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International Journal of Applied Glass Science, 2015; 6(3):229-239

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Originally published at:

<http://doi.org/10.1111/ijag.12128>

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30 June 2016

<http://hdl.handle.net/2440/99092>

Taming the Light in Microstructured Optical Fibers for Sensing

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In this review, we examine recent developments in the field of chemical and biological sensing utilizing suspended-core, exposed-core, and hollow-core microstructured optical fibers. Depending on the intended application, a host of sensing modalities have been utilized including labelled fluorescence techniques, and label-free methods such as surface plasmon resonance, fiber Bragg gratings, and Raman scattering. The use of various functionalization techniques adds specificity to both chemical ions and biological molecules. The results shown here highlight some of the important benefits that arise with the use of microstructured optical fibers compared to traditional techniques, including small sample volumes, high sensitivity, and multiplexing.

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[The copyright line in this article was changed on 24 August 2015 after original online publication.]

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Introduction

Optical detection of chemical or biological species relies on the interaction between a target species and light, either to change the properties of the excitation light in a manner corresponding to the properties of the species or to generate a separate, measurable light signal that can be used as the detection mechanism.^{1,2} Optical fibers are one platform which can exploit this mechanism

to create a sensor. These structures have well-defined optical guiding properties, an ability to guide light to areas of interest, and are compatible with an array of established excitation sources and detection devices.¹

Conventional optical fibers, such as those used traditionally for optical communication, consist of two concentric solid glass materials forming the core and the cladding. Such fibers are exceptionally good at carrying light from one end of the fiber to the other and back with very low loss and have therefore been successful for applications where sensing is performed at the distal end of the fiber, known as extrinsic sensing.^{2,3} However, solid core optical fibers do present some limitations in sensing applications, as the interaction area is limited to the fiber tip's cross section, with a diameter in the order of up to a few hundred micrometers.²

Many optical fiber designs have been proposed and demonstrated to achieve intrinsic sensing, where the optical fiber is not simply a light pipe but plays a significant role in the sensing. For chemical and biological sensing, this usually refers to accessing a portion of the optical field that propagates along the fiber, such as through tapering⁴ or the use of D-shaped fibres.⁵ This approach is attractive as it allows the integration of light-matter interactions along the fiber length. However, modification of the fiber geometry in this way leads to either fragile structures or very low sensitivity, depending on the amount of tapering or portion of the fiber cladding removed.

Microstructured optical fibers (MOFs) offer the advantage that the interaction between the light and chemical species can be extended along the entire length of the fiber, while maintaining the integrity of the device. In suspended-core MOFs (SCMOFs), the glass core is suspended in air by thin struts, allowing a portion of the guided light to extend outside the fiber core into the surrounding holes which serve as low-volume sample chambers.^{6,7} For exposed-core MOFs (ECMOFs), the suspended core is partly open to the environment, enabling easy access to the fiber core and removing the need for sample filling.^{8,9} Hollow-core MOFs (HCMOFs) have also been used for sensing, where the air core not only guides light but also serves as the sample chamber, allowing large overlap of the guided light with the sample.¹⁰

The overlap of the guided light means that properties such as the refractive index and the absorption characteristics of the medium can alter the properties of the guided light.^{11,12} These fibers are an attractive plat-

form for liquid sensing as they can enable strong light-matter interactions, long interaction lengths, and the use of small sample volumes.⁶

In this study, we review our recent progress exploiting the use of MOFs for optical sensing. Methods for the attachment of functional species to the surfaces of MOFs are discussed in the scope of describing how MOFs can function as active sensing elements. We focus on the different modalities of deploying MOFs in sensing applications, using both label-based fluorescence and label-free detection techniques. For label-based fluorescence sensing, we discuss the different chemical and physical mechanisms used for surface attachment of suitable marker molecules, the fiber geometries, and the varied target species which can be detected using MOF-based sensors. For label-free sensing, we explore whispering gallery modes, surface plasmon resonance detection of biological species, Bragg grating-based sensing, and Raman spectroscopy in MOFs, highlighting an additional toolset of sensing mechanisms for MOF-based chemical and biological sensing.

