4.1 Final publishable summary report

1. Executive summary

The Leibniz Institute of Photonic Technology (IPHT, Jena, Germany) has been developing ultra-small optical fiber sensors for life sciences applications for a number of years. Research work has focused on developing the technique of focused-ion beam (FIB) milling, which has the ability to produce highly precise optical cavities. A key requirement for FIB milling is to reduce the size of the optical fiber as this technique is best suited to working with micron-scale devices. To this effect, IPHT has previously demonstrated sensors in both polished and etched optical fibers.

This project has focused on reducing the size of these sensors and introducing the ability to perform multiplexed sensing, through the use of multiple cavities. We have now fabricated cavities as small as 2.8 µm and demonstrated their use for sensing of both bulk refractive index and thin-layer coatings. In order to achieve sensitive measurements we interrogate at visible wavelengths, thereby reducing the free spectral range of the interferometer (relative to infra-red interrogation), increasing the number of interference fringes, and allowing for the implementation of the Fourier shift method. We believe such sensors will provide useful tools for the life sciences given these sensors can be made smaller than a cell. An envisaged application is the measurement of physical and biochemical parameters within an individual oocyte (approximately 100 µm in diameter) for improving understanding in the process of fertilization, particularly in-vitro fertilization (IVF).

In this project we have also demonstrated the fabrication and optical characterization of serially-multiplexed dual cavity micro-sensors. Two cavities can be written serially along the fiber with two different cavity lengths, producing a total of four reflecting surfaces and thus six possible interferometric pairs/cavities. By using fast Fourier transform methods it is possible to obtain de-multiplexed measurements for each cavity. This is particularly significant for performing bioassays, where positive and negative controls are required to be measured within close spatial proximity.

2. Project context and objectives

Optical fibres have revolutionised the way in which the world communicates with now over 150 million kilometres of fibre deployed per year, allowing it to span oceans and continents [1]. The multiplexing capability of fibre optics, particularly in the wavelength domain, is also critical to achieving the extremely high data rates now available. Further multiplexing in polarisation, mode, and phase will likely be critical to achieving even greater data rates [2]. These properties, and more, also make optical fibres an excellent platform for sensing. To date, optical fibres have had particular success in physical sensing applications such as gyroscopes and pressure, strain, and temperature sensors [3].

Optical fibre sensors are playing an increasing role in biological applications, particularly for *in-vivo* applications where the fibre's small cross section can provide a minimally invasive diagnosis. For example, the measurement of protein biomarkers in small samples of serum or other biological fluids can potentially lead to early diagnosis of conditions such as cancer [4]. The potential advantages of using optical fibres for biosensing applications include: being small and flexible for penetrating into difficult to access regions *in-vivo*; the ability to perform multiplexing along a single device, and immunity to electromagnetic interference (e.g. for use in magnetic resonance imaging) [5].

Perhaps the most commonly used label-free optical fiber biosensing technique is the use of surface plasmon resonance (SPR), which is formed by coating an optical fiber with a thinly coated metal such as silver or gold. Such devices are highly sensitive to the external environment (that is, refractive index), but it is difficult to create a multiplexed device due to the broadband nature of the resonance, and instability and high optical loss associated with metal coatings. SPR devices are also intrinsically transmission devices, negating one of the potential advantages of optical fiber sensors to perform remote dip-sensing.

An alternative label-free transduction mechanism is to use interferometric techniques whereby changes in the optical path length of the interferometer, and thus refractive index, are monitored [6, 7]. Any of the traditional interferometric configurations can be implemented into the optical fiber, such as: Fabry-Perot; Michelson; Mach-Zehnder; and Sagnac interferometers. While such sensors have been widely used for physical sensing, for label free refractive index sensing the challenge is to allow the propagating light to interact with the surrounding environment. For this reason Fabry-Perot interferometers are often used as either the cavity walls can be coated with, or the cavity filled with, the analyte of interest. Another advantage is the potential to perform either simultaneous measurement of multiple parameters (usually temperature plus either bulk refractive index or surface coatings) [8] or multiplexed sensing [9, 10]. This is achieved by fabricating cavities with different optical path lengths that can then be de-multiplexed through techniques such as monitoring the shift of multiple interference peaks/troughs [8] or through Fourier transform analysis [10].

Optical fiber Fabry-Perot sensors have been fabricated by a variety of different techniques for different applications. Examples include femtosecond laser micro-machining [11], ultraviolet laser ablation [12], and splicing single-mode fiber to either capillary tubing [13] or photonic crystal fiber [14]. A technique that can provide high surface quality and can be easily tailored for different cavity geometries is to use a focused-ion beam microscope to mill micro-cavities [8, 15-18]. Milling the entire fiber cross section is possible, however this is a highly time consuming process. A number of different fiber geometries have been investigated in order to reduce the milling time such as fiber tapers [15, 17], and polished [16] and etched [18] fibres.

In this project we have investigated methods for reducing the size of, and adding multiplexing capabilities to, Fabry-Perot micro-cavities written into optical fiber tapers using focused ion beam (FIB) milling. First we have analysed the bulk refractive index and surface coating sensitivity of a single cavity sensor and demonstrate sufficient sensitivity to measure individual layers of polyelectrolyte coatings. We have then demonstrated that it is possible to write serially-multiplexed dual cavity micro-sensors and that the optical path length, and thus refractive index, of each cavity can be de-multiplexed using Fourier techniques. To the best of our knowledge, this is the first demonstration of multiplexed refractive index sensing within a tapered optical fiber micro-cavity. We envisage future applications in the field of human fertility, where miniaturised sensors and highly sought after.

<u>The project objectives were (from Sec. B1.2 in the proposal):</u>

1. Modelling and optimising the sensor design, such as the Fabry-Perot resonator size and reflective coatings to increase the Fabry-Perot finesse.
2. Demonstration of a single channel refractive index sensor.

3. Demonstration of a dual channel sensor, with independent measurements for each channel.
4. Investigation into alternative structures such as specialty optical fibres for increased sensor performance.
5. Demonstration of endometrial fertility biomarker sensing.

References

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