2] SESORS combines the sensitivity of surface-enhanced Raman scattering (SERS) with the depth-profiling capability of spatially offset Raman spectroscopy (SORS). Gold nanoparticles (AuNPs) are widely used to enhance Raman signals through their localised surface plasmon resonance (LSPR).[3] However, for spherical AuNPs, the LSPR typically occurs in the visible region, where strong tissue absorbance and scattering can obscure Raman signals. Optimal performance in biological systems requires deliberate tuning of the LSPR into the near-infrared (NIR) windows.[4] The NIR-I (700-1000 nm) and NIR-II (1000-1800 nm) regions offer reduced absorbance and scattering in tissue, providing opportunities for low interference SESORS.[5]

This work presents shell-isolated nanoparticles (SHINs) that have been synthesised, functionalised and optimised to yield intense SERS enhancement at both 785 nm and 1064 nm excitation.

Novel Raman-active dyes were investigated, including a series of chalcogen- containing chromophores with strong NIR absorbance profiles. These dyes exhibited distinct vibrational signatures and potential for high photothermal conversion, indicating that they could be used in dual modality nanotags for both SESORS detection and controlled thermal activation under NIR illumination. This combination of deep Raman and tuneable photothermal output highlights the potential of these probes for future spectroscopy-guided therapeutic applications in highly scattering biological environments. A custom SORS instrument was engineered to support dual-wavelength excitation and detection on one stage, allowing direct comparison of NIR-I and NIR-II performance under the same conditions.

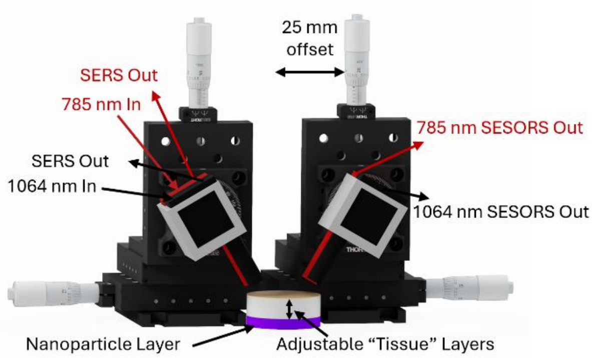

Figure 1 Dual wavelength SESORS setup with adjustable depth "tissue" model with a SERS nanoparticle layer beneath.

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Effect of reactive oxygen species on gold bipyramids's extinction and SERS signal

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KEY WORDS: Gold nanoparticles, reactive oxygen species, SERS

The wavelengths of the light extinguished by gold nanords and gold bipyramids due to their local surface plasmon resonance (LSPR) depend on their aspect ratio, with higher aspect ratios leading to extinction at longer wavelength. The aspect ratio of gold nanorods, and thereby their LSPR wavelength, can be modified by etching with reactive oxygen species (ROS).[1] It is hypothesised this oxidation process leads to the gold nanorods shortening due to the gold surface at the tips being more accessible to the ROS, because the high curvature at the tips of the rod reduces the packing density of the surface-bound stabilising molecules. The resulting shift in colour of the colloid solution has been used to quantify ROS by other groups.[2]

As ROS are an important part of biological processes, we aim to expand the potential of gold nanoparticles as tools to quantify ROS concentration by detecting the LSPR shift via Raman spectroscopy, which should allow us to detect the morphological change non-invasively through biological tissues. To this end, the nanoparticles were functionalised with Raman reporters to achieve Surface Enhanced Raman Spectroscopy (SERS). When the LSPR shift, it results in a change in the intensity ratio between the Raman peaks generated by the Raman reporters, due to the shift in the wavelengths favoured by the plasmon resonance. After evaluating the potential of gold nanorods for ROS sensing applications, we are now investigating bipyramids for the same uses, as we hypothesised their sharp end would make them more sensitive to etching, but also lead to stronger SERS signal enahncement.

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Optimisation of radiative enhancement on metallic nano-surfaces for SERS detection

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KEYWORDS: silver nanoparticles, SERS turn-on, molecule adsorption

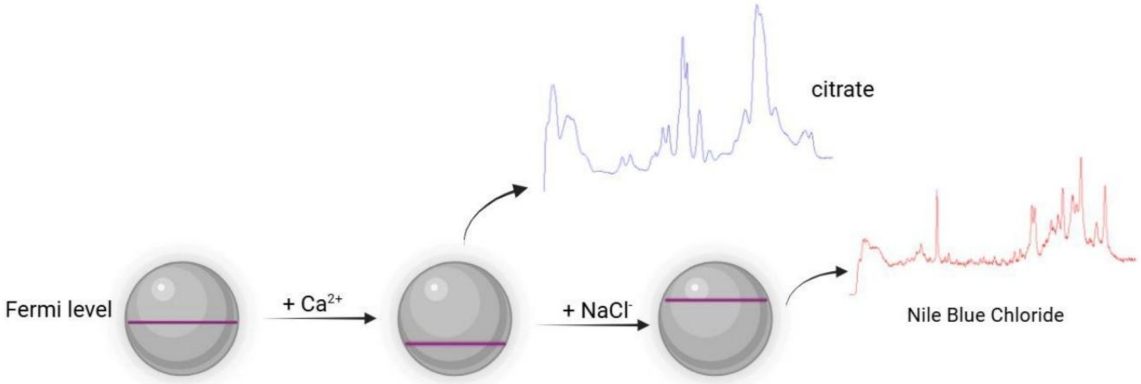
Metallic nano-structures are widely used as optical radiative enhancement. However, the molecule-metal interaction is not yet fully understood. Therefore, this study investigates how surfactant and surface electrochemical potential of silver nanoparticles affect their interaction with molecules and the resulting surface-enhanced Raman scattering (SERS) response.

We examined the role of different surfactants, borohydride, PEG, and citrate, in SERS performance when nanoparticles shared similar localised surface plasmon resonance (LSPR) values. The limit of detection (LOD) varied with surfactant type, with PEG-stabilized nanoparticles providing the lowest LOD for the anionic dye, Alizarine Yellow, while citrate-stabilized colloid for the cationic dye, Nile Blue.

In addition, we investigated the influence of silver surface oxidation state on SERS activation for anionic (citrate) and cationic (Nile Blue) molecules. The surface electrochemical potential of nanoparticles was varied by adding nitric acid (HNO_3), which oxidizes the silver nanoparticles, and sodium borohydride ($NaBH_4$), which reduces the silver ions on the surface.

A more acidic environment increases the citrate adsorption onto silver nanoparticles, promoting its SERS signal. Similar behaviour was observed in the presence of Ca^{2+} ions. Conversely, removal of surface Ag^+ species by $NaBH_4$ displaced citrate from the nanoparticle surface, effectively suppressing its SERS signal. This adsorption–desorption behavior was found to be reversible and cyclic. For cationic analytes, the addition of chloride ions in the presence of surface Ag^+ increased the electrochemical potential of the silver nanoparticles, facilitating Nile Blue adsorption. This process was accompanied by fluorescence quenching and activation of the SERS signal.

These insights contribute to refining SERS detection protocols for improved analytical sensitivity by investigating the effects of nanoparticles' surfactant, environmental pH, analyte affinity, and different chemical synthesis methods.



Graphical abstract showing silver nanoparticles as an SERS substrate used to detect cationic molecules

Liquid Chromatography–SERS Integration for Advanced Healthcare Monitoring

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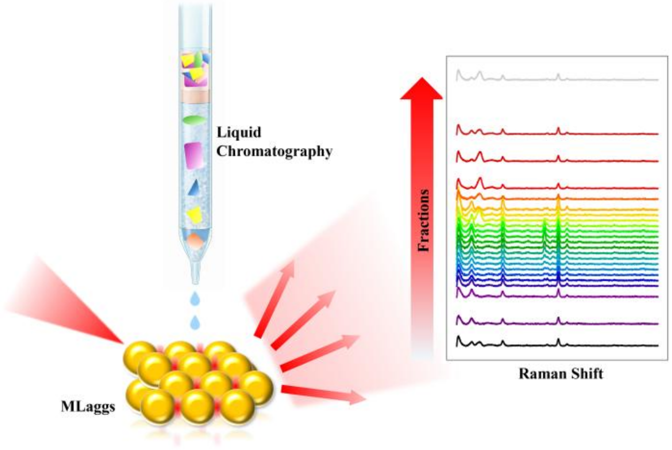
KEY WORDS: SERS, liquid chromatography (LC), plasmonic nanostructures

Surface-Enhanced Raman Spectroscopy (SERS) offers molecularly specific, label-free detection with ultra-low concentration sensitivity, making it attractive for clinical spectroscopy and healthcare monitoring. However, its application to complex biological samples remains limited by substrate fouling, competitive analyte adsorption, and spectral overlap in chemically heterogeneous mixtures[1].

Recent advances in multilayer gold nanoparticle aggregates (Au-MLaggs) enable sub-nanometre plasmonic hotspots while supporting electrochemical (EC) regeneration of active sensing sites[2]. The ability to reproducibly clean and reuse SERS substrates represents a key step toward stable and controllable analytical workflows, particularly for continuous or inline measurements.

Liquid chromatography (LC) remains a cornerstone technique for resolving complex biofluids and industrial process streams. When integrated upstream of SERS detection, LC provides temporal separation of molecular components, reducing spectral congestion and matrix effects. Sequential analyte delivery to the SERS detection point, combined with EC cleaning between elution windows, enables independent measurement of chemically similar species, mitigating substrate fouling and competitive adsorption while improving spectral fidelity, quantitative accuracy, and reproducibility. This LC-assisted strategy addresses several limitations of standalone SERS, especially for multiplexed and low-abundance analyte detection.

This work presents an integrated microfluidic LC–SERS system enabled by reusable plasmonic substrates, demonstrating improved signal clarity and analytical robustness. The resulting workflow shows strong potential for metabolite profiling and biomarker detection in complex biological systems.



Schematic of LC-SERS integration.

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Harriet Willett (SXFP19)

Analytical techniques to study the formation and structure of HGA-derived pigment

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KEY WORDS: Alkaptonuria, spectroscopic monitoring

Alkaptonuria (AKU) is a rare, recessive genetic disorder caused by mutations in the gene encoding for the homogentisate 1,2-dioxygenase (HGD) enzyme. This halts the tyrosine and phenylalanine metabolic pathway leading to an accumulation of homogentisic acid (HGA). Consequently, an alternative metabolism occurs producing a dark brown or black HGA-derived pigment. This pigment is central to the disorder and is deposited into connective tissues in a process called ochronosis. This causes tissues to become hard and brittle leading to ochronotic osteoarthritis which is painful and debilitating. There is currently no cure although a recently approved drug 'Nitisinone' can halt pigmentation and slow disease progression[1].

Owing to being a rare disease, there are many unanswered questions. One major question surrounds the metabolism of HGA to form HGA-derived pigment. Classical ideas of reactivity have arisen due to structural similarity between hydroquinone and HGA but are supported by little evidence[2]. HGA-derived pigment is central to the disorder so increasing understanding could improve disease management and help in working towards a cure.

Recent studies within our group suggest that HGA reacts to form pigment via a radical reaction. This supports studies conducted by other research groups[2,3]. However, the applicability of our current studies is limited. They have taken place in non-physiologically relevant solutions where reactivity is likely to be different to within the body.

Consequently, this presentation highlights studies which investigate the reaction of HGA in more physiologically relevant solutions. These include urine, as excess HGA is excreted in urine, and in the presence of calcium salts, as pigment initially binds within the calcified cartilage[4]. Spectroscopic techniques including Fourier Transform infrared spectroscopy and UV-Vis spectroscopy have been combined with other analytical techniques including mass spectrometry. Together, these techniques have enabled a clearer understanding of how HGA behaves and reacts in the body.

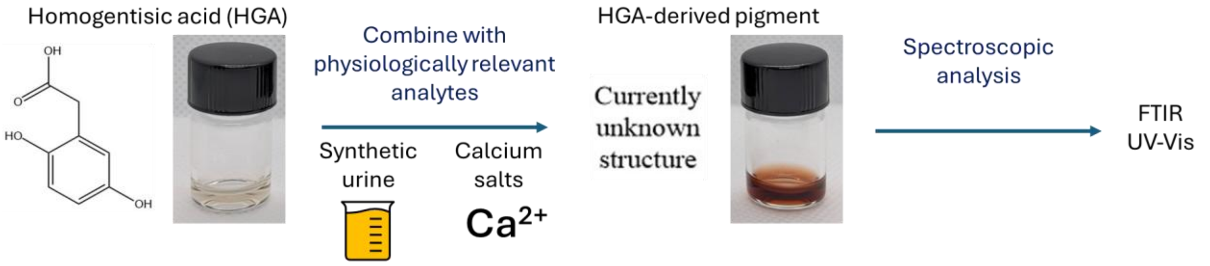

Figure 1: Image summarising the work conducted incubating HGA with various physiologically relevant analytes.

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Ruby Main (SXFP21)

From Label-Free Femtosecond SRS to Prognostic Histology: Single-Frame Femtosecond Virtual H&E Imaging of Breast Cancer TMAs

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KEY WORDS: fs-SRS, machine learning, virtual staining

Haematoxylin and eosin (H&E) staining remains the gold-standard for cancer diagnosis, forming the basis of decades of histopathological knowledge and vast archival tissue resources. Although label-free techniques such as stimulated Raman scattering (SRS) microscopy enable rapid chemical imaging without staining, their clinical translation is constrained by the lack of compatibility with established H&E-based diagnostic criteria and outcome-driven studies. Virtual staining of label-free images into the H&E domain therefore represents a critical route to integrating emerging optical modalities with routine pathology and retrospective prognostic analysis.

We present a fundamentally different virtual histology strategy based on femtosecond SRS (fs-SRS) combined with neural network architectures designed for image generation.

Unlike conventional picosecond SRS approaches that sequentially acquire narrowband CH_2 and CH_3 images, fs-SRS excites the full CH stretching region simultaneously, producing a single high-signal, chemically integrated image per tile. This enables substantially faster acquisition, simplified instrumentation, and eliminates inter-frame artefacts associated with multi-colour imaging.

We employ a pix2pix network for supervised image translation and an unsupervised CycleGAN framework to translate single-frame broadband fs-SRS images directly into H&E-like virtual staining without requiring pixel-wise paired training data. The broadband vibrational excitation encodes composite lipid–protein contrast that captures both tissue architecture and nuclear morphology, providing input for generative translation.

We demonstrate the approach on breast cancer tissue microarrays, encompassing ductal carcinoma in situ (DCIS), invasive ductal carcinoma (IDC), and invasive lobular carcinoma (ILC). The resulting virtual H&E images preserve diagnostically relevant glandular, stromal, and nuclear features across tumour subtypes, while enabling rapid, tile-based imaging compatible with high-throughput pathology workflows.

By mapping label-free chemical images into the H&E contrast domain, this work establishes fs-SRS virtual histology as a scalable bridge between advanced optical microscopy and clinical pathology, opening a direct pathway for applying prognostic models and quantitative metrics developed from archival H&E datasets to SRS-based imaging.

Development of dual modality *in vivo* optical probe for rapid neuromuscular disease assessment

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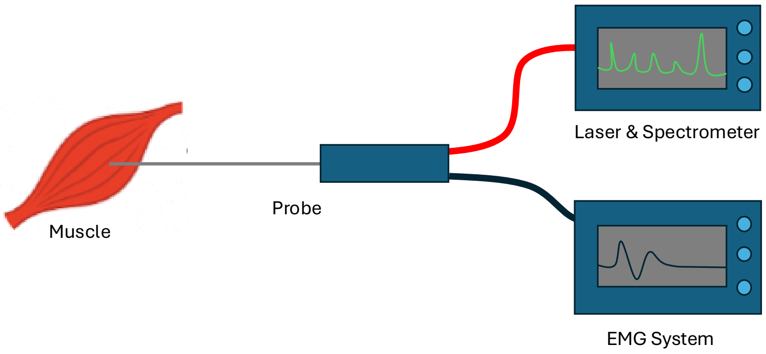
KEY WORDS: Raman spectroscopy, *in vivo* probes, neuromuscular disease

Neuromuscular disorders encompass a wide range of conditions that lead to progressive muscle weakness and are associated with substantial morbidity and mortality.[1] A definitive diagnosis can be challenging, with many patients undergoing prolonged clinical assessment, imaging, and invasive investigations such as muscle biopsy before a clear conclusion can be made.[2] Electromyography (EMG), which measures the electrical activity of muscles, remains a routine and essential diagnostic tool. However, it typically provides limited specificity and offers no biochemical insight on underlying muscle pathology.[3]

To address this, we have developed a "smart" needle device that integrates Raman spectroscopy with routine EMG with Raman spectroscopy to enable rapid identification of muscle pathology. This combined "electro-photonic" approach provides near real-time assessment of muscle health using by capturing electrical activity of the muscle (EMG) and the biomolecular fingerprint (Raman spectroscopy). We hypothesise that this dual-modality approach could enable earlier diagnosis and improved monitoring of disease progression.

Our "Optical-EMG" probe consists of two fibres (100 µm, low-OH) and a central "active" electrode wire within a 23 gauge (0.63 mm) hypodermic needle. The needle forms the second "reference" electrode for the EMG measurements. The probe is connected to a laser and spectrometer via an armoured fibre-optic umbilical, and the electrodes are separately connected to a standard routine EMG system. Spectra can be acquired in approximately 30 seconds, enabling near real-time assessment.

The device has been assessed for optical and EMG performance across a range of laboratory phantoms including PTFE, chicken, and pork meats, and through *in vivo murine* muscle in a preclinical model of a neuromuscular disease. An MHRA submission for a first in human clinical investigation is being prepared to evaluate safety, usability, and diagnostic potential in a clinical setting. This technology represents a promising step toward real-time, minimally invasive assessment of muscle pathology, with potential to enhance diagnostic pathways for a broad range of neuromuscular diseases.



Schematic overview of Optical-EMG probe system

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Alex Henderson (SXFP23)

FAIRSpectra – Sharing IR and Raman data to enable AI

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KEY WORDS: FAIR, metadata, data sharing

There is a growing requirement for data to be shared openly[1]. This is now mandated by funding agencies including UKRI[2], Horizon[3], Wellcome[4], and equivalent organisations around the world[5]. Sharing data means that files must be readable by others, perhaps using different software packages, and their contents understood, ideally by machines in addition to humans. This latter aspect is *machine actionability*.

The FAIR Guiding Principles – that data should be Findable, Accessible, Interoperable, and Reusable – are now recognised to be one of the cornerstones of Open Research[6,7]. Organisations such as ELIXIR[8] and the Research Data Alliance[9] have published materials on how to generate FAIR data[10], but there remains an operational gap between these recommendations and how one should actually go about the task on the ground.

FAIRSpectra's role is to open a discussion about what the chemical analysis field requires in terms of file format support, and specifically the imaging modalities of spectroscopy and spectrometry. It aims to tackle issues with interoperability and reusability. This has been broken down into two areas of activity: open file formats and metadata vocabulary.

This presentation will cover what currently exists, what is still required, and offers an invitation to all interested parties to get involved, share expertise, and become part of the solution.

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Benedetta Gavazzoni (SXFP24)

Raman Imaging for the Monitoring of Cellular Internalization and Fate of MRI-active Fluorinated Nanoparticles

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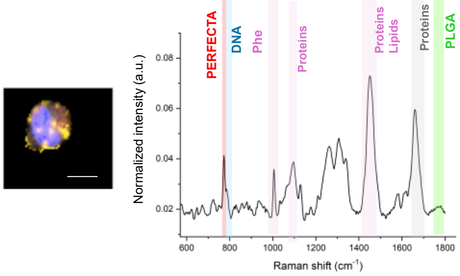
KEY WORDS: bimodal, Raman imaging, cells

Precise localization and characterization of nanoparticles across spatial scales remains a critical challenge in biomedical imaging. While traditional MRI contrast agents enhance macroscopic tumor visualization, they lack molecular specificity at the cellular level. Dual-mode agents (e.g., MRI with fluorescence) have been explored, but integrated systems simultaneously visualized by MRI and Raman microspectroscopy remain largely unexplored [1].

We developed fluorinated nanoparticles (FNPs) that act as a ^{19}F-MRI contrast agent and monitored them in a cellular environment, aiming to understand their internalization fate, and to perform high-resolution cellular analysis. The fluorinated nanoparticles (FNPs) consist of PERFECTA, a perfluorinated probe with both ^{19}F MRI sensitivity and distinct Raman spectral signatures, enabling direct correlation between the modalities[2,3]. The shell is made of poly(lactic-co-glycolic acid) (PLGA), stabilized with polyvinyl alcohol (PVA) or sodium cholate (NaC). Two formulations, PERFECTA-PLGA-PVA and PERFECTA-PLGA-NaC, were evaluated for future *in vivo* applications.

In vitro Raman imaging monitored FNPs uptake in NIH/3T3 murine fibroblasts using a home-built Raman micro-spectroscopy system (660 nm excitation, step size = 0.7 µm, dwell time = 750 ms). This revealed time-dependent internalization of FNPs, allowing separate tracking of both the fluorinated core (PERFECTA) and the PLGA carrier. Unlike fluorescence, which tracks only the nanocarrier, Raman imaging enabled distinct tracking of both components. Raman signals revealed greater accumulation of PERFECTA over PLGA, with increased lipid concentration suggesting endosomal encapsulation. Furthermore, PLGA degradation was monitored through Raman bands at 878 cm^{-1} (PLGA presence) and 1771 cm^{-1} (degradation), with the ratio of these bands quantifying polymer breakdown over different FNPs incubation times.

This study demonstrated the microscale tracking of the FNP system in an *in vitro* cellular environment through Raman microspectroscopy, laying the foundation for future *in vivo* studies on tumor localization, FNPs internalization, and real-time tumor margin monitoring.



NIH/3T3 murine fibroblasts incubated for 8 hours with fluorinated nanoparticles: Univariate analysis on hyperspectral Raman maps of NIH/3T3 fibroblast cells and average spectra on the entire cell volume

High-speed ptychography imaging using photo-modulated probes in the millimeter-wave and terahertz regime

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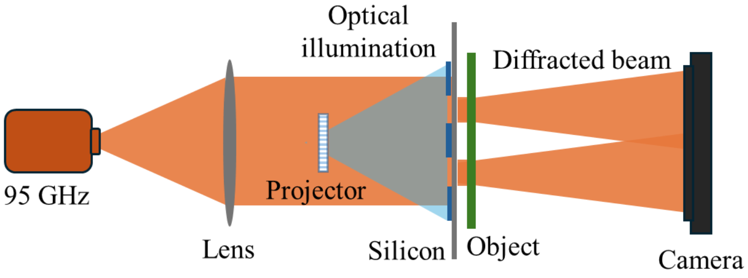
KEY WORDS: Photo-modulation, ptychography, phase imaging

Ptychography is a lensless imaging technique that reconstructs high-resolution amplitude and phase images of an object using multiple diffraction patterns acquired from overlapping beam positions. In conventional implementations, the object is mechanically scanned relative to a localized probe to generate diffraction patterns and to ensure sufficient overlap between adjacent measurements[1]. However, the requirement of mechanical motion significantly limits imaging speed and compromises system stability.

We present a silicon photomodulator-based approach for high-speed ptychographic imaging applicable from the millimeter-wave to terahertz frequency regimes. In this approach, spatially structured optical excitation is used to modify local conductivity of silicon wafer[2], forming virtual aperture equivalent to the physical probe used in conventional ptychography. The object is illuminated by multiple such apertures without any physical movement, while maintaining the beam overlap required for the reconstruction. Furthermore, these optically generated apertures are reconfigured into spatially multiplexed probe beam, which significantly enhances beam throughput and reduces data acquisition time.

A continuous wave ~95 GHz source is employed to reconstruct images of different amplitude and phase sensitive objects. The high-speed imaging capability is demonstrated through measurement of a multiphase fluid dynamic sample, achieving an acquisition speed of 16 frames per second. This optically controlled ptychography approach enables real-time ptychographic imaging, with potential applications in areas such as vivo biomedical imaging.



Schematic of the photo-modulated ptychographic imaging setup.

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Haolin Zhou (SXFP27)

Exploration of Hypoxia Microenvironment with IR Spectral-Spatial Signature

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KEY WORDS: IR spectroscopic imaging, tumour microenvironment, prostate tumour hypoxia.

Tumour hypoxia promotes aggressive, treatment-resistant prostate cancer, yet routine assessment still relies on immunohistochemistry (IHC) markers such as Glucose Transporters (GLUTs) or pimonidazole (PIMO) [1]. These stains are labour-intensive, sensitive to staining/batch effects, and hard to quantify robustly in heterogeneous tissue. This study tests whether label-free mid-infrared (IR) hyperspectral imaging can capture reproducible spectral signatures of hypoxic microenvironments and whether supervised learning can map these signatures to IHC-derived hypoxia proxies at clinically meaningful spatial scales.

Two radical prostatectomy cohorts were analysed: a GLUT-1 macro-array (31 patients, 199 cores) and a PIMO micro-array (25 patients, 188 cores). IR data were acquired on a Bruker LUMOS II ILIM QCL platform (952–1800 cm^{-1}, 4 cm^{-1} resolution). Preprocessing pipelines were benchmarked, combining wax-band removal, Savitzky–Golay smoothing/derivatives, linear baseline correction, denoising and normalisation. Pixel-level baselines were compared with a patch-level spatial-spectral dual-path CNN encoder that fuses local morphology with spectral fingerprints. Tasks included binary hypoxia classification (high vs low from IHC thresholds) and, where feasible, regression to IHC-diaminobenzidine (DAB) optical density (OD). Interpretability used SHAP/gradient attribution and spectral band occlusion.

Evaluated using five-fold patient-wise cross-validation, the GLUT-1 patch model achieved 0.914±0.046 accuracy and F1 0.813±0.169, but performance was fold-dependent, reflecting limited cohort size and label noise; predicted hypoxia heatmaps often elevated probability in “intermediate hypoxic” regions. PIMO performance was moderate and variable (accuracy ≈0.73; F1 ≈0.61). OD regression underestimated high-OD regions due to long-tailed label distribution. Key predictive bands clustered in ~1000–1150 cm^{-1} (carbohydrate/phosphate-rich fingerprint, potentially glycogen-related) and ~1700–1760 cm^{-1} (lipid carbonyl/ester) [2,3], consistent with hypoxia-linked metabolic shifts and lipid remodelling. Although carbohydrate- and lipid-associated bands are informative, their direction is inconsistent across cohorts. Future work will focus on mass spectrometry metabolites confirmation, broader preprocessing validation, long-tail-robust training, and orthogonal assays to verify spectral biomarkers.

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Iona Hill (SXFP28)

Multimodal Spectroscopic Imaging for Advanced Biological and Tissue Characterisation

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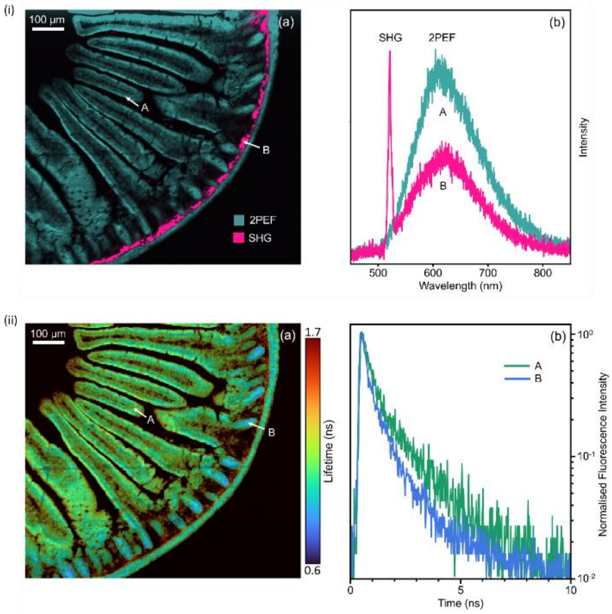
KEY WORDS: Raman spectroscopy, multimodal imaging, bioimaging

Multimodal optical microscopy provides a powerful route to interrogate biological systems by combining complementary sources of chemical, structural, and functional information within a single experimental workflow. By integrating multiple spectroscopic techniques into one platform, it becomes possible to study complex biological samples more efficiently, reducing reliance on labels while enhancing interpretability.

In this work, we present a multimodal microscopy framework built around a confocal Raman system and extended with fluorescence lifetime imaging microscopy (FLIM), second harmonic generation (SHG), and two-photon excited fluorescence (2PEF). Raman spectroscopy delivers detailed molecular fingerprints, while nonlinear and time-resolved modalities provide additional contrast mechanisms sensitive to tissue architecture, biomolecular organisation, and cellular function. SHG enables imaging of ordered biological structures such as collagen, 2PEF supports high-resolution imaging at increased tissue depths, and FLIM offers insights into local biochemical environments and metabolic activity.

The optical and instrumental strategies required to integrate these techniques within a unified platform are described, enabling correlative measurements across spatial, spectral, and temporal dimensions. By bridging vibrational spectroscopy with nonlinear and lifetime-based imaging, this approach expands the analytical capabilities of Raman microscopy and provides a versatile tool for advanced bioimaging. The results highlight the potential of integrated multimodal systems for addressing key challenges in biological research and for supporting future developments in biomedical and translational studies.



Multimodal imaging is demonstrated using mouse intestinal tissue: (i) combined 2PEF and SHG imaging with spectral information, and (ii) 2PEF lifetime imaging and fluorescent decay analysis.

Miranda Eisenköck (SXFP29)

From Impurity to Insight: Real-Time Water Monitoring in Solvent Recycling using MIR Spectroscopy

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KEY WORDS: vibrational spectroscopy, PAT, solvent recycling

Organic solvents play essential roles in numerous processes such as product purification in pharmaceutical and chemical industries. Common methods of disposal such as incineration lead to atmospheric emissions and can pose health risks.[1] The recycling and downcycling of solvents can help reduce the impact on the environment and minimize both cost and waste.[2] According to a study by the European Solvent Recycler Group (ESRG), the carbon footprint of recycled THF is reduced by a factor of 8.8 compared to the virgin solvent.[3]

While downcycling of solvents such as acetone for cleaning applications can yield products with purities of around 95%, recycling or upcycling generally requires significantly higher purity levels, particularly regarding water content when absolute solvents are needed for chemical synthesis.[4] Quantification of traces of water in the recycled solvents is typically performed off-line via Karl-Fischer titrations (KFT). Implementing an on-line measurement system can improve recycling process monitoring.