Surface Functionalization

One solution to adding chemical or biological specificity and selectivity using an optical fiber is to premix reagents with a sample containing the analyte of interest, a small volume of which is then interrogated by the fiber. A different approach is to bind reactive molecules or antibodies to the glass surface before the fiber interacts with the analyte. As most analytes of interest do not typically bind directly with the glass, it is first necessary to create a scaffold onto which the molecules can be bound, through either a grafting or physical functionalization procedure.

Grafting

Grafting, or linking, the sensing molecule of interest to the sensor surface is commonly achieved via covalent bonding to oxide surfaces,^{13–15} polymers,¹⁶ or metals.¹⁷ A number of different attachment chemistries are available, including phosphonates, carboxylates, catechols, alkenes, alkynes, and amines, with a large body of work looking at attachment via silanization.¹⁸

For silanization, hydrolysis of the silane forms silanols, which attach to hydroxyl groups on the surface

via a condensation reaction. This allows for diverse functional groups to be utilized, including perfluoroalkyl, amino, and sulfhydryl for surface passivation or further sensing molecule immobilization.

The surface density of hydroxyl groups on the sensor surface has a large influence on the layer density, with techniques such as plasma activation¹⁹ or treatment of the surface with acids used to increase the surface density.²⁰ A low surface density typically results in low reproducibility in the deposition process.^{20,21}

Silanes can be deposited either in solution²⁰ or in vapor phase²² with previous work in MOF functionalization focused on solution deposition. The solution deposition process typically involves dipping the freshly prepared sensor into the silane solution, yielding a full silane coating in minutes to hours.²⁰

Physical Functionalization

Physical functionalization is a collective term for any approach by which the sensor molecules are attached to the surface by forces that are not chemical bonds, such as electrostatic forces. These methods have less dependence on the chemistry of the surface and can therefore be exploited on a wide variety of substrates including metals,²³ polymers,²⁴ glass,²⁵ and carbon nanotubes.²⁰

One particular approach is to deposit layers of charged polymers, such as polyelectrolytes (PE) from solution. This involves a layer-by-layer process, wherein the PE is attached through electrostatic interaction. The first PE layer, with a charge opposite to the intrinsic surface charge of the substrate is deposited, rinsed, and a subsequent PE layer of the opposite charge deposited.²⁶ The process can be repeated multiple times to stack layers onto any substrate, resulting in an increased PE functional group density on the sensor surface.

Alternatively, a volume-doped polymer layer can be deposited, as shown in Fig. 1b.²⁷ This process can combine both the formation of a protective coating, along with functionalization of the fiber to the target species.²⁷ The thin polymer film functionalized fiber, shown in Figs. 1a and c, has been shown to be suitable for the detection of aluminum cations. This result also shows that the fluorophore (8-hydroxyquiniline) is not held too tightly within the polymer, allowing for multi-ligand binding so that three molecules can still complex with the aluminium.

Fluorescence-Based Sensing Methods

Once a method for attaching molecules to the surface of the MOF is established, functionality needs to be added to allow for specific detection of the target molecules, that either utilizes these surface attached methods, or involves premixing of chemicals and the subsequent use of the MOF for sample interrogation.

One of the primary ways that specificity can be achieved is through fluorescence-based sensing techniques. These typically excite fluorescent molecules or nanoparticles with light guided along the fiber, and analyze the emitted light captured using the same fiber. The captured light can be analyzed at either end of the fiber, with the back-captured emission both improving the practicality of the probe as well as potentially increasing the sensitivity of the device.²⁸ Examples of SCMOFs used for sensing are shown in Fig. 2.

