Case for Support of Proposal “Depth-resolved phase-contrast optical metrology in life sciences and engineering”

1. TRACK RECORD OF THE CANDIDATE

1.1 Short history

After completing a PhD in Physics at the National University of Rosario (Argentina) in 2002, I joined Loughborough University as a Research Associate. My performance as a young independent researcher, as now demonstrated by 17 papers published in peer reviewed journals, was acknowledged in early 2005 with promotion to Research Fellow and then with an appointment to a fast track Lectureship.

I have a long-term interest and a strong track record in full-field non-contact optical metrology and its diverse applications. My research into this field started with my PhD project, which investigated different Electronic Speckle Pattern Interferometry systems for the study of impact induced deformations in metallic components. During the course of my PhD I looked for international collaboration opportunities in other Optical Metrology laboratories to broaden my experience through different work environments and technologies. I spent a total of nine months as a student visitor at the Centro de Investigaciones en Óptica (Mexico, 1999) and the Mechanical Engineering Department at Loughborough University (UK, 2001&2002). These experiences were vital for my development as they allowed me to investigate, implement and optimise different interferometric systems for a wide range of applications. I have explored and contributed to different aspects of displacement evaluation from the measured raw data. These include algorithms for (i) adaptive speckle noise reduction, (ii) phase evaluation with adaptive phase shifting, (iii) 2-D (minimum L^p norm type) phase unwrapping and (iv) numerical evaluation of vibration-induced phase errors in high-speed phase-shifting speckle pattern interferometry. Following my PhD degree I was awarded a scholarship by Fundación Antorchas and The British Council to continue my research at Loughborough University for three months, after which I joined the University as Research Associate in June 2002.

In Loughborough, my research continued with “In-situ quantitative flaw detection using advanced optical inspection techniques”, an EPSRC funded project, where I built robust interferometers (against environmental disturbances) with applications in structural integrity of carbon fibre reinforced composites (CFRP) using high-speed phase-shifted speckle interferometry, temporal phase unwrapping, and Genetic Algorithms for detection and characterization of defects. From this work, it was concluded that *from surface deformation measurements alone*, the solution of the inverse problem that finds the dimensions and depth of delamination cracks in CFRP panels can present multiple solutions and therefore gives ambiguous results.

I also worked on another EPSRC funded project to measure and model strain distributions in adhesively bonded joints. This was in collaboration with the University’s Physics Department and the Structural Integrity Research Group at the Wolfson School. I carried out numerous sets of neutron diffraction experiments for bulk strain measurements at different neutron sources (Rutherford Appleton, UK; Studsvik nuclear reactor, Sweden; Institute Laue Langevin, France), and also Moiré Interferometry experiments for surface full-field strain measurements. We have demonstrated that Finite Element Analysis is capable of predicting both surface and internal strains in the adherends of bonded joints and within the adhesive layer, and confirmed that significant residual strains exist within non-symmetric joints.

1.2 Results and conclusions of recent work relevant to the current proposal

My most recent work was EPSRC Platform Grant funded on a series of proof-of-principle and validation experiments with three novel approaches −Wavelength Scanning Interferometry (WSI), Tilt Scanning Interferometry (TSI) and Phase Contrast Spectral Optical Coherence Tomography (PC SOCT)− to measure **depth-resolved displacement fields within weakly scattering materials and with high displacement sensitivity**.[1-4] This means that we can now see in great detail how the bulk of the material moves and deforms and therefore there is no need to rely on surface measurements to estimate what is going on inside. With this ability it is becoming possible for the first time to map 3-D distributions of strains relevant to structural integrity analysis or, through elastography numerical techniques, to extract the mechanical properties of the material, that can be non homogeneously distributed.

These experimental techniques can all be considered as a type of Optical Coherence Tomography (OCT) because they provide the microstructure in cross sections through the thickness of the sample. The main difference with standard OCT techniques, and the novelty of these approaches, is that the **phase information** in the recorded signal is used to evaluate displacements with a sensitivity that is decoupled from the depth resolution, and which can be as small as some tens of nanometres, ultimately limited by the phase noise. WSI and TSI require the acquisition of a sequence of images and are therefore appropriate to the study of static problems. They can provide 3-D distributions of all displacement components within a scattering material, and have therefore innumerable potential applications if one considers the breadth of applications that surface-only measurements have found over the past few decades in mechanics of materials. As an example of this approach, during the validation phase of TSI, measurements were made within a point-loaded polyester resin beam (see Fig. 1). In-plane and out-of-plane displacement fields for four ‘slices’ within the beam are shown, starting at $z = 0$ mm (left) in steps of -1.7 mm down to $z = -5.2$ mm (right). These results are in close agreement with Finite Element predictions.