Mid-infrared (MIR) spectroscopy is a non-destructive, in-situ process analysis tool, offering valuable insights into the chemical composition of solvent mixtures in real-time. Although water typically poses challenges in MIR spectroscopy due to strong absorption properties, its strong characteristic vibrations enable detection of trace amounts in organic solvents.

We demonstrate the suitability of quantum-cascade-laser-based MIR spectroscopy for monitoring water contents below 0.1w% in THF in a transmission flow-cell using KFT as reference method. Multivariate data analysis such as partial-least-squares-regression (PLSR) enabled the accurate prediction of the water content (RMSECV < 10 ppm). Additionally, samples representing a separation process of a ternary solvent mixture containing acetone, THF and water were analyzed. Furthermore, hydrogen bonding leads to characteristic red and blue shifts in the solvent bands, which can be exploited through chemometric methods such as multivariate-curve-resolution (MCR) and PLSR, providing insights into structural changes in THF due water-induced (1-60w%) H-bonding.

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Investigating the Size and Chemical Identity of Particulates Formed During Battery Thermal Runaway Using Raman Microscopy

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KEY WORDS: Raman microscopy, batteries, particle size

Recent years have seen rapid increases in the demand for lithium ion batteries, particularly as part of the drive towards zero emissions in the automotive industry. Such batteries are susceptible to thermal runaway events, leading to fire and the emission of fine particulate matter[1]. Previous studies have observed the emission of highly toxic compounds from these events[1], and fine particulate matter can negatively impact human health. Particles below 10 µm in diameter are of particular concern as they are more likely to be deposited in the lungs[2]. To fully understand the potential health implications, it is therefore critical to assess the size and chemical identity of the particles produced.

In this work we demonstrate the application of Raman microscopy to investigate the chemical identity and particle size of particulate matter produced from a lithium nickel manganese cobalt oxide (NMC) battery following a thermal event. Particles are dispersed uniformly on metallic substrates using a particle disperser, with particles identified and sized using an image segmentation algorithm and Raman spectroscopy performed on all detected particles. Chemical identities of particles are assigned using multivariate analysis, with the majority of particles smaller than 10 µm in diameter.

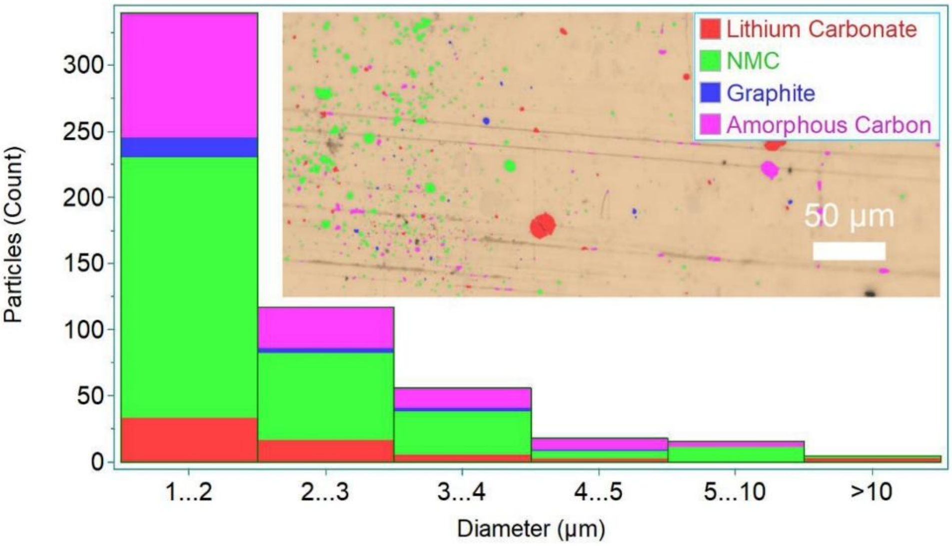

Figure 1 Size distribution and chemical identity of the detected particles. Inset: Optical microscope image of particles dispersed on the substrate showing particles and chemical identities.

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Poster Session & Drinks Reception
(18:15-20:00)
in EXHIBITION HALL

Nibbles, canapés and drinks. Please take your time to visit the poster stands and exhibitors around the venue.

Becca Armstrong (SXP02)

What Lies Beneath: Deep Raman imaging of bacterial biofilms

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KEY WORDS: SESORS, shell-isolated nanoparticles, biofilms

Biofilms cause up to 80% of microbial infections[1] and are notoriously difficult to treat, leading to poor patient outcomes. The transition from planktonic bacteria to mature biofilm involves biochemical modifications that can be tracked using Raman spectroscopy,[1] and it is imperative to detect formation as early as possible as treatment is least effective on mature biofilms. However, Raman spectroscopy is inherently weak, requiring enhancement to improve sensitivity for through-tissue detection of biofilms. To achieve this, surface-enhanced spatially offset Raman spectroscopy (SESORS) can be utilised.

SESORS is a technique that combines the increased signal intensity of SERS with the at-depth signal detection of SORS. By functionalising gold nanoparticles (AuNPs) with a Raman reporter and a capture biomolecule, it is possible to amplify the Raman signal and therefore improve sensitivity while targeting a specific bacterial strain. This allows for non-invasive imaging of a targeted biofilm through tissue via the strong SERS signal of the Raman reporter.[2]

It is crucial that the AuNPs are reproducible, stable, and produce an intense SERS signal when being used for SESORS. This was achieved by producing AuNP aggregates coated in a silica shell, known as shell-isolated nanoparticles (SHINs), via a syringe pump method to improve control and ensure reproducibility between batches. The SERS signal of the Raman reporter is increased due to hotspot formation in the aggregates and the inert silica shell protects the AuNPs from physical or chemical interferants in the environment. Adsorbing a strain specific antibody to the silica shell ensures that the main interaction between AuNPs and the target biofilm is due to antibody-antigen interaction, rather than competing electrostatic interactions. This method of using SHINs in the detection of biofilms via SESORS should increase the sensitivity and the depth collection of the signal to allow for easier detection of biofilms and improved treatment pathways.

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Grant Hendrie (SXP04)

Improving the Manufacturing of DNA Medicines Using SERS Monitoring

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KEY WORDS: Surface enhanced Raman scattering, oligonucleotides, structural validation

Oligonucleotide therapies are an emerging area of interest for leading pharmaceutical companies. There is currently only around 20 oligonucleotide-based drugs available on the market with the most common being antisense oligonucleotides (ASOs) and small interfering ribonucleic acids (siRNAs). Minor structural changes can have significant impact on the function and efficacy of oligonucleotide-based drugs, and one of the current challenges when developing oligonucleotide therapies is structural validation and quality assurance post synthesis. This involves the use of several techniques including mass spectrometry to confirm the correct intact mass, followed by a combination of LCMS, NMR and FT-IR to provide sequence information, which is costly and labour intensive.

Surface enhanced Raman scattering (SERS) could be advantageous in the characterisation of oligonucleotide drugs due to the sensitivity of the technique and the specific molecular information that can be obtained. Previous studies have reported that SERS can be used to detect minor structural changes in oligonucleotide sequences, which could provide an invaluable tool in the pharmaceutical industry for the characterisation of oligonucleotide drugs[1]. The aim of this project is to develop a SERS-based sensor for monitoring oligonucleotide synthesis and detecting structural changes, such as single base mismatches. We are investigating two different approaches: a label-free method that involves conjugating single-stranded DNA (ssDNA) to the surface of positively charged silver nanoparticles and directly detecting the DNA sequence by SERS (Figure 1 (a))[2]; and a hybridisation assay that can be used to discriminate complementary ssDNA sequences to those with minor structural changes (Figure 1 (b))[1]. Each of the methods will be applied to real-world pharmaceutical samples to assess the suitability of SERS as a quality assurance technique to improve current processes and accelerate the development of safe and effective oligonucleotide-based drugs.

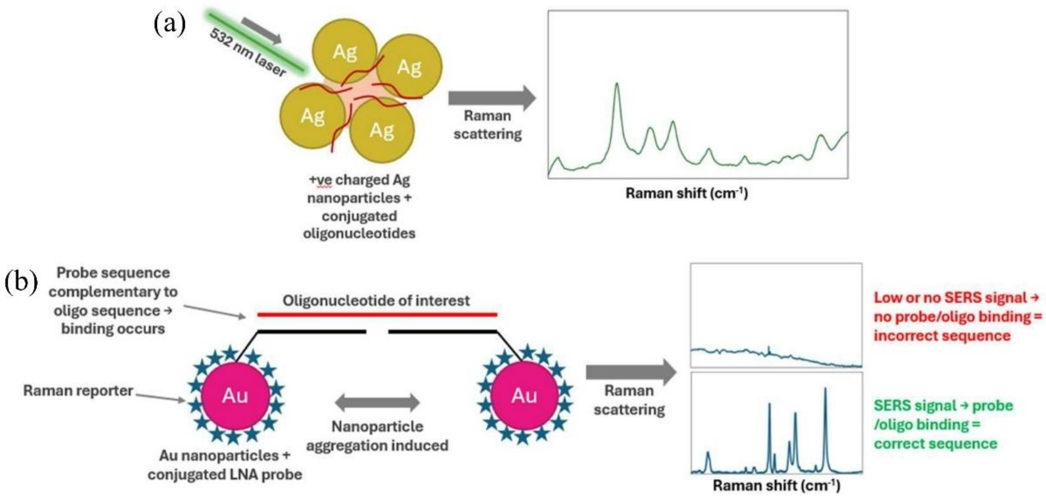

Figure 1: (a) Characterisation of oligonucleotides by label-free SERS. (b) Identification of oligonucleotide sequences by hybridisation assay.

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Reproducible SERS substrates for cortisol detection in aquaculture

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KEY WORDS: SERS, cortisol, aquaculture

Cortisol is a key biomarker of physiological stress in fish and other aquatic organisms, playing a central role in growth, immune response, reproduction, and overall welfare. In aquaculture, chronic stress, often induced by high stocking densities, handling, or suboptimal water quality, leads to elevated cortisol levels, negatively impacting productivity and animal health. Reliable, rapid, and sensitive detection of cortisol in aquatic environments is therefore essential for effective stress monitoring and sustainable aquaculture management. However, conventional analytical methods typically require extensive sample preparation and complex laboratory workflows, limiting their suitability for routine stress monitoring in aquaculture.

Surface-enhanced Raman spectroscopy (SERS) is a promising tool for cortisol detection due to its molecular specificity and high sensitivity, but its practical application is often hindered by poor substrate reproducibility, limited reusability, and competitive adsorption effects in complex aqueous media. Recently developed cleanable multilayer aggregate (MLagg) SERS substrates[1], based on bottom-up self-assembly of gold nanoparticles with rigid molecular spacers (cucurbit[5]uril), provide highly uniform sub-nm nanogaps, enabling improved spectral reproducibility and compatibility with electrochemical systems. These substrates can be electrochemically cleaned and regenerated, allowing multiple analytical cycles using the same device[1].

We show here the exploration of utilising MLagg-based SERS substrates for cortisol detection in aquaculture. Initial work focuses on optimal substrate preparation and spectroscopic characterization, as well as on evaluating cortisol adsorption and spectral behaviours. By integrating the MLagg substrate into electrochemical cells to enable electrochemical-SERS (EC-SERS) studies, improved selectivity in complex media is targeted. This approach aims to provide a reliable, label-free method for cortisol monitoring, supporting better animal welfare assessment and more sustainable aquaculture management.

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James Simons (SXP06)

Development of SERS for the Measurement of Volatile Organic Compounds: Application to Indole Detection Produced from *E. Coli*

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KEY WORDS: SERS, LC-MS, Thioalcohols

Axillary (underarm) malodour is a common issue experienced by many individuals and can have a negative impact on daily life. Although axillary sweat arises from natural physiological processes, it is often perceived unfavourably due to its unpleasant smell produced through biotransformation of odourless precursors by resident skin bacteria. Several underarm products, notably deodorants and anti-perspirants, have been manufactured to tackle problems associated with axillary malodour. However, to improve the efficacy of these products further, a more detailed analysis of the chemical composition of axillary secretions is necessary. Thioalcohols are volatile components of sweat that are of particular interest due to their exceptionally low olfactory detection thresholds (~1-10 pg/L in air) while also being highly potent contributors to malodour.[1] The gold standard for detecting and quantifying volatile compounds, such as thioalcohols, is currently gas chromatography-mass spectrometry (GC-MS)[1,2]; however, GC-MS can be expensive and its sample preparation complex. Therefore, this research aims to employ surface enhanced Raman scattering (SERS) and liquid chromatography-mass spectrometry (LC-MS) with derivatisation as alternative methods to detect, resolve, and quantify these low-concentration compounds in a gaseous state, following their successful application to solid SERS substrates in aqueous solutions.[3] The work reported in this poster focuses on the optimisation of aggregating agents used in a recently developed bubbling through SERS method.

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James W. Beattie (SXP07)

ECHO: the Low-Cost EC-SERS sensing platform

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KEY WORDS: EC-SERS, Miniaturized, Low-cost

Surface-Enhanced Raman Spectroscopy (SERS) offers exceptional molecular sensitivity and specificity, yet its translation beyond the laboratory has been hindered by bulky instrumentation, disposable substrates, and poor measurement repeatability. ECHO (Electrochemically Cleaned Hotspot Optics) system addresses these limitations through a low-cost, miniaturized electrochemical SERS (EC-SERS) sensing platform based on reusable monolayer aggregates (MLaggs).

MLaggs are self-assembled monolayer aggregates of nanoparticles with precisely controlled and highly uniform nanogaps. These structures support strong electromagnetic field confinement via chain modes, enabling robust Raman enhancement while avoiding complex or expensive fabrication processes[1,2]. The uniformity of the nanogaps across the aggregate significantly improves signal reproducibility compared to conventional SERS substrates.
A key innovation of the ECHO platform is electrochemical control, which allows in situ removal of analytes and regeneration of the sensing surface[3]. This capability eliminates the need for disposable substrates and enables repeatable measurements on a single device, addressing a major barrier to practical SERS deployment.

The platform supports rapid detection of small molecules and is applicable to environmental monitoring, biomedical diagnostics, and industrial sensing. Its compact, reusable design enables reliable Raman analysis in field and point-of-care settings, extending high-performance SERS beyond traditional laboratory environments.

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Rosemary Rupesinghe (SXP08)

Label-Free Imaging of Nanopesticides in Plants using Stimulated Raman Scattering

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KEY WORDS: SRS, nanoparticles, agrochemicals.

Nanopesticides are an emerging technology aimed at combatting the growing environmental and health concerns associated with traditional agrochemicals. The incorporation of nanoparticles into pesticide formulations can enable the controlled release of active ingredients, improve their targeting and enhance their uptake into crops.[1] However, the translocation pathways and final destinations of these particles remain poorly understood, which hinders their widespread adoption. Many existing techniques used to study nanopesticide behaviour require destructive sample preparation, lack spatial resolution or rely on fluorescent labels that may alter the intrinsic behaviour of the nanopesticide.

Unlike spontaneous Raman spectroscopy, which is often subject to fluorescence interference when measuring plant tissue, stimulated Raman scattering (SRS) is detected at the same wavelength as the excitation fields and therefore minimises the effects of fluorescence interference. Additionally, an SRS signal is generated only where the pump and Stokes beams spatially overlap at the focal point, enabling chemically specific and high-resolution imaging while remaining non-destructive and label-free.[2] For these reasons, SRS is particularly well-suited for imaging nanopesticides within plants.

In this study, microemulsion polymerisation was used to synthesise poly(octyl acrylate) nanoparticles encapsulating the fungicide fludioxonil. The resulting nanopesticide was characterised using spontaneous Raman spectroscopy and dynamic light scattering (DLS) to confirm nanoparticle formation and composition. A control formulation containing fludioxonil without nanoparticles was prepared to enable direct comparison. Both formulations will be imaged in *Arabidopsis thaliana* leaves using SRS microscopy to investigate differences in uptake and translocation.

This work establishes a label-free and non-destructive method for imaging nanopesticides within plants, while enabling direct comparison between nanopesticide and conventional formulations in terms of uptake and translocation. This paves the way towards more efficient and sustainable farming through improved understanding of nanopesticide behaviour in crops.

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Developing an Electrochemical Biosensor for Endotoxin using Polydopamine-Coated Laser-Induced-Graphene

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KEY WORDS: Electrochemical biosensor, Laser-Induced-Graphene, Endotoxin

Lipopolysaccharide (LPS, commonly known as endotoxin) is a pyrogenic compound on the outer cell envelopes of gram-negative bacteria, provoking highly inflammatory immune responses that can result in septic shock. The gold standard assay for LPS detection and quantification - the limulus amoebocyte lysate (LAL) test - is limited by its complexity, time-to-result and susceptibility to interference[1]. Therefore, a rapid, sensitive electrochemical biosensor (ECB) to detect and quantify LPS would be valuable within point-of-care diagnostics and in food and pharmaceutical safety testing. The biosensor could utilize functional elements modelled on the enzyme within the LAL assay that is sensitive to the Lipid A molecule of LPS. Additionally, expression of horizontally transferred genes that confer antimicrobial resistance (AMR) in some gram-negative bacteria result in the structure and charge of Lipid A changing[2]**.** Therefore, the biosensor could potentially be used to detect evidence of AMR acquisition in bacteria, for applications in decentralized AMR surveillance.

Laser-induced graphene (LIG) is an emerging material of interest within ECB, due to its excellent electrical conductivity, high surface area, and simplicity of synthesis into custom electrodes from low-cost polymer precursors[3]. However, biosensing with LIG remains subject to some common limitations within the field, such as the requirement to use a redox active mediator, which increases sensor complexity and reduces stability and ease of manufacturing. Recent work in our lab explored using polydopamine (pDa) as a low-cost, innately redox-active initial coating for screen-printed electrodes. pDa is simple to synthesize, versatile and enables the stable attachment of functional elements, whilst also facilitating the movement of charged species for ECB techniques.

In this study, we build upon this work, attempting to adhere pDa and functional elements to the surface of LIG electrodes, with the aim of developing a novel, low-cost ECB for LPS that is sensitive, selective and simple to manufacture.

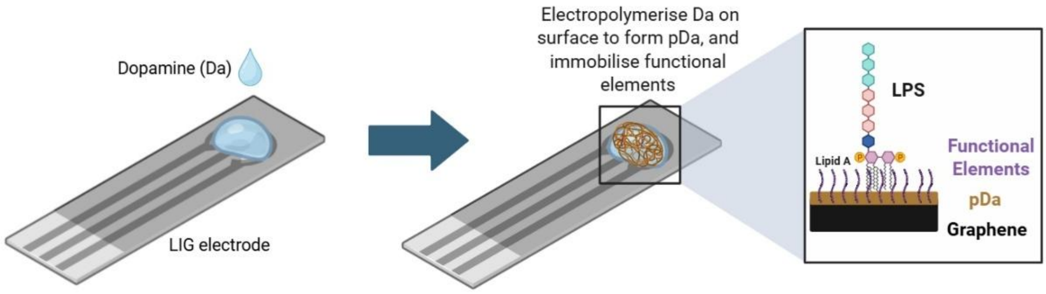

Fig.1: Schematic detailing the process of constructing pDa-coated, functionalized LIG biosensor for LPS Lipid A detection

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Andrew Keating (SXP11)

High-Throughput Screening with Chemical Specificity in Biopharma with PoliSpectra® Rapid Plate Reader

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Key Words: nucleoside triphosphates (NTPs), high-throughput, proteins

Abstract

The PoliSpectra® Rapid Raman Plate Reader (RPR) addresses the critical trade-off in biopharma between high-throughput speed and chemical specificity by providing automated, label-free molecular fingerprinting. Designed for seamless integration into 96-well plate workflows, the RPR utilizes multi-laser excitation and "walk-away" automation to deliver non-destructive analysis of complex samples. This readout demonstrates the platform's efficacy through three key applications: the precise quantification of nucleoside triphosphates (NTPs) in mixture, the determination of protein detection limits for BSA and lysozyme, and the monitoring of glucose levels in varied culture media. By delivering rapid, reproducible results across these diverse bioprocessing tasks, the RPR establishes itself as a high-speed complementary tool to traditional chromatography, enabling more efficient drug discovery and process development ensuring the safety and efficacy of biologic drugs.

Andrew Keating (SXP12)

How can A-TEEM method tackle Biopharma challenges-therapeutic proteins case study

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Key Words: Therapeutic proteins, monoclonal antibodies, PAT

Abstract

Therapeutic proteins are at the forefront of modern biopharmaceuticals, transforming the treatment of diseases such as cancer, autoimmune disorders, and infectious diseases. Biologics; including monoclonal antibodies (mAbs), cytokines, enzymes, and antibody-drug conjugates (ADCs); offer highly specific and effective therapies compared to traditional small-molecule drugs. Their ability to precisely target disease-related molecules or pathways enhances efficacy while minimizing off-target effects, improving patient safety and treatment outcomes.

Characterizing biopharmaceuticals is critical to ensuring their safety, efficacy, and consistency throughout development and manufacturing. Due to their complex structures, therapeutic proteins can exhibit variations in purity, stability, and biological activity. Comprehensive characterization is essential for detecting impurities, aggregation, and structural modifications that could impact therapeutic performance or trigger immunogenic responses. Advanced analytical techniques are therefore required to maintain product quality and regulatory compliance.

A-TEEM fluorescence molecular fingerprinting (Absorbance-Transmittance Excitation-Emission Matrix fluorescence spectroscopy) was employed to investigate monoclonal antibodies, providing valuable insights into their stability, aggregation behaviour, and the differentiation of structurally similar mAbs. When combined with chemometric analysis, A-TEEM enables highly sensitive and precise characterisation, opening new possibilities for research and development (R&D) and quality control in the biopharmaceutical industry. Thanks to an advanced software package tailored for the biopharma industry, the technique can be easily deployed in PAT manufacturing under GMP.

This study highlights the potential of A-TEEM as a powerful analytical tool for advancing therapeutic protein characterization and ensuring the safety and efficacy of biologic drugs.

Emily Evans (SXP13)

Stimulated Raman Scattering for the analysis of lipid droplets in primary and metastatic colorectal cancer cells

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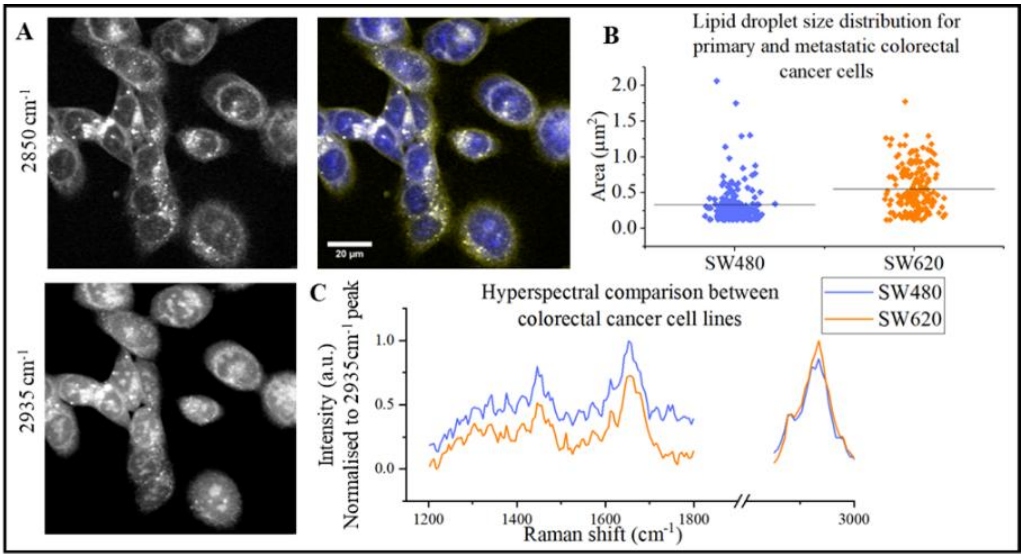
KEY WORDS: SRS, live cells, lipid droplets

Colorectal cancer, which is the 4th most common in the UK, shows resistance in 90% of metastatic cases. This makes treatment for patients diagnosed in late stages incredibly difficult, contributing to the 6.5% 10-year survival rate for these patients[1].

This project aims to use Stimulated Raman scattering (SRS) to analyse the size and composition of lipid droplets (LDs) in primary and metastatic cancer cells. SRS is an imaging technique which offers spatial information as well as chemical specificity without the need for large, fluorescent tags which can alter lipid behaviour. Previous research has shown that the quantity of LDs in cancer cells is higher than in healthy cells and they are comprised of higher proportions of cholesteryl ester and unsaturated fatty acids[2]. Less attention has been given to LD differences between primary and metastatic cancer cells. This research uses two cell lines derived from the same patient with colon adenocarcinoma of Duke's stages B and C. SW480 was isolated from the primary tumour, whilst SW620 is from a lymph node.



Firstly, the LDs present in metastatic cells were ~1.5× larger than those in primary cells (Fig 1B) implying these cells contain greater lipid content. Secondly, analysis of the Amide I and CH-stretching peaks revealed that LDs in metastatic cells contained a higher ratio of lipids to proteins, agreeing with the spatial observations. This supports previous spontaneous Raman studies that found the same spectral ratio for metastatic colorectal cells[3]. This lipid increase is necessary for metastatic cells to generate ATP to rapidly multiply and spread.

Since this work only used two cell lines, it is integral that future work incorporates a wide range of established and patient derived cell lines to account for cell heterogeneity.

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Georgios Papakostas (SXP14)

Miniaturised High-Throughput Amorphous Solid Dispersion Screening via Picolitre Volume 2D-Inkjet Printing of Formulation Micro-arrays

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Many new drug substances exhibit poor solubility, posing multiple challenges in enabling them into formulations or solid-forms. These challenges involve exploring a large compositional space and may require excessive amounts of drug compounds, which may not be adequate at the early stage of drug development.

A high-throughput technique which addresses these performance gaps is automated picolitre volume dispensing 2D-inkjet printing technology. Using a selection of 8 model drugs and 7 polymers, we explored 1,008 unique ASD compositions ranging from 0-80% w/w drug load under accelerated storage conditions, providing over 5,040 unique printed formulations of 1 μg mass each. In addition, confocal Raman microscopy was applied to assess the homogeneity of a printed spot. Across the tested ASD samples, we ranked the polymers based on their effectiveness in preventing drug recrystallisation across various compositions, with physical stability data correlating well with the published literature.

This emerging workflow affords a highly efficient ranking method during the pre-formulation development stage, facilitating rapid screening of new compounds with limited material, in short time-frames.

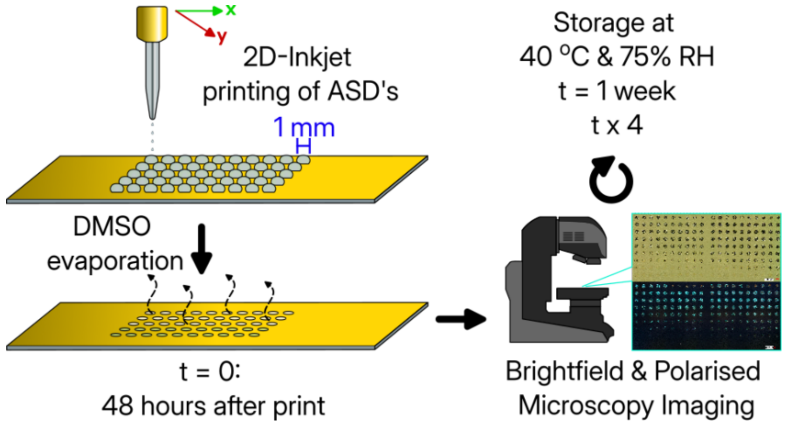

Figure: High-throughput screening workflow of Amorphous Solid Dispersions using pL-scale inkjet printing.

Junya Ji (SXP15)

Wavelet-Guided Spectral Modelling for Biomedical Hyperspectral Imaging

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KEY WORDS: Hyperspectral imaging; Wavelet transform; Spectral modelling

Biomedical hyperspectral imaging (HSI) provides rich biochemical information by capturing tissue reflectance across contiguous wavelength bands. However, biological tissue spectra exhibit strong inter-band redundancy and multi-scale frequency characteristics, which are often overlooked by deep learning approaches that treat spectral channels as unstructured feature vectors. In particular, smooth low-frequency (LF) absorption trends tend to preserve stable biochemical patterns across tissues, whereas high-frequency (HF) fluctuations may be more sensitive to acquisition variability and experimental noise.

In this work, we investigate frequency-aware spectral representation learning for biomedical hyperspectral imaging and propose a wavelet-guided spectral modelling framework. A one-level discrete wavelet transform (Daubechies-2) is applied along the spectral dimension to extract an LF trend prior. Rather than replacing the original spectra or performing full multi-scale fusion, the LF prior is injected as a gated residual signal through a pixel-adaptive modulation mechanism driven by simple spectral statistics. This design encourages LF-consistent representations while preserving task-relevant high-frequency details. To model spectral structure at different ranges, we combine lightweight depthwise 1D convolutions for local spectral continuity with spectral self-attention for long-range inter-band interactions.

Experiments on publicly available biomedical hyperspectral datasets demonstrate that modelling low-frequency spectral trends improves tissue separability and enhances spectral robustness. Our results highlight the importance of frequency-structured modelling in hyperspectral analysis and suggest that wavelet-guided priors offer a principled approach for integrating physical spectral characteristics into data-driven learning frameworks.

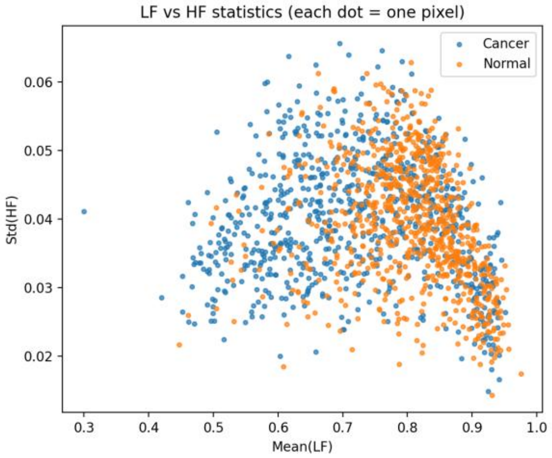

Figure 1: Pixel-wise statistics of low-frequency and high-frequency spectral components. LF statistics exhibit clearer class-dependent structure, whereas HF components show substantial inter-class overlap.