Changing the geometry and material of the MOF allows the desired fiber parameters to be tailored to the specific application. Decreasing the core diameter increases the overlap of the optical field with the medium, which increases sensitivity.³¹ Meanwhile, the hole size can either be made smaller to reduce the required

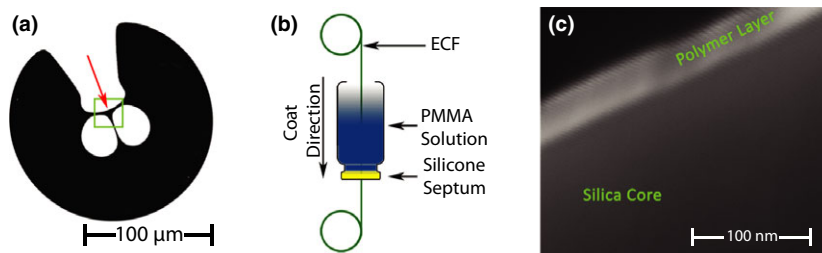


Fig. 1. (a) Contrast enhanced scanning electron microscope image of ECMOF cross section, with core region highlighted in green. (b) Thin film polymer deposition method on ECMOFs. (c) Scanning electron microscope image of the outside edge of the exposed core, with a 50-nm polymer coating.²⁷

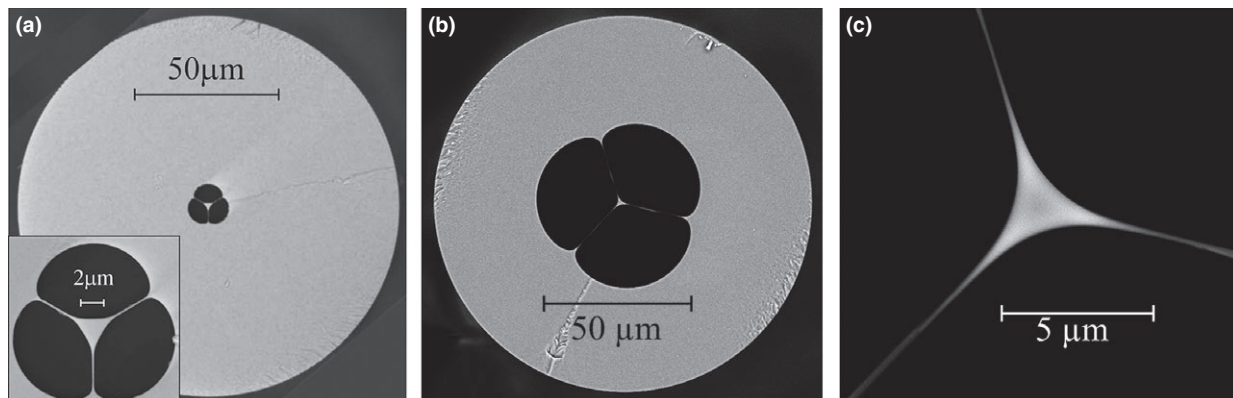


Fig. 2. Scanning electron microscope images of SCMOFs used for sensing applications made from (a) F2 Glass²⁹ and (b, c) Silica.³⁰

sample volume, or larger to reduce filling time.⁶ The fiber material can be selected to optimize the sensor, for example, increasing the glass refractive index (e.g., F2 glass [Fig. 2a] has a higher index than silica [Fig. 2b]) increases the numerical aperture of the fiber and thus the proportion of the fluorescence that can be re-captured.³¹

For SCMOFs, the fibers are filled using capillary action, which is approximately 5 min for a 20-cm length of fiber with an internal volume of 60 nL.³²

Two primary fluorescence sensing avenues have been explored using MOFs. The first seeks to use fluorophores as labels for biomolecules, while the second looks at the emission from fluorophores and attempts to correlate the observed signals with concentrations of chemical species within the solution.

