



The University of  
**Nottingham**

UNITED KINGDOM · CHINA · MALAYSIA

# Applied Optics Group Faculty of Engineering The University of Nottingham

## Research Portfolio January 2014



# Applied Optics Group Overview



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The Applied Optics Group conducts multidisciplinary research in the application of optical, ultrasonic and instrumentation engineering spanning a wide range of physical scales and applied to the life sciences interface, healthcare and advanced manufacturing. We pride ourselves on being able to work on ideas from the basic science right through to application in industry and healthcare.

The group is closely associated with a number of laboratories including the [Institute of Biophysics, Imaging and Optical Science](#) which develops novel imaging technologies to investigate biological problems from the molecular level upwards. Research combines expertise in cellular biology and optical imaging technology. The [Photonic and Radiofrequency Engineering Laboratory](#), which pursues cutting-edge research in photonics and microwaves, focuses on device technologies. We work on a wide range of ultrasonics research within the world leading [laser ultrasonics and nano-ultrasonics group](#).

We have access to well-equipped state-of-the-art resources including optical microscopy and scanning probe systems, biological and chemical laboratories, as well as the engineering capabilities required to custom-build innovative equipment and systems.

## Research themes

### Laser ultrasonics

Supported through the EPSRCs Challenging Engineering, Platform Grant and Fellow schemes as well as numerous Research Council and industry projects we conduct world-leading research into laser and nano-ultrasonics. Here we develop techniques that can create and detect ultrasound using lasers for imaging and measurement of objects from the sub-cellular / nano-scale right up to commercial jets.

Our research operates right along the technology readiness level scales from the basic science that underpins the field (for instance research into the generation and detection of ultrasound with sub optical wavelengths) through to application in the field (for instance routine imaging of advanced aerospace materials using [SRAS](#)).

### Fibre optic sensors

Led by Dr Sergiy Korposh, who recently joined us from Cranfield University, our fibre optic sensors research focuses on applications as diverse as breath analysis, magnetic fields, and pressure measurements.

### Bio-imaging

Utilising advanced imaging techniques such as surface plasmon, two photon, structured light, photothermal total internal reflection, phase contrast and interferometric contrast and scanning ion microscopy and unique custom image sensor technology this research aims to explore and understand the basic mechanism of operation of biological systems.

### Healthcare technologies

Using advanced optical techniques, sensors, electronic and signal processing this research area develops instrumentation for healthcare applications. This includes: foetal heart monitoring systems, tissue imaging, sensor development, systems design and integration and taking technologies into the clinical environment and gaining statutory approval for use in the clinical environment. The EPSRC, TSB, EU and various charities support this research area.

## Cell imaging using picosecond laser ultrasonics

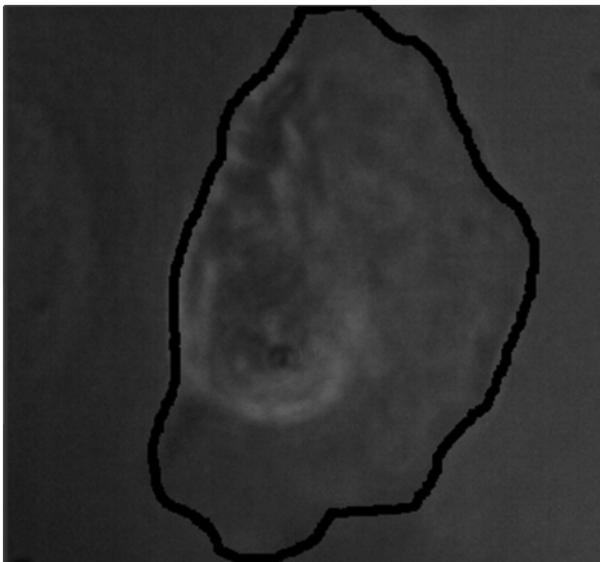
**Fernando Perez Cota, Richard Smith, Leo Marques, Kevin Webb, Matt Clark**

Scanning acoustic microscopy has been a useful tool for biologist for decades, however increasing the resolution has proved difficult as working at higher frequencies introduced many problems. Picosecond ultrasonics is one potential way to increase the frequency of the ultrasound used (and hence the resolution).

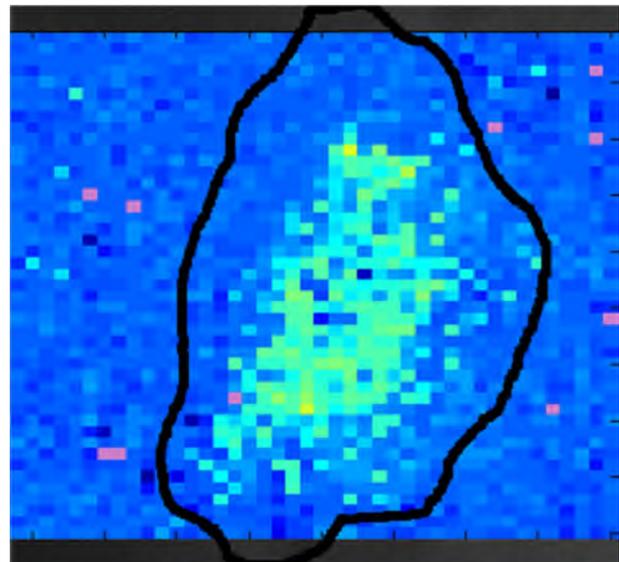
The cells are grown on a transducer substrate similar to those developed as nano-scale ultrasonic transducers however the optimization of the transducer layer is different in this case. Here we are much more concerned with optimizing the optical properties of the transducers. The goal is to reduce the amount of blue light reaching the cell and increase the size of the generated waves while also maximizing the reflected or transmitted probe light.

The picosecond ultrasound instrument is combined with a phase contrast imaging arm, this allows us to obtain good images of the cells as they have very little optical contrast and so a simple bright field microscope is not sufficient to visualize the cells.

This early experimental result shows an acoustic image with the cell outline applied and you can see that in the centre of the cell the frequency increases. At the edges there is no change from the blue substrate back ground, this is likely due to the fact that the cell is very thin at the edges and so does not produce a Brillouin signal.



Phase contrast image



Acoustic image of cell

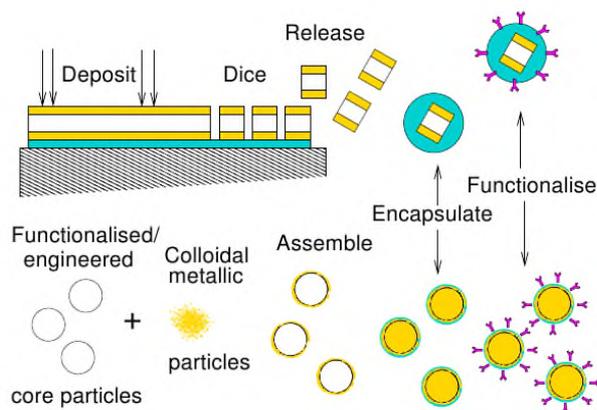
## Nano-scale ultrasonics

**Richard Smith, Fernando Perez Cota, Leo Marques, Rikesh Patel, Matt Clark**

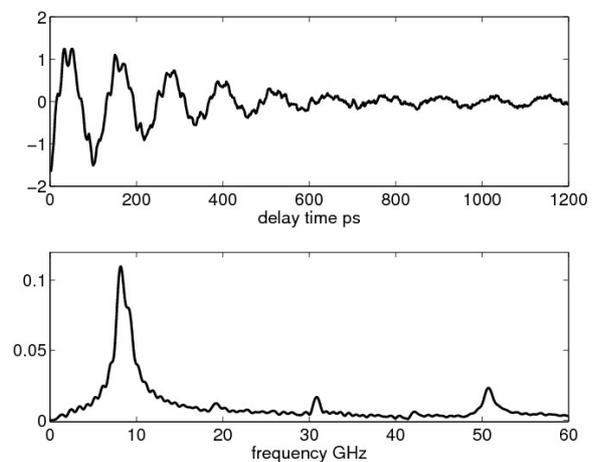
Ultrasound is a powerful tool for diagnosing medical and mechanical problems. Conventional ultrasonics works at megahertz frequencies and with wavelengths of between 1-2 $\mu\text{m}$  and 10s of mm. This means it cannot "see" very small objects at the nano-scale. Our new transducers are so small it is impractical to communicate with them electrically. Instead we have devised a non-contact method of talking to them using short pulses of laser light.

We have adopted two approaches for producing these transducers: one method builds plate devices, the other uses self-assembled nanoparticles. The transducers are made from alternating metal and soft transparent layers. They have optical and mechanical resonances and so the devices have to be made such that they work well both mechanically and optically. We have both FE and analytical models to allow use to choose the optimal layer thickness for the devices to work well for our laser wavelength.

We have measured the response on a 240nm x 10 $\mu\text{m}$  plate transducer and it agrees very well with the modelled response. The main frequency is around 9GHz and there are harmonics up to ~70GHz. The weighting of harmonics do differ from those in the model, this could be due to slight variations in actual material properties, and final created layer sizes being different from those modelled.



**Two approaches to nano-scale transducer fabrication**



**Experimental trace from 10 $\mu\text{m}$  transducer**

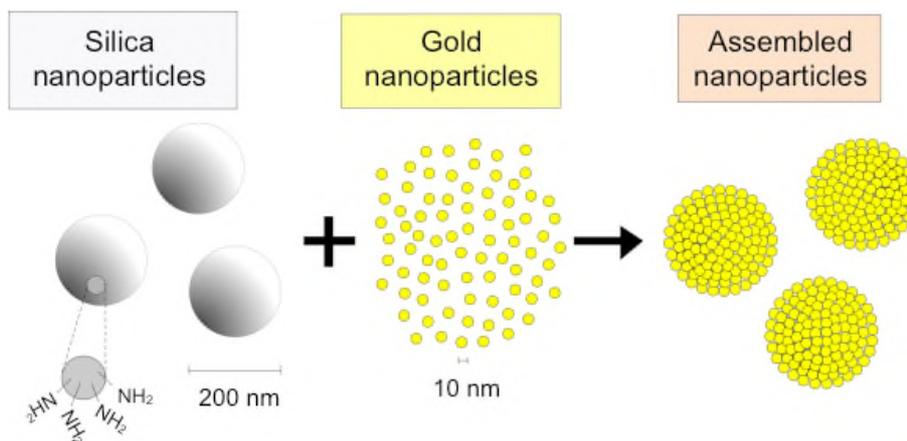
## Nanotransducer development

**Leo Marques, Rikesh Patel, Fernando Perez Cota, Richard Smith, Matt Clark**

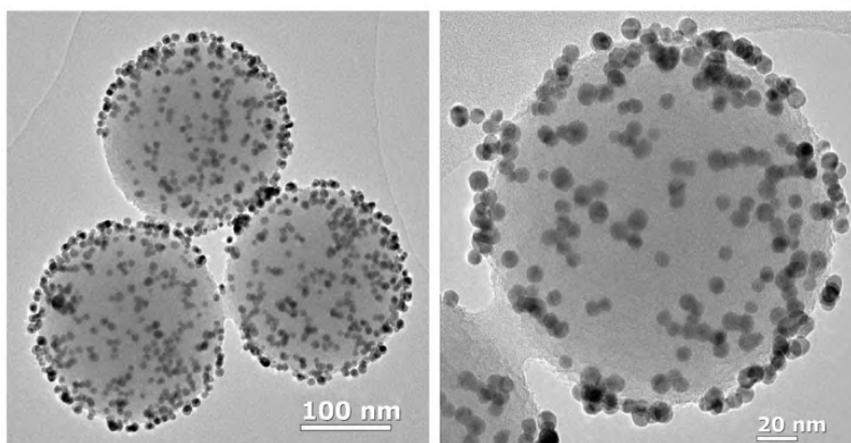
Recognition of the importance of ultrasonic transducers in both biological and industrial applications is growing, with much interest in the recent years. New applications in biomedical sensing and imaging can be developed using nano-scale ultrasonic transducers, particularly when the targets are small structures such as living cells. We have been working on the production of smaller high frequency transducers with the aim of performing ultrasonics at the cellular level.