Laura Brookfield (SXP16)

The Potential of Serum-Based ATR-FTIR Spectroscopy Combined with Machine Learning for Ovarian Cancer Triage

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KEY WORDS: ovarian cancer, ATR-FTIR spectroscopy, liquid biopsy

Ovarian cancer is the deadliest gynaecological malignancy, accounting for ~4,100 deaths annually in the UK [1]. The absence of an effective screening programme means that most cases are diagnosed at an advanced stage, contributing to poor survival outcomes [2]. There is therefore a critical need for minimally invasive tools to enable earlier detection and improved clinical triage.
This study investigated the feasibility of serum-based Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) spectroscopy as a potential triage tool for ovarian cancer. Serum samples were collected from pre-surgical ovarian cancer patients and compared with samples from individuals with benign gynaecological conditions and healthy controls ($n = 232$). Spectral data were pre-processed using multiple optimisation strategies and analysed using supervised machine learning approaches, including partial least squares discriminant analysis (PLS-DA) and random forest (RF). Model performance was assessed using sensitivity, specificity, balanced accuracy, and area under the receiver operating characteristic curve (ROC-AUC).
Across supervised analyses and pre-processing optimisation strategies, PLS-DA consistently outperformed RF, demonstrating higher sensitivity, specificity, balanced accuracy, and ROC-AUC values. The strongest classification performance was observed when comparing pre-surgical ovarian cancer samples with controls, achieving a ROC-AUC of 0.80, with a balanced accuracy of 0.70, sensitivity of 0.70, and specificity of 0.80.
These findings demonstrate the potential of ATR-FTIR spectroscopy combined with PLS-DA as a robust, serum-based approach for distinguishing ovarian cancer patients from individuals without malignancy. This work supports the further development of rapid, minimally invasive triage tools that could enhance clinical decision-making and patient prioritisation within diagnostic pathways.

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Laura Scoble (SXP17)

Micro Questions, Nano Answers: Assessing the application of Optical-PhotoThermal Infrared spectroscopy for single-grain pollen chemotaxonomy

Authors: [a] Laura Scoble; Hao Meng [c]; Simon J. Ussher [a]; Mark F. Fitzsimons [a]; Lauren Ansell [b]; Mustafa Kansiz [d]; Billy Simmonds [a]; Nick Stone [c]; and Ralph M. Fyfe [a]

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Abstract

Single-grain pollen analysis is essential for advancing chemical palynology, which classifies morphologically similar taxa based on taxon-specific pollen and sporopollenin chemistry. Fourier-Transform Infrared (FT-IR) spectroscopy and microspectroscopy (μFT-IR) are widely used to differentiate morphologically similar grains but face limitations from Mie scattering and coarse spatial resolution. Here, we present the first application of Optical-PhotoThermal Infrared (O-PTIR) spectroscopy to chemically treated single pollen grains, using *Molinia caerulea* as a model taxon to fully test and evaluate the value of this new technique. O-PTIR achieves sub-micron "super-resolution" infrared spectroscopy through non-contact, non-destructive measurements by exploiting the photothermal effect. O-PTIR spectra exhibited close similarity to FT-IR datasets, with all major sporopollenin bands present and only minor peak shifts (4 cm-1). Use of spectra derived from sub-micron analyses for future classification purposes relies on a robust understanding of intra- and inter-grain variability. This can now be assessed using O-PTIR to distinguish whether intra-grain heterogeneity or true inter-grain biochemical differences drives grain separation. Multivariate analysis of intra- and inter-grain variability shows greater intra-grain variability does not cause greater inter-grain separation, indicating genuine inter-grain biochemical differences are driving separation rather than technical effects or surface heterogeneity. Similarly, intra- and inter-grain

Megan Campbell (SXP18)

Investigating the Effects of Non-Steroidal Anti-Inflammatory Drugs on Lipid Metabolism in Prostate Cancer using Multimodal Imaging

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KEY WORDS: Single cell, ToF-SIMS, FT-IR, O-PTIR, Lipidomics, Prostate cancer, NSAIDs

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have proposed anti-tumor properties, with evidence showing that they can modulate lipid metabolic pathways[1]. Prostate cancer progression is strongly associated with lipid metabolism dysregulation, and there has been an increasing interest in the COX-2 enzyme and its potential role in tumor metastasis[2]. There is evidence to support that aspirin can block this pathway[3], however, the exact effects and localization of NSAIDs in prostate cancer lipidomics are still poorly characterized.

In this work, we have combined Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) and vibrational spectroscopy techniques, Fourier-Transform Infrared (FT-IR) and Optical-Photothermal Infrared (O-PTIR), to chemically image the spatial lipid profile of prostate cancer cells after treatment with aspirin, specifically monitoring the in-vitro uptake and metabolism of arachidonic acid, which initiates the COX-2 metabolomic pathway. ToF-SIMS enabled label-free imaging of cultured PC-3 cells, with high biological sensitivity and specificity at a single-cell resolution. FT-IR facilitated high-throughput analysis of the same cell populations, supported with complementary data from the sub-micron imaging with O-PTIR. As part of this work, we addressed the challenges associated with multimodal imaging, such as sample preparation and reproducible workflows. We discuss the integration of different imaging modalities and their effective utilization in single-cell analysis, contributing to a better understanding of cellular lipidomics and their role in disease progression.

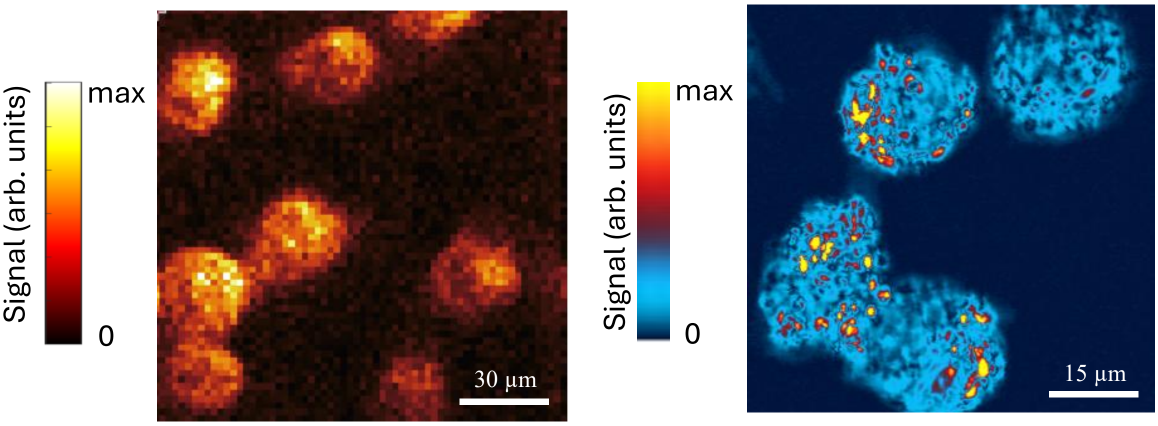

Figure 1 : Example of PC-3 cell lipid localisation imaging using a) ToF-SIMS (*m/z* 91.05) b) O-PTIR (1744 cm^{-1})

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Nai-Hao Yin (SXP19)

Optimising Raman Spectroscopy for Large-Scale Analysis of Untreated Human Hair Samples

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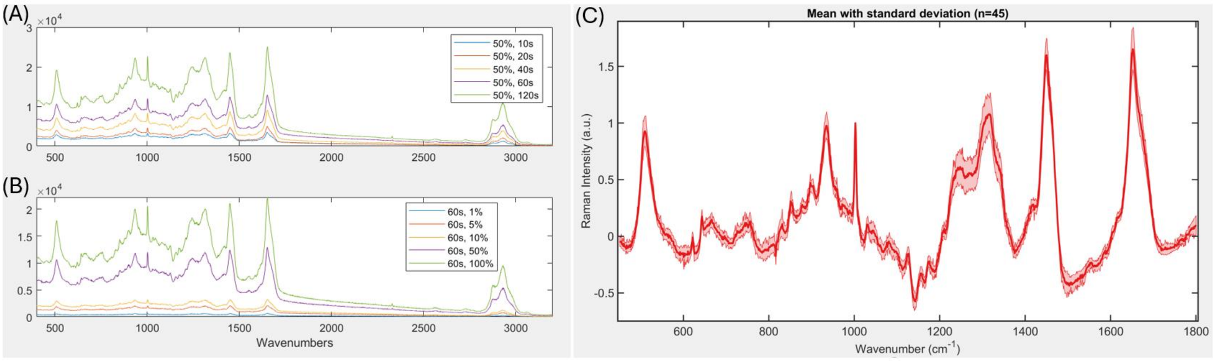
KEY WORDS: Raman spectroscopy, hair, health screening

Hair composition can be indicative of toxin exposure and certain systemic diseases[1]. Population-level health screening could be enabled if a high-throughput method for hair analysis is available. Raman spectroscopy can identify hair compositional changes but existing methodologies are often focused on cosmetic hair products and based on small sample sizes.

The optimisation process involved two strands of white/grey hair with increasing laser power (1%, 5%, 10%, 50%, 100%) and exposure time (10s, 20s, 40s, 60s, 120s), using a Renishaw inVia microspectrometer equipped with a 785nm laser (200mW at source) under a 50× objective. Subsequently, measurements were performed on 61 untreated hair samples from female participants (age: 50–87 years) recruited for another study. Three randomly selected sites within approximately 10mm of the root were measured to minimise contamination from external hair products. Spectra were averaged, baseline-corrected using a sixth-order polynomial, and normalised to the 1002cm^{-1} peak.

Long exposure (≥60s) combined with high power (≥50%) substantially increased fluorescence interference. Optimal conditions of 10% laser power (~7mW at the sample) and a 60s exposure achieved high-quality spectra in 45 of the 61 samples (74%). For the remaining 16 samples with high fluorescence interference or thermally damaged during the measurement, reducing power or exposure did not produce Raman peaks after spectral processing.

Our spectroscopy settings are comparable with those reported[2,3] and provide a practical basis for large-scale untreated hair screening. Additional treatment may be required to limit fluorescence interferences for a small subset of hair samples before subjected to spectroscopy measurements.



(A, B) Optimising results from one hair sample with varying exposure time and laser power. Y-axis represents the raw CCD counts. (C) Baseline corrected, normalised, and averaged Raman spectrum with from 45 female participants using 10% laser power (~7mW at sample) and 60s exposure time.

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Olivia Glass (SXP20)

Raman spectroscopy on dried serum droplets reveals the variation in spatial distribution of biomolecular components with temperature

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KEY WORDS: Raman Spectroscopy, Biofluid biomarkers, Coffee-ring effect

Raman spectroscopy offers a novel approach for detecting changes in blood serum biomarkers relevant to neurodegenerative disease diagnosis. During droplet drying, capillary flow and intermolecular interactions can spread molecules in an advantageous way[1], potentially enabling physical preconcentration and enhanced diagnostic sensitivity. Understanding how controllable drying parameters influence physical effects such as capillary flow and molecular interactions is essential for developing reproducible serum-based Raman measurement protocols.

Human serum droplets (1 µL) were dried at 25 °C and 40 °C for 15 minutes on aluminium-coated glass slides in a preheated convection oven. Raman maps were acquired from $N = 5$ replicate droplets per temperature group, from the droplet center to periphery. Spectra were pre-processed in Python using Savitsky–Golay smoothing (window = 7, polynomial order = 3), IARPLS baseline correction, and mean variance normalization. Pixel-wise statistical comparisons of wavenumber intensities between temperature groups were performed.

Distinct spatial patterns were observed across the Raman maps between groups. A peak at 920 cm^{-1} exhibited statistically significant differences between 25 °C and 40 °C droplets. This indicates that drying temperature alters the spatial distribution of specific biomolecular components within serum droplets. A band at 920 cm^{-1} is identified as a key spectral feature, potentially associated with carbohydrates[2], whose spatial distribution varies with temperature.

These findings highlight the importance of controlled drying conditions for reproducible Raman measurements. Future work will expand further analysis across additional temperature groups and incorporate analytical methods to characterize spatial trends. Together this will lead to optimized droplet preparation protocols and reproducible measurements for diagnostic applications.

Ross Clark (SXP21)

A Time-Resolved Raman Approach for Biological Sample Analysis

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KEY WORDS: Raman scattering, Biological samples, Raman imaging, Fluorescence, Time-resolved Raman spectroscopy

Raman scattering is a vibrational spectroscopy technique capable of providing detailed molecular information from samples such as biological tissues.[1] The advantages of the technique, together with the wealth of information obtainable from Raman scattering, have led to its application across a range of fields, including medical diagnostics. Raman spectra can be collected at multiple points across a sample, enabling the generation of images based on chemical composition and molecular structure.[2] Raman imaging has been widely applied to cell and tissue samples for the characterisation of molecular changes due to the presence of disease, or for monitoring uptake and effects of drugs. However, two key limitations of Raman scattering are its inherently weak signals and interference from background fluorescence of samples.

To address emissions from highly fluorescent samples, Renishaw plc have developed a Time-resolved Raman spectroscopy (TRRS) system.[3] TRRS exploits the faster Raman scattering process relative to fluorescence emission, enabling separation of Raman signals from the fluorescence background. The effectiveness of this approach is illustrated in Figure 1, where TRRS allows Raman spectra to be obtained from highly fluorescent coloured LEGO® bricks that are difficult to analyse using conventional Raman spectroscopy. This project investigates the potential application of this technique in the imaging of biological samples. This will allow the benefits and limitations of the technology to be assessed and to acertain how widely it can be applied across different application areas.

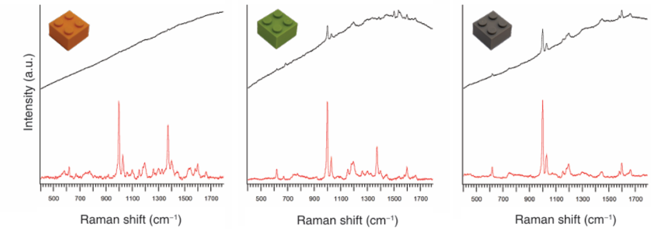

Figure 1- Conventional Raman spectra (black) and TRRS (red) collected using 523 nm excitation from coloured LEGO® bricks, adapted from Renishaw plc.[3]

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Sungho Shin (SXP23)

Development of a hybrid LIBS and Raman spectroscopy system for multi-modal contaminant detection

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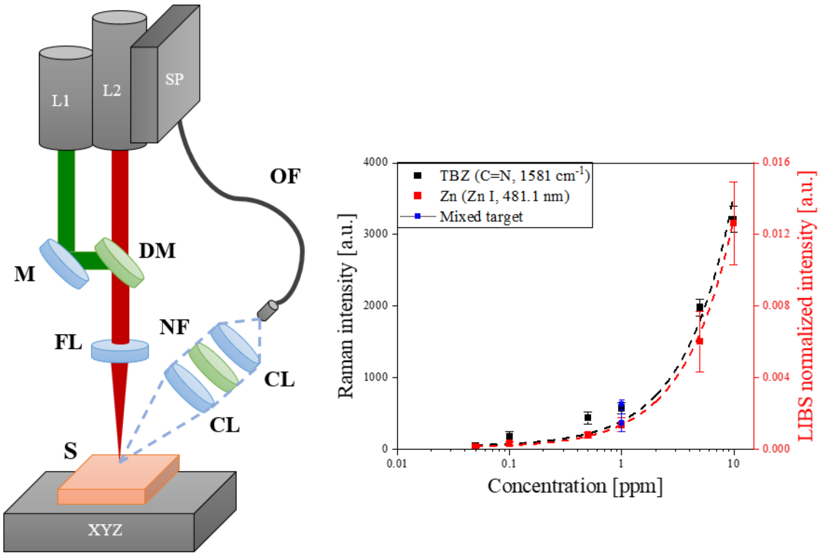
KEY WORDS: Laser-induced breakdown spectroscopy (LIBS), Raman spectroscopy, spectral analysis

Food safety and environmental monitoring require rapid analytical tools capable of providing both elemental and molecular information. We developed a semi-compact hybrid laser-induced breakdown spectroscopy (LIBS) and Raman spectroscopy platform that enables spatially correlated measurements from a single spot through a shared optical pathway. For food applications, pesticide residues (thiabendazole, thiram) and heavy metals (Cu, Zn, Pb) were quantitatively detected with low-ppm limits of detection. Surface-enhancement strategies improved sensitivity for trace analysis. The platform was further validated for microplastic and mixed-particle analysis. Raman spectroscopy discriminated polymer types (PS, PE, PP), while LIBS simultaneously quantified adsorbed heavy metals, enabling direct correlation between polymer identity and contaminant burden at the single-particle level. This hybrid LIBS–Raman approach demonstrates a versatile and field-adaptable analytical strategy for simultaneous elemental and molecular characterization in complex food and environmental samples.



Schematic of the hybrid LIBS-Raman spectroscopy system, and representative calibration curves of a TBZ and Zn mixed solution.

Sunny Angel (SXP24)

Extra-Terrestrial Biosignature Detection at Low Temperatures using Raman Spectroscopy

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KEY WORDS: Raman spectroscopy, biosignature detection, Mars

The ExoMars Rosalind Franklin Rover, led by the European Space Agency, will carry the Raman Laser Spectrometer (RLS) to Mars. This follows two Raman spectrometers currently onboard NASA's Perseverance Mars rover as part of the Mars 2020 mission. A key objective of both missions is to search for signs of past life. Previous research at the University of Southampton has demonstrated that the temperature of Raman measurements can affect the shape of biomolecule spectra[1,2], this makes detecting and identifying molecules in extreme low temperatures difficult without supporting databases. Furthermore, spectra obtained using in-field spectrometers, such as the RLS, may not directly translate to spectra obtained using lab grade instruments.

This project aims to build on previous work at the University of Southampton to produce a database of Raman spectra of molecular substances relevant to life detection at a range of temperatures, particularly those representative of the temperatures experienced by samples in the RLS. The spectral data obtained at a range of temperatures is also relevant to current and future missions such as Mars 2020, Chang'e 7 and MMX, which are deploying Raman spectroscopy for planetary exploration and extraterrestrial biosignature detection.

Suitable molecular substances have been selected, and their Raman spectra are being recorded under ambient conditions using a lab grade instrument. Their spectra will then be measured under a range of temperatures, using lab grade and in-field grade instruments to produce a database. This database will support science performed on the ExoMars mission as well as current and future missions equipped with Raman spectrometers. It will also inform potential development of future instrumentation.

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Yifan Wei (SXP25)

Developing novel prognostic biomarkers for Penile Cancer using Infrared Spectroscopy

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KEY WORDS: penile cancer, FTIR, QCL-IR

Penile cancer is a rare but aggressive malignancy with substantial morbidity and mortality, particularly in patients with regional lymph node involvement[1]. Despite histopathology remaining the diagnostic gold standard[2], conventional assessment is limited by inter-observer variability and a reliance on morphological features. Infrared (IR) spectroscopy offers a label-free and non-destructive approach to probe biochemical alterations in tissue, providing an opportunity to develop objective prognostic biomarkers[3]. In this project, Fourier-transform infrared (FTIR) spectroscopy was first applied to whole-tissue sections from penile cancer patients to evaluate its capability for tissue characterization. A comprehensive preprocessing pipeline, including quality control, baseline correction, denoising, normalization, spectral differentiation, and digital paraffin removal, was established to generate machine-learning-ready spectral data. Unsupervised clustering analysis demonstrated that FTIR data could reliably distinguish major tissue components, such as tumour epithelium, stroma, and keratin, with strong concordance to adjacent H&E-stained sections. Building upon this foundation, the second phase of the project focuses on supervised learning using quantum cascade laser infrared (QCL-IR) spectroscopy alongside conventional FTIR. Available penile cancer QCL datasets were collected, and histopathological annotations derived from H&E staining were used to assign pixel-level labels for model training. Supervised classification models are being developed to discriminate multiple tissue types, including cancerous epithelium, normal epithelium, stroma, and keratinized regions. A direct comparison between QCL-IR and FTIR systems is performed to evaluate their relative strengths in spatial resolution, spectral quality, and suitability for large-scale clinical translation. Furthermore, high-resolution and highly specific annotations derived from multiplex immunofluorescence staining are being incorporated to refine supervised learning labels. Classification tasks targeting p16 and p53 expression status are designed to infer HPV association and prognostic relevance at the spectroscopic level. By integrating biochemical information from IR spectroscopy with histological and molecular annotations, this work aims to establish a robust framework for objective tissue classification and prognostic stratification in penile cancer.

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Shun-Suke Kanai (SXP26)

Diversification of the 10th core atom of 9-cyanopyronins expands the resonance Raman vibrational palette

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KEY WORDS: EPR-SRS, resonance Raman probe, live-cell imaging.

9-Cyanopyronin derivatives bearing a nitrile tag at the 9th position of the xanthene ring are known to enable highly sensitive detection of nitrile (C≡N) Raman signals via the resonance Raman effect. These derivatives have been utilized as multicolor imaging probes since the Raman shifts can be tunable through isotopic editing of C≡N group, ring expansion of the xanthene ring, or substation of the 10th core atom[1,2]. Compared to rhodamine derivatives, which are known to exhibit diverse optical properties when various atoms are introduced at the 10th position, the variety of core atoms at 10th position of 9-cyanopyronin derivatives has been limited. Therefore, we aimed to develop a new series of resonance Raman probes suitable for multicolor live-cell imaging by substituting the 10th position of 9-cyanopyronin with various atoms (Fig. 1).

We synthesized a series of fourteen 9-cyanopyronin derivatives in which the 10th core atom is substituted with various group 13, 14, 15 or 16 elements, and systematically evaluated their properties as resonance Raman probes using electronic pre-resonance stimulated Raman scattering (EPR-SRS) microscopy. We found that substitution at the 10th position modulates not only the vibrational frequency of the C≡N group in the silent region, but also the conjugated double-bond stretching frequency (C=C) in the fingerprint region, and additionally alters the subcellular localization of the probes. By employing different combinations of probes for the silent and fingerprint regions, we were able to utilize the distinct patterns of C≡N or C=C bond vibrations together with the different subcellular localizations of the probes to achieve live-cell three-color imaging. These 9-cyanopyronin derivatives would greatly expand the vibrational palette available for multiplexed SRS imaging.

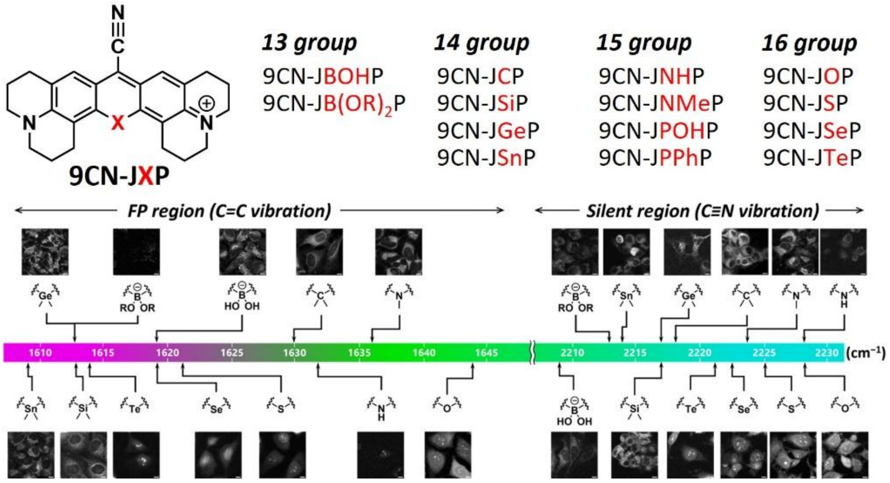

Figure 1. Chemical structures and live-cell SRS imaging of 9CN-JXP derivatives.

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Jorge Servert (SXP27)

The Virtual Laboratory: Simulating a Million Photons to Build One Perfect Diagnostic

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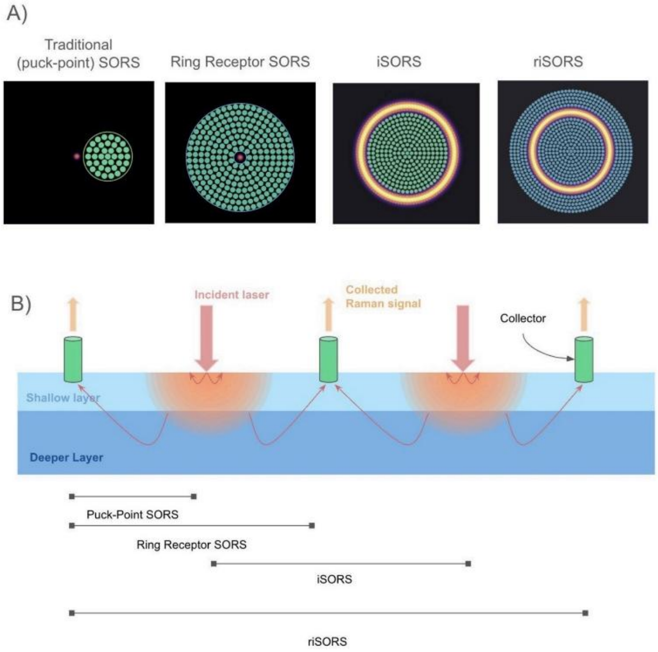
KEY WORDS: Raman spectroscopy, spatially offset Raman spectroscopy (SORS), biomedical safety, diagnostics, numerical simulation.

Spatially offset Raman spectroscopy (SORS) offers non-invasive, molecularly specific access to subsurface tissues, showing strong potential for biomedical diagnostics. However, clinical translation remains limited by the need to balance Raman signal strength with laser safety constraints. This study introduces an open-source, Python-based framework integrating photon transport simulation, probe geometry optimization and photothermal safety modelling within a unified workflow. Monte Carlo photon transport is coupled with Pennes' bioheat and Arrhenius/CEM43 thermal damage models to assess four SORS configurations—conventional puck-point, ring-collector, inverse SORS (iSORS) and a new reinforced iSORS (riSORS)—on a multi-layer skin model. Results show that ring-based illumination markedly reduces thermal loading, extending safe laser exposure times by one to two orders of magnitude relative to point illumination, thus permitting up to 60–100× greater Raman energy accumulation before predicted damage onset. Among tested geometries, riSORS achieved the best trade-off between subsurface selectivity and photon collection efficiency, outperforming conventional designs in both signal yield and safety margin. Sensitivity analyses across optical properties further demonstrate robustness to patient variability. Although simplified assumptions require experimental validation, this framework quantitatively links probe design to safety-limited performance, offering a practical roadmap for clinically viable, thermally safe SORS system design.[1]



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Near-Infrared Gold Nanopinecones as Photothermal Therapy Agents for the Treatment of Pancreatic Cancer?

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KEYWORDS: Pancreatic Cancer, Gold nano-pinecones, Photo-thermal

We report the development of near-infrared gold nano-pinecones (NIR-AuNPCs), a new class of plasmonic nanostructures synthesised through a simple, one-pot, seedless method conducted entirely at ambient conditions. Incorporating a gold–platinum precursor system generates hierarchical, nanostructures with strong and broad absorbance across the near-infrared (NIR) region—significantly higher than conventional spherical gold nanoparticles or gold-only nano-pinecones. This enhanced NIR response enables efficient conversion of light energy into heat, a critical requirement for deep-tissue photothermal therapy (PTT).

NIR-AuNPCs exhibit robust and concentration-dependent photothermal behaviour; under 800 nm continuous-wave irradiation, temperature increases of up to ~48 °C were achieved, with excellent stability maintained over repeated heating cycles. Motivated by this strong photothermal performance, we evaluated their therapeutic potential against pancreatic cancer, a malignancy characterised by dense stromal tissue, poor drug penetration, and limited treatment options.

In vitro studies demonstrated minimal cytotoxicity of NIR-AuNPCs up to 100 µg/mL, enabling their safe use as photothermal agents. In 2D monolayer BxPC-3 cultures, NIR-AuNPC-mediated PTT induced substantial cell death under optimised, non-damaging laser parameters, whereas nanoparticles or laser exposure alone produced negligible effects. To better replicate the pancreatic tumour microenvironment, 3D co-culture spheroids containing BxPC-3 cells and pancreatic stellate cells were generated. NIR-AuNPC-mediated PTT caused progressive structural disruption and significant loss of viability in these spheroids, demonstrating effective heat delivery into dense tumour-like tissue.

Together, these findings establish NIR-AuNPCs as promising, easily synthesised, and highly effective photothermal agents for treating pancreatic cancer in both 2D and 3D tumour models.

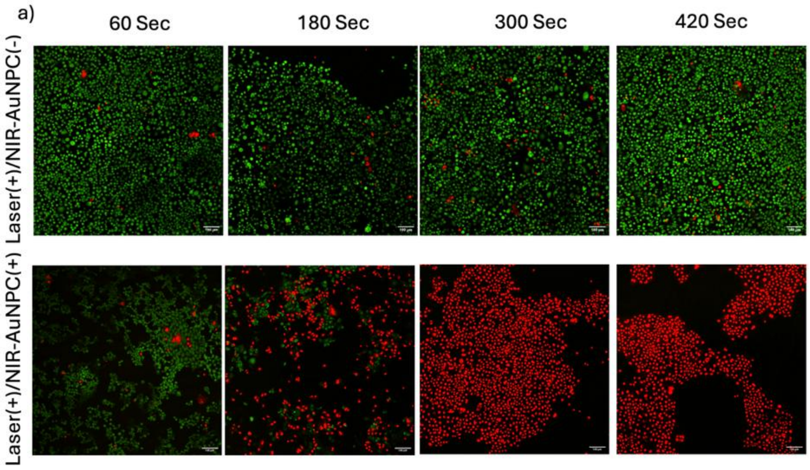

Figure 1. 2D cell monolayers irradiated with 800 nm light, 1.5 W/cm^2, for increased exposure times in absence (top row) and presence (bottom row) on AuNPC.