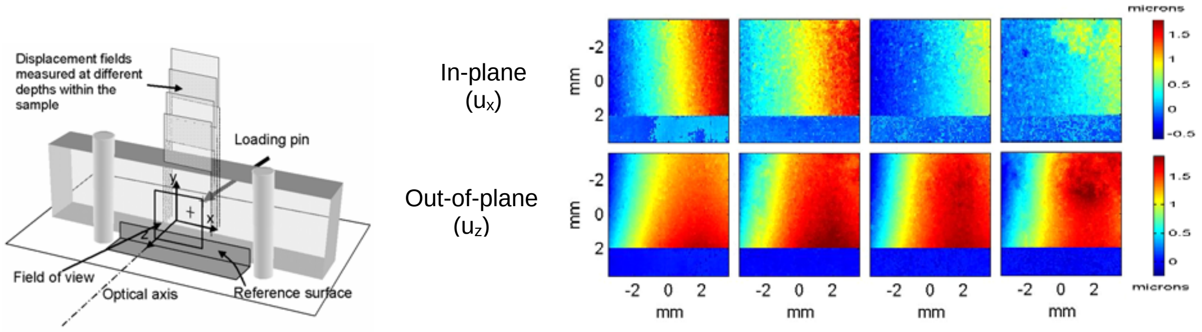

Figure 1. Depth-resolved displacements measured inside a polyester resin beam by means of Tilt Scanning Interferometry (from Ref. 3).

PC SOCT is a "single shot" technique, and therefore suitable for dynamic applications. It provides a 2-D cross section of the sample. In a recent PhD student project that I supervised, we developed a phase contrast SOCT system and demonstrated depth-resolved displacement field measurements with it.[4] We have also observed displacement fields in cross sections of porcine corneas after changes in the intraocular pressure, as it is shown in Fig. 2, Section 2.2.3. This work has won the **prize** for the best paper in the oral sessions (out of 63) at the Speckle06 International Conference, Nimes, France, Sept 2006.

These experiments have exposed numerous aspects that limit the performance of the prototype setups, which could be greatly enhanced in order to fully exploit the new technology. If those limitations are successfully addressed, we will be able to investigate the application of these novel techniques in challenging materials in which it is critical to measure through-the-thickness mechanical properties in order to correctly predict mechanical behaviour.

1.3 Future plans

This is a shortened version of an ARF proposal that was rated overall as "outstanding" by the 4 reviewers in early 2006 but was ultimately rejected. I acknowledge that this project is ambitious and intend to resubmit an ARF proposal with a new programme of work in 2007 that will support this one. My aspiration is to establish an internationally renowned research career in the field of depth-resolved optical metrology in which I have recently made pioneering contributions. My main focus will be on the development of different instruments and techniques for full-field volume (depth-resolved) metrology and on tackling different applications in which the kind of measurements supplied are crucial for further understanding of the behaviour of the materials under study.

1.4 Collaboration with other institutions

I have contacted and motivated several groups to collaborate on this project, all of which have perceived the potential of the above-mentioned techniques to study materials of their interest. Collaboration with the School of Optometry and Vision Sciences at Cardiff University, through Dr. Tim Wess, will be essential to study through-the-thickness properties of the vertebrate eye cornea. Joint work with Prof. Fabrice Pierron and Dr. Stéphane Avril, ENSAM, Châlons en Champagne, France, will aim to extract volume distributions of material constitutive parameters from full-field measurements by using novel inverse methods. Dr. Gustavo Galizzi (Rosario Institute of Physics, Argentina) will contribute to instrument construction and development of data analysis tools through a visit as a Visiting Researcher and further work in Argentina.

1.5 Expertise and infrastructure available at the host Institution

The Wolfson School of Mechanical and Manufacturing Engineering, Loughborough University, was rated 5 in the 2001 RAE. Within the School, the Optical Engineering group for which I am a member has been awarded the 2000 Queen's Anniversary prize for Further and Higher Education for its excellence, and is holder of an EPSRC Platform Grant (renewed for 5 years from 2005), awarded through international peer review to groups of recognised internationally leading status. Two spinout companies (LOE Ltd and Phase Vision Ltd) provide options for eventual commercial exploitation of the project deliverables. High quality optical laboratory space and equipment has been made available to me in my current role and this would continue if granted a FG. I believe that this bank of expertise is unmatched nationally, and I consider Loughborough University would provide the most suitable environment, resources and facilities for a successful undertaking of the proposed research.

1.6 References

[1] P. D. Ruiz, Y. Z. Zhou, J. M. Huntley, et al., Journal of Optics A: Pure and Applied Optics **6**, 679 (2004).
[2] P. D. Ruiz, J. M. Huntley, and R. D. Wildman, Applied Optics **44**, 3945 (2005).
[3] P. D. Ruiz, J. M. Huntley, and A. Maranon, Proceedings of the Royal Society A **462**, 2481 (2006).
[4] M. de la Torre-Ibarra, P. D. Ruiz, and J. M. Huntley, Optics Express, 14, (21), 9643-9656, (2006).