In this work, the design and fabrication of nanometre sized ultrasonic sensors (nanochots) using a self-assembly process of hybrid nanostructures is described. The design leads to the formation of core/shell structured nanoparticles.

To date we have produced devices on the micron scale operating at up to 50GHz that are excited and probed using femtosecond lasers.



**Nanochot assembly procedure.**



**TEM image of nanochots.**

## Cheap Optical Transducers (CHOTs) and portable CHOTs demonstrator

**Teti Stratoudaki, Victoria Ageeva, Matt Clark**

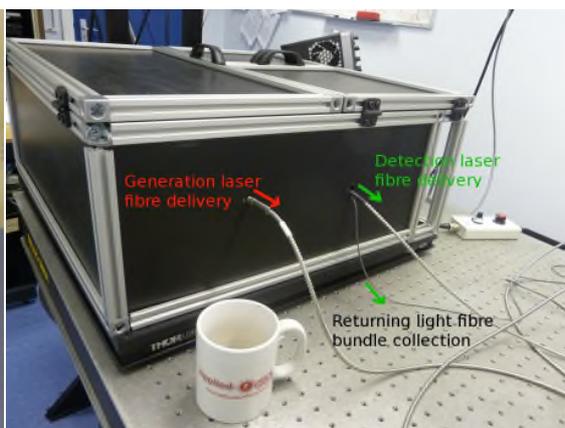
Cheap Optical Transducers (CHOTs) are a non-contact, wireless, couplant-free alternative to the traditional piezoelectric transducers that have been developed by at the Applied Optics Group, University of Nottingham and can be used for ultrasonic inspection. Because they are cheap and very small, they can be used in large numbers and in different ways to normal ultrasonic probes. For example, they could be mounted permanently on the component for easy repeatable measurements or considered as disposables: use once and throw away. CHOTs are structures attached to the surface of the test component that are optically excited using a simple laser set-up to either generate or detect ultrasound. The use of CHOTs enables testing of components inaccessible by other techniques and potentially enabling on-site and in-service ultrasonic testing currently unavailable to the industry.

CHOTs are nanometre-height patterns printed or attached onto the component. Using principles of laser ultrasonics they are able to remotely generate and detect ultrasound when illuminated by a laser, providing a simple non-contact and couplant-free alternative to the conventional piezoelectric transducers. They are fully customisable for the required application providing control over the directivity and the mode of the generated ultrasound (surface acoustic waves or longitudinal bulk waves), type of the wave (plane or focused wavefront), generation efficiency and bandwidth of the signal.

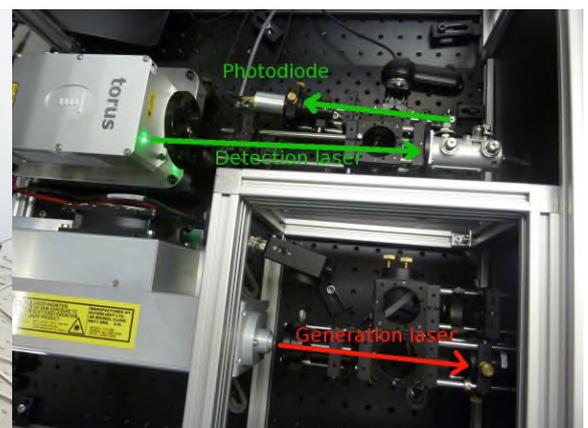
A basic CHOT measurement system for generation and detection of ultrasound consists of a pair of CHOTs on the surface of a sample, a pulsed generation and a CW detection laser to illuminate the corresponding CHOTs, minimal optics to expand and collimate the beams and to collect the returning probing beam (containing ultrasonic information), and a photo-detector. We have designed and constructed a portable CHOTs demonstrating system that houses the CHOTs pulser, the equivalent of a conventional ultrasonic transducer pulser.



**CHOT for generation and detection of focused 20MHz SAW on a glass slide.**



**CHOTs portable demonstrator.**



**Inside the CHOTs portable demonstrator.**

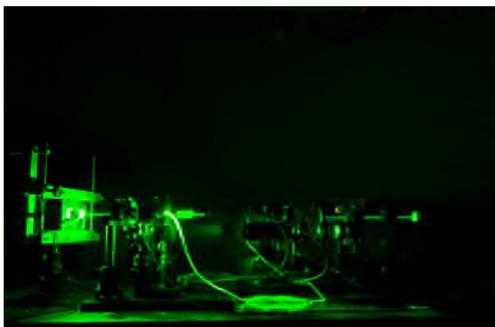
## Endoscopic system for *in situ* ultrasonic inspection of aero-engines using Cheap Optical Transducers (CHOTs)

Victoria Ageeva, Teti Stratoudaki, Matt Clark

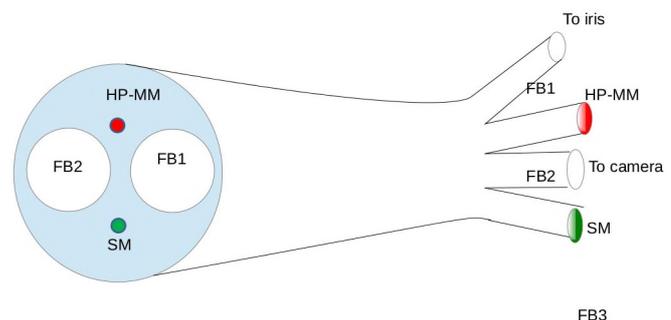
This is a research project jointly funded by the EPSRC and Rolls-Royce plc to enable on-site non-contact ultrasonic inspection of the aeroengine components by an endoscopic system based on the Cheap Optical Transducer (CHOT) technology.

Cheap Optical Transducers (CHOTs) use principles of laser ultrasonics to remotely generate and detect ultrasound, providing a simple non-contact, couplant-free alternative to the traditional piezoelectric transducers. They are practically weightless nanometre-height patterns attached or printed on the component, and activated by lasers. CHOTs for Surface Acoustic Waves (SAWs) are used in this project.

The framework of this project includes: application of the SAW CHOT technology to the non-destructive testing in an aero-engine environment combined with the development of the endoscopic light delivery system to provide access to the components via existing service ports in the engine, as well as the investigation and development of the corresponding CHOT manufacturing techniques to enable remote or in-situ application of the sensors.

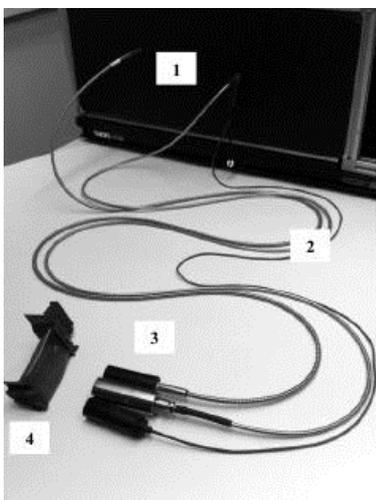


**CHOTs endoscopic system for in situ inspection of aero-engines.**

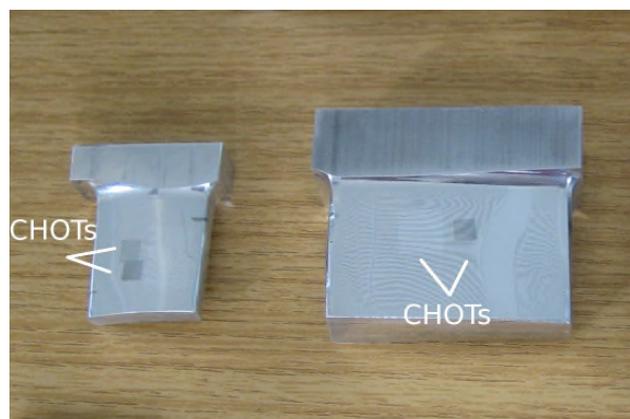


FB1=Fibre bundle for collection of CW light from d-CHOT and imaging  
 FB2=Fibre bundle for imaging.  
 HP-MM=High power multi mode fibre for ultrasonic generation using g-CHOT.  
 SM=Single mode fibre for detection using d-CHOT (d-CHOT illumination).

**Schematic of the future fibre arrangement at the inspection end.**



**Photo of the existing endoscopic CHOTs system.**



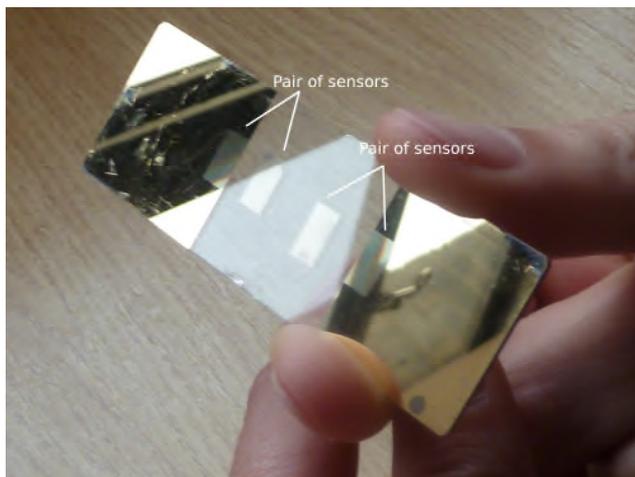
**Mock turbine blade samples with CHOTs.**

## Cheap Optical Transducers (CHOTs) as chemical sensors

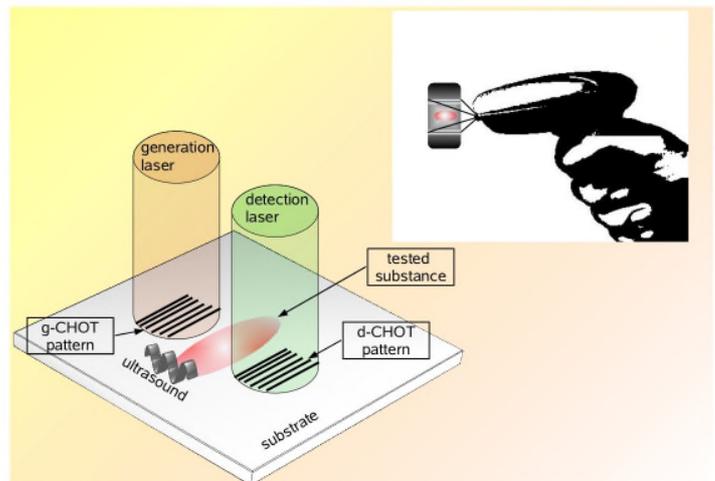
**Teti Stratoudaki, Leo Marques, Victoria Ageeva, Fernando Perez Cota, Matt Clark**

Optically excited surface acoustic wave (SAW) sensors are used as chemical sensors for testing chemical or biological substances. The technique is based in the use of Cheap Optical transducers (CHOTs), a technology that was developed in the Applied Optics Group. CHOTs are a new breed of ultrasonic transducers that are optically activated for generation and detection of ultrasonic signals. CHOTs offer a range of advantages over the traditional contact piezoelectric transducers: wireless, remote, reliable, couplant-free operation.

They are activated by light, with a great potential of becoming inexpensive to manufacture so as to be considered as disposable or be used in large numbers. CHOTs are 2-D patterns of nanometre height, attached on a substrate such as a glass coverslip and are optically excited by means of lasers for generation and detection of acoustic waves, including surface acoustic waves (SAWs). In this application, CHOTs are used to measure the thickness of thin metal layers as well as for substance identification on polymers.



Two pairs of CHOTs on a microscope slide, used as SAW chemical sensors.



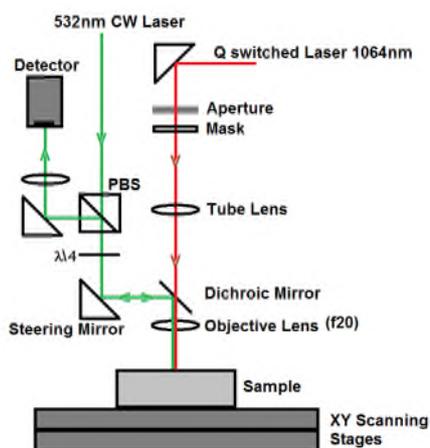
Schematic of the excitation of CHOTs for substance identification and thickness measurement.