Josep Sulé-Suso (SXP29)

Fourier Transform Infrared Microspectroscopy detects single circulating tumour cells in the blood of a lung cancer patient. A new Liquid Biopsy tool?

J. Sulé-Suso[1,2,*], C. Evans[1], L. Dowling[1], L. Vaccari[3], G. Cinque[4], C. Stani[3], G. Birarda[3], V.A. Muruganandan[4], S. Pillai[5], D.G. van Pittius[6], A. Jegannathen[2], P. Roach[7].

1. School of Life Sciences, Guy Hilton Research Centre, Keele University, Stoke-on-Trent, UK. 2. Oncology Department, Cancer Centre, Royal Stoke University Hospital, University Hospitals of North Midlnads (UHNM), UK. 3. SISSI-BOFF Beamline, Elettra Sincrotrone, Trieste, Italy. 4. B22 beamline, Diamond Light Source, Didcot, Oxfordshire, UK. 5. Haematology Department, Cancer Centre, Royal Stoke UHNM, Stoke on Trent, UK. 6. Histopathology Department, Royal Stoke University Hospital, UHNM, UK. 7. Department of Chemistry, Loughborough University, Loughborough, Leicestershire, UK.

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KEY WORDS: FTIR microspectroscopy, cancer, liquid biopsy.

The detection of Circulating Tumour Cells (CTCs) through liquid biopsy is revolutionising the screening, diagnosis, and treatment monitoring of cancer. However, existing CTC isolation methods rely on antigen expression or physical properties. These techniques are highly operator-dependent, lack robustness and suffer from automation challenges. A universal, unbiased methodology for CTC detection across tumour types is critically needed to streamline the process for higher throughput and more robust capabilities.

Here, we present the first proof-of-concept study demonstrating the use of Fourier Transform Infrared (FTIR) microspectroscopy to study cytospun blood samples coupled with a Random Forest classifier, for the detection of a single CTC in the blood of a lung cancer patient confirmed via immunohistochemistry. Notably, our method utilizes glass coverslips as substrates, routinely employed in pathology departments, meaning that this could be easily adopted into clinical workflows. Using FTIR spectral data from in vitro grown lung cancer cells as a training model, we achieved precise CTC identification based on biochemical composition, specifically within the fingerprint region (1800 cm^{-1} to 1350 cm^{-1}) and confirmed by immunohistochemistry.

This study introduces FTIR microspectroscopy as a novel, label-free approach for CTCs detection in liquid biopsies, with the potential to redefine cancer diagnostics. This methodology may represent a significant advancement in personalized oncology, offering a clinically viable tool for real-time cancer monitoring and improved patient stratification. A clinical study including patients with different types of cancer (lung, breast, prostate, and bowel) is now underway.

Lyra O'Leary (SXP30)

Spatial-Spectral Deep Learning for Prostate Cancer Tissue Classification in Infrared Spectroscopy

<u>L. O'Leary*</u>[1], D. Ferguson[1], C. Hart[1], M. Brown[1], P. Oliveira[4], N. Clarke[1,2], A. Sachdeva[1,3], P. Gardner[1], H. Yin[1]

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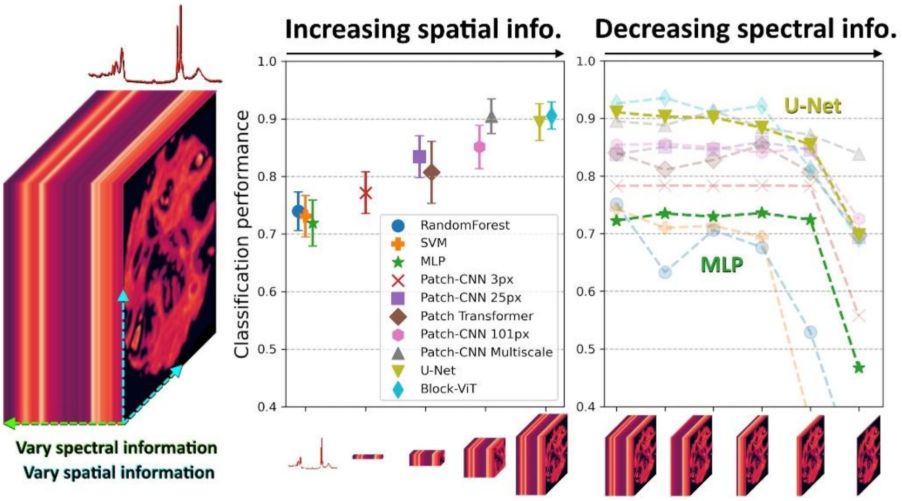
KEY WORDS: Deep Learning, FTIR, Prostate Cancer

Modern methods of infrared (IR) spectroscopy yield full IR absorbance spectra in arrays, forming hyperspectral images. Deep learning shows promise for exploiting the wealth of spatial and spectral information in these images, but recent research suggests that convolution-based architectures may have a spatial bias[1]. Towards improving prostate cancer tissue classification in IR spectroscopy, we compare a variety of deep learning classifiers with a range of spatial receptive fields and probe the impact of a bottleneck which compresses the spectral dimension. We find a strong correlation between model spatial receptive field and classification performance, with highest performance achieved by a modified vision transformer model. Conversely, we find only limited correlation between spectral information and classifier performance: a spectral bottleneck of just 16 features had only a negligible effect on all neural network models, including convolution-eschewing transformer architectures and a multilayer perceptron model utilizing no spatial information. Rather than any particular network component inducing a spatial bias, the breadth of architectures exhibiting little dependence on spectral information implies that tissue classification itself is characterized by only a small set of spectral features. This, in turn, suggests that success at tissue classification may be a poor benchmark in the development of deep learning models designed to effectively utilize the spectral dimension.



Left plot: tissue classification performance (macro-averaged F1-score) using a range of machine learning architectures ordered by increasing spatial receptive field size. Right plot: machine learning model performance when incorporating a spectral information bottleneck. Traversing left to right on the figure corresponds to a reduction from a full 965-channel spectral input to a compression to a 256, 64, 16, 4, and 1 channel input to the machine learning models.

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Day 2 – Wednesday 15th April

Plenary 3 – Prof Thomas Bocklitz
(09:30-10:15)
in NEWMAN BLUE

Combining vibrational spectroscopic techniques with artificial intelligence based data pipelines to maximize the extracted knowledge

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KEY WORDS: vibrational spectroscopy, spectroscopic imaging, deep learning, data pipelines

Vibrational spectroscopic techniques are important photonic techniques that are being used in an increasing number of disciplines, including life sciences and medicine. This increased use can be attributed to advancements in measurement setups and data science methodologies, including artificial intelligence (AI). Photonic data science is an interdisciplinary field that combines data science principles with photonics to extract meaningful information from photonic data using sophisticated methodologies. The efficacy of photonic data science depends on the specific task and the characteristics of the sample being examined. Examples of such tasks include predicting diseases, tissues and sample properties.

Notable subsets of photonic technologies include vibrational spectroscopic techniques such as Raman spectroscopy and vibrational spectroscopic imaging. These techniques offer several advantages, including their role as non-destructive fingerprinting methods. To realise the full potential of these techniques, it is essential to study the entire photonic data life cycle, from generation and modelling to archiving. Specifically, the cycle begins with the experimental design stage, including sample size planning. After the data has been measured, pre-treatment and pre-processing are performed, followed by data modelling using AI-based methods. Finally, the models are investigated and interpreted using explainable AI (XAI) methods. This presentation will offer insights into generating a data pipeline for Raman spectroscopy and vibrational spectroscopic imaging [1,2]. We will emphasise potential pitfalls and demonstrate how AI can assist within this data pipeline, particularly to enhance data [3,4,5] and assessing data quality [6], as well as AI-based classification and segmentation methods [7-10]. Furthermore, we describe how XAI methods can be utilized to understand AI models [11,12] and how uncertainty estimation can be utilized to improve the model prediction [13].

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ACKNOWLEDGMENTS: This work is supported by the BMBF, funding program Photonics Research Germany (13N15706 (LPI-BT2-FSU), 13N15466 (LPI-BT1-FSU), 13N15710 (LPI-BT3-FSU)) and is integrated into the Leibniz Center for Photonics in Infection Research (LPI). The LPI initiated by Leibniz-IPHT, Leibniz-HKI, Friedrich Schiller University Jena and Jena University Hospital is part of the BMBF national roadmap for research infrastructures.

Parallel Session 2
(10:45-12:15)
Session 2A – Biomedical Raman Imaging 1
in NEWMAN BLUE (Chair: Dr Priyanka Dey)

Yasuyuki Ozeki – Keynote

Stimulated Raman Scattering Microscopy Empowered by Raman Probes and AI

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KEY WORDS: Stimulated Raman scattering, Raman probes, AI

Stimulated Raman scattering (SRS) microscopy[1,2] is a powerful imaging modality for probing molecular and lattice vibrations. Its versatility has enabled a broad range of applications across both biological[3] and materials sciences[4,5,6].

In this talk, I will present recent advances in SRS microscopy empowered by Raman probes and artificial intelligence (AI). We first introduce a high-speed SRS and fluorescence imaging platform that employs a wavelength-tunable Yb fiber laser synchronized to a picosecond Ti:sapphire laser[7,8]. When combined with recently developed Raman probes, this system enables super-multiplex imaging[3], multiplexed enzyme activity sensing[9], and super-resolution imaging[10], allowing detailed investigation of dynamic intracellular organelle interactions.

More recently, we have explored enhancing the capability of SRS with the aid of deep learning[11]. Specifically, we acquired a large hyperspectral SRS/fluorescence dataset comprising over 600 paired images with an increased number of spectral points (91), enabling accurate prediction of fluorescence images from label-free SRS data using deep learning. This approach extends the label-free imaging capability of SRS, by leveraging both vibrational signatures and morphological information.

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Julia Gala de Pablo (SXT06)

Catalyzing Biomedical Discovery Through Multimodal Vibrational and Fluorescence Imaging at the Leeds Hyperspectral Bioimaging Facility

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[1] *Molecular and Nanoscale Physics Group, School of Physics and Astronomy, University of Leeds, Leeds, UK.*
[2] *Leeds Institute of Medical Research, St James Hospital, University of Leeds, Leeds, UK.*
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KEY WORDS: Raman spectroscopy, Stimulated Raman Scattering, Coherent anti-Stokes Raman scattering, Second-Harmonic Generation, Fluorescent Lifetime, Two-photon fluorescence, Vibrational imaging.

Live, coherent vibrational imaging is a powerful technique for label-free characterization of cells and tissue in clinical research. The main translational challenge often is demystifying these techniques for the clinical researchers, showing how they integrate into their research pipelines. The simultaneous combination of traditional confocal fluorescence imaging with vibrational chemical imaging and multiphoton modalities provides same-sample structural, biochemical and functional information, while containing an output that the clinical researcher is already familiar with.

At the University of Leeds, the Hyperspectral Bioimaging Facility (HYBIFA) is built around a multimodal CRS–STELLARIS microscope that combines stimulated Raman scattering (SRS), coherent anti-Stokes Raman scattering (CARS), second harmonic generation (SHG), fluorescence lifetime imaging microscopy (FLIM), two-photon fluorescence (TPF) and advanced confocal imaging within a single platform, complemented by the facility spontaneous Raman microscopy capabilities for high-spectral resolution analysis. The facility allows users to transition between familiar fluorescence-based modalities and novel label-free approaches, reducing the technical barrier to adopting techniques that have not yet been integrated into standard biomedical pipelines, with the ultimate goal to expand the experimental repertoires of biomedical researchers.

I will provide an overview of the first 1.5 years of the facility, reviewing the most exciting and challenging applications co-developed with our biomedical collaborators. These include simultaneous fluorescence and SRS imaging of kidney organoids to resolve label-free structural markers alongside immunostaining; chemical and morphological characterization of pancreatic cancer spheroids to assess tumor–stromal organization, drug uptake, and treatment response; single-cell vibrational phenotyping across a colorectal cancer progression model; combined SHG and SRS characterization of decellularized pig tendon for safe tissue bio-scaffolds; and hyperspectral imaging of calcinosis deposits in scleroderma skin samples from patients, among others. Together, these studies illustrate how combining familiar optical methods with advanced vibrational and multiphoton techniques enhances biological insight while empowering researchers to adopt new imaging approaches.

Radu Boitor (SXT50)

Classification of breast cancer utilising Raman spectroscopy and optical coherence tomography (OCT) data

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KEY WORDS: Raman spectroscopy, Optical Coherence Tomography, tumour margin assessment.

Breast cancer is the most prevalent cancer among women, with 55,000 new cases in the UK each year[1]. The most common method of treatment for breast cancer is breast conserving surgery (BCS), which aims to remove the tumour mass with a minimal amount of healthy margin, to achieve the best aesthetic outcome. The current best intraoperative method used to determine whether a margin is positive is X-ray imaging, which can give the surgeon an indication of how close the tumour is to the surgical margin. However, positive margins are still detected by post-operative histopathology for 20-30% of patients undergoing breast cancer surgery. These patients require additional surgeries (re-excision) to achieve complete excision of the tumour. More accurate and objective techniques of detecting the status of surgical margins during breast conserving surgery are sought after.

Raman spectroscopy has been used in the past to discriminate between cancerous and healthy breast tissue[2], however multimodal approaches could further increase detection accuracy. We are investigating whether a combination of optical coherence tomography (OCT) and Raman spectroscopy can produce complementary structural and molecular information that can improve the detection of breast cancer on fresh tissue specimens. Co-localised OCT and Raman spectroscopy measurements have been made on fresh breast tissue specimens excised from 75 patients. Structural and molecular information was extracted from each modality and machine learning models were trained on OCT data alone, Raman data alone and combined OCT-Raman data. The performance of these models was ascertained by comparison to paraffin embedded histopathology.

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Julian Moger – Keynote

Beyond Colour: Resonance-Enhanced BCARS on Routine H&E Slides for Nucleus-Level Chemical Phenotyping and AI-Ready Pathology

Paul Ebersbach[1], Jayakrupakar Nallala[1], Neil Shepherd[2], Nick Stone[1], Julian Moger[1]*

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KEY WORDS: CARS, four-wave mixing, spectral analysis, phase-retrieval, pathology

Routine haematoxylin and eosin (H&E) histology is the workhorse of diagnostic pathology, yet it primarily reports morphology and only indirectly reflects the biochemical state of tissue. Meanwhile, vibrational spectroscopy offers molecular specificity but has struggled to integrate into clinical workflows due to acquisition speed, compatibility with standard slides, and the practical realities of archival specimens. In this talk, I will describe a hybrid nonlinear spectroscopic strategy that bridges these worlds by extending broadband coherent anti-Stokes Raman scattering (BCARS) into electronically resonant regimes *on conventional H&E-stained sections*.

The key idea is to treat haematoxylin not merely as a colour stain but as a nuclear-targeted chromophore whose electronic response is governed by chromatin chemistry and organization. Under resonance and pre-resonance conditions, electronically enhanced four-wave mixing (EE-FWM) produces strong, information-rich spectral modulations that coexist with Raman-like vibrational features recovered via phase retrieval. Rather than rejecting this "background," we exploit electronic–vibrational coupling as a quantitative reporter of nuclear phenotype.

Using breast tissue microarrays as a feasibility study, we show that hybrid BCARS spectra are dominated by hemalum–DNA interactions and enable three complementary readouts: (i) pixel-resolved wavenumber-shift mapping that tracks intra-nuclear absorption-linked heterogeneity and resolves chromatin compartmentalization and necrosis-associated pyknosis; (ii) Raman-like signatures consistent with nucleic-acid–associated modes in the fingerprint region; and (iii) nucleus-level discrimination of ductal carcinoma in situ (DCIS), invasive ductal carcinoma (IDC), and invasive lobular carcinoma (ILC) using a practical PCA–LDA pipeline after segmentation and per-nucleus spectral averaging.

While not a clinical validation, the results establish a new contrast paradigm—unifying "colour" and "chemistry" on routine slides—and point toward scalable, AI-ready spectroscopic features that could unlock vast archival H&E repositories for retrospective molecular phenotyping, biomarker discovery, and mechanistic digital pathology.

Dougal Ferguson – Keynote

Infrared Imaging of Tissue Within Clinical Timeframes

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KEY WORDS: QCL, IR, Clinic

For many years a major roadblock for the clinical uptake of infrared spectroscopic imaging modalities was the acquisition time required to obtain reasonable images of tissues, with good enough spatial resolution and signal-to-noise ratio (SNR) to enable clinically useful applications. The time to acquire a reasonable signal to noise spectroscopic scan of a standard microscope slide region of tissue can take many hours, even with trade-offs (assuming an FTIR microscope). Recent instrumentation developments now allow for the full fingerprint imaging of tissue micro arrays in under 30 minutes, and entire microscope slides within an hour, enabling rapid, high quality spectroscopic imaging of tissues within clinical timeframes without sacrificing frequency bands (1,2) It will be demonstrated that QCL microscopes offer a 20x improvement to acquisition times over state-of-the-art FTIR microscopes, including improvements to image contrast, SNR, and supervised learning applications. It will also be shown that QCL data can be used for a clinically significant application: identifying "at-risk" prostate cancer patients at the point of biopsy by combining IR data and limited clinical details (age and PSA). While the reported novel QCL system addresses the throughput requirement for clinical uptake, the subsequent limiting factor is also anticipated and addressed: the limitation of computing power for loading, preprocessing, and analysis of large sections of tissue. It will be demonstrated that applying an unsupervised analytical pipeline to large hyperspectral datasets (specifically a 49,420,800 pixel image of penile cancer tissue equating to 62GB of data covering 22 x 40 mm^2), see fig 1,is possible to complete in reasonable time (under 30 minutes) using only a memory limited system (a HP work laptop)(3).

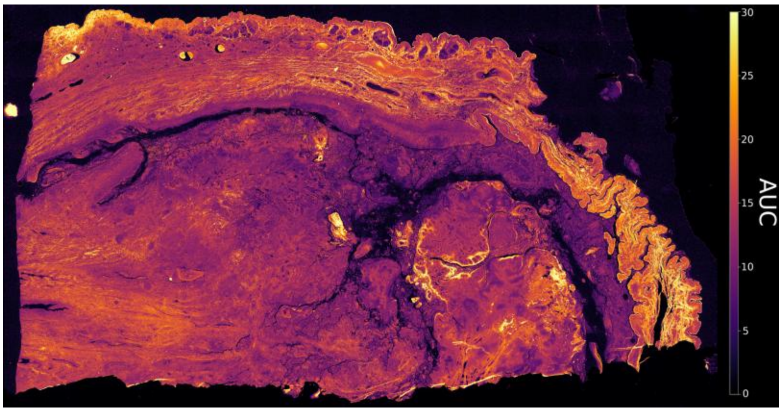

Figure 1 – Amide I integration image of a penile cancer sample imaged using a QCL microscope.

These advances in both data acquisition speed and data analysis strategies remove significant roadblocks in the translational pathway towards clinical adoption.

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2. (Ferguson D, Sachdeva A, Hart CA, Sanchez DF, Oliveira P, Brown M, et al. Identification of at-risk prostate cancer patients using Fourier transform infrared spectroscopy and machine learning. In: Optical Biopsy XXIII: Toward Real-Time Spectroscopic Imaging and Diagnosis [Internet]. SPIE; 2025 [cited 2025 Apr 16]. p. 4–11. Available from: https://www.spiedigitallibrary.org/conference-proceedings-of-spie/13311/1331103/Identification-of-at-risk-prostate-cancer-patients-using-Fourier-transform/10.1117/12.3048498.full

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Ruihao Luo (SXT04)

3D Hyperspectral Data Analysis with Spatially Aware Deep Learning for Diagnostic Applications

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KEY WORDS: hyperspectral imaging, deep learning, Raman spectroscopy

Nowadays, with the rise of artificial intelligence (AI), deep learning algorithms play an increasingly important role in various traditional fields of research. Recently, these algorithms have already spread into data analysis for Raman spectroscopy[1]. However, most current methods only use 1-dimensional (1D) spectral data classification, instead of considering any neighboring information in space. Despite some successes, this type of methods wastes the 3-dimensional (3D) structure of Raman hyperspectral scans. Therefore, to investigate the feasibility of preserving the spatial information on Raman spectroscopy for data analysis, spatially aware deep learning algorithms were applied into a colorectal tissue data set with 3D Raman hyperspectral scans[2,3]. This data set contains Raman spectra from normal, hyperplasia, adenoma, carcinoma tissues as well as artifacts. First, a modified version of 3D U-Net was utilized for segmentation; second, another convolutional neural network (CNN) using 3D Raman patches was utilized for pixel-wise classification. Both methods were compared with the conventional 1D CNN method, which worked as baseline. Based on the results of both epithelial tissue detection and colorectal cancer detection, it is shown that using spatially neighboring information on 3D Raman scans can increase the performance of deep learning models, although it might also increase the complexity of network training. Apart from the colorectal tissue data set, experiments were also conducted on a cholangiocarcinoma data set for generalizability verification. The findings in this study can also be potentially applied into future tasks regarding spectroscopic data analysis, especially for improving model performance in a spatially aware way.

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Investigation of different data fusion methods on MALDI data to improve classification accuracy

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KEY WORDS: MALDI, feature fusion, decision fusion, classification

Matrix-assisted laser desorption/ionization (MALDI) mass spectrometry is widely used in biomedical research to analyze proteins, peptides, and other biomolecules [1]. MALDI produces complex spectra that reflect the molecular composition of biological samples, enabling disease classification and biomarker discovery. However, the high dimensionality of MALDI spectra produces challenges for accurate classification. Conventional machine-learning pipelines typically apply a single feature extraction method and then classify. While these approaches may not fully capture the structure of MALDI data. Different feature extraction techniques highlight different and complementary properties. Integrating features from different approaches provides potential benefits to improve the performance of the classification. In this study, we propose a data fusion framework to combine PCA, ICA, NMF, and MCR features for classification with a support vector machine (SVM). The workflow begins with preprocessing, including interpolation, smoothing, baseline correction, peak alignment, peak binning, and normalization, to reduce noise and inter-sample variability. Afterwards, each feature extraction method is applied separately, followed by data fusion of two fusion strategies. In feature-level fusion, features from all methods are concatenated into a single representation to train an SVM (see figure 1.). In decision-level fusion, separate SVMs are trained on each feature set, and their predictions are combined via majority voting [2]. We also assess how different feature normalization schemes (e.g., median, min-max) influence performance for both individual and fused features. Performance is compared by using balanced accuracy, F1-score, and sensitivity.

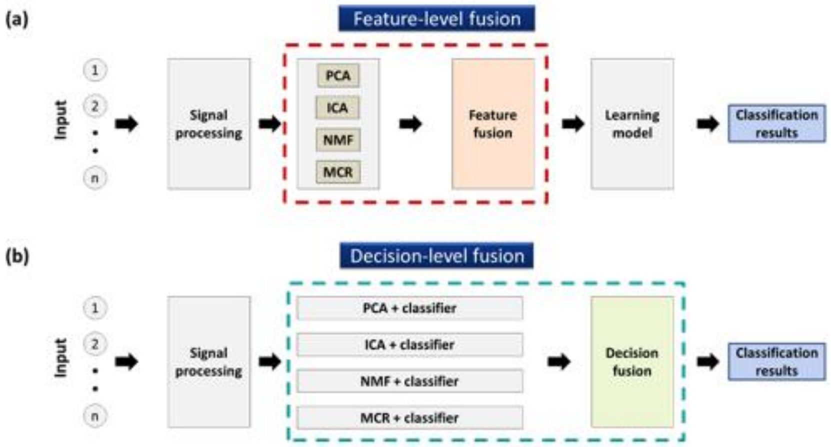

Figure 1. Comparison of feature-level fusion (a) and decision-level fusion (b) in MALDI data classification workflows.

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Vasilisa Kostromina (SXT02)

Machine Learning-Based Detection of Thymus Cancer Using Raman Spectroscopy

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KEY WORDS: Raman spectroscopy, machine learning, cancer detection

Raman spectroscopy is emerging as a promising non-invasive approach for detecting cancer across many organs. The multivariate nature of Raman spectra calls not for mere spectral interpretation, but for robust machine learning-based approaches. Complicating matters further, the real-world datasets are often significantly imbalanced, favouring either the normal or the pathological samples, depending on the study design. To remedy these issues, a pilot dataset of normal (n = 488) and cancerous (n = 194) rat thymus was collected on multiple days using 785 nm In Via (Renishaw, UK) Raman spectrometer. The dataset was pre-processed using a custom-developed pipeline consisting of baseline correction, Savitzky-Golay smoothing, and min–max normalization. To ensure robust and unbiased model evaluation, training and testing were strictly separated at the measurement-day level to prevent data leakage, resulting in multiple splits. Several classifiers were optimized using grid search combined with stratified k-fold cross-validation. The results demonstrate that the pipeline using the best-working classifier can confidently distinguish spectra of cancerous and healthy tissue (mean accuracy for SVM = 0.98).

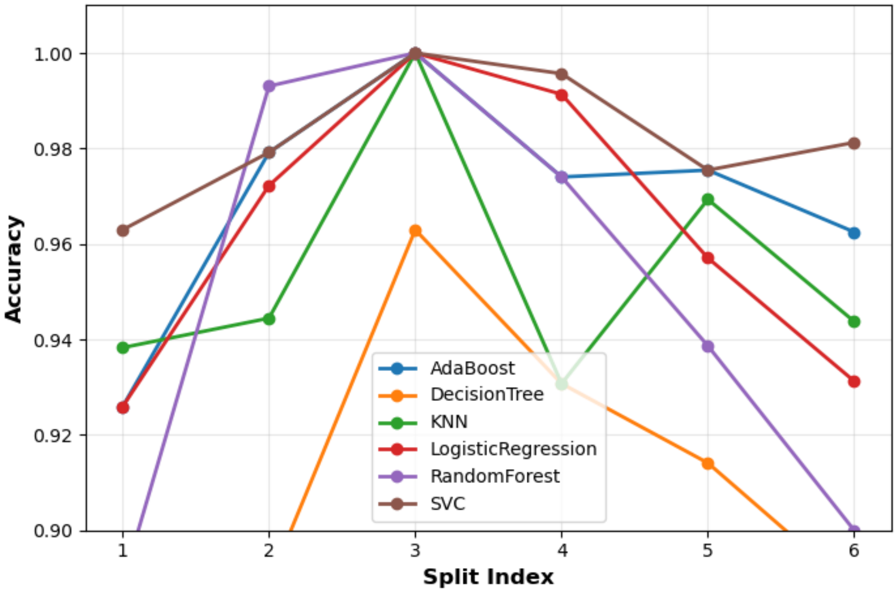

Figure 1: Accuracy comparison of classifiers for Raman spectra of rat thymus.

Oleg Ryabchykov (SXT03)

Advancing Vibrational Spectroscopy for Diagnostics via Deep Learning

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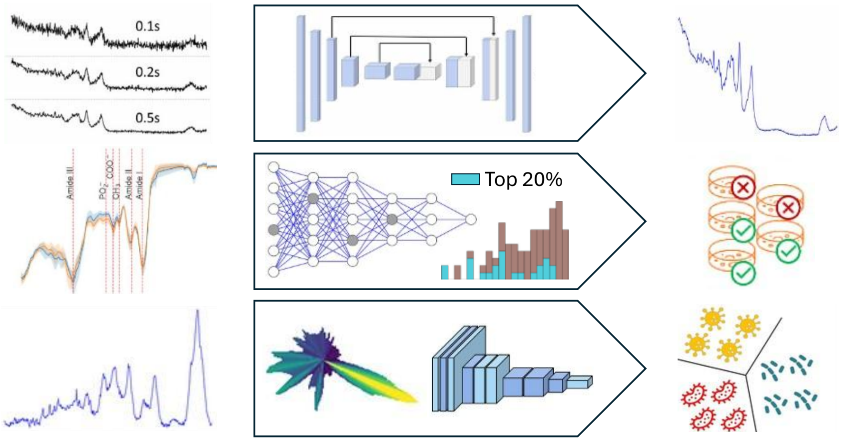
KEY WORDS: Raman spectroscopy, FTIR, Deep learning, Denoising, Diagnostics

Vibrational spectroscopy provides rich chemical information for noninvasive diagnostics but faces challenges such as long acquisition times, limited interpretability, and calibration sensitivity. We show how deep learning addresses these issues through denoising, uncertainty-aware data cleansing, and utilization of models pretrained with augmented images.

U-Net models remove noise from IR and Raman[1] spectra while preserving key features. For saliva-based Sjögren's screening with ATR-FTIR, a neural network using Monte Carlo dropout estimates prediction confidence[2], enabling exclusion of uncertain spectra for improved reliability. We also explore converting 1D spectra into 2D representations for pre-trained image models[3], achieving robustness to wavenumber shifts and better device compatibility.

By integrating deep learning for preprocessing and uncertainty estimation, our approach enhances data quality, reliability, and interpretability, bringing vibrational spectroscopy closer to clinical application.



Different applications of deep learning in spectral analysis: denoising, utilizing pretrained image-based networks, and rating certainty of spectra based on Monte-Carlo dropout.

ACKNOWLEDGMENTS: This work is supported by the BMBF, funding program Photonics Research Germany (13N15708 (LPI-BT3-IPHT), 13N15466 (LPI-BT1-FSU), 13N15710 (LPI-BT3-FSU), 13N15713 (LPI-BT4-IPHT)) and is integrated into the Leibniz Center for Photonics in Infection Research (LPI). The LPI initiated by Leibniz-IPHT, Leibniz-HKI, Friedrich Schiller University Jena and Jena University Hospital is part of the BMBF national roadmap for research infrastructures.

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Parallel Session 3
(13:30-15:00)
Session 3A – Clinical Spectroscopy 1
in NEWMAN BLUE (Chair: Prof Nick Stone)

Renzo Vanna – Keynote

From Whole-Body MRI to *In Situ* Raman Detection: Toward Intraoperative Tumor Margin Evaluation

Renzo Vanna[1]*, **Benedetta Gavazzoni**[1,2], **Francesco Manna**[1,2], **Beatrice Lucia Bona**[3], **Francesca Garello**[4], **Cristina Chirizzi**[5], **Alberto Lux**[6], **Dario Polli**[2], **Giuseppe Digilio**[7], **Claudia Conti**[6], **Francesca Baldelli Bombelli**[3].