2. DESCRIPTION OF THE PROPOSED RESEARCH

Abstract

Novel "phase contrast" optical techniques that can provide 3-D displacement distributions within the volume of weakly scattering materials will be developed and applied. Their feasibility and promise have been recently demonstrated with proof-of-principle experiments either by using wavelength scanning, broadband spectral detection, or by changing illumination direction. The techniques have some exciting features: they are full-field, non-contact, have a displacement sensitivity of order 10nm due to the use of optical phase information, and can be used to study static and dynamic depth-resolved deformation fields within semitransparent materials. They also provide the volume microstructure of the material to which the deformation fields can be superimposed. This project builds upon lessons learned from those preliminary experiments and aims to establish and mature these techniques as a "platform technology" by developing the necessary instrumentation and data analysis tools and to overcome identified technical limitations. Two important but hitherto insoluble problems in life sciences and engineering will be investigated with this new technology: 1) Compliance characterization of the vertebrate eye cornea, in which 3-D displacement fields measured within the corneal tissue will be used to extract material property distributions inside it by using novel inverse problem approaches; and 2) Micromechanics of granular materials, in which contact forces between individual grains will be evaluated from 3-D displacement field distributions to check the hypothesis of force chains in 3-D granular packs.

2.1 Background

Semitransparent scattering materials are widely encountered in industrial applications (adhesives, polymers, composite materials) and biological systems (tissues such as skin, cartilages, cornea) and their function is often critical in the performance and structural integrity of the system they belong to. There has been a long history of research into the mechanical and functional behaviour of these materials, but they are not in many cases fully understood due to (i) the inherent complexity of the materials that cannot always be modelled with continuum mechanics assumptions, as in the case of many composite materials and biological tissues, and (ii) the limitations of current experimental techniques to measure the distribution of the constitutive parameters of the materials within their volume with enough sensitivity and spatial resolution, in order to relax the need for simplistic bulk properties assumptions.

Displacement fields can be used to evaluate the constitutive parameters of an anisotropic material (mainly elastic constants) by solving an inverse problem. In general it requires the measurement of three-component displacement fields (to over-determine the problem) under a set of known boundary conditions, and the geometry of the sample. The inverse problem is usually posed as the identification of the most representative components of the material constitutive matrix. Generally this is due to insufficient spatial resolution and/or incomplete multi-component displacement mapping, as is the case for most interferometric techniques that only provide surface displacement fields. Therefore, a technique that allows us to measure multi-component displacement fields inside the volume of the material will enable us to determine non-uniform distributions of constitutive parameters, which is essential to accurately predict mechanical behavior.

A broad range of methods to measure internal structure and displacement fields have been developed in the last few decades such as X-ray diffraction, photoelastic tomography (PT) [5, 6], Phase Contrast Magnetic Resonance Imaging (PCMRI)[7, 8], and 3-D Digital Image Correlation (DIC) using data acquired with X-ray Computed Tomography (XCT) [9] and Optical Coherence Tomography (**OCT**).[10, 11] Each technique has a restricted range of materials to which it can be applied: PT, for example, is suitable only for materials that exhibit photo-elasticity; PCMRI requires significant water or fat content in the sample. For many technologically- and medically-important materials the existing techniques are often either non-applicable, have insufficient spatial resolution or else are too insensitive.

OCT is an exciting technique that provides depth-resolved microstructure images primarily for medical applications. It is based on a Michelson interferometer and a low temporal coherence broadband source and is usually implemented in the time domain, in which case the reference mirror is scanned to provide cross-sections of the sample. It can also be realised in the spectral domain (**SOCT**) where all the information of a 'slice' inside the material is registered simultaneously by using a spectrometer, an area photodetector array and no scanning devices. A 2-D interferogram is recorded with depth encoded as spatial frequency along the wavelength axis of the spectrometer, rather than as a function of time.[12] The microstructure is then extracted from the spectral magnitude of the Fourier transform along the wave-number axis.

2.2 Methodology

Although correlation methods can be used to quantify displacement fields from before- and after-deformation OCT microstructure images, the displacement sensitivity would be limited by the depth resolution of typically 10 µm or more. This constrains the ability to detect and quantify deformation fields due to small loads (mechanical, thermal or chemical) even for compliant materials. Working with Prof. J. M. Huntley under EPSRC platform grant funding, I have recently demonstrated with a series of proof-of-principle experiments, that optical phase information can be extracted from OCT systems to measure displacements with a sensitivity of order 10nm, i.e. some 2-3 orders of magnitude better than the intrinsic depth resolution. I have developed three different methods that make use of phase information to measure depth-resolved displacements. I will refer to them as Phase-Contrast (PC) methods,[13] and they are described below. Doppler OCT, proposed in 1997, also makes use of this phase information for velocity mapping of e.g. retinal blood flow[14].