## SRAS: spatially resolved acoustic spectroscopy for materials characterisation

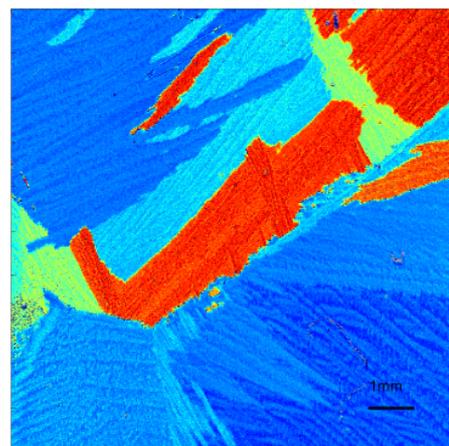
**Wenqi Li, Richard Smith, Jethro Coulson, Paul Marrow, Matt Clark, Mike Somekh, Steve Sharples**

Measuring the grain structure of aerospace materials is very important to understand their mechanical properties and in-service performance. Spatially resolved acoustic spectroscopy is an acoustic technique utilising surface acoustic waves to map the grain structure of a material. When combined with measurements in multiple acoustic propagation directions the grain orientation can be obtained by fitting the velocity surface to a model. The research instrument based in our lab can take thousands of acoustic velocity measurements per second. The spatial resolution ( $\sim 25\text{-}100\mu\text{m}$ ) and velocity resolution ( $<1\%$  single shot) can be adjusted by simple modification to the system optics.

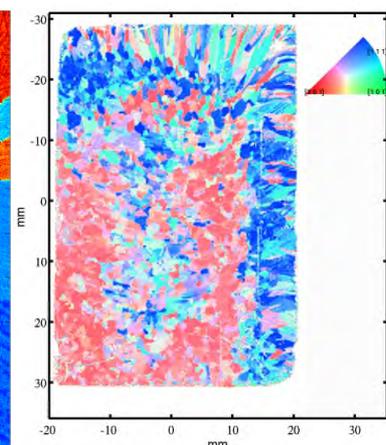
The instrument has been used extensively over the past few years, on both a commercial and a research basis. We continue to develop the instrumentation itself, but more recently focusing on the interpretation of the data for quantitative texture and orientation determination.



**Optical configuration of the SRAS instrument.**



**Image of TiLG685 showing internal structure within the large grains, the crystallites are clearly visible, spatial resolution  $\sim 50\mu\text{m}$ .**



**Inverse pole figure of a large grained aluminium sample.**

## Technology transfer: SRAS from lab to commercial prototype

**Jethro Coulson<sup>1,2</sup>, Steve Sharples<sup>1</sup>, Colin Bulled<sup>2</sup>**

<sup>1</sup> Applied Optics Group

<sup>2</sup> Renishaw plc

Until recently SRAS has remained a mainly laboratory based technique limited to fairly small samples moved by linear stages. Only one fully capable SRAS instrument currently exists and is available for use. This project is a collaboration between the University of Nottingham and Renishaw plc to assess the viability of SRAS as a commercial product, and to develop the technique into a marketable scientific instrument. The ultimate goal is to produce a SRAS instrument, coupled to existing Renishaw motion platforms, which can be deployed autonomously on complex geometry parts, of unlimited size, as a quick and quantitative quality check.



The current laboratory based SRAS instrument.

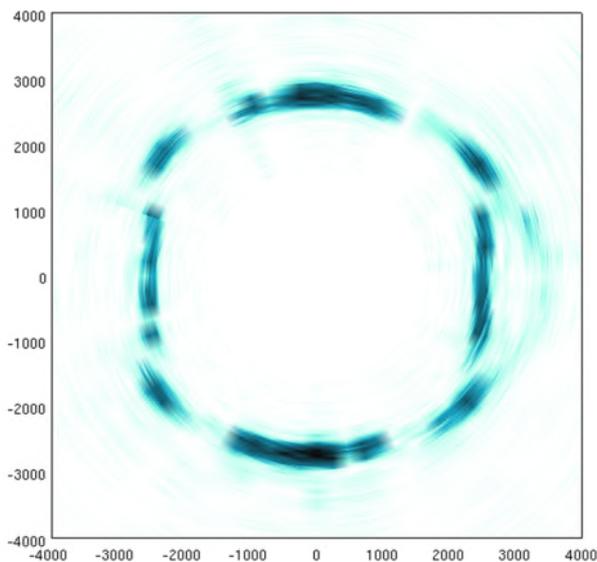


The Renishaw Equator platform, a possible motion solution for SRAS.

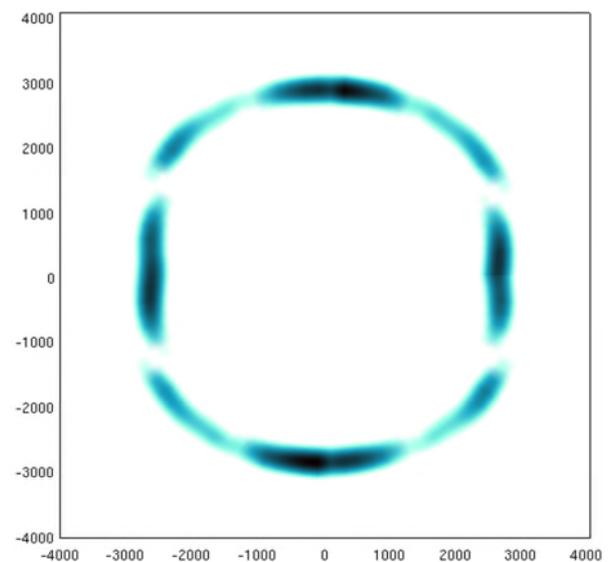
## Modelling laser generated SAWs

**Jethro Coulson, Wenqi Li, Mike Somekh, Steve Sharples**

SRAS has proved itself as a useful technique for imaging the grain structure of engineering metals and, in many cases, determining the full crystallographic microstructure. This is done by comparing experimentally determined slowness surfaces with a database of theoretical slowness surfaces for a particular material. Currently the database is built using the 'forward model' which is based upon finding the wave modes which are allowed to propagate on a particular plane in a particular direction. The generation model is being developed to determine which of these theoretically allowed modes are actually generated and will help in the orientation determination. The models itself uses the finite element method to model the SAWs produced by a short pulse length, laser point source on a given plane of a material. Huygens' superposition principle is then applied to fully model the generation patch used in the SRAS technique.



**An experimentally-derived slowness surface for cubic nickel. The determined Miller index of the crystallographic plane is (1 4 0).**



**A modelled slowness surface for cubic nickel. The Miller index of the crystallographic plane is (1 4 0).**

## HiDepAM - SRAS for online monitoring for additive manufacturing processes

**Supriyo Ganguly<sup>1</sup>, Stewart Williams<sup>1</sup>, Steve Sharples<sup>2</sup>**

<sup>1</sup> Cranfield University   <sup>2</sup> Applied Optics Group, University of Nottingham

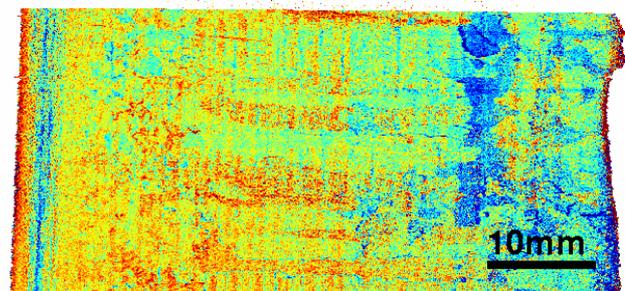
This new 2.5-year EPSRC sponsored project is led by Cranfield University and also includes the University of Nottingham, IIT Bombay and IIT Indore. The overall aim of the project is to radically enhance the state of the art in high deposition rate additive manufacturing (AM) processes by (a) carefully controlling the metal deposition parameters, and (b) by transforming the properties of the manufactured part as it is built up, layer by layer, by introducing cold work into the metal.

Critical to the successful application of metal AM for significant engineering structures is to guarantee that the material properties are always at the level required. Spatially resolved acoustic spectroscopy (SRAS), developed by the University of Nottingham with support from RCNDE, East Midlands Development Agency, Rolls-Royce and Renishaw, has been shown to be capable of providing microstructural details of AM parts non-destructively.

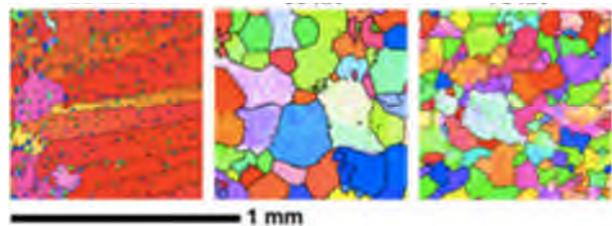
We will further develop the SRAS technique to extract the requisite microstructural information needed to prove that the material properties are satisfactory within the AM process. The SRAS system will be combined with a wire feed metal AM system at Cranfield University to demonstrate the capability for online monitoring of grain structure in the actual AM environment.



**SRAS inspection of wire and arc additive manufactured sample.**



**SRAS scan of polished titanium wire and arc additive manufactured sample.**



**Texture and grain sizes for Ti structures built using the WAAM process, with and without interpass rolling.**

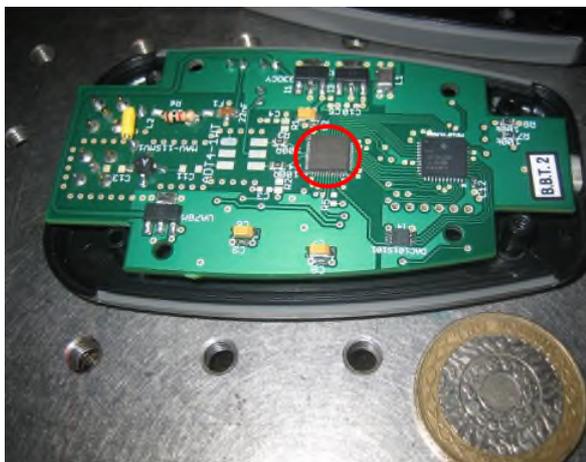
## SKED: speckle knife edge detector for detection of ultrasound on rough surfaces

**Samuel Achamfuo-Yeboah, Roger Light, Steve Sharples**

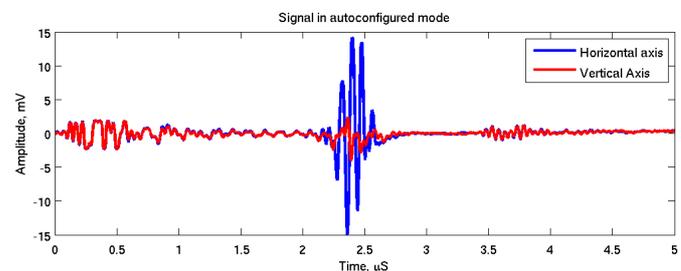
The optical detection of laser ultrasound from optically rough surfaces is severely limited using a conventional setup because the detected light is speckled. This means that complicated and expensive setups are required to detect laser ultrasound on rough surfaces. We present a CMOS integrated circuit that can detect laser ultrasound in the presence of speckle. The detector circuit is based on the simple knife edge detector. It is self-adapting and is fast, cheap, compact and robust.

The CMOS circuit is implemented as a widefield camera with 1024 pixels. Each pixel pairs up with one of two adjacent pixels and depending on the light intensity distribution over the array, a decision is made as to the output. The angular deflection of the surface due to the ultrasound preserves the speckle distribution whilst shifting it. The spatial disturbance of the speckle pattern due to the ultrasound is detected by considering each pair of pixels as a knife edge detector. The sensor can adapt itself to match the received optical speckle pattern in  $0.1\mu\text{s}$  or even less, and then detect the ultrasound within  $0.5\mu\text{s}$  of adaptation. This makes it possible to detect ultrasound from optically rough surfaces very quickly.

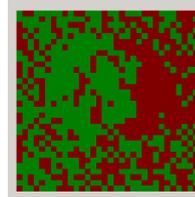
Because it is setup just like a camera, it is cheap, robust and easy to use. The detector is capable of independent operation controlled by a microcontroller (on the host printed circuit board), or it may be connected to a computer for more complicated configuration and control.