Fluorescence-Based Sensing of Biomolecules

By labeling target biomolecules with fluorescent markers, the detection of the biomolecule itself can be inferred from the detection of the fluorophore to which it is attached. The sensitivity of fluorescence-based MOF-biosensing is typically limited by either background fluorescence emissions, or photobleaching.

Previous work by Jensen *et al.*³³ utilizing Cy5 labelled DNA, looking at the absorption rather than the emission of the fluorophores restricting the detection limit to 0.1 μM . Smolka *et al.*¹⁰ were able to observe concentrations as low as 1 nM by measuring the fluorescence emission of Rhodamine 6G using an HCMOF with a large light-matter overlap.

The use of alternative labels, such as semiconductor-based quantum dots (Qdots), allows for detection

of biomolecules to be performed at much lower concentrations. Filling near infrared emitting Qdots within the holes of an SCMOF allowed for detection down to 1 nM of quantum dot labelled proteins,³⁴ which was further improved to 10 pM after modifications to the glass composition and fiber design.²⁹ This result was limited primarily by background fluorescence emissions from the glass.

Lanthanide-doped upconversion nanoparticles provide a significant advantage over alternative labels, as they emit at a shorter wavelength compared to the excitation source. The high brightness of these particles, combined with a significant reduction in competing background signals allows for an improvement in detection to 660 fM using erbium-/ytterbium-doped nanoparticles.³⁵ Using optimized thulium-ytterbium-doped nanoparticles allows further sensitivity improvements. These high brightness, highly doped nanoparticles along with the lack of competing background signals allows detection of single nanoparticles from one end of the fiber as they enter into the vicinity of the evanescent field inside a SCMOF from the fiber's other end.³⁶

Another application where SCMOFs have also found use in is enzyme activity assays, where they have been shown to be able to detection of PC6 down to 50 U/mL using a sample size of 210 nL.³⁰ This is particularly important for potential *in vivo* applications, where difficulty removing larger samples restricts the total available volume leading to a particular advantage in using MOFs for these particular applications.

Further work has explored the use of these fibers for specific DNA detection²⁵ and genotyping, where molecular beacons have been multiplexed to differentiate between wild- and mutant-type sequences in MOFs.³⁷

Fluorescence-Based Chemical Sensing

In addition to their use as biosensors, MOFs can also be applied to chemical sensing applications. These sensors typically function by detecting and amplifying the interaction of the desired substrate with a receptor, where the receptor is usually a small-molecule responsive fluorophore.

By choosing the appropriate fluorophore to react with the target species, these MOF-based sensors have been used to detect metal ions such as aluminum³⁸ through the use of a surface attached fluorophore layer, sodium ions,³⁹ or hydrogen peroxide.⁴⁰

A recent advance in sensing technology involves the use of photoswitchable molecules and MOFs to create light-driven sensors that are capable of targeting the desired substrates selectively and reversibly among other unique characteristics. The photoswitchable component provides an ability to modulate reversible binding and release of the desired ion from the binding domain. Such a sensor would allow for multiple measurements to be made on a single sample without the need to change the sensor. This would then permit continual and noninvasive study of biological systems, with an associated increase in the sensors' useful lifetime. In this respect, the first nanoliter-scale regenerable ion sensor based on MOFs was recently reported,⁴¹ where the air holes of the MOF are functionalized with a monoazacrown bearing spiropyran to give a switchable sensor that reversibly detects lithium ions down to 100 nM in nanoliter-scale volumes. Similar sensors for probing zinc⁴² as well as multiple ions have also been demonstrated using MOFs, with a dual sensor for calcium and cadmium capable of detecting ion concentrations as low as 100 pM.⁴³

The deposition of thin layers of reactive polymer layers gives an alternative to standard organic fluorophores, as the polymer layer itself can be used for detection. This has been demonstrated using poly[2-methoxy-5-(2-ethylhexyloxy)-1,4-phenylenevinylene] for explosives detection, showing a detection limit of 6.3 ppm using only 27 nL of sample volume.⁴⁴

Label-Free Sensing Methods

Methods which do not require prior attachment of fluorescent molecules to perform detection are commonly referred to as label-free techniques. These encompass methods which either look at a refractive index change on

a surface to correlate binding, typically of biomolecules, or methods such as Raman spectroscopy which look at vibrational modes of the molecules themselves.