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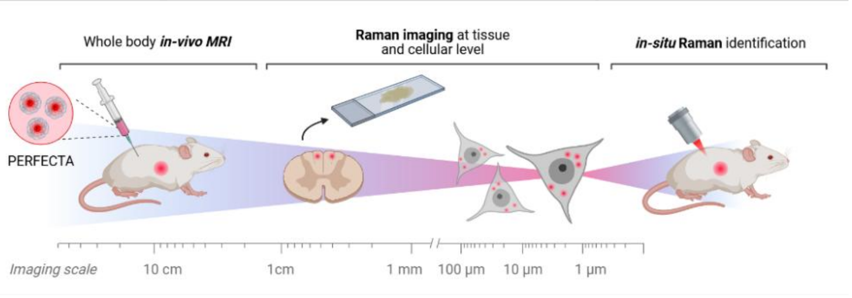
KEY WORDS: Multimoldal, Multiscale, Raman spectroscopy.

Accurate assessment of tumor-free margins during surgery is essential for minimizing recurrence rates and enhancing patient outcomes. The current gold-standard histopathological evaluation is slow, involves extensive sample handling, and can overlook residual tumor cells due to sampling constraints. As a result, there is a pressing need for real-time, reliable methods to evaluate surgical margins directly within the operative field.

We introduce a multimodal approach utilizing fluorinated nanoparticles—PLGA nanocarriers loaded with PERFECTA, a superfluorinated molecular probe that offers superior 19F MRI sensitivity and distinct Raman signatures[1,2]. These nanoparticles, stabilized with either polyvinyl alcohol (PVA) or sodium cholate (NaC), are also designed for potential future surface functionalization for targeted tumor applications.

We began by characterizing the Raman signatures of these nanoparticles and assessing their cellular uptake in NIH3T3 fibroblasts using a custom 660 nm inverted Raman microscope optimized for live-cell imaging. The results demonstrated time-dependent internalization of both the fluorinated core and the PLGA shell. *In vivo* studies were carried out in BALB/c mice with orthotopic mammary tumors. After administering the nanoparticles (intratumoral or intravenous), tumor localization was confirmed via ^{19}F MRI at 7 T. *Ex vivo* Raman detection of the tumor was then performed using both a 660 nm microscope and two 785 nm systems configured for SORS or micro-SORS, with signals from PERFECTA consistently detected at the tumor surfaces.

This multimodal approach highlights the potential of using a single molecular probe for both MRI-based tumor localization and Raman-based in situ detection during surgery, enabling label-free, histology-independent intraoperative assessment of tumor margins.



Schematic representation of the multimodal and multiscale strategy under development.

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Yoshiki Cook (SXT10)

Multi-Excitation Raman Chemometrics for Rapid Identification and Antimicrobial Resistance Profiling of *Pseudomonas aeruginosa*

Yoshiki Cook*[1, 2, 3], Callum Highmore[3,4,5], Niall Hanrahan[1,2], Ysanne Pritchard[1,2,6], Adam Lister[1,2], Kirsty Cooper[3,4], George Devitt[2,4], Alasdair P. S. Munro[5,7], Saul N. Faust[5,7], Jeremy S. Webb[3,4,5], & Sumeet Mahajan[1,2,5]

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KEY WORDS: MX-Raman, Chemometrics, Antimicrobial Resistance

In clinical settings, where diagnostic delays and uncertainties can lead to inappropriate therapy, rapid and accurate identification of bacterial pathogens is essential in enabling informed decision-making and improving patient outcomes, While chemometric and machine learning approaches using Raman spectroscopy offer a promising route toward faster, culture-independent characterisation, strain-level identification and **antimicrobial resistance** (**AMR**) profiling remain challenging due to subtle biochemical variation and overlapping spectral signatures among closely related bacterial populations.

As different excitations preferentially enhance distinct vibrational features, single-excitation Raman measurements capture only a subset of the biochemical information present in microbial systems. Consequently, relying on a single excitation wavelength limits spectral diversity and constrains the discriminatory power of downstream computational models.

To address this limitation, we present a **Multi-Excitation Raman** (**MX-Raman**) spectroscopy approach[1] to expand the biochemical information captured by Raman measurements and enhance microbial discrimination. Spectra were acquired at multiple excitation wavelengths and combined using feature-level spectral fusion to generate a unified chemical fingerprint. The approach was applied to 20 clinical isolates of *Pseudomonas aeruginosa* for strain identification and susceptibility profiling against four antibiotics: ceftazidime, ciprofloxacin, imipenem, and tobramycin.

Our results found that integrating multi-excitation spectra enhanced class separability and improved model stability across all tasks. Using **Support Vector Machine** (**SVM**) analysis, **MX-Raman** consistently delivered higher predictive performance for both strain identification and resistance profiling. Strain-level accuracy increased from 80% and 81% with single-excitation measurements to 86% with MX-Raman, while AMR profiling similarly improved from 86–96% to 92–96% when multi-excitation data were incorporated.

These findings indicate that spectroscopic acquisition strategy is a key determinant of chemometric performance in Raman-based microbial analysis. Multi-excitation data fusion provides a feasible means of enhancing discriminatory power in Raman workflows, particularly where phenotypic differences are subtle.

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James Alix (SXT14)

Application of Raman spectroscopy to the diagnosis of nerve and muscle diseases: a journey from the bedside to the bench and back again

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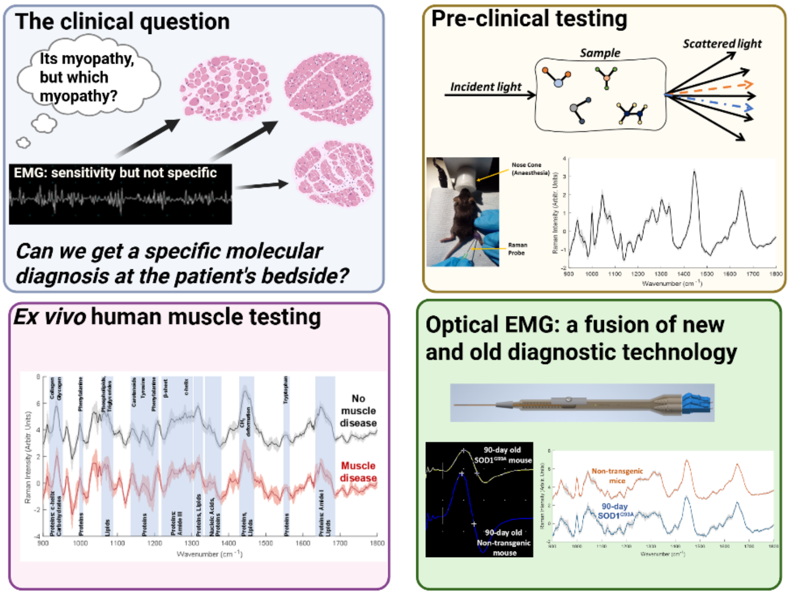
KEY WORDS: Translation, Neurology, Raman spectroscopy

Nerve and muscle diseases have common features, such as muscle weakness, but have a wide range of causes. A large number of investigations can be required, and diagnostic delays are long[1,]. The molecular profile obtained from Raman spectroscopy could revolutionise the diagnostic process, particularly within a fibre optic system suitable for point of care testing. However, when we started there was no evidence for such an application. This work details our journey from the concept of using Raman spectroscopy of muscle to identify different diseases, through development of in vivo preclinical paradigms[2], ex vivo human sample analysis[3] and work towards first-in-human testing. We will consider how we have tried to obtain clinically relevant data from early preclinical testing onwards, framing experimental design around real clinical problems. We will present our ideas on how we aim to facilitate clinical uptake and decision making through the development of interpretable spectral biomarkers linked to disease pathophysiology[4] and analytical workflows matched to clinical problem solving[5]. Finally, we will describe our integration of Raman alongside existing diagnostic technology[6], with a view to improved targeting to areas of abnormality and a faster, more efficient diagnosis.



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Raman microscopy using light-sheet illumination with slit detection

<u>Tomoaki Okumura</u>[1], Kenta Temma[1], Yasuaki Kumamoto[1,2], Nicholas Isaac Smith[2,3], and Katsumasa Fujita[1,2*]
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KEY WORDS: Raman microscopy, hyperspectral Raman imaging, biological specimens

Raman microscopy visualizes molecular components in samples and various applications using Raman microscopy have been reported[1]. A key to the recent emergence of Raman microscopy is the development of high-speed Raman imaging techniques, which expand the utility of Raman microscopy in the life-science field. In particular, slit-scanning Raman microscopy, which collects Raman scattering from multiple positions along a line-shaped laser, has accelerated Raman imaging speed by more than 100-fold compared with confocal Raman microscopy[2]. However, in conventional epi-illumination configurations, background signals originating from the substrate, surrounding media, and signals from out-of-focus planes reduce Raman image contrast, thereby limiting the sensitivity in Raman imaging.

In this study, we propose light-sheet illumination Raman microscope with slit scanning that enables selective illumination of the focal plane and reduces the out-of-focus background signals in Raman imaging (Fig. 1). We first estimated point spread functions in both epi- and light-sheet illumination configurations to theoretically confirm that light-sheet illumination reduces background signals from out-of-focus planes. A 2.5-fold improvement in a signal-to-background ratio with light-sheet illumination configuration was experimentally confirmed using polystyrene bead samples. We further demonstrated that this approach reduces background signals in Raman imaging of cells and spheroids, resulting in higher-contrast visualization of molecular distributions within the samples. We expect that the proposed technique will contribute to improving the sensitivity in Raman imaging and facilitate its applications in biology, medicine, and clinical diagnostics.

Reference
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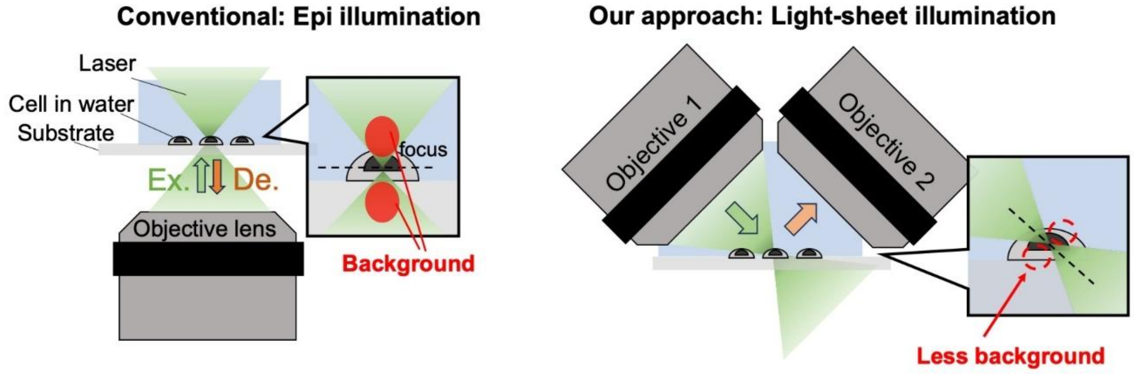

Fig. 1 Shematic illustration of epi- and light-sheet illumination.

Single-cell Raman Spectroscopy Reveals Differential Stress Responses and Dysplasia Associated Signatures in Barrett's Oesophagus

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KEYWORDS: Raman spectroscopy; Barrett's Oesophagus; Microfluidics

Barrett's oesophagus (BO) results from chronic gastro-oesophageal reflux, exposing oesophageal epithelium to repeated acidic bile salt episodes that promote inflammation, oxidative stress, and progression toward oesophageal adenocarcinoma (OAC). Understanding how individual BO-derived cells tolerate these fluctuating conditions is essential, as disease progression is strongly influenced by cellular heterogeneity. Here, we combine microfluidic single-cell trapping, live-cell imaging, and Raman spectroscopy to characterise the biochemical and morphological responses of BO-derived cell lines to physiologically relevant intermittent exposure to acidic bile salts. Across four Barrett's-derived lines (CP A, CP B, CP C, CP D), repeated 1-minute pulses of pH 4 bile salt solution induced distinct, exposure-dependent alterations in Raman features associated with lipids, proteins, and nucleic acids. Sensitive lines such as CP A and CP C exhibited progressive loss of lipid associated CH_2/CH_3 stretches, reductions in DNA phosphate bands, and perturbations of Amide I/III regions, consistent with increasing biochemical stress. Corresponding bright-field images revealed membrane blebbing, shape distortion, and loss of viability. In contrast, more resilient dysplastic lines (CP B, CP D) maintained significantly greater biochemical and morphological stability, highlighting inherent heterogeneity in stress tolerance that does not align strictly with dysplasia grade.

Machine learning analysis demonstrated that principal component and linear discriminant analysis (PCA/LDA) distinguished non-dysplastic (CP A) from highly dysplastic (CP D) cells with >93% accuracy, driven by differences in cytochrome c, nucleic acid content, lipid organisation and aromatic amino acids. Acidic bile salt exposure amplified these differences: CP A showed marked cytochrome c depletion consistent with early apoptosis, while CP D displayed non-lethal stress adaptations.

Overall, this work establishes single-cell Raman spectroscopy, integrated into a microfluidic platform, as a powerful label-free approach for resolving biochemical stress responses and dysplasia-associated signatures in BO. This methodology provides a foundation for minimally invasive diagnostic strategies and for probing mechanisms of cellular resilience in reflux-associated disease.

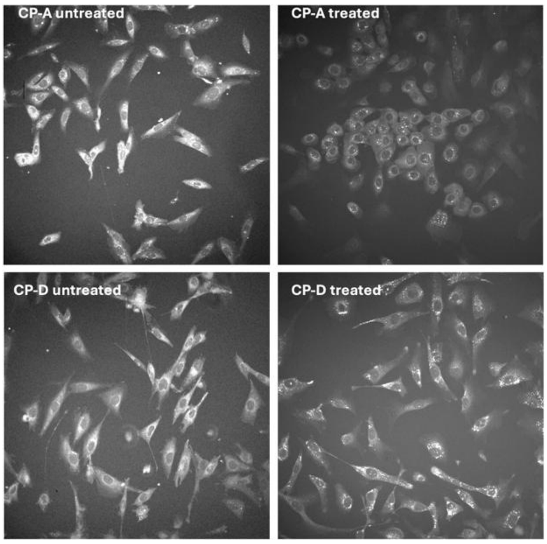

Figure 1 SRS images taken at 2850 cm^{-1} demonstrating different responses to acid/bile treatment.

Session 3B – Non-linear Optical Spectroscopy
in NEWMAN GREEN (Chair: Julian Moger)

Federico Vernuccio – Keynote

Advances in Broadband Coherent Anti-Stokes Raman Microscopy

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KEYWORDS: CARS microscopy, spectral analysis, wide-field CARS imaging

Over the past decades, coherent anti-Stokes Raman scattering (CARS) microscopy has undergone continuous advancements, establishing itself as a powerful tool for chemical imaging of crystalline samples, unstained cells, and biological tissues. Narrowband CARS relies on two picosecond pulses—namely, the pump and the Stokes beams—whose frequency difference is resonant with a specific vibrational mode of the sample under investigation. However, this configuration allows access to only a single vibrational mode at a time. Broadband CARS can be implemented either by combining a narrowband pump beam with a broadband Stokes beam (multiplex CARS), enabling the parallel acquisition of multiple vibrational modes, or by using narrowband pump and Stokes pulses while tuning one of them to achieve sequential acquisition of vibrational modes (hyperspectral CARS)[1].

Conventionally, CARS imaging is performed in a point-scanning configuration, in which the two beams are tightly focused at the sample plane. However, point-scanning approaches are limited by motion blur, slow acquisition due to the mechanical inertia of galvanometric scanners, and the risk of sample photodamage. Wide-field CARS implementations based on camera detection can overcome these limitations, enabling faster imaging with reduced phototoxicity. Nevertheless, such approaches typically lack axial resolution and are constrained to relatively small fields of view (FoV ~100 × 100 μm^2) to avoid damage to objective lenses.

In this presentation, I will describe our recent developments in broadband CARS microscopy. First, I will introduce an experimental setup for multiplex CARS that enables imaging of the entire Raman spectrum of biological samples in less than 1 ms[2]. I will discuss the experimental implementation, the presence of undesired non-resonant background in CARS spectra, and the numerical methods and deep learning algorithms we have developed to suppress it[3].

I will then present our recent advances in wide-field CARS microscopy that address the challenges of objective damage and optical sectioning by employing a temporal focusing (TF) scheme within a galvo-scanning system. TF, originally introduced for optically sectioned wide-field two-photon microscopy[4], uses a diffraction grating to spatially disperse the spectral components of a femtosecond laser pulse, generating a focused spectral line at the back pupil plane of the objective. The spectral components recombine into a short pulse only at the focal plane, thus generating the nonlinear contrast exclusively within a thin plane, enabling optically sectioned wide-field imaging.

I will describe how temporal focusing can be implemented for the CARS contrast mechanism using a tunable 220 fs optical parametric amplifier (pump, 700–900 nm) pumped by a 100 kHz ytterbium fiber laser at 1030 nm (Stokes). I will show wide-field hyperspectral TF-CARS images of microplastics and steatotic liver tissues across the full CH-stretching vibrational range (2800–3050 cm^{-1}), with optical sectioning better than 5 μm, over a FoV exceeding 700 × 700 μm^2 and 2Hz frame rate. Finally, we show that the temporal focusing scheme employing femtosecond pulses enables a spectral resolution of approximately 30 cm^{-1}, introducing the concept of *k*-space spectral focusing.

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William Tipping (SXT41)

Live-cell imaging of prostate-specific membrane antigen using stimulated Raman scattering microscopy

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KEY WORDS: SRS microscopy, chemometrics, hyperspectral imaging, prostate cancer.

Prostate cancer is one of the leading causes of cancer-related death in men globally, with more than 1.2 million new cases diagnosed annually. [1] Treatment for localised disease includes active surveillance, radical prostatectomy or radiotherapy as curative approaches.[2] Long-term control of the disease can be achieved providing there is complete resection of the tumour-positive margin. Currently, histopathology is the most reliable method by which a positive margin can be identified, although it is a time-consuming process which requires tissue to be resected, and is only available for small biopsies. As a result, the development of intraoperative imaging agents for margin assessment targeted to prostate-specific membrane antigen (PSMA) have seen a great deal of research focus to overcome the limitations of histopathology.[3]

This presentation will report the first small-molecule Raman probe for specific SRS imaging of prostate cancer.[4] The molecular design incorporates a glutamate-ureido-lysine (GUL) ligand for specific PSMA targeting, and a bisaryl butadiyne (BADY) group for high sensitivity detection in the cell-silent region of the Raman spectrum, which are united via short chemical linker. The resulting probe, referred to as PSMA-BADY, was assessed against a panel of prostate cell models for specificity and PSMA targeting ability. In addition, the temporal aspects of uptake and binding of PSMA-BADY in live cells using SRS imaging is demonstrated. Finally, wash-free imaging of PSMA-BADY in a multicellular population will be presented. PSMA-BADY is a selective probe for visualising PSMA expression in single cells that has significant potential for further development towards clinical Raman imaging of prostate cancer margins during surgery.

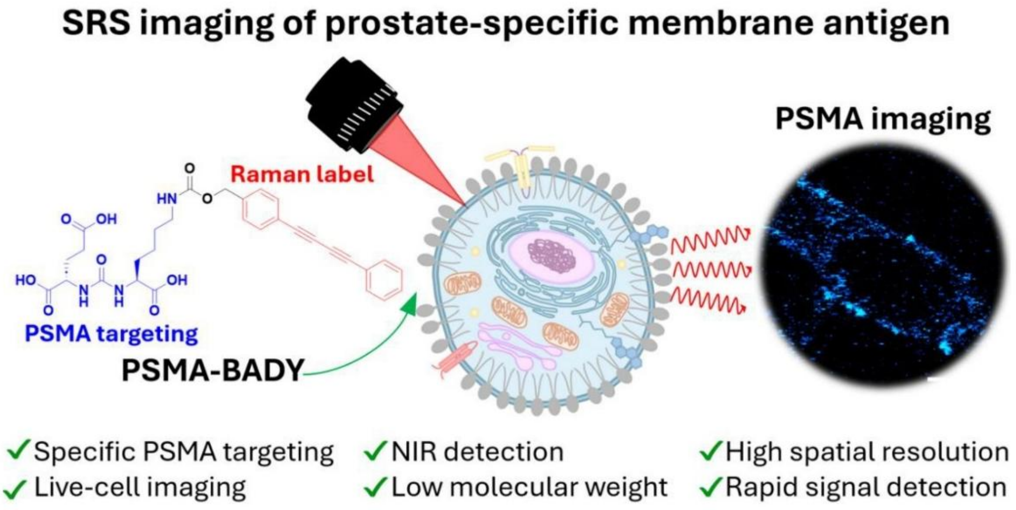

Figure 1 SRS imaging of prostate-specific membrane antigen.

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Yang Ma (SXT42)

Deep Learning-Based Fluorescence Image Prediction from Large-Scale Stimulated Raman Imaging

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[2]*Research Center for Advanced Science and Technology, The University of Tokyo, Tokyo 153-8904, Japan*
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KEY WORDS: stimulated Raman scattering, deep learning, spectral analysis

Stimulated Raman scattering (SRS) microscopy is a powerful tool for biochemical analysis because it probes the inelastic scattering of photons arising from intrinsic molecular vibrations in the sample. However, extracting organelle-specific information solely from Raman spectra is challenging, since SRS signals are mixtures of multiple biomolecular components with strongly overlapping vibrational spectra. Traditional analysis methods, such as principal component analysis (PCA) and multivariate curve resolution (MCR), rely only on spectral information and therefore struggle to robustly separate all overlapping chemical contributions in the Raman signal[1].

Deep learning has emerged as a powerful approach for both spectral analysis and image segmentation, offering a way to overcome the limitations of traditional methods[2,3]. In this work, we aim to bridge traditional spectral approaches and deep learning–based methods. To this end, we employ both a PCA-assisted deep learning model and a purely deep learning–based model to predict mitochondrial distributions in HeLa cells from a jointly acquired SRS/fluorescence dataset. Our image dataset contains 670 pairs of SRS/fluorescence images, which is bigger than previous reports[2,3].

The prediction accuracy is quantified using the feature similarity index (FSIM) [4], and Pearson's correlation coefficient (PCC). Both FSIM and PCC take values in [0, 1], with higher values indicating better performance. The prediction results, summarized in Table 1.1, show that the PCA + U-Net model achieves higher Pearson's correlation coefficient (PCC), whereas the CNN + U-Net model attains a higher FSIM value. This suggests that the PCA-based approach performs better in terms of linear intensity correspondence, while our end-to-end deep learning model more effectively preserves cellular structural details, as reflected by its higher FSIM. Further details will be presented at the conference.

Table 1.1 Comparison between two different approaches.

Quality metrics\ Approaches	PCA + U-net	CNN + U-Net
FSIM (a.u)	0.55	0.96
PCC (a.u)	0.89	0.81

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Jessica Mansfield (SXT40)

Label-Free Chemical Imaging of Plant–Fungal Interactions Using Stimulated Raman Scattering Microscopy

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KEY WORDS: Indicate up to 3 key words, Stimulated Raman Scattering (SRS), Hyperspectral imaging, live cell imaging

Understanding the earliest chemical events that determine whether a plant successfully resists or succumbs to fungal infection is critical for crop protection, yet remains experimentally challenging due to the need for non-invasive, chemically specific imaging. Here, we demonstrate the use of stimulated Raman scattering (SRS) microscopy as a label-free, three-dimensional spectroscopic tool to visualise and chemically characterise fungal infection and plant defence responses in situ in fresh cereal leaves.

We investigate early infection stages (24–48 h post inoculation) of *Blumeria graminis f. sp. Hordei (BGh)*, a powdery mildew pathogen that infects barley but is resisted by wheat. SRS imaging tuned to the CH_3 stretching vibration (2930 cm^{-1}) enables direct visualisation of fungal conidia, germ tubes, appressoria, and haustorial development without staining or fixation. Complementary hyperspectral SRS measurements across the 2780–3150 cm^{-1} region provide chemical contrast sufficient to segment plant cell walls, epicuticular waxes, fungal surface lipids, and intracellular components based purely on vibrational signatures.

Plant defence responses are resolved spectroscopically through pronounced increases in aromatic content localised to papillae formed beneath attempted penetration sites. Hyperspectral imaging in the fingerprint region (1480–1710 cm^{-1}) reveals distinct spectral signatures that differentiate uninfected tissue, unsuccessfully defended attack sites, and successfully reinforced cell walls, highlighting chemically specific markers of resistance.

Finally, time-lapse SRS imaging captures dynamic intracellular transport towards fungal attack sites as early as 24 h post infection. Quantitative kymograph analysis yields material transport velocities on the order of ~3 µm s^{-1}, demonstrating the ability of SRS to provide both chemical specificity and real-time functional insight.

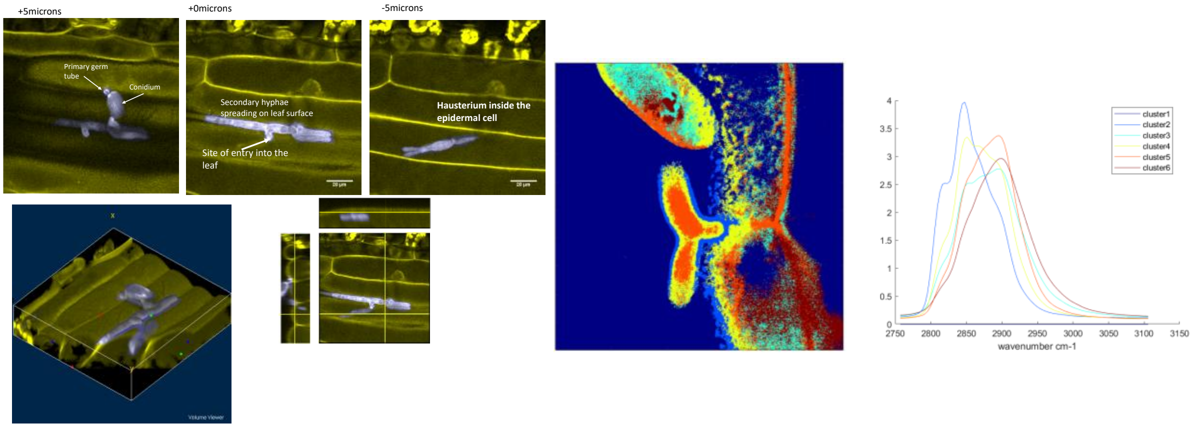

Figure: LHS 3D imaging of *BGh* infection in a barley leaf with fully formed haustorium, RHS hyperspectral imaging of fungus on leaf surface

Mustafa Kansiz (SXT39)

High-Speed Laser-Scanning Photothermal Submicron Infrared (O-PTIR) and Stimulated Raman (PT-SRS) Platform for Real-Time Label-Free Chemical Imaging

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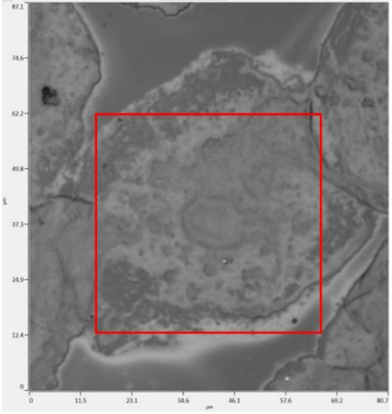
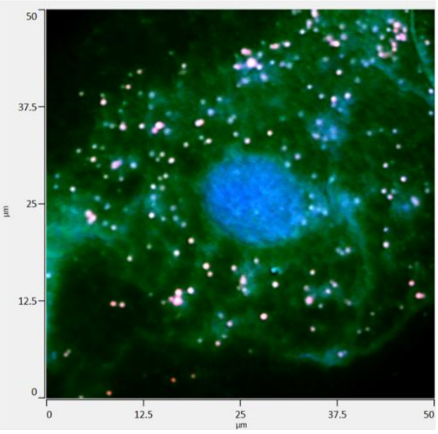
KEY WORDS: O-PTIR, PT-SRS, Chemical Imaging

We describe a new laser-scanning microscope developed for real-time, label-free vibrational chemical imaging, integrating Optical Photothermal Infrared (O-PTIR) and Photothermal Stimulated Raman Scattering (PT-SRS) also known as Stimulated Raman Photothermal (SRP), modalities into a single multimodal, correlative platform. These techniques were originally developed in the laboratory of Prof. Ji-Xin Cheng at Boston University, whose group also contributed valuable collaboration during the development of the current commercial system.*

The platform enables true sub-micron spatial resolution and high-speed chemical imaging across a range of biological and materials science applications. High-speed synchronized IR and probe beam laser scanning supports efficient large-area imaging, with full hyperspectral data cubes acquired in minutes. The system also supports three-dimensional depth-resolved chemical imaging. To accommodate a broad range of sample types, the instrument supports both co-propagating and counter-propagating beam geometries, enabling measurements on IR-transparent and IR-opaque substrates. The combination of OPTIR and PT-SRS provides complementary vibrational contrast within one system, enhancing chemical specificity and enabling broader applicability to complex samples. The platform also includes multi-line widefield and laser-scanning confocal fluorescence, enabling fluorescence-guided infrared and Raman measurements. This facilitates correlative imaging in cellular biology, pathology, and functional materials research. We will present representative datasets from O-PTIR and PT-SRS imaging, including mixed polymer standards, subcellular structures (e.g., lipid dynamics in live cells), brain tissue sections, and microplastic mapping. These examples demonstrate the system's ability to support both high-resolution imaging and efficient analysis over extended areas.

Brightfield image





RGB Overlay

1743 – Lipid
1650 - Protein
1085 – Nucleic Acids

100nm pixel size
501x501 pixels
13 sec per image
52 µsec pixel dwell time
Obj: 50x, 0.8NA
Counter-prop mode

Parallel Session 4
(15:30-17:30)
Session 4A – Emerging Technologies
in NEWMAN BLUE (Chair: Dr Sara Mosca)

Kareem Elsayad – Keynote

Surfing the hypersonic landscape: Brillouin Microspectroscopy and what it can tell us about life and disease

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KEY WORDS: Brillouin Spectroscopy, Dynamic Structure, Biological Matter

The last decade has seen a sharp increase in the popularity of Brillouin Light Scattering (BLS) microscopy, driven by significant technological advances in spectrometer designs that increase the speed and versatility of measurements on living systems. Despite this there are still some fundamental issues regarding the interpretation of the measured parameters in biological samples.