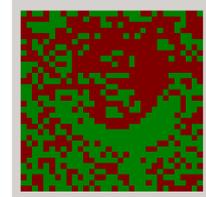
**SKED printed circuit board, with SKED chip outlined.**



Configuration data (Vertical Axis)



Configuration data (Horizontal Axis)



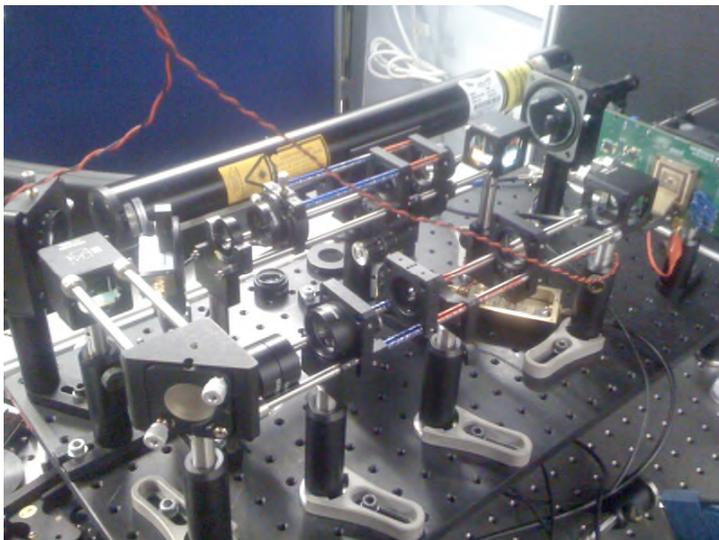
**Top: traces from a sample, showing sensitivity to orientation of the propagating surface acoustic wave depending on the axis of sensitivity set by the user.**

## Full field ultrastable interferometry for industrial environments

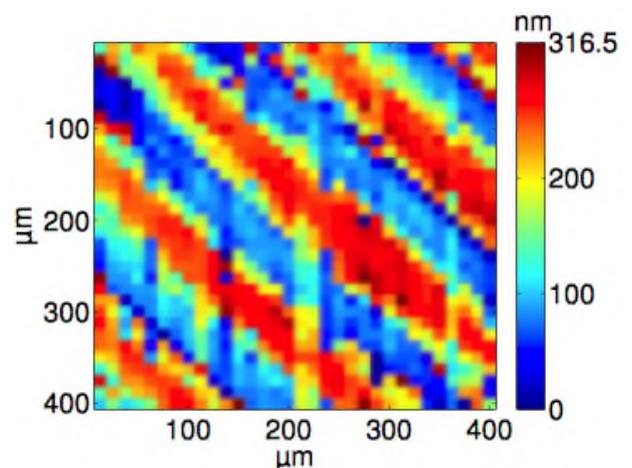
**Rikesh Patel, Matt Clark**

Interferometers are used in a wide variety of fields for imaging objects in the sub-wavelength region, and for measuring refractive indices. However, being sensitive to small measurements can be problematic as simple interferometers can be sensitive to vibrations and other environmental effects. Complex common-path arrangements or high speed acquisition systems could be used, but may involve the use of complex optics, require precision alignment, and could be costly.

An ultrastable interferometer system has been developed that uses a modulated light camera (MLC) to capture widefield heterodyne interferograms. The prototype CMOS camera continuously measures and demodulates the modulated optical pattern (with frequencies in the MHz region) using a local reference signal. By feeding back the raw signal measured on one pixel as the reference signal, the temporally varying phase (e.g. vibration) seen on all pixels is cancelled out (electronic self-referencing). The detection system has been tested in simple Michelson / Mach-Zehnder arrangements and has demonstrated piston vibration velocity immunity of up to 3m/s (theoretical limit is approximately 10m/s). The ultrastable system has demonstrated its capability of capturing the interference patterns generated by two separate lasers.



**Mach-Zehnder interferometer incorporating the ultrastable system. A vibrating mirror is used to test the vibration immunity limits.**



**Image of a chrome grating pattern; heights of each finger (measured using an AFM) are between ~140-160nm.**

## Pressure measurements at single point using a fibre-optic Fabry-Pérot interferometer

**Sergiy Korposh**

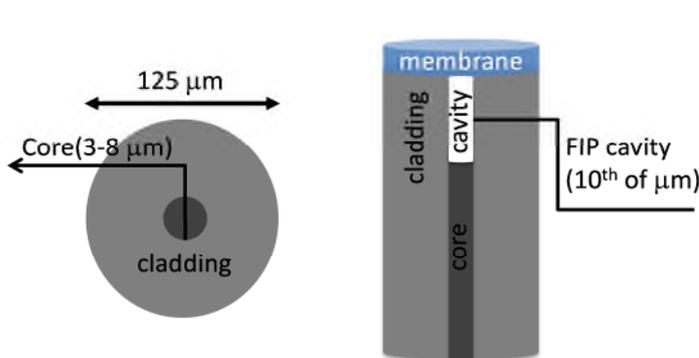
This work, which is undertaken in collaboration with Cranfield University and The University of Kitakyushu, Japan, focuses on the development of highly sensitive pressure sensors for bio-medical and industrial applications. The pressure sensor is formed at the tip of an optical fibre (typical outer diameter  $125\mu\text{m}$ ), offering compact device and flexible deployment.

The pressure sensor is formed by creating a Fabry-Pérot interferometer on the end of the optical fibre. A Fabry-Pérot interferometer (FPI) sensor consists of two partially reflecting surfaces separated by tens of micrometres, forming an *optical cavity*. The reflection spectrum of the FP is characterised by a sinusoidal channelled spectrum, the period of which depends on the cavity length. Small changes in the cavity length are characterised by a change in the phase of the sinusoid. A number of techniques may be employed to form an optical fibre FP cavity, ranging from complex machining and splicing to chemical etching using highly toxic reagents. One of the major drawbacks of the fabrication methods is low reproducibility.

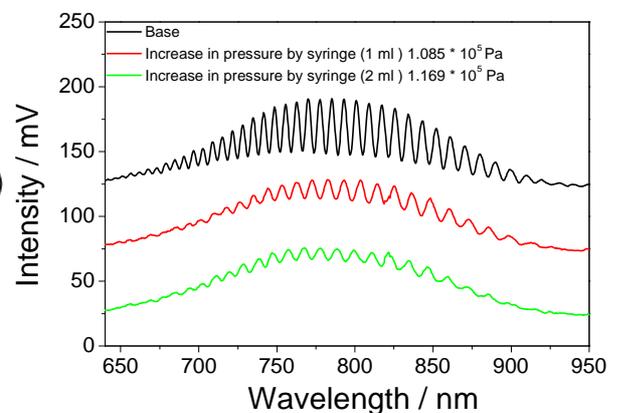
A novel method for the reproducible fabrication of a highly sensitive pressure sensor on the tip of an optical fibre is proposed. A narrow void is created at the end of a single optical fibre and a pressure sensitive membrane is attached directly to the end-face of the optical fibre. The interface between the core of the fibre and the cavity forms one of the reflecting surfaces while the flexible membrane forms the second, as illustrated in Figure 1a. Increasing the ambient pressure pushes the flexible membrane towards the fibre, thus changing FP cavity length, leading to wavelength shift of the channelled spectrum as shown in Figure 1b.

Here a free-standing thin film is used as the pressure sensitive membrane. The high sensitivity of the FPI is achieved as a result of the use of an ultrathin parylene membrane, with thickness ranging from 10s to 100s of nanometres. The free-standing membrane is directly and firmly attached to the tip of the optical fibre via electrostatic forces.

The dimensions of the pressure sensor are determined by the size of the optical fibre, typically  $125\mu\text{m}$ . The sensitivity and dynamic range can be varied by changing the thickness of the pressure sensitive membrane.



**Schematic illustration of the FP cavity in an optical fibre.**

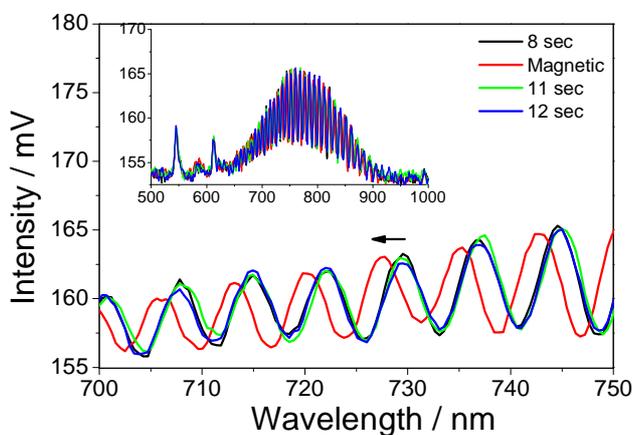


**Typical response of the fibre optic FPI pressure sensor.**

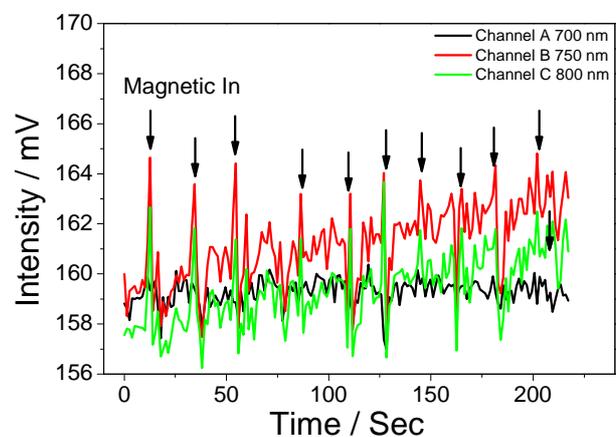
## Ultra-miniature magnetic field sensor based on a fibre-optic Fabry-Pérot interferometer

**Sergiy Korposh**

This work, undertaken in collaboration with Cranfield University and The University of Kitakyushu, Japan, is aimed at the fabrication of miniature magnetic field sensors with highly sensitivity and fast response times. The principle of operation is based on the Fabry-Pérot interferometer (FPI), with the sensor consisting of a single optical fibre with a magnetic field sensitive membrane attached directly to the end-face of the optical fibre. The presence of the magnetic field leads to the deflection of the membrane thus changing the length of the optical cavity, which can be measured via changes in the reflection spectra, as shown in the figures.



**Typical spectral response of the fibre-optic FPI sensor to the presence of the magnetic field.**



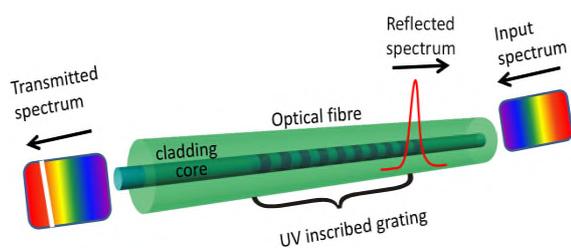
**Dynamic response measured at single wavelength.**

## Measurements of the contact pressure at multiple locations using multiplexed optical fibre Bragg gratings

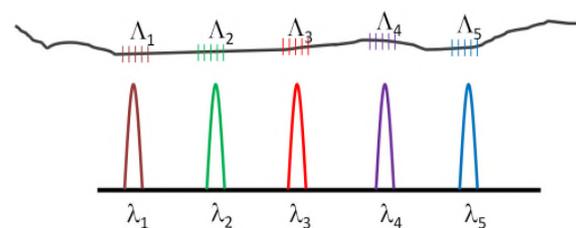
Sergiy Korposh

Fibre optic grating based sensors, fibre Bragg gratings, (FBGs), and long period gratings (LPGs), have been extensively investigated for the measurement of physical and chemical parameters. An FBG consists of a periodic modulation of the refractive index of the core of the optical fibre with a period of the order of the wavelength of light. The FBG acts to reflect light of a specific wavelength (equal to twice the optical period of the grating) back along the fibre, see the figures below. The lengths of the FBG can vary from 0.5mm to 20mm [1].

A key feature of FBG sensors is the ability to wavelength-division-multiplex a serial array of sensors in a single optical fibre (right hand figure), and this is exploited in the measurement of strain, pressure and temperature across a wide range of industrial sectors. FBG sensor interrogation and data logging instrumentation is now available commercially.