2.2.1 Measurement of depth-resolved displacement fields in semitransparent materials using optical phase information

A. Tilt Scanning Interferometry (TSI)

TSI is realised by tilting the illumination wavefronts from a monochromatic source whilst a sequence of interferograms records depth-encoded temporal carrier signals.[3] A linear variation in Doppler shift with depth is induced by a tilting mirror. TSI can be adapted to any laser source and controlled tilting of the wavefront is technically much easier than tuning the wavelength of a laser as in Wavelength Scanning Interferometry (WSI), a sequential version of spectral OCT that can also deliver depth-resolved displacement fields.[1, 2] For example, closed loop piezo-electric tilt stages are now available with sub-μrad resolution that can scan a beam through 100 mrad in a fraction of a second. At an incidence angle of 45°, and a wavelength of 532 nm the effective depth resolution is ~30 μm. To achieve the same resolution, a WSI system would need a tuning range of ~30 nm, requiring mode-hop-free dye or Ti:sapphire lasers, which cost typically £70-100k and operate on multiple longitudinal modes with the potential for major speckle decorrelation.

TSI will therefore result in an instrument that is less expensive and has significantly higher performance than one based on WSI. TSI is appropriate to study static problems and it can provide *3-D distributions of all displacement components* within a scattering material. As an example of this approach we made measurements within a point-loaded polyester resin beam, [3] and the results are shown in Fig. 1, Section 1.2.

B. Phase-Contrast Spectral Optical Coherence Tomography (PC SOCT)

PC SOCT is fundamentally analogous to WSI, the main difference being that in PC SOCT a low cost broadband source is used and the interference signal is present along the wavelength axis of a spectrometer detector, rather than along the time axis of a sequence of frames, as in WSI. The key feature of PC SOCT is that it is "single shot", which enables fast acquisition of instantaneous deformation states to study dynamic events and follow the temporal evolution of displacement and strain fields with nanometre sensitivity within a slice in the sample. It provides 2-D cross sections of the material, usually perpendicular to the surface of the sample. Out of plane sensitivity is straightforward to measure and in-plane sensitivity could be realized for non-dispersive media. Very recently, and under my supervision, proof-of-principle experiments were performed which proved that *depth-resolved displacements* can be measured by means of PC SOCT. We achieved a depth resolution of ~30 microns and a displacement sensitivity of ~30nm, limited by the phase noise.[4] PC SOCT has exciting practical advantages over WSI and the potential to expand the capabilities of SOCT to map displacement and strain fields with nanometre sensitivity within the microstructure of *in-vivo* samples.

2.2.2 Identification of constitutive parameters using inverse methods

Once the displacement fields have been measured, they can be used to find the constitutive parameters of the material. In the general case where the stress/strain fields are heterogeneous due to boundary conditions, specimen geometry, localized plasticity or damage, the inverse problem can only be solved if full-field data is available. **Finite Element Updating (FEU)**[15] and the **Virtual Fields Method (VFM)**[16] are two approaches currently used to obtain the constitutive parameters from 2-D full-field strain measurements. In the former the direct problem is solved by means of Finite Element Analysis (FEA) by using initial guesses of the unknown parameters and simulations are performed iteratively until the displacements computed at various nodes of the mesh match their experimental counterparts. In the latter, given measured strain fields, the stress fields are expressed as a parameterised function of the unknown constitutive parameters. The principle of virtual work is then applied so that the stress fields verify the global equilibrium of the structure. Finally the use of several virtual fields yields a system of equations that involve the unknown parameters and which leads to the solution. In collaboration with Prof. F. Pierron's group, these methods will be extended to 3-D and used to extract constitutive parameters from biological tissue as described in Section 2.2.3.

2.2.3 Life sciences and engineering problems to be addressed by the research

A. Compliance characterization of the vertebrate eye cornea

Nowadays refractive surgery is becoming more and more widespread as a means for permanently correcting refractive errors in our eyes, with over 100,000 operations in the UK per year at a cost of approximately £2,500 per eye. The primary objective of this interventions is the modification of the corneal central anterior surface by removing material, as in laser in-situ keratomileusis (LASIK) and photorefractive keratectomy (PRK). The achieved refractive outcome may however differ from the expected outcome because of tissue deformations induced by the hydrostatic eye pressure that constantly strains the cornea. Changes in corneal shape after flap cutting and laser ablation must be accounted for in surgical planning because spherical aberration and asphericity after laser refractive surgery may deviate from predictions based solely on the laser ablation target profile (between 5% and 20% of the interventions lead to residual refractive errors). Accurate prediction of these changes is still very limited as it requires a detailed knowledge of through-the-thickness mechanical properties of the corneal tissue, which may vary significantly with depth and be markedly anisotropic. Figure 2 shows a wrapped phase map (proportional to displacements parallel to the corneal axis) through the thickness of an *ex-vivo* porcine cornea that I recently obtained using PC SOCT. The phase change was due to viscoelastic deformation of the cornea after a change in the intraocular pressure.

In this project, I aim to answer the following research questions with regard to this problem: 1) Is there a non-uniform distribution of elastic modulus through-the-thickness of the cornea?; 2) If so, what is the distribution and how does it affect corneal compliance and corneal behaviour after ablation?; Section 2.4 (WP6) describes how these questions will be approached.