In the optical domain, we have successfully exploited four different physical phenomena in conjunction with MOFs to create new sensing modalities.

Whispering Gallery Modes

Whispering Gallery Modes (WGMs) refer to a resonance mechanism that occurs when light is trapped within a microresonator by total internal reflection, and returns in phase after one or multiple roundtrip(s).⁴⁵ Multiple geometries of optical resonators have been investigated, including microspheres,^{45,46} capillaries,⁴⁷ micro disks, and toroids.⁴⁸ WGMs have been widely used for refractive index sensing and biological sensing applications in particular via surface functionalization.⁴⁹ The amount of time the light remains circulating within the resonator determines the quality (Q) factor (i.e., the linewidth of the resonance features), with a higher Q-factor resulting in longer interaction lengths with the molecules as they bind to the surface.⁵⁰

WGMs can be excited and interrogated through two different mechanisms. The first approach involves using a phase matched fiber taper or prism to couple light to the microresonator at one of the resonance wavelengths.⁴⁸ This approach runs the risk that a small deviation in the optimum position of the gap separating the resonator and the taper will not only affect the coupling conditions, but also be seen by the resonator as a change of local refractive index, yielding measurement error.⁵¹

The second approach relies on using microresonators which contain a gain medium such as a fluorescent dye, and through remote excitation of the dye the re-emitted light can be coupled back into the resonant modes. This allows for remote excitation and collection of the WGM-modulated spectra as seen in Fig. 3a, alleviating the limitation of the taper coupling requirements but at the cost of lower Q-factors.

We have initiated the use of SCMOFs for both the excitation and collection of the WGM signal emitted by a dye-doped polymer microsphere positioned onto the tip of the fiber, as shown in Fig. 3b.⁵² Further work on this platform has shown a strong coupling mechanism between the microsphere and the SCMOF as a function of the diameter mismatch between the microsphere and the hole into which the microsphere is positioned, resulting in preferential enhancement of the