Schematic illustration of an FBG inscribed inside the core of an optical fibre.



Wavelength-division-multiplexing of a serial array of FBG sensors in a single optical fibre; each grating has different grating period  $\Lambda$  with the corresponding reflection wavelengths  $\lambda$ .

### Reference

[1]. Sunita Ugale et. al., 2010, "Fiber Bragg Grating Modeling, Characterization and Optimization with different index profiles," *International Journal of Engineering Science and Technology*, **2** (9), 4463-4468.

## Optical fibre chemical sensors modified with sensitive films for bio-medical applications

Sergiy Korposh

Sensing techniques based upon the use of optical fibre devices to probe the optical characteristics of nanomaterials that exhibit changes in their optical properties upon exposure to targeted chemical species are particularly attractive, due to their potential high sensitivity, selectivity, the ready ability to multiplex arrays of sensors, and the prospect for remote sensing. The variety of different designs and measurement schemes that may be employed using optical fibres provides the potential to create very sensitive and selective measurement techniques that can be deployed in real environments. In our work we have focussed on the development of fibre-optic chemical sensors utilising different measurement designs based on multimode optical fibres, (Figure 1a), tapered optical fibres (Figure 1b) and optical fibre long period gratings (Figure 1c) functionalized with nanoassembled thin films, Figure 2 [1].

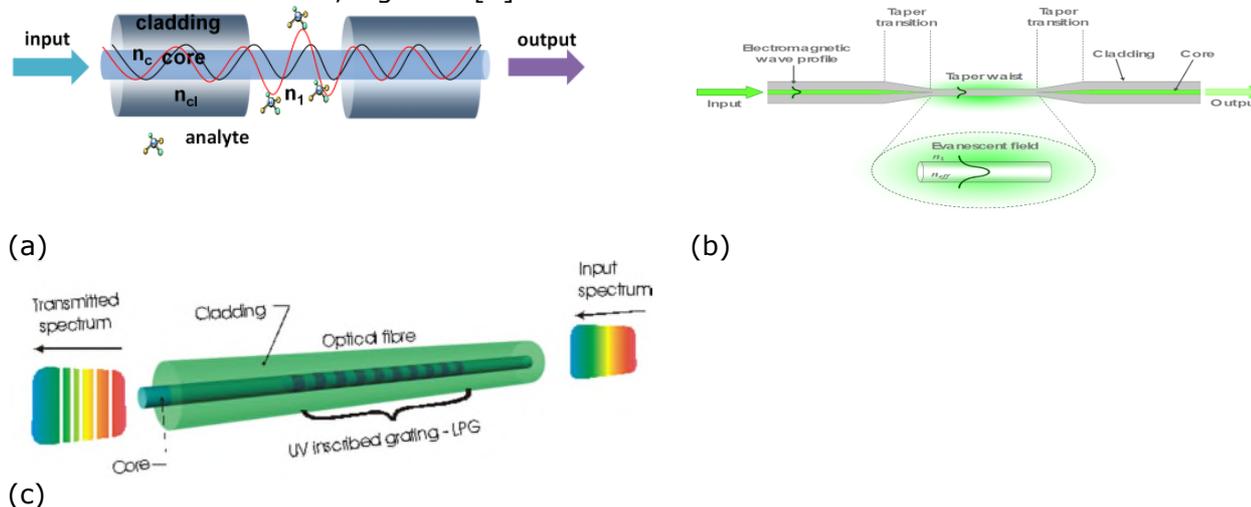


Figure 1: Schematic illustration of (a) an evanescent wave type sensor, (b) a tapered optical fibre sensor and (c) an optical fibre LPG sensor.

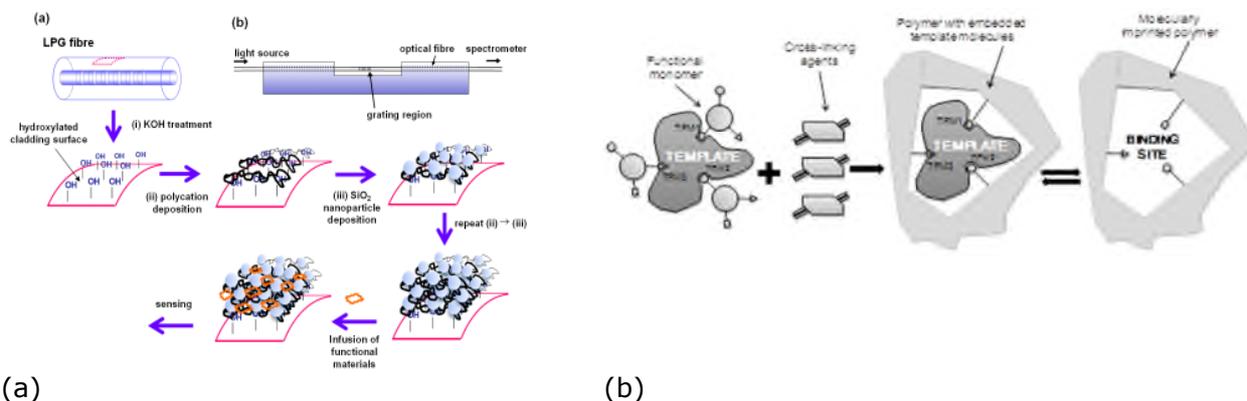


Figure 2: Schematic illustration of the (a) layer-by-layer (LbL) electrostatic deposition process; and (b), molecular imprinting process.

### Reference

S. Korposh, S. James, R. Tatam, and S.-W. Lee, 2013, "Fibre-optic chemical sensor approaches based on nanoassembled thin films: A challenge to future sensor technology" in: *Current developments in optical fiber technology*, Dr. Sulaiman Wadi Harun (Ed.), ISBN: 978-953-51-1148-1, InTech, DOI: 10.5772/53399, 2013.

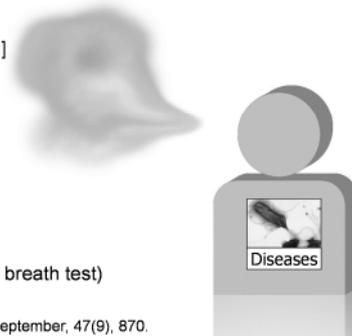
## Breath analysis using fibre optic sensors

### Sergiy Korposh

Chemical compounds excreted from the human body are believed to reflect certain metabolic conditions as well as the blood gas content, See left hand figure [1]. The changes in concentration of some compounds, referred to as biomarkers, and the chemical composition of human samples such as breath, blood, urine, sweat and saliva can be linked to particular diseases and have been intensively used in medicine for early and minimally invasive diagnosis [2]. There is considerable interest in the development of sensor devices to identify compounds both *in vivo* and *ex vivo* that can facilitate non-invasive diagnosis.

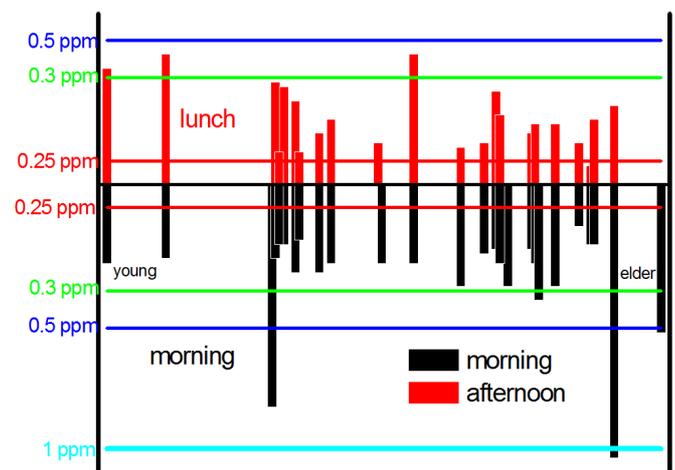
In collaboration with Cranfield University and The University of Kitakyushu, an optical fibre sensor for the measurement of ammonia, a known biomarker, in the breath of a patient has been demonstrated with the aim of developing point-of-care device, (right hand figure).

Disease	Biomarker
schizophrenia	pentane, CS <sub>2</sub> [1]
angina pectoris	CO
hyperbilirubinemia	CO [2]
diabetes (type 2)	acetone
asthma	NO
liver diseases	OCS, NH <sub>3</sub>
lung cancer	VOCs
<i>Helicobacter pylori</i> infection	CO <sub>2</sub> , NH <sub>3</sub> (urea breath test)



1. Journal of Clinical Pathology (1994) September, 47(9), 870.  
2. Pediatrics International (2001) 43, 329-333

### Biomarkers exhaled in breath.



**Response of the fibre optical sensor modified with the sensitive film to ammonia measured using 50 healthy volunteers before and after lunch.**

### References

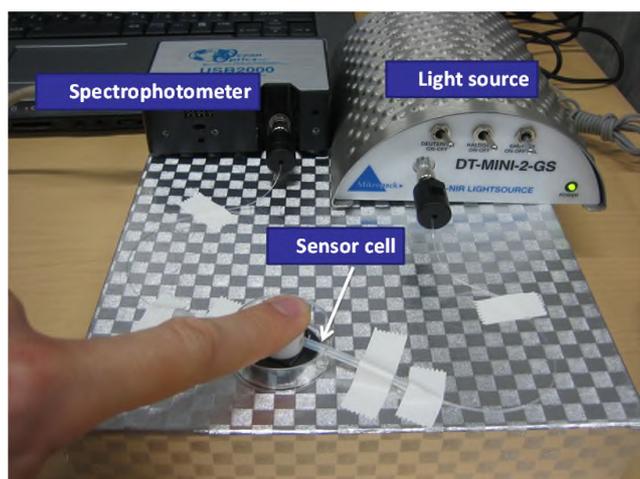
- [1]. S Ohira, K Toda, 2008, "Micro gas analyzers for environmental and medical applications," *Anal. Chim. Acta*, **619**, 143.  
[2]. C Probert, I Ahmed, T Khalid, *et al.*, 2009, "Volatile organic compounds as diagnostic biomarkers in gastrointestinal and liver diseases," *J Gastrointest Liver Dis.* **18**, 337.

## Skin gas analysis using fibre optic sensors

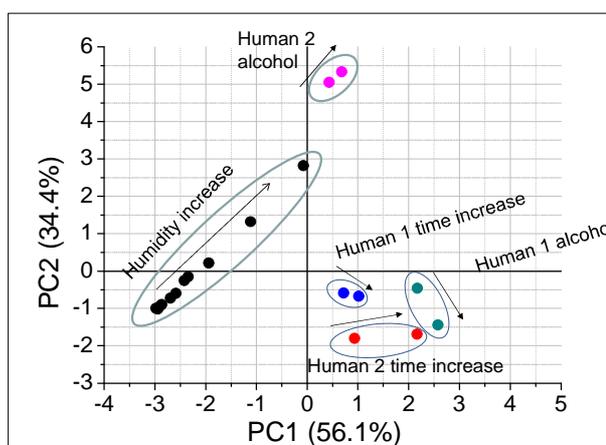
Sergiy Korposh

New diagnostic methods are of considerable interest in medicine. A lot of information about the chemicals excreted by human skin is available in the literature [1]. In gas chromatography (GC) based experiments, a variety of compounds such as acetone, ammonia, hydrocarbons, aromatics were shown to be emitted by human skin, with the quantity of some being correlated to blood content. Some studies suggested that it was possible to identify human subjects through the examination of their odor volatile organic compound (VOC) patterns, formulating the idea of a personal "smellprint" as analogue of fingerprint.

An evanescent-wave optical fibre sensor modified with tetrakis-(4-sulfophenyl) porphine (TSPP) and poly(allylamine hydrochloride) (PAH) bilayers using layer-by-layer (LbL) electrostatic self-assembly was tested to measure the gas emitted from human skin, shown in the left hand figure. Responses of the current optical sensor system could be considered as composite sensor array, where different optical wavelengths act as channels that have selective response to specific volatile compounds. Data obtained from the sensor system was analyzed using principal component analysis (PCA). This approach enabled to distinguish skin odors of different people and their altered physiological conditions after alcohol consumption, (right hand figure).