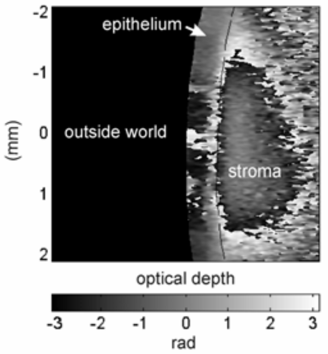

Figure 2. Phase change measured by the PI with PC SOCT due to viscoelastic deformation of an ex-vivo porcine cornea after a change in the intraocular pressure.

B. Micromechanics of granular materials

Granular materials are economically important in some major market sectors such as the food, chemical and pharmaceutical industries. Design codes for storage structures and ducts are based on empirical models (of granular packing, flow, jamming) that ultimately require a micromechanical understanding at the single grain level. In many cases the structures fail due to concentrated stresses that the models could not predict. Experimental work using photo-elasticity is providing great insight, and initiated the concept of 'force chains', i.e. networks of contacts through which most of the load is carried within the bead pack.[17] Such experiments are however inherently two-dimensional, and there is now great interest in exploring experimental techniques that could deliver information on the contact force network within three-dimensional packs. Contact forces between the grains and the boundaries of a container have been recently measured at Loughborough[18-20] and this project will extend this to 3-D measurements of inter-grain contact forces in the full pack. The research questions I aim to answer are: 1) How is stress distributed inside individual grains in a 3-D pack? and 2) What are the contact force networks inside a 3-D granular pack? The approach proposed to address these questions is described in Section 2.4 (WP7).

2.3 Aims and objectives

This project aims to:

1. Establish depth-resolved phase-contrast optical metrology as a suitable technology to map *strain fields* and *mechanical properties* (via inverse problem solution) *inside* the volume of weakly scattering materials, in a *non-contact* way and with *high sensitivity* and *high spatial resolution*;
2. Contribute to improving the outcome of refractive surgery by taking into account the cornea compliance after laser ablation and to validating current theoretical models of stress propagation in 3-D packs of granular materials.

These will be achieved through a set of detailed objectives:

1. **Instrument development:** Design, build and validate novel high-spatial-resolution systems for Tilt Scanning Interferometry and Phase Contrast Spectral Optical Coherence Tomography, based on the lessons learned from successful low-spatial-resolution proof-of-principle experiments.
2. **Performance optimization:** Develop experimental procedures and data processing tools to extract displacement and strain information with optimised axial and depth resolution, depth range, and signal-to-noise ratio. These will include investigating the effect of multiple scattering, dispersion, refraction, photoelastic effect, signal non-linearity, optimum 3-D data volume registration, 3-D phase evaluation and phase unwrapping methods.
3. **Inverse methods:** Develop and apply inverse numerical methods to extract material properties from measured displacement and strain distributions within weakly scattering materials.
4. **Medical applications:** Obtain elastic modulus distributions from displacement measurements through-the-thickness of the vertebrate eye cornea. Use them to numerically predict corneal behaviour after laser ablation of a target profile.
5. **Engineering applications:** Measure 3-D displacement fields inside 3-D granular packs under known loads to evaluate contact forces and the resulting stress distribution within the pack.

2.4 Project Management and Work Programme

The project is expected to last 36 months under overall supervision of the PI, who will devote 20% of his time to it. It will involve Visiting Researcher Dr. G. Galizzi (Rosario Institute of Physics, Argentina) during 6 months in the first year, for instrument development and hardware integration (WP1-2). Back in Argentina, he will work for another 6 months on tasks [3-4]. The project will also involve a PhD student at Loughborough (PhD1, fully funded by EPSRC) and a second one (PhD2) who will spend 50% of the time at Loughborough and 50% at Châlons en Champagne, fully funded by the Wolfson School (Loughborough University) and the Mechanics and Manufacturing Laboratory (ENSAM, Châlons, France). Prof. F. Pierron and Dr. S. Avril, at Châlons, will develop and apply inverse methods using experimental data measured at Loughborough and will supervise PhD2 during an 18 month stay in Châlons. This will strengthen the collaboration between groups, already initiated by an 8 month visit of Dr. S. Avril to Loughborough in 2006. Prof. T. Wess (Cardiff University) will provide *ex-vivo* corneal trephinates, expertise on corneal properties from a molecular level and training to the Loughborough team to handle, store and dispose biological samples. Technician services are required for manufacturing of electro-mechanical components and computer maintenance. Project meetings will be held every 6 months unless research questions arise that need detailed consideration by researchers from all teams (allowance is made for travel and subsistence). Working meetings at Loughborough and Châlons en Champagne will take place as and when needed but at least every 2 weeks. Day-to-day communication between Loughborough, Châlons, Cardiff and Rosario will be mostly by e-mail or phone. For organisational purposes the project is split into several work packages, each with their own tasks numbered within square brackets **[ ]** and milestones indicated with a diamond ◈. A Gantt chart is included separately, and indicates the responsible person/s for each task.