Brillouin Light Scattering (BLS) spectroscopy measures the speed and attenuation of GHz acoustic phonons (*hypersound*) in a material. Implemented in a microscopy-setup it becomes possible, using modern BLS spectrometers, to non-invasively spatio-temporally map these properties in living biological cells and tissue. From the measured acoustic speed and attenuation, it is possible to calculate the corresponding *longitudinal elastic modulus* and *longitudinal viscosity*. While from a physics perspective the definition and interpretation of these material parameters may be quite clear, interpreting their significance in complex biological systems is less so. For one, they probe the dynamic-structure (mechanics) subject to different boundary conditions and timescales (picoseconds). This can result in distinct values and trends compared to elastic and viscous moduli obtained using e.g. perturbation-based techniques. As such there is sometimes confusion when it comes to interpretation of BLS derived parameters.

Here I will discuss several biological processes and systems where BLS measured parameters can in of themselves give useful mechanistic insight, and compare these to ones where they can serve as useful proxies. I will do so also by way of introducing several novel variations of BLS spectroscopy/microscopy and correlative measurements using other modalities, that can provide additional information.

Finally, I will discuss the potential of BLS for medical diagnostics and prognostics, presenting some recent results from our lab and others, together with efforts by the community to develop reporting and analysis standards.

Andrei Markin (SXT19)

Time-Resolved Raman spectroscopy: Removing spectral background for clear chemical identification

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KEY WORDS: Time-resolved Raman spectroscopy, fluorescence suppression, chemical identification

Fluorescence emission can be orders of magnitude more intense than Raman scattering which can hinder chemical analysis. A cutting-edge technique to overcome this issue is time-resolved Raman spectroscopy (TRRS). This work demonstrates how TRRS can be used to leverage the fast timescale of Raman scattering and isolate the Raman signal from other background light, whether that is fluorescence emission caused by the excitation laser, or black-body emission originating from the sample.

An example application of this technique is shown in figure 1 where LEGO bricks of different colour have been measured using conventional continuous-wave (CW) Raman spectroscopy and TRRS, both at 532 nm excitation. LEGO bricks are polymers loaded with pigments which limit penetration depth and introduce a strong fluorescence background, making chemical identification challenging. In each case, TRRS suppresses the fluorescence background and allows the polymer to be identified.

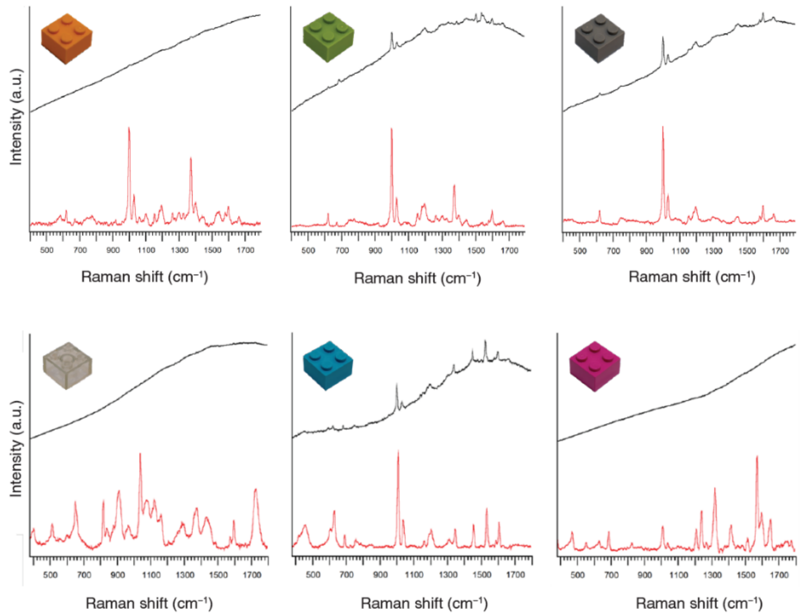

Figure 1: Conventional CW Raman spectra (black) and TRRS (Red) measured from six coloured LEGO bricks (pigmented polymers) using 532 nm excitation. In conventional Raman spectroscopy, fluorescence from the pigment dominates the spectrum. TRRS eliminates the fluorescence background and allows the polymer to be identified as acrylonitrile butadiene styrene (ABS). In the orange and blue bricks, the dyes can also be identified as solvent orange 3 and phthalocyanine blue respectively.

Miriam Unger (SXT20)

Smaller Plastics, Bigger Risks: Revealing Micro- and Nanoplastics with Submicron IR (O-PTIR) Microspectroscopy

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KEY WORDS: Optical Photothermal Infrared (O-PTIR), Microplastics, Nanoplastics, Raman spectroscopy, Submicron IR imaging

Microplastic (MP) contamination has become a global environmental and health concern, with particles now detected in water, air, soil, and biological systems. These particles can enter the human body through ingestion or inhalation, where submicron microplastics and nanoplastics (<1 µm) are of particular concern due to their ability to cross biological barriers and accumulate in tissues.

Infrared (FTIR/QCL) and Raman spectroscopy are the most widely used tools for MP analysis, yet both face major challenges at small particle sizes. Conventional FTIR microscopy is generally limited to particles >20 µm due to diffraction and suffers from scattering artefacts that compromise spectral reproducibility. Raman spectroscopy offers higher spatial resolution (<10 µm) but is often limited by fluorescence interference, reduced sensitivity, and frequent false-positive assignments, including the misidentification of long-chain molecules such as stearates as polymers like polyethylene. These limitations leave a critical analytical gap in characterizing submicron plastics, the size range most relevant to biological uptake and toxicity.

Optical Photothermal Infrared (O-PTIR) spectroscopy overcomes these constraints by delivering true submicron infrared spatial resolution (<500 nm) in an optical microscope format. Operating in reflection mode, O-PTIR provides FTIR transmission- or ATR-like spectral quality without contact or scattering artefacts and is unaffected by fluorescence or dark or highly absorbing samples. In addition, its multimodal capability enables simultaneous, same-spot, same-time, same-resolution Raman measurements for complementary chemical information.

We have developed automated workflows for the detection and chemical characterization of micron and submicron MP particles using combined O-PTIR and Raman spectroscopy. Following optical or fluorescence-based screening, particles of interest are automatically measured to acquire both IR and Raman spectra. Real-world case studies demonstrate how this approach enables high-confidence detection, identification, and spatial mapping of micro- and nanoplastics in environmental and biological samples, revealing what has long remained inaccessible to conventional vibrational spectroscopy.

Najla Albugami (SXT21)

Single Live-Cell FTIR Spectroscopy for Inhaled Medicine Development

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Key words: FTIR spectroscopy; live cells; inhaled medicines

The development of inhaled medicines is frequently constrained by limitations in early-stage assessment of drug toxicity and cellular responses, contributing to high attrition during pre-clinical development. Conventional approaches, such as histological evaluation, often lack sensitivity to underlying biochemical changes and may not reliably distinguish between different cellular response profiles. For example, foamy macrophage morphology is currently used as an indicator for drug cytotoxicity, but it is a non-specific feature and does not provide mechanistic insight[1,2]. Fourier Transform Infrared (FTIR) spectroscopy is a label-free technique capable of probing biochemical composition at the single-cell level.

In this study, single live-cell FTIR spectroscopy was applied to investigate biochemical differences in macrophage-like cells following exposure to a panel of reference compounds and approved inhaled drugs, alongside untreated controls. Single live cell spectra were measured by using the zinc sulphide hemispheres approach, developed in our laboratory, which produces high signal to noise data with minimal spectral artefects associated with light scattering [3]. Machine-learning and multivariate statistical analysis was applied to discriminate between different compound exposure groups and control cells based on distinct lipid- and protein-associated spectral features. These findings demonstrate that single live-cell FTIR spectroscopy can resolve subtle biochemical differences that are not apparent from morphology alone, highlighting its potential as a complementary tool for early-stage investigation in inhaled medicine development.

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Hidenori Koresawa (SXT22)

Use of a Photon-Counting 2D Detector in Line-Illumination Raman Microscopy

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KEY WORDS: Raman microscopy, photon-counting, weak signal detection, high-sensitivity, live-cell imaging

Line-illumination Raman microscopy[1] enables higher-throughput imaging than conventional point-illumination Raman microscopy by allowing parallel acquisition along the illuminated line using a CCD camera. However, under weak Raman signal conditions (e.g., when the detected photon number is on the order of several tens or fewer), the readout noise of CCD cameras, typically 3–5 e$^-$, becomes the dominant factor limiting sensitivity, and operation at this noise level requires long readout times.

To address this limitation under low-photon-number conditions, we implemented a photon-counting two-dimensional detector (qCMOS, Hamamatsu Photonics) in line-illumination Raman microscopy. Because its readout noise is below 1 e$^-$ rms, the detector enables accurate counting of individual photon detection events, allowing shot-noise-limited detection in the low-photon regime. In addition, its readout time is faster than that of a CCD. Consequently, qCMOS-based systems are expected to provide higher sensitivity and faster acquisition than CCD-based systems.

To evaluate SNR, we compared a qCMOS-based system with a conventional CCD-based system using EdU-labeled HeLa cells as a weak Raman signal sample. The EdU Raman band was observed at 2121 cm^{-1}. Figure 1(a) shows Raman spectra obtained by the qCMOS- and CCD-based system. Raman images were reconstructed using differences of photon count between 2121 and 2145 cm^{-1} measured by the qCMOS-based system (Fig. 1(b)) and CCD-based system (Fig. 1(c)). The qCMOS-based system provided higher contrast of EdU-labeled nuclei. Because the qCMOS has a smaller pixel size than the CCD, pixel binning was applied to match the pixel size. Despite binning, which generally accumulates readout noise, the qCMOS-based system achieved a higher SNR (1.2) than the CCD-based system (1.0). The total measurement times were 961 s and 2184 s for the qCMOS- and CCD-based systems, respectively. These results demonstrate the benefit of incorporating two-dimensional photon-counting detectors in line-illumination Raman microscopy for weak signal detection with high sensitivity.

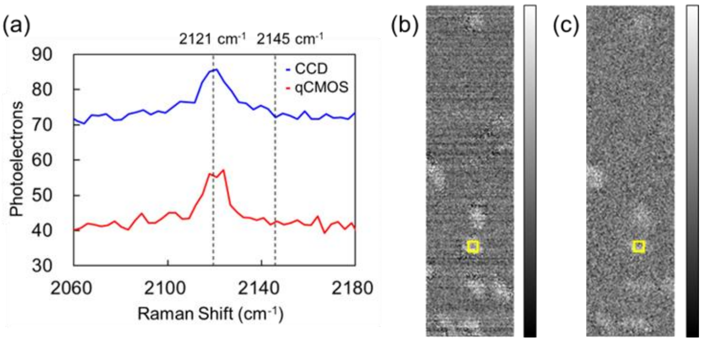

Figure 1 (a) Raman spectra of EdU-labeled HeLa cells obtained using a CCD- and a qCMOS-based system. These Raman spectra averaged over the rectangular regions in Fig. 1(b) and 1(c). (b) Raman image obtained using qCMOS-based system (c) Raman image obtained using CCD-based system.

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[1] Y. Kumamoto, M. Li, K. Koike, K. Fujita, *Jornal of Applied Physics*, **132** (2022) 171101.

Georgina Charlton – Keynote

Using Single-Cell Proteomics to Analyse DNA Damage Response in Cells Using the Thermo Orbitrap Astral

Georgina Charlton[1], Riccardo Chiozzi Zenezini[1,3], Jonathan Ditcham[1], Jenny Ho[3], Konstantinos Thalassinos[1,2*]

1. Institute of Structural and Molecular Biology, University College London, London, UK. 2. UCL Mass Spectrometry Science Technology Platform, University College London, London, UK. 3. Thermo Fisher Scientific, Hemel Hempstead, UK.
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KEY WORDS: Single-Cell Proteomics, DNA Damage, Orbitrap Astral

Single-cell proteomics has become possible in recent years due to advancements in cell isolation techniques and more sensitive mass spectrometers. Single-cell technologies have the potential to significantly enhance our understanding of different cell types within complex biological systems, vastly improving the resolution with which protein behaviour within a cell can be characterised and linked to phenotypic behaviour.

Using single-cell proteomics and inducing DNA damage, we analysed changes in the proteome of cells, which can lead to a better understanding of how cells respond to neurodegenerative diseases, such as Huntington's Disease where DNA damage is implicated.

When DNA damage was induced and analysed by bulk proteomics, DNA damage response pathways were not enriched. This is most likely because bulk measurements average across all cells in the sample, meaning that dead or non-responsive cells can mask the DNA damage response in other cells. In contrast, single-cell analysis revealed clear upregulation of three DNA damage pathways, mismatch repair, base excision repair, and nucleotide excision repair, with nucleotide excision repair showing the strongest enrichment.

We found that 6TG caused S-phase arrest. Because the analysis was performed at the single-cell level, we were able to identify control cells that were also in S-phase and directly compare cells at the same stage of the cell cycle. This ensured that the observed protein changes were not confounded by differences in cell cycle stage. Several significantly altered proteins were identified, consistent with S-phase arrest and a transition from proliferation to a survival state.

Overall, single-cell analysis enabled a more detailed characterisation of 6TG-induced DNA damage than is possible with bulk proteomics, providing deeper insight into cellular stress responses and demonstrating that single-cell approaches are essential for analysing cell responses to treatment.

Session 4B – IRDG Martin & Willis
in NEWMAN GREEN (Chair: Prof Chris Sammon)

Jorge Servert (SXT31)

Smartphone-Sized Diagnostic for the Most Common Cause of Pediatric Neurosurgery

Jorge Servert Lerdo De Tejada[1*], **Derren J. Heyes**[2], **Shumaila Chaudhry**[3], **Shahid Iqbal**[4], **Naima Mehdi**[5],
Danylo Komisar[6], **Oleksii Ilchenko**[6] **& Jaleel A. Miyan**[1*]

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**Presenting Author: jorge.servertlerdodetejada@manchester.ac.uk;* `https://www.linkedin.com/in/jorge-a-servert/`

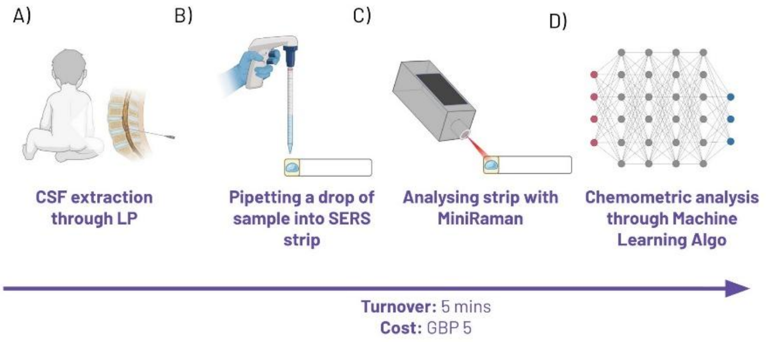
KEY WORDS: SERS, machine learning, hydrocephalus.

Hydrocephalus is a severe neurological disorder marked by cerebrospinal fluid (CSF) accumulation in the brain's ventricles, causing elevated intracranial pressure, neurological deficits, and substantial societal and medical costs. Rapid detection in neonates and children remains challenging, as primary diagnostic indicators such as increased head size often manifest late, delaying intervention.

Hydrocephalus stems from diverse causes, including prematurity, intracranial bleeds, CNS infections, and brain tumours. CSF collected for diagnostic purposes provides an opportunity to explore innovative rapid detection methods. In this paper, we show that integrating Surface-Enhanced Raman Spectroscopy (SERS) and machine learning offers a novel molecular diagnostic tool for hydrocephalus.[1]

Using silver nanoparticle-layered-cellulose strips as SERS substrates and a portable Raman spectrometer, we analysed CSF samples from 117 patients (70 controls, 47 hydrocephalus cases). Within 5 min of sample placement in strip, the optimized Random Forest algorithm achieved 97% accuracy in blind testing, with 100% specificity and 95% sensitivity. The miniaturized Raman spectrometer and standarised strips enable portability and support clinical use, particularly in resource-limited settings.

Our grid search-based ML workflow and scoring system enable the prediction of overfitting, as well as assessment of feature importance within the spectra, improving model interpretability, which could prove helpful in other vibrational spectroscopy applications. Overall, this study provides evidence of an accurate, rapid, portable, and interpretable diagnostic technique for hydrocephalus. Further validation with larger cohorts will refine predictive models and expand clinical utility, advancing diagnostic precision for hydrocephalus and related neurological conditions.



Enter Caption

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[1] Servert Lerdo De Tejada, J., Heyes, D.J., Chaudhry, S. et al. Surface enhanced Raman spectroscopy and machine learning as an accurate and rapid diagnostic tool for hydrocephalus. *Sci Rep* **16**, 2659 (2026). `https://doi.org/10.1038/s41598-025-32177-6`

Aidan Morton (SXT33)

Using vibrational spectroscopic imaging to understand drug release from hydrophilic matrices.

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KEY WORDS: MIR ATR Imaging, Spectroscopy, Multivariate Analysis.

Pharmaceutical tablets are typically made by compacting a blended combination of an active pharmaceutical ingredient (API), binder and other excipients such as fillers, pH modifiers or disintegrants. The distribution of these components within the tablet ultimately determine how it will perform.

In this study we have used a combination of NIR spectroscopy coupled with partial least squares (PLS) analysis and Raman point mapping to characterise the composition and distribution of components within tumble-blended trinary mixtures of HPMC, weak acid (citric acid and cystine HCl) and API (itraconazole and fluconazole).

ATR-FTIR imaging has been used to monitor, *in situ* and in real-time, the influence that hydration media (water and simulated GI fluids) has on the gelation and API migration from these tablets, simulating their behaviour within the body.

We have observed that hydration rates and API migration kinetics are both highly dependent on tablet composition. Hydration of HPMC based tablets appears to be pH independent. The addition of highly soluble excipients to tablets leads to faster hydration. More soluble APIs are observed to migrate faster from the tablet matrix, whilst the addition of pH modifiers has a modest impact on the migration of sparingly soluble API.

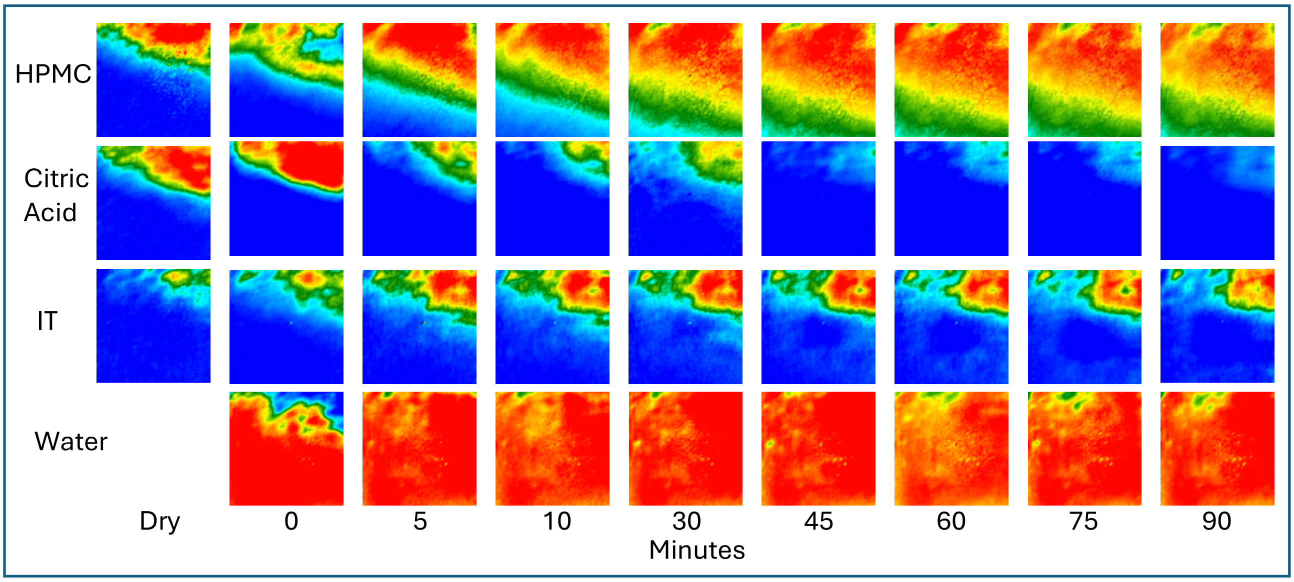

Figure 1 – Imaging Data Example

Nitin Patil (SXT37)

Monitoring cellular glycolysis pathway kinetics using high content Raman spectroscopy

Nitin Patil[1,2,3], Zohreh Mirveis[1,2], Hugh J Byrne[1], Nitin Patil*

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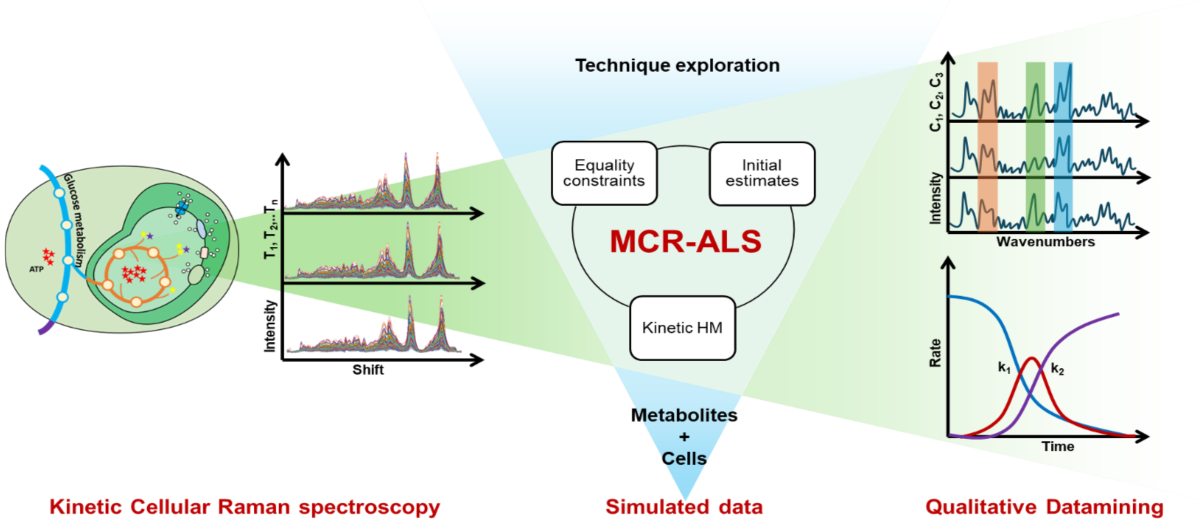
KEY WORDS: Raman spectroscopy, multivariate curve resolution- alternating least squares, metabolic pathway kinetics

The potential of Raman spectroscopy to elucidate cellular glycolysis pathway kinetics was explored in this study. A549 cells were cultured in an unbuffered minimal medium with glucose as a sole carbon source under three modulated conditions Control, Stimulation (oligomycin) and Inhibition (2-deoxyglucose), and thirty cell spectra were acquired for each time point from three biological replicates.

Partial least squares discriminant analysis (PLS-DA) resolved the different timepoints for individual metabolic condition with an accuracy of >85% in all cases. It was observed that the analysis could not resolve different modulated conditions in the complex cell soup, however, given the most prominent contributor to the spectrum was the cell itself.

The data was further regressed using multivariate curve resolution-alternating least squares (MCR-ALS) toolbox which revealed the challenges associated with datamining complex cellular data. Simulated cellular data was generated to mimic the experimental dataset to explore the bottlenecks of the toolbox in a controlled manner. The simulated data was used to explore the inbuilt constraints and a datamining pipeline using specific constrains for complex cellular data was optimised. The experimental data showcased similar results and the datamining pipeline was validated. The resolved components from the cellular data captured the effect of the modulations on the cellular metabolism. Furthermore, since the approach was label-free in nature, a spectral fingerprint of a processes not affiliated with the pathway modulations was also captured, highlighting the significance of label-free kinetic spectroscopy.

This study aims at pushing the limits of vibrational spectroscopy and finds applications in high-content drug screening/ drug discovery, disease diagnostics and monitoring cellular bioprocesses in real-time for enhancing the process efficiency. Additionally, this approach augments the present gold standard approaches for kinetic metabolic analysis.



Amy Colleran (SXT32)

Analysing Volatile Organic Compounds (VOCs) with SERS by Bubbling into Colloidal Silver or Gold Nanoparticles

A. Colleran*[1], **N. Gotts**[1] , **S. Murray**[2], **A. Millichope**[2], **R. Goodacre**[1]
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KEY WORDS: SERS, VOCs detection

The analysis of volatile organic compounds (VOCs) and other gaseous molecules by surface enhamced Raman scattering (SERS) is of high interest due to the ability to perform real-time analysis with portable Raman devices enabling quicker measurement in comparison to laboratory-based techniques such as mass spectrometry. To facilitate this process, numerous solid SERS substrates have been developed and applied across multiple fields. Nevertheless, solid SERS substrates may require complex fabrication due to poor adsorption of gases onto solid surfaces. This can lead to high production costs and inconsistencies in sensitivity and reproducibility. In comparison, colloidal nanoparticles are facile to make and can be cheaper, and there are established methods for synthesis. This has made them easier to implement across a range of fields. Consequently, a simple method has been developed whereby gaseous analytes are bubbled directly into colloidal nanoparticles. This was achieved by pumping air into a flask containing the analyte, which in turn was bubbled into a vial containing nanoparticles and measured with a portable Raman spectrometer. Initially, 3-mercapto-hexanol (3MH) was successfully measured with hydroxylamine-stabilised silver nanoparticles (hAgNPs) using this method. 3MH was then used to optimise the flow rate of the air by testing at 2, 4, 5, 6, 8, 10, 20 and 50 mL.min^{-1}. The results from this indicated that flow rate had an impact on the timing of the appearance of the spectrum of the analyte and the rate of change in peak height at 634 cm^{-1} (ν(C-S) band) for 3MH. The most reproducible results were seen with 50 mL.min^{-1}. The technique was further tested with two other analytes: 2-methyl-3-mercapto-pentanol (2M3MP) and indole, with indole being tested with the subsequent addition of an aggregating agent (NaCl) to the nanoparticles. The results from this study show promise for this method as a different way to detect gaseous analytes using colloidal nanoparticles.

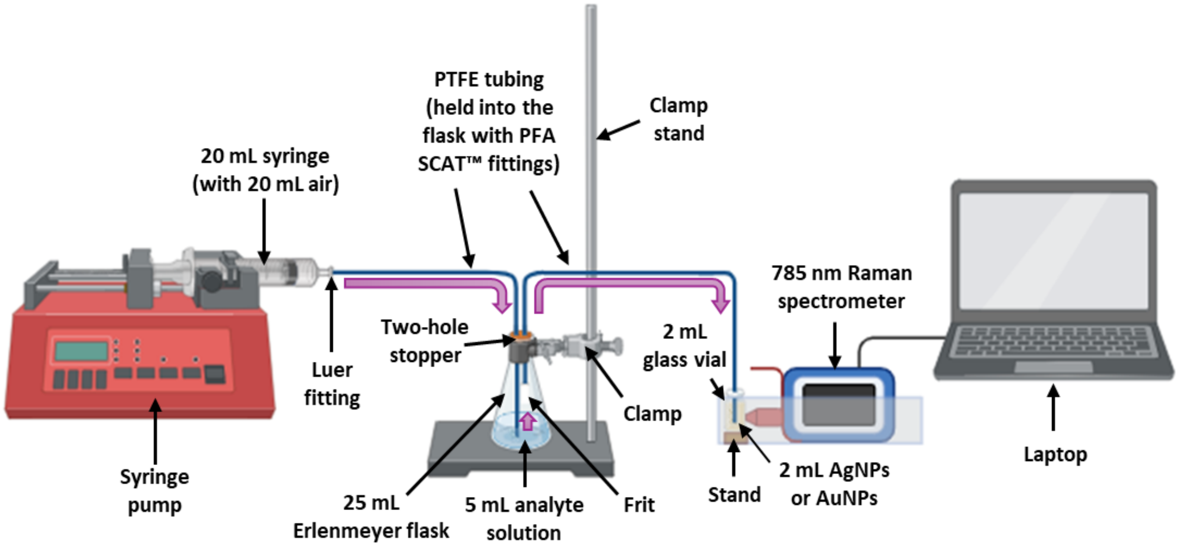

Figure: Illustration of method used to bubble gaseous analytes into colloidal nanoparticles where the purple arrows indicate the direction of gas flow. Figure created with Biorender.com.

Anna Zetterstrom (SXT34)

Preliminary Investigation into Multimodal Imaging of Renal Tissue using Infrared, Raman and Mass Spectrometry

A. Zetterström*[1,2], **N. Lockyer**[2,3], **P. Gardner**[1,2]
1 Department of Chemical Engineering, Faculty of Science and Engineering, University of Manchester, Oxford Road M13 9PL United Kingdom
2 Photon Science Institute, University of Manchester, Oxford Road M13 9PL United Kingdom
3 Department of Chemistry, Faculty of Science and Engineering, University of Manchester, Oxford Road M13 9PL United Kingdom
**anna.zetterstrom@manchester.ac.uk*

KEY WORDS: FTIR, QCL, O-PTIR, SRS, DESI, imaging, tissue

Chemically specific imaging techniques, such as vibrational spectroscopy and mass spectrometry imaging (MSI) applied to biological tissue have seen an increasing interest in recent years. Multimodal imaging combining these techniques across spatial scales generates complimentary information, promising a better understanding and explainability of the chemistry of the tissue[1]. In this work we have used both vibrational spectroscopy and mass spectrometry-based modalities to provide chemical maps ranging from the micron to sub-micron scale on renal cancer tissue. Fourier-transform infrared (FTIR) imaging and quantum cascade laser infrared (QCL-IR) imaging enable rapid, label-free assessment of broad chemical distributions at micron resolution, while optical photothermal infrared (O-PTIR) and stimulated Raman scattering (SRS) imaging provide sub-micron spatial resolution. These vibrational techniques are complemented by desorption electrospray ionization mass spectrometry imaging (DESI-MSI), which delivers molecularly specific information on lipids, metabolites, and other small molecules from the tissue, but at significantly poorer spatial resolution, see figure 1. Here we discuss the challenges associated with multimodal analysis with greatly differing spatial resolution and dynamic range. We assess analysing different data individually and combining results compared to analysing the combined data. The results are discussed in terms of explainable AI and increased diagnostic accuracy.