Sensor used for the skin gas analysis.



Principal component analysis performed using the measured data.

### References

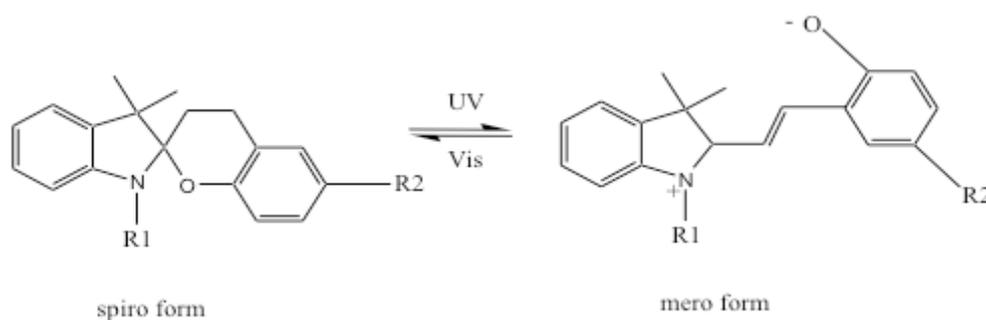
- [1]. S.I. Ohira, K. Toda, 2008, "Micro gas analyzers for environmental and medical applications," *Anal. Chim. Acta* **619**, 143–156.
- [2]. R. Selyanchyn, S. Korposh, W. Yasukochi, S.-W. Lee, 2011, "A preliminary test for skin gas assessment using a porphyrin based evanescent wave optical fiber sensor", *Sensors & Transducers Journal*, **125** (2), 54-67.

## Superresolution and R/W microscopy

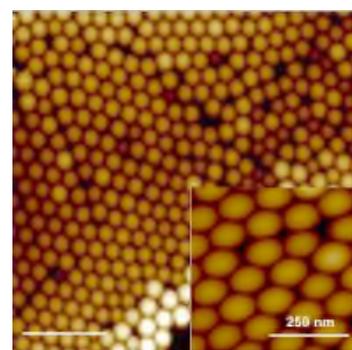
Leo Marques, Rikesh Patel, Matt Clark

Optical microscopy is one of the most powerful tools used in the field of life sciences, allowing researchers to image and study cells and other microorganisms. For direct imaging of objects, the technique is subject to the Rayleigh resolution limit. New techniques in the field of superresolution microscopy, such as STED, PALM, and STORM, tackle the resolution limit by using a photo-switchable fluorescent signal. In our work we use spiropyran (SP) as the photo-switchable molecules incorporated into nanoparticle/polymer films. These molecules can be switched into fluorescent 'on' and 'off' states by using light with two different wavelengths. Widefield fluorescence microscopy is conducted by switching 'on' the particles and applying 2-D intensity patterns at the 'off' wavelength. Due to the nonlinear intensity response of the nanoparticles, the molecules lying at the very darkest regions of the pattern remain 'on'; these regions can be smaller than the Rayleigh resolution limit. A repeated incremental shift in the pattern position allows for fully characterisation.

The optical switching molecule, spiropyran (SP) can be triggered between the 'on' and 'off' states multiple times. The molecule is switched to and from the closed spiro form and the open mero form through exposure to UV light and visible light.



**Spiropyran molecule showing transition.**



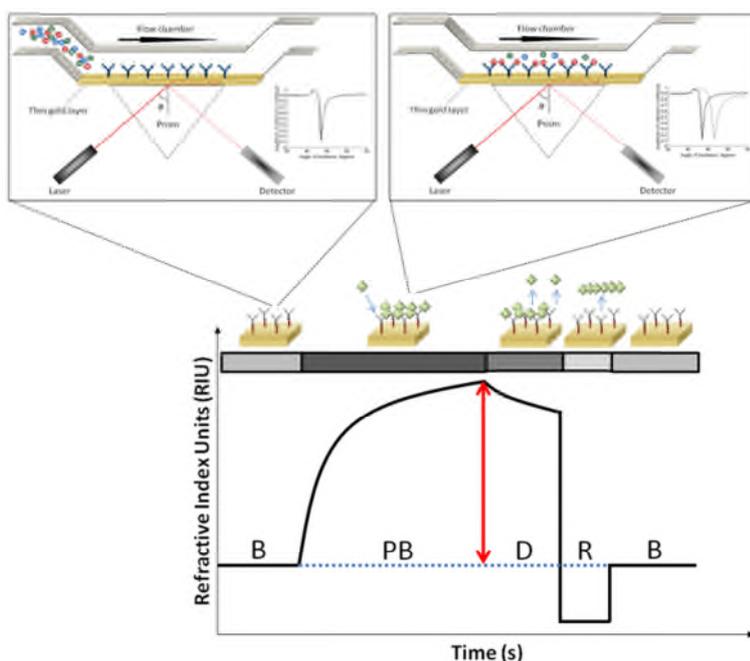
**AFM image of SP 100nm beads**

## Wide field surface plasmon resonance imaging for biomarker panel measurements

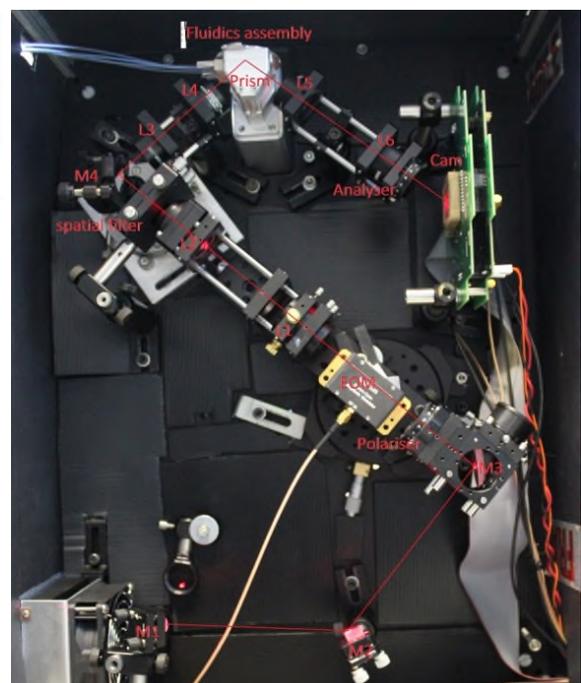
**Richard Smith, Jing Wang, Jing Zhang, Roger Light, Joanna Richens, Paul O'Shea, Mike Somekh**

The surface plasmon resonance (SPR) instrument we have developed forms part of a platform of technologies used for disease diagnosis. This platform is based around a panel of biomarkers, none of which can inform on the patients state on their own but when combined together can provide the power to diagnose disease. The instrument utilises surface plasmon resonance leading to a very sensitive instrument for the detection of antibody / protein binding.

The antibody printed biochip is placed on a prism and the underside is used for the optical instrumentation, a laser beam is reflected off the biochip gold surface and imaged onto a camera. The sample is delivered to the biochip by a microfluidic system and proteins within the sample will bind to the antibodies on the biochip. As the proteins attach the SPR signal changes as the characteristic dip shown in the figure inserts moves, giving rise to a change in the light levels reaching the camera. The rate and amount of binding depends on the protein concentration in the sample and so a measure of the binding rate can be used to provide the information required for the diagnosis. The SPR instrument we have developed uses an unconventional configuration; it uses polarization modulation and is built around a custom made CMOS modulated light camera that enables us to have both high sensitivity and wide dynamic range across a large imaging area.



**SPR signal change during antibody protein binding**



**Picture of the SPR instrument**

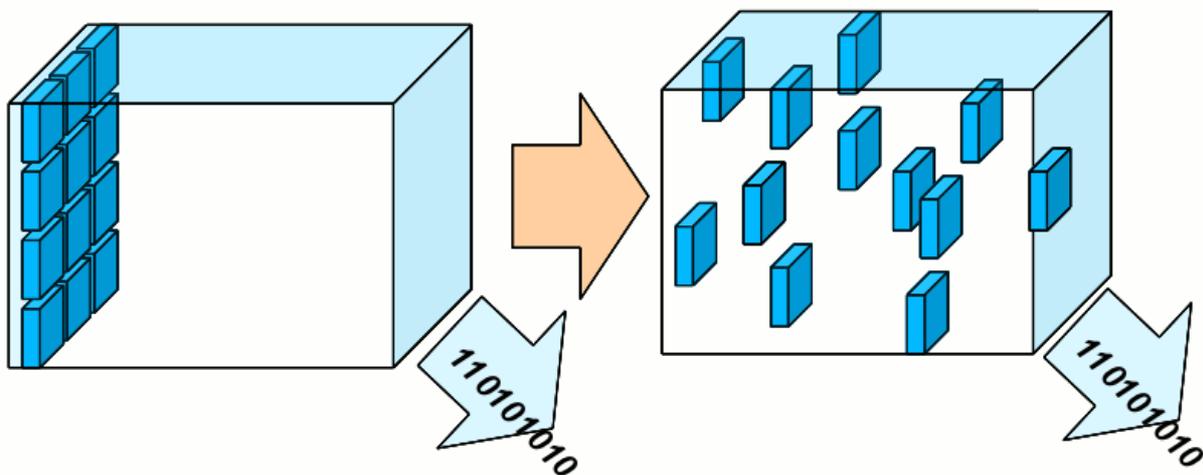
## Temporal pixel multiplexing - simultaneous high-speed, high-resolution imaging of excitable cells

Roger Light<sup>1</sup>, Mike Somekh<sup>1</sup>, Gil Bub<sup>2</sup>

<sup>1</sup> Applied Optics Group, University of Nottingham    <sup>2</sup>University of Oxford

Measuring the behaviour of cardiac cells or whole hearts is a subject of interest to our colleagues in Oxford. A useful signal to measure is the action potentials of the cells, these are directly related to the muscle contractions that generate the detector heart beat. These action potentials can be measured by imaging the cells after staining with voltage sensitive dyes. The measurement of the action potential signal is not trivial however. The signals are small, very fast, but very sparse. Using a high speed camera to carry out the measurement is not ideal because the high data rate needed to read out the image data means that the signal may be lost among the noise, and there will be a large amount of unnecessary data produced.

The TPM project aims to solve this problem by taking a different approach to camera exposures using a fully configurable custom IC camera design. Rather than exposing the whole frame at once, a TPM camera exposes patterns of pixels at different times, until the entire frame is exposed. The data can then be read off at a low pixel rate to give good noise performance. This exposure method encodes some temporal information in the spatial camera array, meaning that the full frame can be treated as a (blurred) high resolution image, or turned into a lower resolution video.



Conventional camera (left) and TPM exposure (right) exposure principle.

## Real time, label-free, detection of stem cell differentiation using high resolution, multi-modal light microscopy

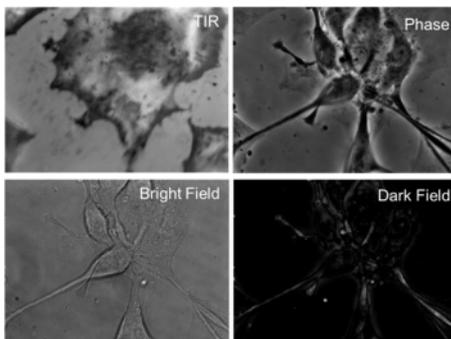
Jing Zhang<sup>1,2</sup>, Emilia Moradi<sup>1,2</sup>, David Morris<sup>2</sup>, John Crowe<sup>2</sup>, Kelly Vere<sup>1</sup>, Mike Somekh<sup>1,2</sup>, Melissa Mather<sup>1,2</sup>

<sup>1</sup> Institute of Biophysics, Imaging and Optical Sciences    <sup>2</sup> Applied Optics Group

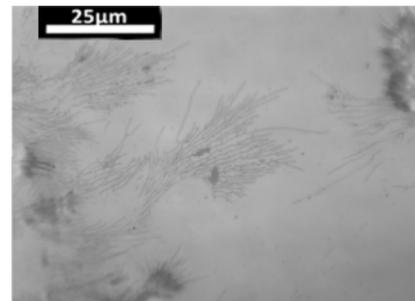
Stem cell therapies may deliver radical approaches to treat neurodegenerative disease. Clinical implementation requires methods to assess the purity of cell populations and to identify suitable cell culture conditions to control cell proliferation, survival, migration and the direction of stem cell differentiation.