WP 1: TSI system development

[1] A prototype TSI interferometer (see Section 2.2.1 A) will be constructed as an extended and optimised version of the system used for proof-of-principle experiments [3] (it will measure all displacement components with ~40 fold improvement in depth resolution, with high repeatability and linearity, ~24dB improvement in signal dynamic range and enhanced phase signal-to-noise ratio). The required system components are outlined in Section 3 "Justification of resources". In order to measure the three displacement components with TSI it is necessary to illuminate from at least three different directions. This will be implemented by mounting the interferometer head with a single oblique illumination beam in a highly repetitive rotation stage with the rotation axis collinear with the observation direction z. By repeating measurements at various θ_z angles, all displacement components will be obtained. There are several practical difficulties that can be anticipated in optimising TSI: **[2]** the tilt of the object beam must be linear with time to ensure a constant modulation frequency throughout the scan. This will be achieved through the use of a closed loop tilting stage. A 100mrad tilt range will provide depth resolutions in the tens of μm. Repeatability in the starting tilt angle is also required for each of the before- and after-load scans to avoid introducing fictitious strains. This will be checked with a method developed for the feasibility study based on the signal from an unstrained optically rough reference surface within the field of view of the camera. **[3]** Multiply scattered light presents a problem to all OCT systems since the signal resides in the single-scattered photons. As a consequence, the displacement information is blurred, limiting the depth to which valid measurements can be made. To reduce this effect, the project will investigate a strategy based on the fact that speckle patterns from multiply-scattered photons decorrelate rapidly with changes in the illumination angle, allowing independent datasets to be averaged.[21] The planned θ_z rotation stage will allow such technique to be introduced easily. **[4]** Spatial registration between microstructure volumes imaged under the different illumination directions may be needed to compensate for differences in refractive index gradients perpendicular to the illuminating wavefronts. It will, however, only be required in the depth (z) direction since the path from the scattering point to the camera pixel is identical for all illumination directions. A simple 1-D cross-correlation algorithm will be implemented for this purpose. M1**:** TSI system optimised and operational◈.

WP 2: PC SOCT system development

This will run in parallel with WP1. **[5]** A PC SOCT interferometer (see Section 2.2.1 B) optimised for measurements in the vertebrate eye cornea will be constructed from the version used for successful proof-of-principle experiments[4] (the new system will have an order of magnitude increase in depth resolution, ~36dB increase in signal dynamic range, and will operate at near infrared wavelengths where the cornea exhibits optimum scattering properties). A Linnik configuration will be used, which benefits from a high numerical aperture (and hence more spatial resolution and power efficiency), larger magnification and dispersion compensation. The required system components are outlined in Section 3, "Justification of resources". **[6]** Real time Fourier Transform evaluation will be implemented, via 1-D fast Fourier Transform along the wave-number axis, in order to visualize the spectrum or scattering potential during the experiment setup. This is essential to position the sample in the field of view of the system but most importantly to optimize the interferometer setup (noise sources, beams ratio, polarization, etc) during alignment. **[7]** In order to avoid phase decorrelation due to rigid body motion of the sample during image acquisition in dynamic applications, the "before" and "after" images will be re-registered within the 3-D data volume with sub-pixel resolution before phase evaluation. **[8]** A precise determination of the depth resolution and depth range in a PC SOCT system requires an accurate evaluation of the spectral bandwidth falling on the 2-D image sensor. This will be achieved using two etalons transmitting at known wavelengths and the spectral lines will be used to calibrate the wavelength axis of the sensor. **[9]** Non-linear effects introduced in the interference signal by the diffraction grating in the wavelength axis of the spectrometer broaden the spectral peaks and therefore decrease the depth resolution. Numerical compensation will be implemented, as done in TSI for non-linearity of the tilting stage.[3] Multiple scattering will be reduced by implementing a 1-D confocal setup based on an aperture slit to reject photons coming from outside the coherence gate and the diffraction limited illuminated region. This will also reduce the "out-of-focus glare". **M2**: PC SOCT system optimised and operational◈.

WP 3: Control Software and Graphical User Interface (GUI)

[10] A Matlab® Toolbox and GUI will be developed to control the TSI and PC SOCT systems and to process the raw data. Real time spectrum visualization will be implemented for PC SOCT. Post processing will include multiple scattering reduction, non-linearity compensation, spatial/temporal re-registration, phase unwrapping modules (2-D and 3-D algorithms are now in place at Loughborough University thanks to recent MRC and EPSRC grants), displacement and strain evaluation, and refraction phase compensation. The toolbox will incorporate different modules as the project progresses and will build upon the routines and algorithms already developed by the PI for the preliminary experiments. **M3:** real time spectrum visualization◈; GUI updates◈.