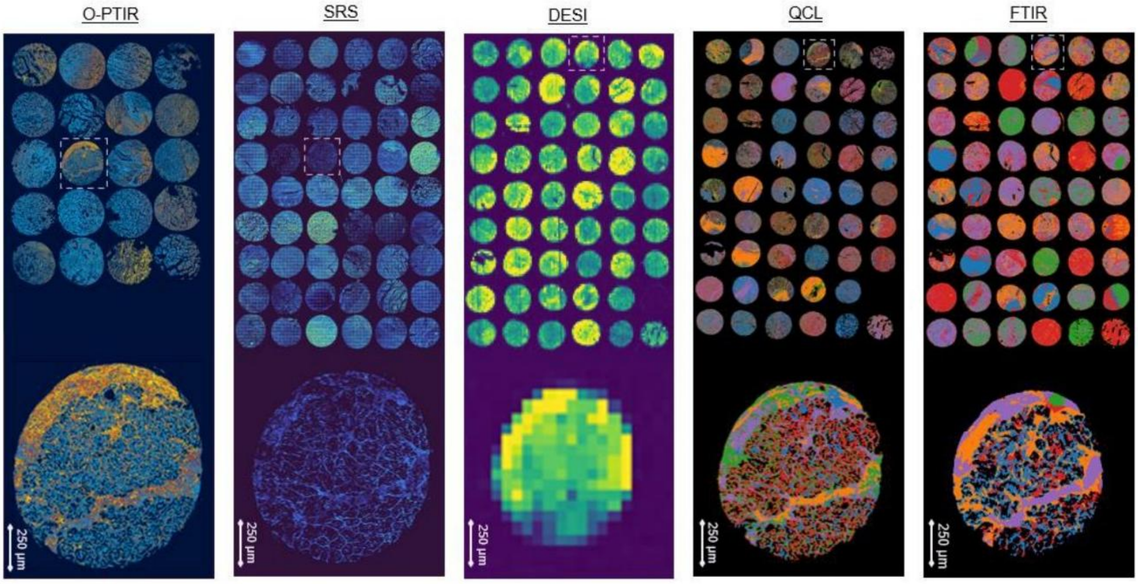

Figure 1. Comparison of O-PTIR, SRS, DESI, QCL and FTIR imaging

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[1] A Zetterström, N Lockyer and P Gardner, *Applied Spectroscopy Reviews.* **60** (2025) 710-734

Jana Galina Hofmann (SXT35)

The Optical Nose: Monolayer sensitisation of Au surfaces for plasmonic gas sensing

Jana G. Hofmann*[1], **Elle Wyatt**[1], **Sarah May Sibug-Torres**[1], **Marika Niihori**[1], **James W. Beattie**[1], **Tabitha Jones**[1], **Nicolas Spiesshofer**[1], **Bart de Nijs**[2], **Jeremy J. Baumberg**[1]

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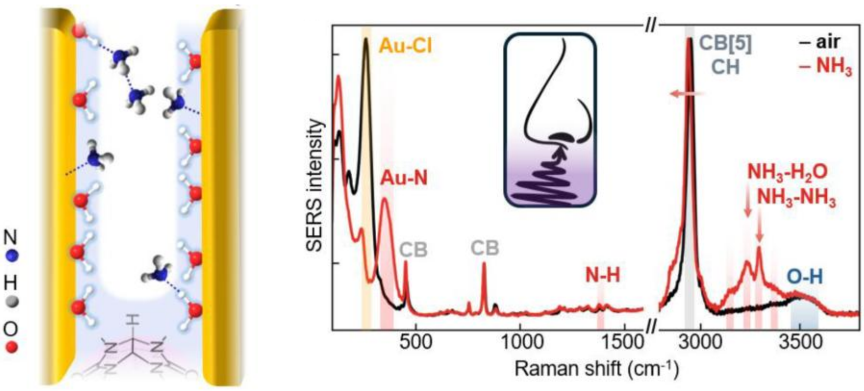
KEY WORDS: SERS, gas sensing, monolayer sensitisation

Robust real-time gas sensing is essential for fields ranging from agritech to medical breath analysis. Ammonia, a key biomarker for kidney disease and a significant environmental pollutant, is typically present at ppb to ppm levels. However, current detection technologies such as GC-MS are limited by high costs, complexity, and slow measurement times.

Our work demonstrates a dramatic improvement in surface-enhanced Raman spectroscopy (SERS) for gas detection. We demonstrate a robust gas-phase sensing platform utilizing reusable multilayer aggregates (MLaggs) of 80 nm gold nanoparticles. These substrates are self-assembled using cucurbit[5]uril (CB[5]) molecular scaffolds to create precise, sub-nanometer (0.9 nm) hotspots that provide significant electromagnetic enhancement. Through precision plasma precleaning protocols we remove all organic surfactants and contaminants, allowing for the surface-sensitization of metal facets using a persistent water monolayer.[1-3]

This 'optical nose' platform enables sub-ppm detection of ammonia at room temperature.[4] By also accessing the high-wavenumber (>2500 cm^{-1}) region, we observe N-H, C-H, and O-H vibrations that provide enhanced discriminatory capabilities. This approach is generalized to a variety of volatile organic carbon (VOC) molecules, including ethanol, methanol, and acetone, which are distinguished by their unique C-H vibration lines. The sensor achieves a dynamic range of over five orders of magnitude and demonstrates high reproducibility with a relative standard deviation (RSD) of ~5%.[1] This methodology offers a low-cost, real-time alternative for high-sensitivity trace gas analysis without the need for preconcentration.



Schematic of nanogap, identifying different ammonia interactions with the water monolayer and with the Au facets (left). SERS spectrum of the MLagg in air (black) and in ammonia vapour (red), showing appearance of peaks characteristic to ammonia (right).

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[1] Grys, et al, *J-Raman Spect.*, **52** (2021) 412-419.
[2] Grys et al, *ACS Sensors,* **8** (2023) 2879-2888.
[3] SM Sibug-Torres et al, *Nat Comm.,* **15** (2024) 2022
[4] E. W. Wyatt et al, submitted (2025)

Zachary Douglas (SXT36)

Improving the Transferability of Calibration Models Between Varying ATR-FTIR Instruments

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KEY WORDS: FTIR-ATR Spectroscopy, Calibration Transfer, Spectral Corrections.

Process Analytical Technology (PAT) is important as it provides real-time process understanding and control. In process analytics, quantitative predictive models applied to spectral data are used to analyse and predict the composition and properties of media in the manufacturing environment. Calibration transfer refers to the ability to apply a chemometric model developed on one instrument to another, which may be a different type, vendor or configuration, without rebuilding the model from scratch. This ensures model robustness across instruments, reduces cost and time, supports scalability and multi-site manufacturing and maintains measurement accuracy. This issue is particularly prominent for quantitative models developed using FTIR-ATR spectroscopy, a common process analytical tool. When coupled with an FTIR-ATR probe for in situ and process monitoring, errors can be as high as 10%. Calibration transfer in mid-infrared process analysis using chemometric approaches, by applying standardisation techniques (e.g. DS, PDS and SST) has been previously investigated.[1]

We have investigated this key industrial problem by utilizing the technique developed by Hore and co-workers,[2] to calculate the angle of incidence and degree of polarisation which, when informed by other recent studies,[3] and combined with chemometric approaches can be used to standardise the data collected between each configuration. We show the key importance of correcting for the variation in these parameters in the calibration process.

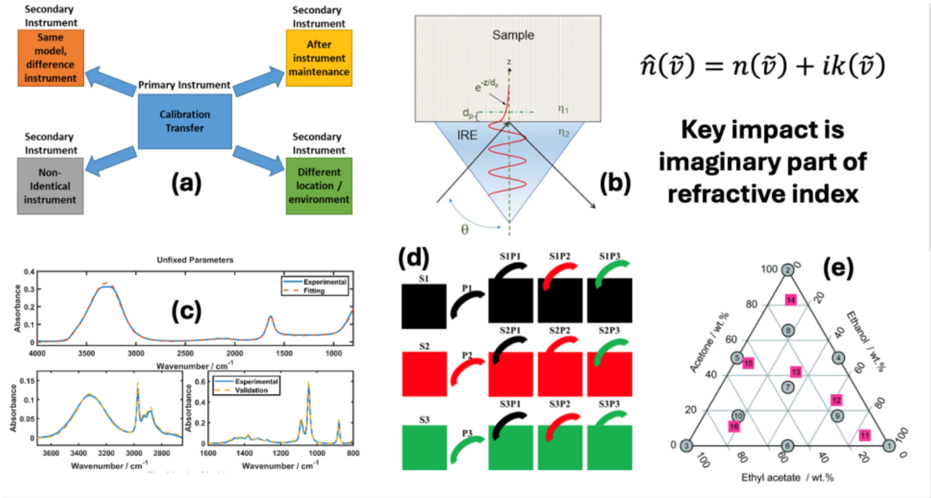

Figure 1. (a) The possible scenarios that require calibration transfer. (b) Diagram of a single reflection FTIR-ATR set-up with the complex refractive index equation, adapted from literature.[4] (c) Utilisation of the technique developed by Hore and co-workers on a single reflection FTIR-ATR set up. (d) The possible ReactIR spectrometer / FTIR probe configurations that were used in this work. (e) Concentration diagram of samples for a predictive model, adapted from literature.[1]

We thank EPSRC and Mettler Toledo AutoChem for support and the technical staff at Nottingham for their help

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[1] A.J. Parrott, A.C. McIntyre, M. Holden, G. Colquhoun, Z.P Chen, D. Littlejohn and A. Nordon, *Anal. Methods*, 2022, **14**, 1889-1896

[2] M. S. Azam, M. D. Ranson and D. K. Hore, *Appl. Spectrosc.*, 2022, **76**, 1254–1262.

[3] T. G. Mayerhöfer, W. D. P. Costa and J. Popp, *Appl Spectrosc.*, 2024, **78**, 321–328.

[4] M E. V. Miseo and P. J. Larkin, *Appl. Spectrosc. Pract.*, 2025, **3**, 27551857251336262.

Clearing Enhanced Vibrational Imaging of 3-Dimensional Tumour Models

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Centre for Nanometrology, Department of Pure and Applied Chemistry, Technology and Innovation Centre, The University of Strathclyde,
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KEY WORDS: SRS, spheroids, 3D imaging

Raman imaging of drug distribution and effect in cancer cells has been extensively documented using many different types of Raman scattering.[1] Imaging has largely been limited to 2-dimensional focal planes of cells which often give a good approximation of drug uptake and effect, but when moving to *in vivo* models, unacceptable toxicity or uptake is observed.[2] To counteract this, 3-dimensional cellular models - multicellular tumours spheroids (MTS) - have been developed to more accurately emulate the tumour microenvironment, but these have significant challenges.[2] Apart from the synthesis of MTS, often requiring specialised equipment and reagents, there is the problem of poor laser penetration caused by high scattering of light through high refractive index cellular components. Many clearing techniques have been developed to mitigate this problem, but require harsh conditions including dehydration, delipidation, and immersion in high refractive index organic solvents. These solvents also often contain C-H vibrations which will interfere with endogenous C-H vibrations in lipids and proteins.[3] This work uses urea as a clearing agent, as it has no C-H vibrations that will interfere with endogenous C-H vibrations, whilst having an appropriate refractive index to effectively clear, allowing for deeper imaging. This work also compares the distribution of a selection of molecules which contain alkynyl moieties that can be used for bio-orthogonal Raman imaging in both 2D and 3D models. Spectral phasor analysis was also employed to assess differences in spectral profiles of control and drug treated models.

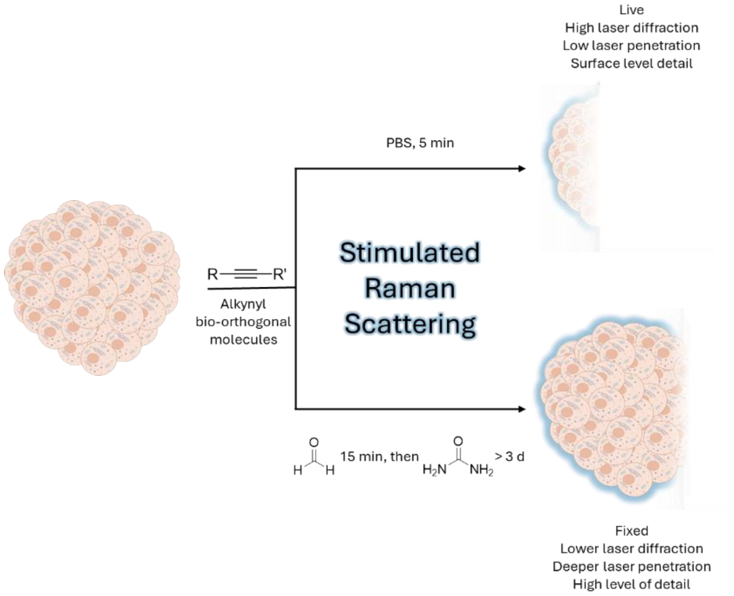

Figure 1: Clearing enhanced stimulated Raman imaging allows for high imaging penetration into MTS and allows for minimally labelled visualisation and localisation of exogeneous and endogenous molecules.

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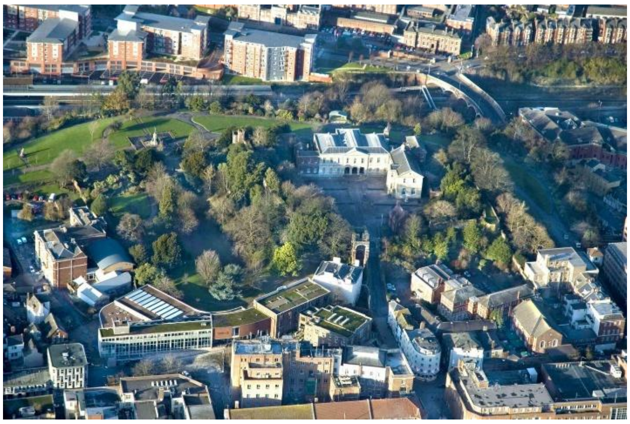
[1] W. J. Tipping, M. Lee, A. Serrels, V. G. Brunton and A. N. Hulme, *Chem. Soc. Rev.*, 2016, **45**, 2075-2089.
[2] S. Breslin and L. O'Driscoll, *Drug Discov. Today*, 2013, **18**, 240-249.
[3] J. Seo, M. Choe and S.-Y. Kim, *Mol. Cells*, 2016, **39**, 439-446.

Gala Dinner
(18:45-23:30)

Please note, we regret that due to the historic nature of this venue, it is not a fully accessible venue, please contact a member of the team at springscix-conf@exeter.ac.uk for further details.

NOTE You must have registered for the conference by 16th March to be able to attend the Gala dinner



Day 3 – Thursday 16th April

Parallel Session 5
(09:30-11:00)
Session 5A – Biomedical Raman Imaging 2
in NEWMAN BLUE (Chair: Dr Renzo Vanna)

Katsumasa Fujita – Keynote

Cryogenic Raman Microscopy for Resonance-Enhanced Molecular Imaging of Biological Systems

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**fujita@ap.eng.osaka-u.ac.jp, https://photon-ap.eng.osaka-u.ac.jp*

KEY WORDS: Raman microscopy, rapid freezing, resonant Raman scattering

Raman microscopy enables molecularly specific, label-free imaging of biological samples based on vibrational fingerprints of chemical bonds. While recent advances have expanded its analytical capabilities, Raman imaging of living cells remains limited by photodamage and photobleaching, particularly when exploiting resonant Raman scattering from endogenous chromophores. Biomolecules such as cytochromes and carotenoids exhibit strong electronic absorption in distinct spectral regions, requiring multiple excitation wavelengths to maximize resonance enhancement and chemical contrast[1,2]. However, repeated multi-wavelength illumination in live cells rapidly perturbs molecular states and degrades samples, restricting sensitivity and chemical reliability.

To overcome these limitations, we used a cryogenic Raman microscopy platform that enables chemically faithful imaging under cryogenic conditions[3]. Low-temperature operation allows longer signal integration times and higher excitation powers without inducing photobleaching or photochemical damage. An on-stage rapid cryofixation method enables *in situ* freezing, preserving physiological and chemical states while minimizing sample handling artifacts[4]. This approach permits sequential Raman imaging with multiple excitation wavelengths, enabling selective enhancement of cytochromes, carotenoids while non-resonant Raman signals provide complementary information on intracellular biomolecules. Cryogenic stabilization suppresses molecular state alteration, allowing repeated wavelength switching and prolonged data acquisition.

We demonstrate multimodal Raman imaging of HeLa cells and cardiomyocytes, revealing spatial distributions of respiratory chain cytochromes, carotenoids, and Raman-tagged biomolecules with high signal-to-noise ratios. These results establish cryogenic Raman microscopy as a powerful analytical strategy for high-sensitivity, resonance-enhanced molecular imaging in complex biological systems.

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[1] Okada, M. et al., *Proc. Natl. Acad. Sci. USA*, **109** (2012) 28-32.
[2] Li, M. and Nawa, Y. et al., *Commun Biol,* **5** (2022) 1-11.
[3] Mizushima, K. et al., *Sci. Adv.,* **10** (2024) eadn0110.
[4] Tsuji, K. and Yamanaka, M. et al., *Light Sci. Appl.,* **14** (2025) 275.

Ellie Hansen (SXT07)

Imaging and detecting PM2.5s in the brain, and exploring their role in neurodegenerative disease

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**ellie.hansen@ed.ac.uk, https://www.horrockslab.org*

Keywords: Pollutants, Parkinson's Disease, Raman spectroscopy

Abstract

Environmental factors, including exposure to pollutants, are increasingly linked to an increase in risk of developing Parkinsons Disease (PD)[1]. PM2.5s are super-fine pollutant particles that are released as 'burning' emissions, for example, from internal combustion engines, wood burners, or from industrial processes[2]. While international health studies have shown there is a correlation between living in areas more highly polluted PM2.5s and an increase in risk of developing PD, we have yet to understand the mechanism behind this effect[3]. By imaging and detecting PM2.5s in the brain, using Raman spectroscopy, as well as other fluorescent microscopy techniques, we will elucidate the mechanism by which exposure to PM2.5s leads to neuronal loss. We have shown that PM2.5s can be detected by their characteristic spectra using Raman spectroscopy, and by developing new methods, we aim to identify the location of PM2.5s in various tissues, particularly the brain, in mouse models. Additionally, by using fluorescent plastic nanoparticles of the same diameter as PM2.5s as a model, we will address questions about 'microplastics' and their dispersion in tissues. Overall, this work will look more deeply into what size and type of particles can pass into the brain by using Raman spectroscopy, and interrogate particle interaction with cells within the brain.

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Eric Michele Fantuzzi (SXT08)

Single-Shot Multiplex SRS: From Tissue to Microplastics

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KEY WORDS: Multiplex SRS, hyperspectral chemical imaging, FFPE tissue imaging, Microplastic identification, Virtual staining and segmentation

Stimulated Raman Scattering (SRS) microscopy lets us map the chemical composition of samples without labels or stains. Standard dual-band C–H systems, which measure only around 2845 and 2930 cm^{-1}, can tell lipids and proteins apart, but they don't capture enough spectral information to reliably identify different polymers or subtle biochemical changes in tissues. That makes them unsuitable for detailed microplastic detection in flow setups or complex tissue, and limits stain-free histology.

We built a multiplex SRS setup using an all-fiber, double-wavelength self-synchronized laser with a compact multichannel lock-in amplifier. This lets us capture the full C–H region in a single shot, down to 2 μs per pixel. With this setup, we can automatically detect, classify, and map microplastic size distributions on slides or in flow cells. In tissues, it distinguishes residual paraffin from biomolecules, enabling stain-free virtual histology and quantitative segmentation.

By combining the SRS data with clustering and machine learning, we produce reproducible, high-throughput chemical maps without any labeling. While our main focus so far has been tissue imaging, the system is flexible and could be applied to a range of samples. It also sets the stage for future studies on microplastics in biological tissues, letting us explore particle distribution without altering sample preparation.

This approach brings together fast imaging and chemical insight in one shot, and could support both materials research and ex-vivo histology in a standardized, high-throughput way.

Mako Kamiya – Keynote

Mako KActivatable Raman probes for multiplexed bioimaging

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KEY WORDS: resonance Raman probes, SRS, live cells

Raman probes based on alkyne or nitrile tags hold promise for highly multiplexed imaging. In order to functionalize the Raman probes, we have established a general strategy to control Raman signals intensity based on the resonant Raman effect, which exhibits enhanced stimulated Raman scattering (SRS) signals upon reaction with enzymes or by photoirradiation. First, by optimizing the xanthene derivative bearing a nitrile group at 9th position, we developed activatable Raman probes for detecting enzyme activities and succeeded in simultaneous imaging of different enzyme activities with different vibrational frequencies in live cells.[1] We also expanded the molecular design by combining the resonant Raman effect and aggregate formation to develop new series of activatable Raman probes for enzymes using rhodol as a scaffold. The developed probes show increased SRS signal intensity and high aggregate-forming ability after enzymatic activation, resulting in good retention in target cells, which enabled us to distinguish target cell regions in live Drosophila tissues.[2] We also developed a photoswitchable Raman probe based on diarylethene scaffold which exhibits SRS signal activation upon UV light irradiation and SRS signal depletion upon visible light irradiation with the transition between closed and open form. We demonstrated that the spatial resolution has been improved in combination of the photoswitchable Raman probe and RESORT (REversible Saturable Optical Raman Transitions) microscopy, which has been devised by Prof. Ozeki group (UTokyo) by introducing two additional CW lasers to SRS microscopy to regulate the SRS signal of photoswitchable Raman probe.[3] In this presentation, I would like to introduce our molecular design strategy and their application to live cells and tissues, together with our recent effort.

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Session 5B – Process Analytical Control/Industrial Applications in NEWMAN GREEN (Chair: Georgina Charlton)

Lucy Flint – Keynote

Mapping Tissue Pharmacology and Metabolism from Discovery to Translation with Mass Spectrometry Imaging

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KEY WORDS: Spatial metabolomics, biomarker discovery, multimodal integration

Advances in spatial metabolomics by mass spectrometry imaging (MSI) are reshaping how we interrogate heterogeneous tissues. MSI enables label-free, spatially resolved detection of metabolites, lipids, and drugs directly from tissue, providing molecular maps that support target identification, biomarker discovery, and mechanism-of-action studies across drug development and disease characterisation. Aligned with histopathology and quantitative image analysis, MSI localises pathway and pharmacological signatures to discrete anatomical or cellular niches, sharpening interpretation of exposure, distribution, and pharmacodynamics.

We have demonstrated MSI's utility across discovery and translation. In advanced cell models, we developed a high-throughput imaging workflow to profile metabolic responses to standard-of-care chemotherapy in naïve and resistant osteosarcoma, revealing treatment-associated phenotypes[1]. In animal studies, high-resolution MSI combined with histology resolved drug biodistribution across retinal layers in a rat model, informing localisation and functional implications[2]. In pancreatic ductal adenocarcinoma models, we characterised disease-associated metabolism and distinguished molecular patterns between responsive and resistant mouse cohorts[3]. In patient-derived samples, we utilised MSI to spatially profile prostate cancer biopsies, linking metabolite localisation with histopathological features and supporting identification of translational biomarkers for aggressive subtypes[4,5].

Building on these examples, we have deepened biological insight by complementing MSI with other spatial and analytical technologies. Imaging mass cytometry (IMC) delivers high-plex protein phenotyping of cell states and immune contexture, spatial transcriptomics (ST) captures gene expression that contextualises MSI-derived metabolic signatures, and liquid chromatography-mass spectrometry (LC-MS) provides orthogonal, quantitative profiling to validate and extend molecular findings. Integrating MSI and histology with IMC, ST, or LC–MS yields a layered view of tissue biology that unites molecular identity, pathway activity, and cellular composition, strengthening mechanistic interpretation across models and patient-derived samples.

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Jorge Diniz (SXT47)

Characterization of Li-based battery materials using *in situ* colocalised Raman and SEM analysis

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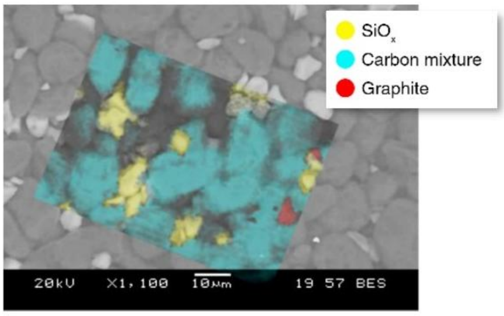
KEY WORDS: Raman in-SEM; correlative Raman analysis, battery materials

The high demand for energy storage solutions and the decrease in fossil-fuel dependency has driven the need to improve the performance, safety and lifetime of battery systems, such as lithium-ion batteries. The properties of Li-based batteries are governed by multiscale phenomena such as porosity, particle fracture, binder homogeneity and interphase transformations during de/sorption of Li ions, to name a few.[1] Therefore, understanding the link between morphology and chemistry across length scales can enable the engineering of more durable, stable and higher capacity battery systems.

Correlative SEM and Raman analysis co-registers the structural and spectroscopic information for enhanced understanding of batteries. Scanning electron microscopy (SEM) offers high-resolution insights into particle size distributions and morphology, porosity, and interfacial properties, while Raman spectroscopy provides non-destructive identification of polymorphs, quantifies carbon quality (D/G bands), detects stress and local bonding environments, and probes the state of lithium and metal oxide species.[2] However, it is difficult to perform both analyses in the same regions-of-interest when using separate instruments. Furthermore, the active materials are susceptible to degradation when exposed to the atmosphere, requiring specialised sample transferring between instruments.

Here, we present results demonstrating the benefit of integrating Raman spectroscopy into an SEM chamber, enabling colocalised and simultaneous Raman and SEM imaging without the need to move or transfer the sample. Due to the precise spatial correlation between modalities, this enables a rapid and comprehensive approach for component identification, process control, and failure analysis, with the intent to accelerate the optimisation of Li-ion battery materials.



Correlative SEM and Raman images of a carbon-coated battery anode illustrating the distribution of different forms of carbon and silicon.

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William Leigh (SXT49)

Optimizing Powder Classification Efficiency: A Synergistic Approach Using Laser Diffraction and Dynamic Image Analysis

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KEY WORDS: Laser Diffraction, Dynamic Image Analysis, Powder Classification

Powder classification is a pivotal unit operation across diverse industries, ranging from pharmaceuticals to ceramics, where controlling particle size distribution (PSD) directly impacts final product quality and process efficiency. The objective of this process is twofold: ensuring the complete removal of oversize particles that could cause defects, while simultaneously minimizing the loss of valuable fine product into the coarse reject stream. Accurately characterizing this separation efficiency—specifically confirming the absence of coarse aggregates and quantifying the entrainment of fines—is critical for maximizing yield and ensuring specification compliance.

In this study, we present a comprehensive analytical framework for evaluating classification performance by integrating Laser Diffraction (LD) and Dynamic Image Analysis (DIA). We compared the PSDs of feed, fine, and coarse fractions to assess the cut point and separation sharpness.

Laser Diffraction, generating a volume-based distribution, proved essential for quantifying the bulk movement of the mass and identifying the proportion of fines misclassified into the coarse fraction. However, its sensitivity to trace amounts of oversize particles can be limited when the primary mass resides in the fine fraction. Conversely, Dynamic Image Analysis provides a number-based distribution that offers exceptional sensitivity to the coarse end of the spectrum. Our results demonstrate that DIA is well-suited for clearly visualizing the tail fragmentation of large particles and for identifying the presence or absence of oversized particles—a detail often obscured in volume-based data.

By combining the global volumetric perspective of LD with the high-resolution sensitivity of DIA towards outliers, process engineers can obtain a holistic view of classification dynamics. This dual-methodology enables precise optimization of classifier settings, ensuring both the elimination of critical defects and the preservation of product yield.

Classification of Meliaceae and Gymnosperms Timbers using Laser-Induced Breakdown Spectroscopy and Partial Least Squares Discriminant Analysis

María Fernanda Delgado Cornelio[*1], **Erin Pierce**[2], **Skyler Coleman**[2], **Karl S. Booksh**
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KEY WORDS: Laser-Induced Breakdown Spectroscopy (LIBS), Partial Least Squares Discriminant Analysis (PLS-DA), Timber Identification

The U.S. Department of Agriculture Animal and Plant Health Inspection Service (USDA-APHIS) permits the use of Special Use Designations (SUDs) under the Lacey Act when the exact genus or species of imported wood products cannot be determined. While SUDs facilitate trade for visually similar and commonly commingled woods, they may also create opportunities for illegal timber to enter supply chains. Rapid, field-deployable screening methods are therefore needed to support enforcement and risk assessment efforts.

This study evaluates laser-induced breakdown spectroscopy (LIBS) combined with chemometric classification as a screening tool for differentiating timber species commonly subject to SUDs. Two major taxonomic groups were examined: *Meliaceae*, representing high-value tropical hardwoods, and *Gymnosperms*, which include widely used structural softwoods. LIBS spectra were collected from 370 *Meliaceae* lumber samples representing five genera (*Cedrela, Entandrophragma, Khaya, Leplaea,* and *Swietenia*), with two to three species per genus, and from 223 Gymnosperm samples spanning six genera (*Abies, Larix, Picea, Pinus, Pseudotsuga,* and *Tsuga*). Spectral data were preprocessed using baseline correction, unit-area normalization, and variable selection, followed by modeling with partial least squares discriminant analysis (PLS-DA).

Although both datasets represent taxonomically related classification problems, their optimal modeling strategies differed. For *Meliaceae*, a flat model distinguishing all 13 species achieved a Cohen's Kappa of 0.70, while a hierarchical approach, genus-level classification followed by species-level models, improved performance, yielding a genus-level Kappa of 0.89 and species-level values exceeding 0.90. In contrast, the *Gymnosperm* dataset performed well using a flat classifier, separating 11 species with a Kappa of 0.93. These results highlight how family-specific chemistries influence classification behavior and model design. Overall, this work demonstrates the potential of LIBS as a rapid screening method to support enforcement decisions for SUD-regulated timber.