As part of the EPSRC Centre for Innovative Manufacturing in Regenerative Medicine a novel multi-modal light microscope for non-invasive, label-free characterisation of live cells has been constructed. This microscope allows phase imaging and proximity microscopy (total internal reflection (TIR) microscopy) to be performed with the full resolution of a high NA (1.49) immersion microscope objective.

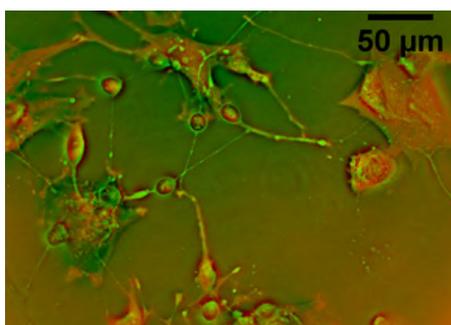
We have demonstrated the use of our multi-modal microscope to study the differentiation of neural stem cells through determination of cell adhesion and 3D morphology. These findings have been validated by endpoint immunostaining and preliminary results suggest the microscope has the potential to predict cell quality and fate earlier than possible with conventional assays. These findings are of tremendous importance in the context of the regulation and translation of stem cell therapies into the clinic.



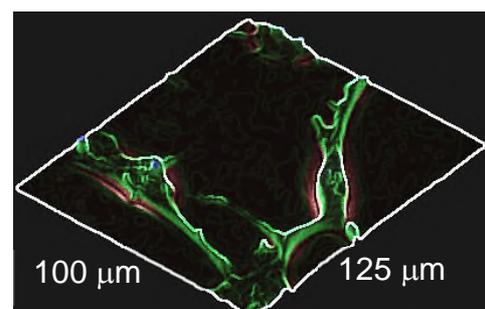
Live neural stem cells imaged by TIR, phase contrast, bright field and dark field imaging of the same field of view



High resolution imaging of neural stem cells using TIR microscopy. Contrast is produced can be used to study cell adhesion



Overlay of TIR and phase contrast imaging producing complementary information of a mixed population of neural cells



Reconstructed neural cell 3D morphology achieved through quantitative phase contrast imaging

## Microscopy techniques for the life sciences

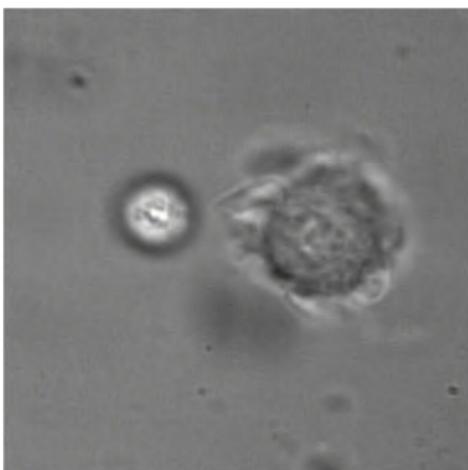
### Amanda J Wright

As part of IBIOS my focus is on optical microscopy techniques that can be applied to Life Science research and I work closely with colleagues in the School of Life Sciences. The two techniques I am currently working on are optical trapping or optical tweezers and adaptive optics. Optical trapping involves using a laser beam and a high numerical aperture microscope objective lens to trap, manipulate and control micron sized cells/objects in three dimensions. It has been around since the early 1980s and has found application across the Science and Engineering disciplines. Examples of recent projects include:

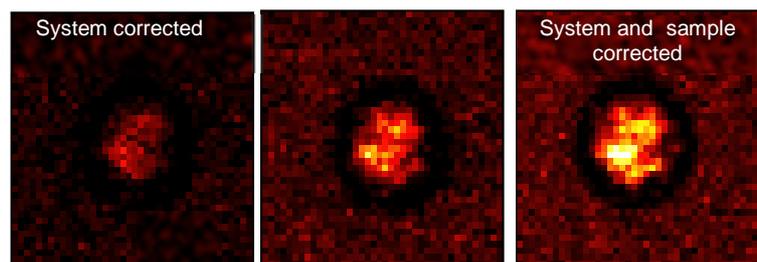
- 1) Using an optically trapped local probe to study the micro-rheology of the vitreous humor to aid the development of more effective drug delivery systems
- 2) Accurately quantifying the interaction force between individual immune cells and observing differences in force associated with therapeutic intervention

Adaptive Optics was originally developed for Optical Astronomy to overcome the aberrations caused by the earth's atmosphere and to improve the quality of images. I specialise in transferring this technology to non-linear microscopy systems where image resolution and quality are known to greatly deteriorate with imaging depth. I have worked on confocal, multi-photon, CARS and second harmonic microscopes successfully installing Adaptive Optics systems leading to improved image quality at depth.

This work has been supported by the Royal Academy of Engineering, EPSRC, EU, Royal Society and Allergan.



Controlling and quantifying the interaction force between immune cells. Here the T cell is optically trapped and the dendritic cell is adhered to the coverslip.



A 10µm diameter polystyrene bead imaged at a depth of 592µm in a CARS microscope. Left to right: no aberration correction applied; correcting for only system induced aberrations; correcting for system and sample induced aberrations.

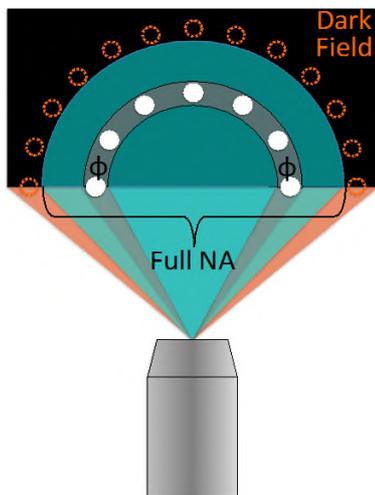
## Condenser-free phase contrast microscopy

Flavius Pascut, Kevin Webb

Phase contrast microscopy allows the study of highly transparent yet detail-rich specimens by producing intensity contrast from phase objects within the sample. We have developed a generalised phase contrast illumination schema in which condenser optics are entirely eliminated, yielding a condenser-free yet highly effective method of obtaining phase contrast in visible light microscopy. A ring of light emitting diodes is positioned within the optical light-path such that observation of the objective back focal plane places this ring in appropriate conjunction with the phase plate.

We have demonstrated that true Zernike phase contrast is obtained, whose geometry can be flexibly manipulated to provide an arbitrary working distance between illuminator and sample. Condenser-free phase contrast has been demonstrated across a range of magnifications (4-100x), numerical apertures (0.13-1.65NA), and conventional phase positions. Also facilitated by the same schema is condenser-free darkfield microscopy, as well as the simultaneous application of condenser-free phase contrast in conjunction with scanning probe methods, such as scanning ion conductance microscopy (SICM).

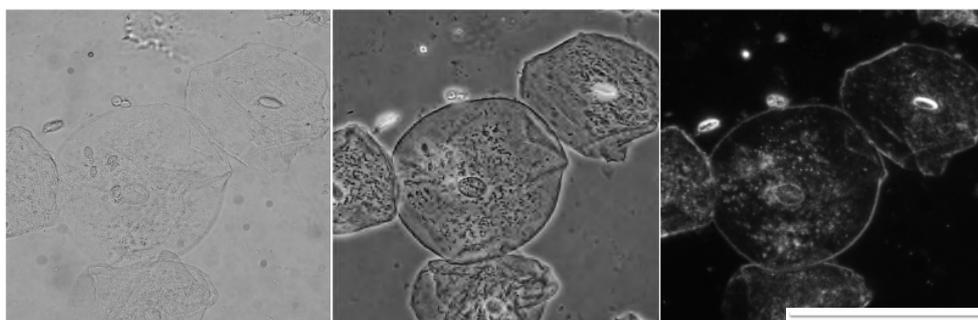
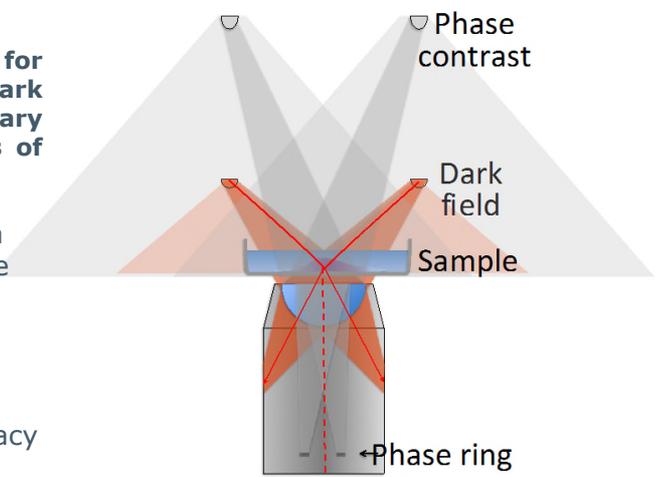
By eliminating the condenser assembly, and thus providing enhanced working space above the preparation, a range of concurrent imaging and electrophysiological techniques are technically facilitated. The compact, versatile LED illumination schema further lends itself to novel next-generation transmitted-light microscopy designs, while the condenser-free illumination method using rings of independent emitters may be exploited in future in other electromagnetic wavebands, including X-rays or the infrared.



**Condenser-free illumination schema for phase contrast and dark field imaging at arbitrary geometries, using rings of LED's:**

*Left* Illumination schema for condenser-free phase contrast and dark field imaging using rings of LED's

*Right* Back Focal Plane schema showing conjugacy of illumination sources



**Condenser-free contrast enhancement in buccal epithelial cells:**

*Left* bright-field

*Middle* phase contrast

*Right* Dark field image

This work has been supported by the Royal Academy of Engineering and the EPSRC

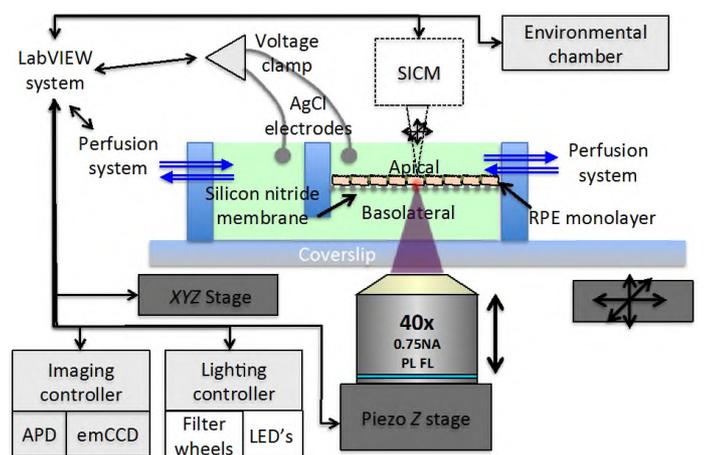
## Direct imaging of epithelial fluid transport

Flavius Pascut, Emilia Moradi, Kevin Webb

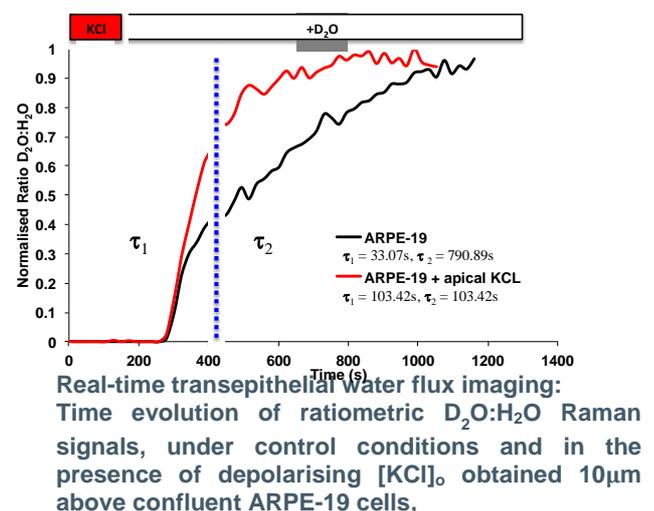
Epithelial fluid transport lies at the heart of bodily homeostasis; maintaining fluid and ion balance in response to normal physiology and to insult. Dysfunctions in epithelial transport are implicated in cystic fibrosis, kidney disease, and eye disease. The cornea, ciliary epithelium, and retinal pigment epithelium (RPE) are all important fluid transporting epithelial structures in the eye.