WP 4: Validation

TSI and PC SOCT systems performance will be validated on ‘cooperative’ samples undergoing rigid body rotation and well-characterised deformation −3 point bending and compression disk reference specimens from the Standardisation Project for Optical Techniques of Strain measurement (SPOTS). **[11]** Validation samples will be manufactured by either casting or bonding polymers with known (and different) elastic modulus, or by using rapid manufacturing graded photopolymers, in which elastic modulus spatial distributions can be produced by varying the intensity of a UV laser as it scans a liquid photopolymer. All these samples will then be loaded under well-known conditions and measured with TSI and PC SOCT systems. **[12]** Surface deformation of the sample results in phase changes due to refraction. This effect can lead to unwanted fictitious displacements and has to be accounted for and compensated. **[13]** Samples containing varying packing fractions of glass micro-spheres (diameter ~ 100μm to confer a well defined microstructure) will allow the re-registration technique from tasks **[4]** and **[7]** to be validated. Following 3-D unwrapping of the phase maps, displacement maps will be compared with those from forward FE calculations (FEUM). This will allow the random and systematic errors of the techniques to be quantified. The former are likely to be dominated by multiple scattering, the latter by strain-induced refractive index changes and refraction. **M4:** Random and systematic errors quantified for TSI and PC SOCT systems◈.

WP 5: Inverse Problem solution

[14] This WP will run in parallel with WP 6 and WP 7. VFM and FEUM approaches described in Section 2.2.2 will be used first for the validation of the experimental data and most importantly for the characterization of material parameters in *ex-vivo* corneas. Existing algorithms for finding virtual fields that provide uncoupled equations and filter noise from 2-D data (3 components of strain) will be modified for processing 3-D data (6 components of strain) considering some modifications to the theoretical modelling and the numerical implementation. **[15]** Phase changes due to strain-induced refractive index changes are typically at the 5-10% level dependent on stress-optic coefficient and can be ignored as a first approximation. The fact that the phase change is measured for at least three non-coplanar illumination directions would allow these effects to be removed. In the presence of photo-elastic effects, it may not be possible to derive the stress fields as an explicit function of the unknown parameters by using the measured displacement fields. These effects could be compensated using the photo-elastic constants of the material that link the refraction indices and the principal stresses. A non-linear version of VFM will be used, adapted to problems where it is not possible to derive explicitly the stresses in function of the unknown parameters. Another strategy is based on the fact that in materials with high stress-optic coefficient the microstructure as seen by an off-axis imaging system will be distorted due to refraction through refractive index gradients. Comparison between 3-D correlation and FEUM predictions will expose the spurious strain field due to the distortion produced by the stress-induced refractive index gradients. That field will then be used to find a first guess of the refractive index distribution for the VFM and to estimate the difference between the principal components of stress. Collaborators: Prof. F. Pierron and Dr. S. Avril. **M5:** Parameter characterization in corneas◈; stress-optic phase compensation◈.

WP 6: Corneal compliance characterization

[16] A pressure chamber filled with saline solution will be constructed to mount corneal trephinates and load them with a static and/or dynamic hydrostatic pressure that mimics intraocular pressure variations. It will also allow for controlled and stable loads to be used. Depth-resolved displacement fields will be measured with PC SOCT in *ex-vivo* corneas (pig/cow/human) under known hydrostatic pressure. They will be used to extract through-the-thickness elastic modulus distributions by solving the inverse problem using novel plane strain and axi-symmetric VFM. Corneal OCT slices at different angles to the nasal-temporal direction will be explored to check for tangential variations in the elastic modulus distributions. Viscoelastic properties will be characterized by measuring temporal sequences of displacement fields after the cornea has been loaded, and during tissue relaxation (we have recently observed corneal viscoelastic compression after an increase of the intraocular pressure). Once corneal mechanical properties have been mapped, a finite element model will be used to predict its behaviour after ablation of a target profile. Results will be compared with those from a model that assumes uniform elastic modulus distribution and with those from more complex models found in the literature that account for the multilayer structure of collagen fibres.[22]

Collaborators: Drs. T. Wess, J. Morgan and J. Albon, Cardiff University. **M6:** Evaluation of elastic modulus distributions ◈; characterization or viscoelastic properties◈; numerical comparison of uniform and non-uniform modulus cases◈.

WP 7: Micromechanics of granular materials

[17] TSI with sensitivity to all displacement components will be used to measure contact force chains within three-dimensional granular beds. To reduce the complexity of the experiment, spherical beads (~2-5mm diameter) made of low stress-optic coefficient material embedded with micro-spheres or titanium oxide as scattering centres will be immersed in an index-matching fluid in a glass test cell. This will avoid complications due to stress-optic coupling and also refraction at the beads surface. The stress distribution within the beads will be evaluated from the measured 3-D displacement fields and mechanical properties of the beads material. Simple geometries involving one or two beads under a known load will be measured first and results will be checked against analytical and numerical predictions. This will serve to validate the system before moving to more general multi-bead (1000-10000 beads) configurations in 3-D packs. **M7:** Construction of test cell ◈; validation with simple geometry (2 grains in contact) ◈; construction of larger cell and measurements of multiple bead pack ◈.

