Category: Medical Equipment

Reference: 1469

**MSO – Microscopy Smart Optics**

**Space Origin:**

A GRIN (Graded-index) fibre was developed by an Italian Institution based on commercial parts, with simple mechanical set-up, and fully exploiting the reduced GRIN fibre dimensions (0.5 mm diameter). The application of a series of well-known observational techniques such as confocal, two-photon fluorescence or Optical Coherence Tomography (OCT) supported by small and non-invasive optical probes is highly useful for in-vivo analysis of hollow tissues and for medical and metrology issues.

**Description:**

Optical microscopy for in vivo analysis of hollow tissues, small animals but even human cases, requires the application of a series of well known observational techniques such as confocal, two-photon fluorescence or Optical Coherence Tomography (OCT) supported by small and non-invasive optical probes. As Optical fibres and in particular Graded-index fibre (GRIN fibres), offer the possibility to be modelled as conventional optical elements, they can provide this feature. Recently, a GRIN objective was developed by an Italian Institution based on commercial parts, with simple mechanical set-up, and fully exploiting the reduced GRIN fibre dimensions (0.5 mm diameter).

The objective is based on Aspheric optics matching the input NA (Numerical Aperture) of the GRIN fibre, modelled with ZEMAX optical Computer Aided Design (CAD), and mechanically assembled in a small sized support provided with a standard microscope mounting collar. Mounting the objective in a two-photon microscope demonstrated that fabrication defects, material un-homogeneity and other construction problems (e.g. illuminating optics mismatches and relative misalignments between illumination beam, illuminating lens and GRIN fibre) introduce departures of the performance of the GRIN fibre objective from the predictions of optical theory and/or ray tracing algorithms, which result in blurring/distortions of the image produced by the GRIN objective. The technology offer is based on the application of a low-order adaptive optics system applied to the GRIN objective mounted in a multi-photon microscope system. A key feature of the invention is the calibration procedure during which the behaviour of a merit function, based on the measurement of the final point spread function, was monitored while acting in modal way on the deformable device. Optimization tables thus constructed were then iteratively applied during the real observation. Attention is drawn on the static distortions produced by the objective and on the methodology and algorithms developed to correct them. It was possible to reach stable observations of test targets (fluorescent sample spheres immersed in liquid) and biological samples at the theoretical limiting resolution imposed by the GRIN system optics.

**Innovative Aspects:**

MSO (Microscopy Smart Optics) is a system based on the new generation of ‘smart’ focal plane technologies. GRIN optical fibres with their sub-millimetre sizes and the ability to fill much reduced spaces are part of this category. The same is valid for the new generation of Micro- Electro-Mechanical Systems (MEMS)/ Micro-Opto-Electro-Mechanical Systems (MOEMS) devices like deformable mirrors based on arrays of micrometric single mirror elements or even micro-scanning mirrors and micro-piston mirrors for applications like GRIN fibre OCT (Optical Coherence Tomography).
By inserting an adaptive optics system, typically a deformable mirror, in the illumination light path of a multiphoton microscope, and using a specific error minimization algorithm, this invention permits to adaptively correct distortion inherent in the images formed by a generic GRIN fibre objective for microscopic observations, and even wavefront distortions present in the laser beam itself, greatly improving image quality.

Innovative aspects of the experimented microscopy technology are:

- Construction of small size optical probes with imaging capability
- Insertion of adaptive optics techniques in the optical path of commercial microscopes
- Development of computational algorithms and methodologies for calibration and table-driving of adaptive optics systems applied to microscopy

The three elements of innovation listed above are in synergy in making a system for coherent image collection that can be scaled to quite different areas, ranging from microscopy to metrology.

Application Areas:

Applicative areas for the system here proposed can span in quite different scientific and metrological sectors:

1. ‘In Vivo' two and multi-photon microscopy for biological samples. The system is currently used for live imaging experiments on mice at the Venetian Institute of Molecular Medicine (VIMM) in Padova. ‘In-vivo’ biological samples analysis is an extremely challenging approach in biological microscopy requiring both optical objectives with high ‘penetration’ capability (at the level of hypodermic needles, possibly) and fast scanning execution in order to ‘freeze’ sample movements induced by blood pulsation in the living animal under test. The possibility to have fast dynamical control of the scanning illumination beam (focusing, spherical aberration) by adaptive optics insertion is of great benefit in achieving the best possible spatial resolution.

2. Confocal microscopy in biology. GRIN adaptive optics techniques applied to this observational technique have not yet been tested at the Padova VIMM Institute; this could be a development line to be analyzed in future developments.

3. Construction of an ‘optical-tweezer’ for applications on nano and micro structured systems. In this application the GRIN objective can be immersed in solutions and used to create nano/micro particle trapping beams. The reduced size of the GRIN based optical objective is of great help in the construction of multi-beam systems where several nano-systems can be trapped and driven simultaneously. This is a quite hard option to obtain with standard microscope objectives.

4. Metrology: the system can be used to analyze surfaces on hardly reachable positions and interstices.

5. Medical: medical endoscopic probes

In the last two cases the system can work either in OCT (Optical Coherence Tomography) mode or with laser light stimulation. For this application a further development will be required integrating on the basic experimented system flexible fibre-optics, MOEM micro-scanning mirror and MOEM deformable mirror..

Cooperation:

The technology owner is looking for partners for a license agreement.