Elizabeth Legge – MSG Duncan Bryant Award Recipient

Non-invasive quantitative chemical measurements of liposomal formulations using Raman spectroscopy

Elizabeth J. Legge*[1], Ryan T. Coones[1], William A. Lee[1], Yiwen Pei[1], Natalie A. Belsey[1,2], and Caterina Minelli[1]
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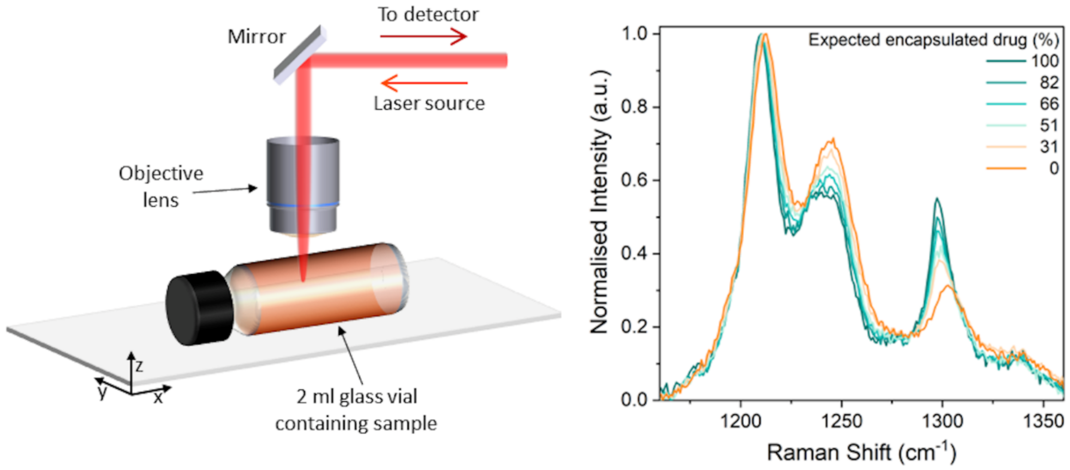
KEY WORDS: Raman spectroscopy, liposomal formulations, nanoparticles

With a growing interest towards low batch-volume personalised medicines and continuous manufacturing of pharmaceuticals, the need for robust non-invasive quality control analytical methods is becoming increasingly important. Current methods for the quantification of total and encapsulated drug in a liposomal formulation include reversed-phase high-performance liquid chromatography with ultraviolet or fluorescence spectroscopy, which requires sample consumption after procedures such as ultrafiltration to separate the free drug from the encapsulated drug. We have developed and tested a method to perform non-invasive Raman spectroscopy measurements on liposomal doxorubicin. Raman spectroscopy provides chemically specific, potentially quantitative information, with measurements able to be performed on the contents of a sealed glass vial. We developed and validated the method by using a model system of polystyrene (PS) nanospheres and produced calibration curves for the concentration of PS at sizes of 40 nm, 125 nm and 200 nm. We then applied the same method to a liposomal doxorubicin formulation to measure the concentration of lipidic and drug components, and differences in the percentage of encapsulated drug. Our results show that by this method we can measure differences in doxorubicin concentration of 0.25 mg/mL and distinguish between free and encapsulated doxorubicin down to a minimal relative concentration of 2.3 %.[1]



Set-up and position of the sample in relation to the laser when performing Raman spectroscopy measurements (left). Raman spectra of samples containing a combination of free and encapsulated doxorubicin (right).

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Parallel Session 6
(11:30-13:00)
Session 6A – Clinical spectroscopy 2
in NEWMAN BLUE (Chair: Dr Ben Gardner)

Diana Frimpong (SXT11)

Exploring the implications of tissue heterogeneity in ovarian cancer metastases on Raman modelling

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KEY WORDS: Ovarian cancer, Raman spectroscopy, spatial heterogeneity

Raman spectroscopy has demonstrated high diagnostic accuracies for classifying epithelial cancers; however, there is limited work exploring ovarian and peritoneal tissue in the context of epithelial ovarian cancer.[1, 2] Ex vivo work to date has demonstrated high accuracy for classification of ovarian cancer against benign and borderline tissue however differences in spectral signatures because of spatial heterogeneity of cancer within these samples prompt the consideration of whether these accuracies can be maintained when three-dimensional blocks of tissue are presented for probe measurements.[3-6] Retrospective analysis of spectral data taken from peritoneal metastases of ovarian cancer compared to areas of fibrosis, within the same tissue section, achieved cross validation accuracy of 0.78, a significant reduction in the accuracy achieved for primary ovarian tissue, 0.98. We propose that the ability of Raman to accurately separate cancer from benign in such small sections might prove a stumbling block in translational work. Furthermore, the reduction in the discriminatory power of the technique in more heterogenous tissue suggests that spatial heterogeneity interferes with Raman modelling.

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Jan Valis (SXT13)

Re-use or Risk? FT-IR & Chemometric Assessment of Microcentrifugal Filter Reusability for Fractionation of Human Serum

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KEY WORDS: ATR FTIR, Serum Fractionation, Repeatability

Fourier Transform Infrared (FT-IR) spectroscopy is a promising method for human serum-based diagnostics. However, due to high-molecular-weight components in serum overshadowing the signal of diagnostically relevant minority components, single-use microcentrifugal filters need to be employed. For economic and environmental reasons, these filters are often re-used, but no study so far has investigated whether such re-use compromises analytical quality. To address this, we analysed the filter reusability using FT-IR and machine learning. First, two sets of Amicon Ultra 100 kDa filters (Merck Millipore, IRL) were used up to twenty times to process samples of human pooled serum. Subsequently, for each filter cycle, nine ATR FT-IR spectra of the filtrate were acquired. To assess the effect of the filter re-use on spectra, the number of cycles was considered to be a class and/or an integer to be classified and/or estimated by a regression model. While no clear differences in the FT-IR spectra could be observed by the naked eye, both the classifier (Support Vector Machine: accuracy = 1.00, precision = 1.00, recall = 1.00, F1 = 1.00, AUCROC = 1.00) and the regression model (Gaussian Process Regression: RMSE = 0.18, MSE = 0.03, MAE = 0.12, R^2 = 0.97) achieved excellent metrics, indicating significant differences between the spectra with respect to the number of times each filter was used. Thus, our findings strongly suggest that filter re-use should be avoided to maintain analytical reliability.

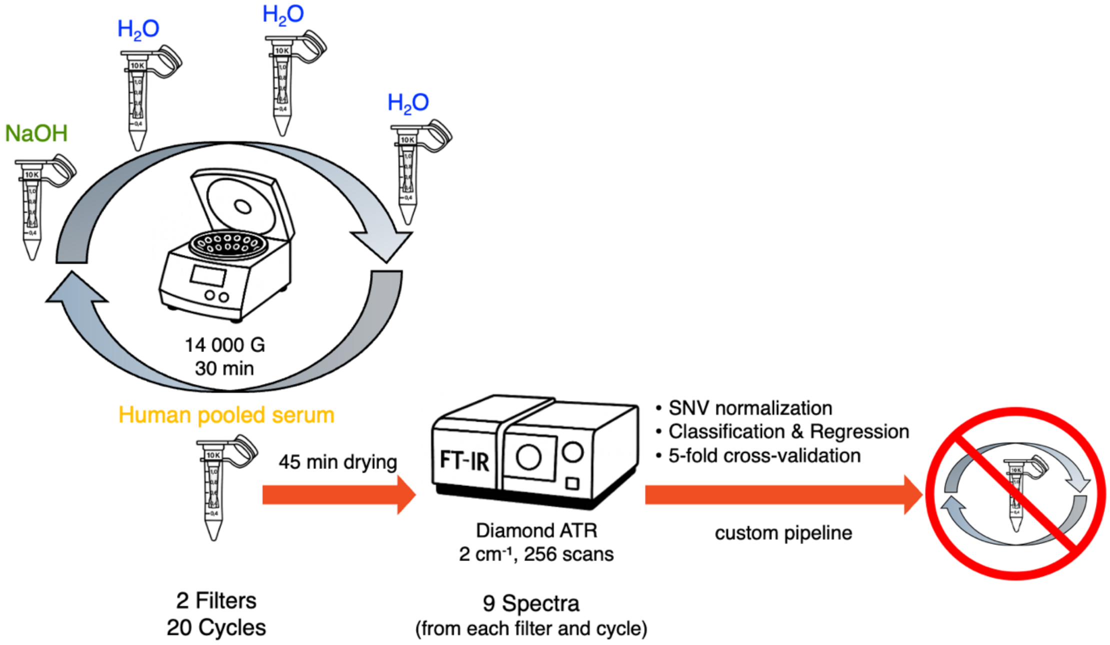

Figure 1 Repeated human serum fractionation resulting in filter depreciation (left), ATR FT-IR measurements of the filtrate (centre), and chemometric assessment of the spectra using a MATLAB pipeline (right) hinting, that filter re-use should be avoided.

SERS sensing of 2-Hydroxyglutaric acid in urine

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KEY WORDS : SERS, oncometabolite, 2-Hydroxiglutaric acid

2-Hydroxyglutaric acid (2HGA) is an oncometabolite increased in patients suffering from gliomas and acute myeloid leukemia. Beyond its diagnostic purposes, abnormal accumulation of 2HGA serves as an indicator of aberrant DNA hypermethylation and contributes to clinical decision-making in cancer therapy. In this study, a label-free surface-enhanced Raman spectroscopy (SERS) approach was optimized for the detection of 2HGA in urine samples.

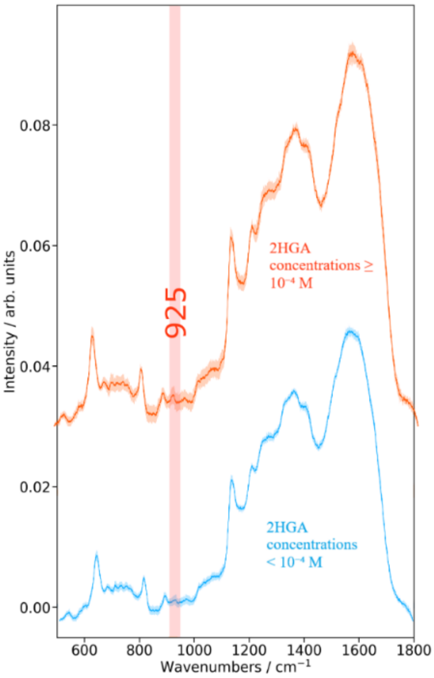

Figure 1. The mean SERS spectra of the groups based on 2HGA concentration: 35 samples with levels ≥10^{-4} M (considered representative of cancer) and 17 with levels <10^{-4} M (considered within the non-cancerous range)

An InVia Raman system coupled to a Leica microscope was employed, using a 532 nm laser line. Sodium borohydride–silver nanoparticles (BH_4–AgNPs) were used as the SERS substrate. 2HGA in the concentration range of 10^{-6} M to 10^{-3} M was analyzed, both in pure solution and also spiked into urine samples ($n = 52$). Out of these samples, 35 had concentrations higher to 10^{-4} M, associated with cancer-related levels, while 17 samples had concentrations below this threshold, corresponding to non-cancerous conditions.

The limit of detection for 2HGA was determined to be 10^{-6} M. In urine samples spiked with 2HGA, the characteristic SERS band at 925 cm^{-1} was identified, enabling direct detection down to 10^{-4} M, which corresponds to the clinical threshold used for medical classification. To evaluate the discrimination capability of the proposed method, principal component analysis combined with a support vector machine model was applied, yielding an overall classification accuracy of 82.4%.

These results demonstrate the potential of BH_4-AgNPs as a simple, cost-effective SERS substrate for non-invasive detection of cancer-associated metabolites in urine. This approach supports future clinical translation and spectroscopic screening applications.

Acknowledgement

This study was supported by the Romanian Ministry of Research and Innovation, CCCDI-UEFISCDI, under project number PN-IV-P2-2.1-TE-2023-0342.

Heqi Xi (SXT17)

Label-Free Evaluation of Osteogenic Differentiation Using Extended-Focus Raman Imaging

Heqi Xi[1,2], **Phan Bhongsatiern**[3], **Menglu Li**[1,4], **Tomoaki Iwayama**[3], **Masahide Takedachi**[3], **Yoshinori Yamaguchi**[1] **and Katsumasa Fujita***[1,2]

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KEY WORDS: Raman imaging, extended-focus, osteogenic differentiation

In periodontitis treatments, periodontal ligament stem cells (PDLSCs)-based therapy has emerged as a promising alternative to regenerate damaged periodontal tissue.[1] However, the challenges including the time-consuming, destructive evaluation method of cell osteogenic ability and the thick, heterogeneous cell culture hinder the application of this method.[2,3] In this study, we proposed a non-invasive extended-focal line-scanning Raman imaging approach that can achieve label-free and high throughput detection of the average Raman spectra of the whole cell volume at a certain measurement area (Figure 1).[4] Through this method, we evaluated the osteogenic differentiation of PDLSCs with low and high osteogenic abilities. By introducing multivariate analysis into Raman spectral analysis, we identified the differences between two cell populations were mainly determined by extracellular matrix (ECM). Combining extended-focal Raman imaging and fluorescence imaging, we further confirmed the relationship between ECM deposition represented by collagen type I and hydroxyapatite (HA) generation, a conventional osteogenic marker, linking the ECM accumulation to the osteogenic ability of PDLSCs. These findings highlighted the potential of extended-focal Raman imaging combined with multivariate analysis methods for label-free cell screening of proper PDLSCs, holding promise for non-invasive cell screening in periodontal tissue regeneration treatment.

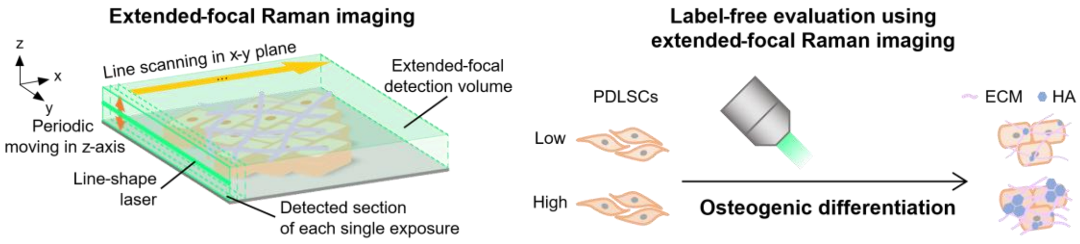

Figure 1. Label-free evaluation of osteogenic differentiation using extended-focal Raman imaging.

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James Read (SXT16)

A simple method for multi-photon label-free super-resolution imaging using Airyscan

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KEY WORDS: label-free, Airyscan, CARS

Label-free super-resolution techniques have several advantages over their fluorescence counterparts as they do not have the challenges that come with using dyes and stains. Many of these techniques however tend to be complex with intensive data processing. Therefore, there is a need for a simple robust technique. Airyscan is a detector-based commercial technology from Zeiss this is based on the pixel-resignment method for achieving super-resolution pioneered by Colin J.R[1]. Airyscan uses an array of 32 small detectors each the size equivalent to a pinhole of 0.2 Airy units. Therefore, each individual detector gives an image with improve resolution because of the smaller pinhole and the total signal is collected by the array with each pixel offset from the centre detector. After pixel re-assignment and processing, an improvement in resolution is seen. As this is a detector-based technique, it is compatible with the label free methodologies.

Here we present a straightforward method using the Zeiss Airyscan detector for multi-photon label-free super resolution imaging super resolution imaging. An improvement in the axial resolution of ~1.4 times and a lateral resolution improvement of 1.5 times was observed using coherent anti-Stokes Raman spectroscopy (CARS) on 200 nm plastic beads. CARS was then used to image lipid droplets within A549 cells and a greater separation of lipid droplets was seen with Airyscan-CARS. Finally human liver tissue from steatosis (fatty) liver imaged using Airyscan with CARS and second harmonic generation (SHG) for collagen analysis. This is a novel demonstration of multimodal super-resolution imaging with two label-free techniques in a co-registered manner (on the same sample and in the same field of view).

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Session 6B – Plasmonics & Nanomaterials
in NEWMAN GREEN (Ioana Blein-Dezayes)

Priyanka Dey – Keynote

Plasmonic Gold nano-assemblies as SERS-efficient agents

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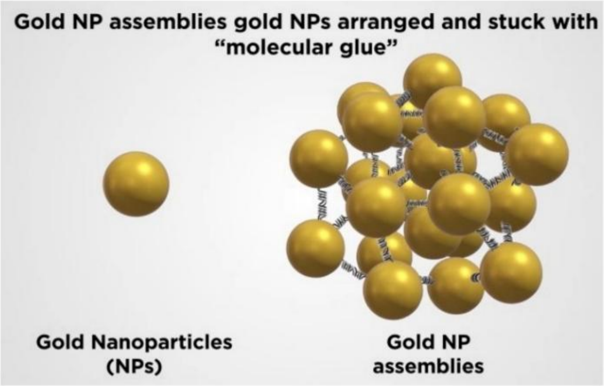
Raman spectroscopy offers high molecular specificity for sensing applications, but its practical sensitivity is limited by inherently weak scattering signals. Surface-enhanced Raman scattering (SERS) using plasmonic gold nano-assemblies provides a powerful solution by generating intense localized electromagnetic fields ("hot spots") that amplify Raman signals. Achieving reproducible and high enhancement, however, critically depends on the structural design of the nano-assemblies and the stability of reporter attachment.

We report a controllable strategy for assembling gold nanoparticles using ssDNA and structural polymers as molecular "glues," enabling reproducible nano-assembly formation without complex linker chemistries. Precise control over nano-assembly morphology and the number of nanoparticles per assembly governs interparticle spacing and plasmonic coupling, increasing hot-spot density and enhancing near-infrared optical response. The assemblies exhibit strong and tunable SERS activity with multiple reporter molecules, highlighting the importance of SERS label selection, robust anchoring chemistry to the gold surface, and controlled surface coverage to ensure signal stability and reproducibility. Key parameters influencing colloidal stability and spectral performance—including aggregation control, surface functionalization, and label loading—are also identified.

In the talk I will discuss how effective SERS performance relieson (i) precise nano-assembly morphology control, (ii) optimized nanoparticle packing to maximize electromagnetic enhancement, (iii) appropriate reporter molecule selection, and (iv) stable and uniform label anchoring on gold surfaces.[1-6] Importantly, customized gold nano-assemblies provide significantly stronger and more reproducible signal enhancement than single gold nanoparticles, establishing them as superior SERS and SESORS agents.[1-8]



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Emma Burns (SXT46)

The Development of SERS Substrates for the Detection of Diagnostically Relevant Volatile Organic Compounds

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KEY WORDS: Surface enhanced Raman scattering, volatile organic compounds, breath diagnostics

Human breath contains a complex mixture of volatile organic compounds (VOCs) including aldehydes, ketones, alcohols, and other hydrocarbons.[1] These analytes have potential as a rich source of information for non-invasive point of care diagnostics, as changes in VOCs can be indicative of a person's health. For example, acetone levels in breath can increase from hundreds of parts per billion to hundreds of parts per million in diabetics[1] and aldehydes are biomarkers for lung disease,[2] a number of different cancers,[2] and Covid-19.[3] Surface-enhanced Raman scattering (SERS) allows for detection of analytes at ultralow concentrations, however its use for the detection of VOCs is typically limited by the high mobility of gaseous analytes. For this reason, substrate design and functionality must be carefully considered.

This work explores the production and application of substrates that can detect VOCs by SERS. Critical to this is the addition of a highly porous zeolitic imidazolate framework layer used to capture the gaseous analytes, followed by gold nanoparticles functionalised with amine molecules. When exposed to the analytes of interest, namely aldehydes and ketones, the adsorbed amine undergoes a Schiff-base reaction, forming a new imine bond and altering the SERS spectra. In this proof-of-concept study, benzaldehyde, acetone, and glutaraldehyde were successfully captured, and then differentiated by SERS using flexible and inexpensive paper-based substrates. This work establishes potential avenues for detecting a broader range of VOCs by SERS.

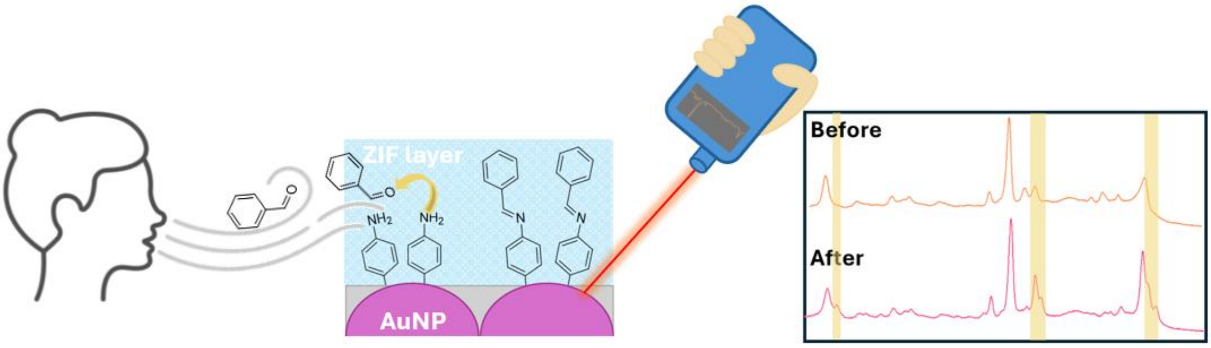

Figure 1: Depiction of 4-ATP and ZIF-8 modified AuNP substrate exposed to gaseous benzaldehyde, and corresponding key changes in the SERS spectra

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Vinicius Anjos (SXT44)

SERS and LDA Investigation of pH-Induced β-Lactam Ring Cleavage in Amoxicillin

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KEY WORDS: SERS, drug stability, chemometrics.

Substandard medicines pose a significant threat to global public health. The widespread occurrence of poor-quality antibiotic formulations in low- and middle-income countries, coupled with the increasing number of defined daily doses, presents an alarming concern. Surface-Enhanced Raman Spectroscopy SERS enables non-invasive, ultrafast, label-free quality control approach [1,2]. This study investigated the effect of acidic conditions on the SERS signatures of amoxicillin, aiming to identify pH-induced molecular and structural changes and their implications for spectral differentiation. Nanoparticles of hydroxylamine-reduced silver were synthesized and used with antibiotic solutions prepared at pH 2.66, 4.33, and 7.30, at concentrations of 10 mM. SERS samples were obtained by mixing the drug solution with the colloid, and spectra were acquired in the 400–1800 cm^{-1} range using a 785 nm laser, a 10 s integration time, and stratified ~25 spectra/class. Preprocessing included Savitzky–Golay smoothing, baseline correction, and SNV normalization, followed by Linear Discriminant Analysis (LDA) with a stratified train–test split (20%). LDA revealed SERS signatures capable of discriminating pH conditions, elucidating the pH-dependent hydrolysis mechanism of the amoxicillin β-lactam ring. Under strongly acidic pH (pH 2), a degradation response by water was observed, with formation of penicilloic acid reflected in characteristic shifts of bands around 1735 cm^{-1} and conformational disruptions in the 420–450 cm^{-1} (carbonate) region. Perfect discrimination of the pH 2 condition, in contrast with partial overlap between pH 4 and pH 7, mirrors the degradation kinetic profiles, indicating rapid and nearly complete inactivation at pH 2. The results demonstrate that SERS combined with LDA is a sensitive approach for monitoring acid-catalyzed degradation of β-lactams, offering promising route antibiotic monitoring in pharmaceutical quality control scenarios.

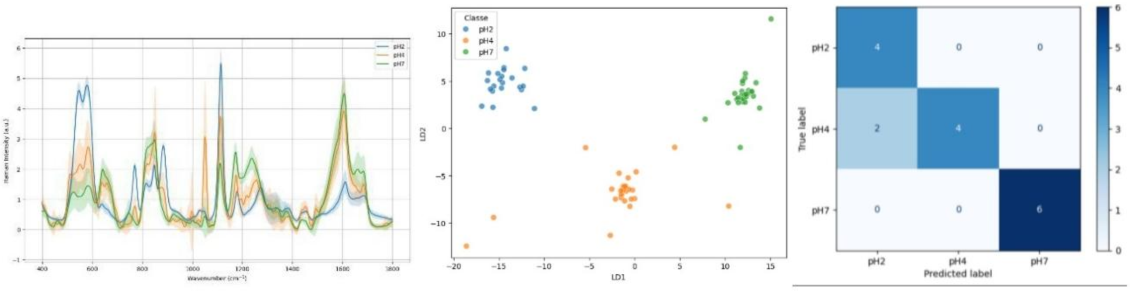

Figure 1: a) SERS spectra under different pH conditions, b) LDA discrimination, c) Confusion matrix.

This work was supported by CNPq (INCT-INTERAS 406761/2022-1; INCT-INFO 409174/2024-6; Sisfoton 440228/2021-2; PQ 314517/2021-9), FAPESP (2020/07065-4; 2025/03135-1), and CAPES: (PDSE 88881.126379/2025-01, finance code 001).

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Development of a SERS Sensor for Point of Care Therapeutic Drug Monitoring in Canine Epilepsy

Megan Miles[1,2,3], **Dr Stacey Laing**[1], **Prof. Karen Faulds**[1], **Dr Mark McLaughlin** [2], **Prof. Catherine Stalin**[2], **Dr William Peveler**[3], **Prof. Duncan Graham***[1]

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KEY WORDS: Therapeutic drug monitoring, surface enhanced Raman scattering, point of care

Epilepsy is the most prevalent neurological disorder observed in canines.[1-3] With no cure, anti-epileptic drugs such as phenobarbitone (PB) are commonly prescribed for seizure management.[4, 5] PB is effective at serum concentrations of 86 - 151 μM,[4, 5] however, above this level patients are at risk of hepatotoxicity.[5, 6] Therapeutic drug monitoring (TDM) is therefore essential to ensure patients receive safe and effective PB dosages. Current TDM methods require invasive intravenous blood draws and off-site laboratory analysis causing a delay between sample collection and clinicians receiving results.[7] To overcome these limitations, this work investigates saliva as a non-invasive alternative matrix and aims to develop a rapid point of care TDM test using surface-enhanced Raman scattering (SERS) to enable sensitive and selective PB detection at clinically relevant concentrations. Thus far, investigations into the optimisation of canine saliva collection and both label-free and labelled methods of SERS based PB detection have been carried out. A label-free SERS test was developed, allowing for the detection of PB at concentrations of 18 nM in the absence of saliva and 100 μM in the presence of saliva. The next stages of this project will involve the development of a lateral flow immunoassay employing Raman reporter functionalised nanoparticles, hypothetically allowing for labelled SERS detection of PB. The work hopes to contribute to the development of more rapid and less invasive methods of TDM in veterinary medicine, reducing the stress levels of patients and improving overall care.

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Alexandra M. Chiriac (SXT45)

Temperature-Driven Changes in SERS Substrate Synthesis

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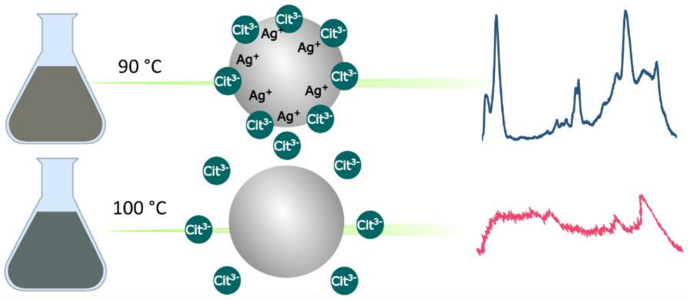
KEY WORDS: adsorption, silver nanoparticles, surface Ag^+

Surface-enhanced Raman scattering (SERS) signals arise exclusively from analytes adsorbed onto the surfaces of colloidal nanoparticles, while free molecules remain spectroscopically inactive. In molecular mixtures, adsorption is competitive and governed by the relative affinities of species for the metal surface. As a result, analytes often need to displace stabilizing surfactants—most commonly citrate—adsorbed on silver nanoparticles (AgNPs). In this work, we demonstrate that the synthesis temperature of citrate-capped AgNPs critically influences citrate surface binding, thereby regulating analyte adsorption and SERS sensitivity[1].



AgNPs were synthesized using a modified Lee-Meisel method at two temperatures, producing cit-AgNPs90 (90 °C) and cit-AgNPs100 (100 °C). Dynamic light scattering revealed comparable hydrodynamic diameters for both colloids, and zeta potential measurements confirmed stable, negatively charged surfaces. Despite these similarities, the two nanoparticle systems exhibited markedly different surface potentials. X-ray photoelectron spectroscopy (XPS) showed a significant presence of surface Ag^+ species on cit-AgNPs90, resulting in a more positive surface potential that promoted spontaneous adsorption of anionic species. Citrate, chloride (Cl^-), bromide (Br^-) and iodide (I^-) readily adsorb onto cit-AgNPs90 at concentrations ranging from 10^{-7} to 10^{-3} M.

In contrast, the cationic dye Nile Blue (NB) did not adsorb spontaneously onto cit-AgNPs90 at 10^{-8} M and was only detected at higher concentrations after displacing pre-adsorbed citrate. Conversely, cit-AgNPs100—composed predominantly of metallic silver—enabled spontaneous adsorption of NB at 10^{-8} M, while anionic species such as citrate and Cl^- showed no detectable adsorption even at millimolar concentrations. Notably, the addition of Ca^{2+} (5×10^{-4} M) to cit-AgNPs100 induced the formation of surface Ag^+ species, shifting the surface potential and enabling adsorption of anionic analytes.

The findings demonstrate that AgNP synthesis temperature strongly governs surface chemistry and competitive adsorption, providing a powerful means to tailor SERS sensitivity toward either cationic or anionic analytes through controlled nanoparticle preparation and surface modulation.

Acknowledgement Funding from the Romanian Ministry of Research and Innovation, CCCDI-UEFISCDI, under project number PN-IV-P2-2.1-TE-2023-0342 is highly acknowledged.

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Closing Remarks and Prizes

(13:00-13:30)

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Awarding of various prizes.

END

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