2.5 Novelty of the project and deliverables

- Novel instruments and data analysis tools will be developed. 3-D multi-component displacement and strain distributions will be measured within scattering materials, rather than only on the surface as with current interferometric techniques.
- The techniques will offer a displacement sensitivity some 2-3 orders of magnitude better than the depth resolution.
- The volume information obtained will enable the solution of the inverse problem of finding the mechanical properties of the material within its volume without the limitation of non-unique solutions.
- Through-the-thickness elastic modulus distributions in the cornea will be available for the first time. This will contribute to the improvement of refractive surgery outcomes by taking into account the corneal compliance.
- It will be possible for the first time to unambiguously characterize materials with non-uniform elastic modulus.
- Experimental measurements able to test current 3-D models of stress propagation in granular packs at the microscopic (single particle) level will be performed for the first time.

2.6 Relevance to Beneficiaries

This proposal is multidisciplinary in nature and involves collaboration with optometrists, physicists, biologists, numerical modellers, rapid manufacturing engineers and optical metrologists. In the ophthalmology field, research and technology of the kind proposed will result in a far greater understanding of the mechanical properties of the cornea. The general public will be a direct long-term beneficiary, as corneal interventions such as refractive surgery are already widely adopted and could benefit from better predictive capabilities on the outcome of the surgery. Experimental measurements of contact forces and contact networks within granular agglomerates will be a vital step both for validating current theoretical models of stress propagation in such materials, and ultimately improving structural analysis techniques for the food and chemical engineering industries. Finally, development of depth-resolved phase contrast techniques will provide mechanical and optical engineers with new tools for full volume displacement and strain measurements within scattering materials, with potential to investigate a broad range of new exciting applications.

2.7 Dissemination and Exploitation

The results of the research will be submitted for publication in optical engineering, material science and ophthalmology journals (JOSA, OE, Appl. Opt, JSAED, Opt. Exp, IJSS, Strain, Exp. Mech, Cornea, BJOpht) and presented at international conferences (SEM annual conf. in Exp. Mech; Br. Soc. Strain Meas.; Speckle Metrology; Annual Congress Royal College of Ophthalmology, etc −see application form for all conferences). Exploitation of the research results will be through further use by our Institution in future projects, and by other academic and medical research groups, including those at the collaborating Institutions. Wherever appropriate, worldwide patents will be sought through the university's Intellectual Property Office. A potential candidate is a "Corneal compliance measurement system". The Optical Engineering group spinout companies Phase Vision Ltd or Laser Optical Engineering Ltd are potential partners for licensing the technology from the University, for leasing the equipment to perform consultancy tests for any UK company wishing to explore its benefits, and to commercialise the data processing Matlab toolbox. In order to improve his communication skills, the PI is requesting funds to take public communication training at the Royal Society.

2.8 Additional References

[5] T. Abe, Y. Mitsunaga, and H. Koga, Journal of the Optical Society of America A **3**, 133 (1986).
[6] H. Aben, A. Errapart, L. Ainola, et al., in *Optical Metrology in Production Engineering* (SPIE-INT, Bellingham, 2004), Vol. 5457, p. 1.
[7] M. T. Draney, R. J. Herfkens, T. J. R. Hughes, et al., Annals of Biomedical Engineering **30**, 1033–1045 (2002).
[8] D. D. Steele, T. L. Chenevert, A. R. Skovoroda, et al., Physics in Medicine and Biology **45**, 1633–1648 (2000).
[9] B. K. Bay, T. S. Smith, D. P. Fyhrie, et al., Experimental Mechanics **39**, 217–226 (1999).
[10] J. M. Schmitt, Optics Express **3**, 199 (1998).
[11] A. F. Fercher, W. Drexler, C. K. Hitzenberger, et al., Reports on Progress in Physics **66**, 239 (2003).
[12] T. Dresel, G. Hausler, and H. Venzke, Applied Optics **31**, 919 (1992).
[13] B. J. Vakoc, S. H. Yun, J. F. de Boer, et al., Optics Express **13**, 5483 (2005).
[14] Z. Chen, T. E. Milner, D. Dave, et al., Optics Letters **22**, 64 (1997).
[15] P. Pedersen and P. S. Frederiksen, Measurement Science & Technology **10**, 113 (1992).
[16] F. Pierron, S. Zhavoronok, and M. Grédiac, International Journal of Solids and Structures **37**, 4437 (2000).
[17] T. S. Majmudar and R. P. Behringer, Nature **435**, 1079 (2005).
[18] R. Brockbank, J. M. Huntley, and R. C. Ball, Journal de Physique II **7**, 1521 (1997).
[19] M. S. Osman, J. M. Huntley, and R. D. Wildman, Optics and Lasers in Engineering **43**, 752 (2005).
[20] Z. Yanzhou, R. D. Wildman, and J. M. Huntley, Journal of Optics A: Pure and Applied Optics **7**, S453 (2005).
[21] A. E. Desjardins, B. J. Vakoc, G. J. Tearney, et al., Optics Express **14**, 4736 (2006).
[22] K. Anderson, A. El-Sheikh, and T. Newson, Journal of the Royal Society Interface **1**, 1 (2004).