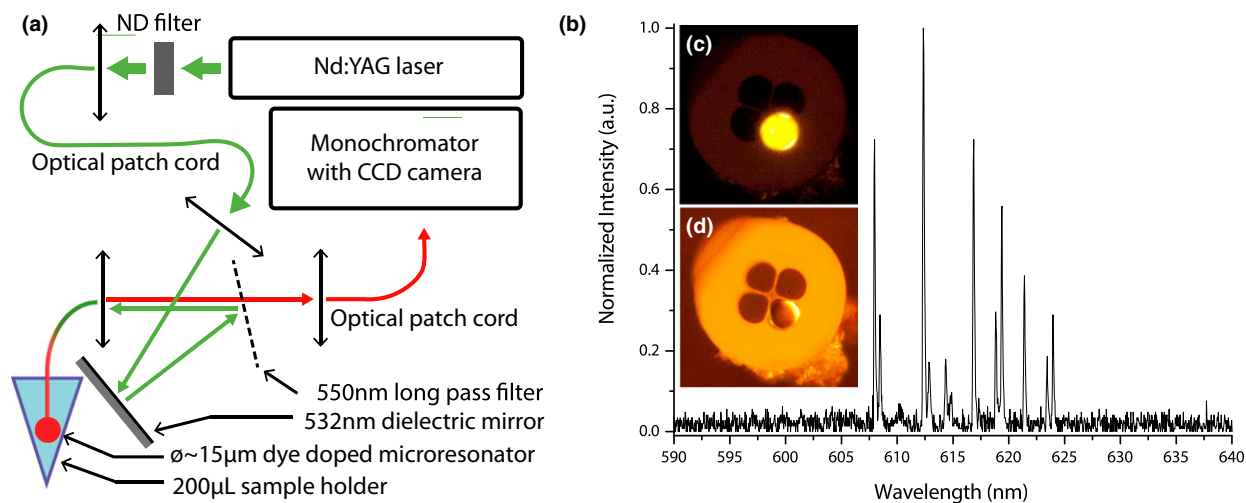


Fig. 3. (a) Optical setup used for the excitation and interrogation of a dye-doped microsphere on an SCMOF tip, (b) WGM spectra of a 15- μm diameter dye-doped polystyrene microsphere, (c, d) Bright field and fluorescence images of a microsphere positioned onto the tip of a silica SCMOF.⁴⁶

WGM depending on their polarization⁵³. This effect, combined with the operation of the dye-doped microspheres above their lasing threshold allowed to increase the stored energy within the resonator, increasing the Q-factor⁴⁵ by almost 6 \times , allowing for improved detection limits and the potential for *in-vivo* biosensing applications.²⁴

Surface Plasmon Resonance

Surface plasmon resonance (SPR), which refers to the oscillation of free electrons in thin metallic coatings, is another refractive index sensing method that has been widely exploited for biosensing applications. The resonance wavelength depends on the different dielectric functions of the metallic coating and dielectric substrate, as well as the surrounding refractive index adjacent to the metallic coating.⁵⁴

Although SPR methods initially used a prism to match the propagation constant of the monochromatic radiation with the propagation constant of the plasmons, a similar mechanism has as been demonstrated with optical fibers.⁵⁵ Hassani and Skorobogatiy⁵⁵ started investigating the use of SPR in a MOF, with theoretical work showing the potential for improved performance.

To circumvent observed issues with physical deposition methods inside MOFs, an electroless plating

technique for silver deposition based on the Tollens reaction has been developed.⁵⁶ Initial work showed that scattering of the plasmonic wave induced by the higher surface roughness of silver thin film can be exploited on bare core optical fibers. This process essentially turns an intrinsically nonradiative process into a radiative one, with significant advantages compared with the standard transmission measurements in terms of signal-to-noise ratio, the potential for multiplexed and self-referencing sensing.^{23,57,58}

Recently, we showed that a silver layer could be deposited on the core of an ECMOF (similar to that shown in Fig. 4a) by thermal evaporation. This fiber possessed a significantly smaller core diameter ($\text{O}_{\text{core}} \sim 10 \mu\text{m}$) compared to the bare core fibers previously used ($\text{O}_{\text{core}} \sim 140 \mu\text{m}$) and resulted in a reduction of the resonance linewidth by a factor 3, while the refractive index sensitivity ($\delta\lambda/\delta n$) remained constant,⁵⁹ improving the refractive index detection limit by the same factor.

Bragg Gratings

Fiber Bragg gratings (FBGs) are formed by creating a small periodic modulation of the optical fiber's refractive index along its length, which results in a narrow band reflection at a particular Bragg wavelength. FBGs are well known within the optical fiber sensing