This programme of research addresses a fundamental limitation in the field; that of a lack of direct water transport measurements at the nano- to microscale within and across transporting epithelia. While it is known that the flow of solvent (water) is coupled to that of ions and other solutes, exactly how epithelia transfer fluid between two solutions of identical composition remains an enigma. A range of proxy measures of water flux have been employed, but water transport has yet to be imaged directly at the subcellular scale.

Our hybrid optical and electrophysiological system is being assembled to address the mechanistic foundations of epithelial fluid transport by providing multiscale, multimodal measurements of electrodynamic events at subcellular resolution. Confluent RPE layers have been established on nanoporous silicon substrates which are highly permeable, incredibly thin (50nm) and optically transparent. Small (1mm<sup>2</sup>) RPE cultures are held under voltage or current clamp for simultaneous high-resolution imaging of water flux using confocal Raman microspectroscopy. The resulting system is amenable to both apical and basolateral perfusion, allowing physiological and pharmacological manipulation. Optogenetics is further being applied for the first time to drive and manipulate epithelial transport in individual cells, non-invasively, using stimulus pulses of light.



**System schema showing geometry and control systems for perfusion, imaging, and positioning**



This work is supported by the BBSRC and EPSRC

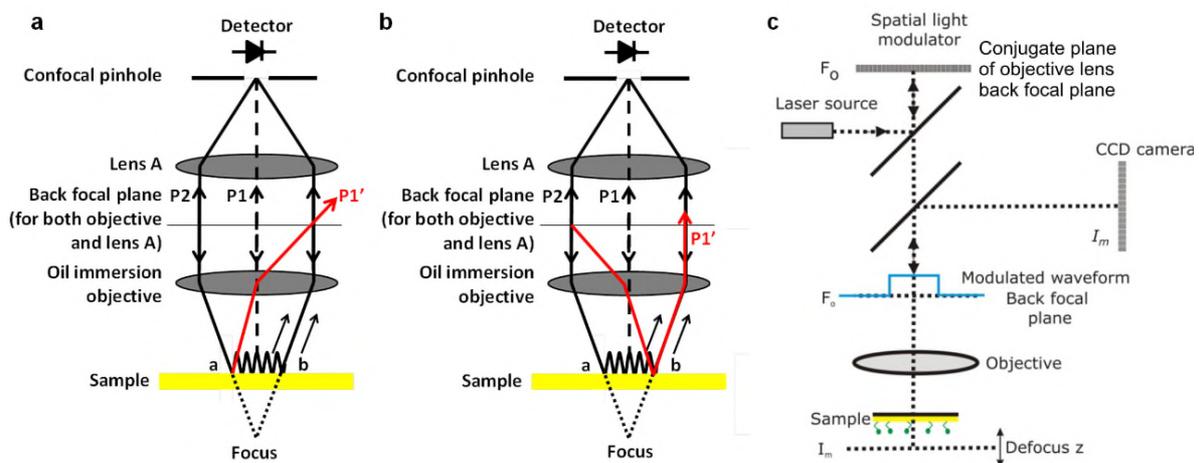
## Confocal surface plasmon microscopy

Suejit Pechprasarn, Chung W See and Mike Somekh

Surface plasmons (SP) provide us with a very powerful tool for sensing small changes in local refractive index and since scientists are currently aiming for measuring small numbers of molecules for supporting medical diagnosis. Our research and developmental work is focused on developing a very sensitive surface plasmon sensor based on a modified confocal microscope as shown in the figure.

We have shown that a modified confocal microscope (Zhang et al., 2012b) shown in the figure can give us an excellent sensitivity over a well confined region. Integrating a phase spatial light modulator (phase-SLM) into the back focal plane of microscope objective lens provides us with a very flexible embedded interferometer (Zhang et al., 2012a; Zhang et al., 2013). We can see that the p-polarised light forms an SP; some of which appears to come from the focus and passes through the pinhole. The s-polarised light will miss the pinhole; however we use the SLM to deflect this light into the pinhole and block path P1 shown as path P1' in the figure. This reduces the effect of microphonic vibrations and creates an ultrastable interferometer.

We have also developed a theoretical framework (Pechprasarn and Somekh, 2012) based on rigorous vector diffraction theory to assess the performance of the confocal SP microscope and determine how few molecules can be detected.



**(a) Simplified schematic showing operation of a confocal microscope with SP excitation; the red lines indicate the direct reflection of incident s-polarization. The azimuthal planes corresponding to pure p- and s- incident polarizations are orthogonal. The reflected s-polarised beam is deflected after interacting with the sample at the back focal plane of the objective lens. (b) Similar to (a) but the s-polarised beam is deflected before interacting with the sample. (c) Schematic of optical system showing the relationship between different planes in the system. The blue waveform indicates phase modulation in the back focal plane.**

### References

- [1] Zhang B., Pechprasarn S., Zhang J., Somekh M.G., 2012, *Optics Express*, **20**, 7388-7397
- [2] Zhang B., Pechprasarn S., Somekh M.G., 2012, *Optics Express*, **20**, 28039-28048
- [3] Zhang B., Pechprasarn S., Somekh M.G., 2012, *Optics Express*, **21**, 11523-11535
- [4] Pechprasarn S., Somekh M.G. 2012, *Journal of Microscopy*, **246**, 287-297



## MindTech - NIHR Healthcare Technology Cooperative for mental health and neurodevelopmental disorders

**Michael Craven, John Crowe**

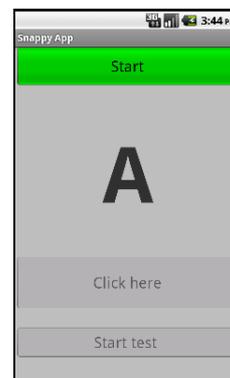
MindTech Healthcare Technology Co-operative (HTC) is a national centre of excellence focussing on the development and evaluation of new technology for mental healthcare. MindTech brings together patients, healthcare professionals, researchers and industry to identify unmet clinical needs and develop and/or evaluate new technologies, and so assist the translation of products into routine clinical practice. The idea of HTCs arose from the Department of Health's Healthcare Industries Task Force (2003), which aimed to stimulate the healthcare technology economy in the UK. The areas of focus were market access, R&D and the industrial base, regulatory issues and international trade. The central themes that emerged were how to stimulate innovation in the NHS and industry, and how to increase adoption of new useful medical technologies.

We are currently looking at technologies for dementia, mood disorders such as depression and neurodevelopmental disorders such as Tourette Syndrome and ADHD (attention deficit hyperactivity disorder). However, we are interested in all aspects of mental health and we aim to map the non-drug technology landscape including informatics as well as devices and software applications. MindTech is a multi-disciplinary centre involving clinical, engineering and implementation specialists and includes a patient reference group to ensure end-user involvement. MindTech is based at the University of Nottingham Innovation Park and is hosted by the Institute of Mental Health whilst it includes personnel from the Faculty of Medicine and Health Sciences, Faculty of Engineering and the School of Computer Science and Information Technology. The Faculty of Engineering Division of Electric Systems and Optics lead the Technology Theme of MindTech and bring expertise in sensor technologies and software development and also contributes human factors and cost-effectiveness modelling methods into evaluation processes. Pilot work has included the use of multiple sensors to monitor the activity of people with bipolar disorder to enable early detection of changes in behaviour. We are also collaborating on the use of smartphone Apps to allow people (young people or adults) with ADHD to self-monitor their condition by means of motion tracking whilst taking a continuous performance test. Other interests include video applications for remote therapy and assisted living technologies for use in the home.

Following an open competition the eight NIHR HTCs were launched on 1 January 2013, and will receive a total of £6.4m of funding over 4 years. In addition the Engineering and Physical Sciences Research Council (EPSRC) are inviting network proposals to enable collaborations between academia and the HTCs (closing date 7 January 2014).

Further information: <http://mindtech.org.uk>

Frequency of app use	%
Every day	53
Weekly	17
Monthly	4
Not at all	26



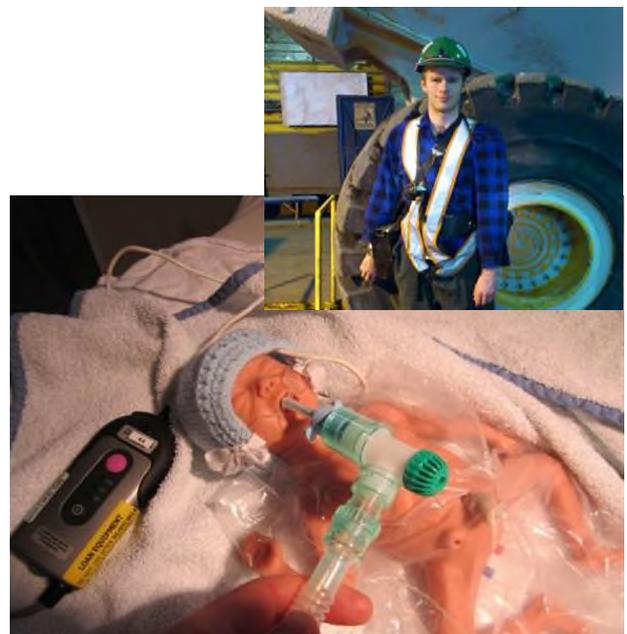
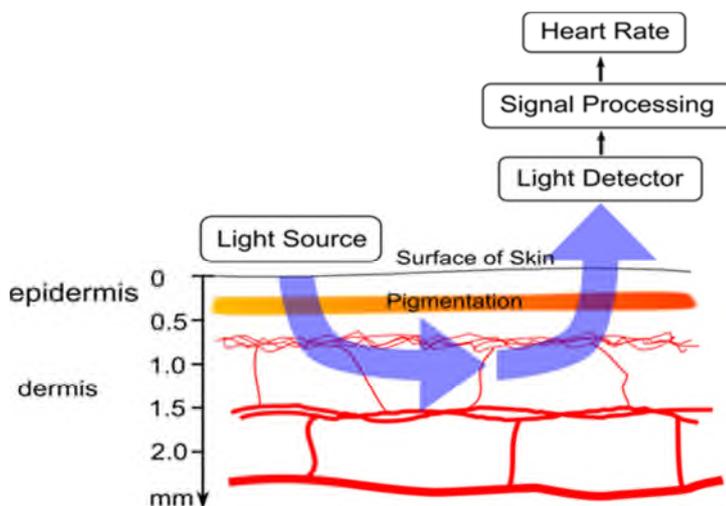
## Heartlight: Heart-rate sensing from miners to minors

**James Carpenter, John Crowe, Barrie Hayes-Gill**

A small optical non-invasive heart-rate sensor (Heartlight) has been developed by University of Nottingham academics. Started through a PhD in 2004, the technology has been applied to multiple fields of use, including monitoring the health and wellbeing of miners working in hot environments and the assessment of newborn babies requiring resuscitation at the time of birth.

Miners can be exposed to temperatures exceeding 60 degrees Celsius, which means that many suffer from heat stress. This causes a number of problems such as fatigue, a decline in alertness and vigilance, muscle cramps and in the worst cases, heat stroke. A recent collaboration with a contract electronics manufacturer, Tioga Ltd, in the form of a KTP, has enabled the production of a wireless hard-hat incorporating Heartlight technology. The hard-hat has already undergone trials in underground mines with promising results.

A serendipitous meeting with a clinician in 2007 has prompted the development of a Heartlight sensor suitable for use in newborn resuscitation. 10% of newborn babies require some form of resuscitation at birth and heart rate is the best indicator of the success of interventions. However the current heart-rate assessment technique, the stethoscope, is often inaccurate, and causes mismanagement and delays during the resuscitation. An improvement to resuscitation practice through the use of Heartlight will reduce short term morbidity and save on healthcare costs. A large number of recordings have been performed on newborns to date, and future research will concentrate on clinical user needs and industrial prototyping.



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