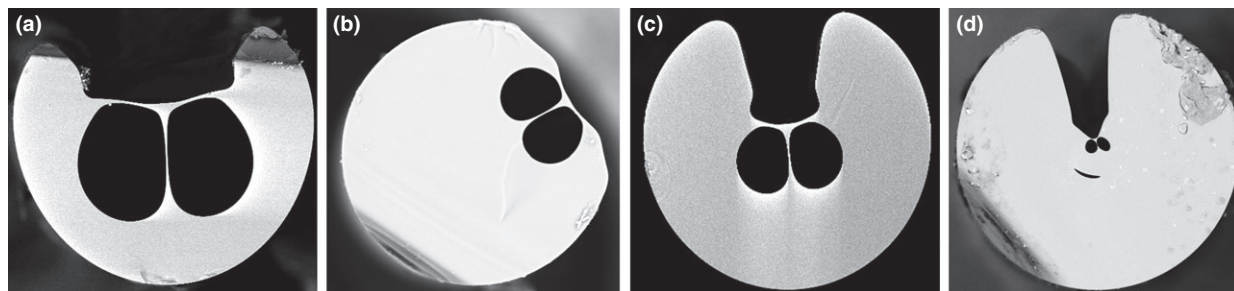


Fig. 4. Scanning electron images of fabricated silica ECMOFs.⁶⁸ The fibers have core diameters of (a) 12.5 μm , (b) 9.3 μm , (c) 7.5 μm , and (d) 2.7 μm . The outer diameters of the fibers at the maximum point are (a) 200 μm , (b) 200 μm , (c) 160 μm , and (d) 200 μm .

community for their role in temperature and strain sensing, as the pitch is highly dependent on strain, while the effective refractive index of the fiber is dependent on temperature via the thermo-optic effect.²

In the case of refractive index sensing, the position of the Bragg wavelength depends on the fiber's effective index, which in-turn depends on the refractive index experienced by the evanescent field. For FBGs written on conventional optical fibers, the analyte is well isolated from the light guided within the fiber, and as such the fiber cladding needs to be thinned down to improve the refractive index sensitivity.^{60,61}

There is particular advantage in using MOFs which can be tailored to enhance this light-matter overlap without weakening the fiber structure. For example, an ultra-violet written FBG in an SCMOF was shown to detect a refractive index variation of 3×10^{-5} refractive index units (RIU).⁶²

Two challenges arise using SCMOFs for FBG-based biosensing. Firstly, they must be filled from the distal end to interact with analytes, and secondly, complexity can arise due to inscription methods being susceptible to scattering by the MOF geometry.⁶³

To address these issues, ECMOFs have been developed where the core is accessible from one side along the length of the fiber. These have been fabricated from a diverse range of materials including polymer,⁶⁴ chalcogenide,⁶⁵ lead-silicate,⁸ and silica.^{9,66–68} Silica ECMOFs show good stability⁹ and can be readily spliced to conventional single mode fiber for easy integration with commercial interrogation equipment.^{67,68} ECMOFs have been fabricated with core diameters ranging from 2.7 to 12 μm , as seen in Fig. 4.⁶⁸

Fiber Bragg gratings have been written onto the core of these ECMOFs using a femtosecond laser technique:

using sufficiently short duration pulses multiphoton absorption can lead to ionization of electrons and the physical removal of material, a process known as laser ablation.⁶³ An example of such gratings is shown in Figs. 5a and b for the 7.5 μm core diameter ECMOF from Fig. 4c. The Bragg reflection shift with respect to external refractive index is shown in Fig. 5c, and the shift with polyelectrolyte layer deposition shown in Fig. 5d.

While FBGs on ECMOFs are less sensitive than techniques based on surface plasmon resonance, with shifts reported in the range of 1.1 to 101 nm/RIU depending on core diameter, the capability to be multiplexed and operate in reflection mode makes them a particularly attractive research direction for label-free assays in *in-vivo* biosensing applications.

Raman Spectroscopy

Raman spectroscopy is a form of vibrational spectroscopy in which each Raman-active chemical bond vibrational mode changes the energy of incident photons from a laser source by a fraction equal to that mode's vibrational energy.⁶⁹ Raman spectroscopy has the great advantage of being a label-free technique that can uniquely identify chemical species in a sample without the need for target-specific chemistry or surface modification.⁷⁰ Optical fibers have been deployed for Raman-based optical sensing as, besides their advantages in terms of delivering and collecting light,² in the case of MOFs they can enhance the Raman signature from target molecules.^{71,72}

We have shown that Raman spectroscopy in SCMOFs can be used as a method for detecting explosives in liquid samples.³² We were able to detect explosive quantities as small as 1 μg (Fig. 6a) in a small

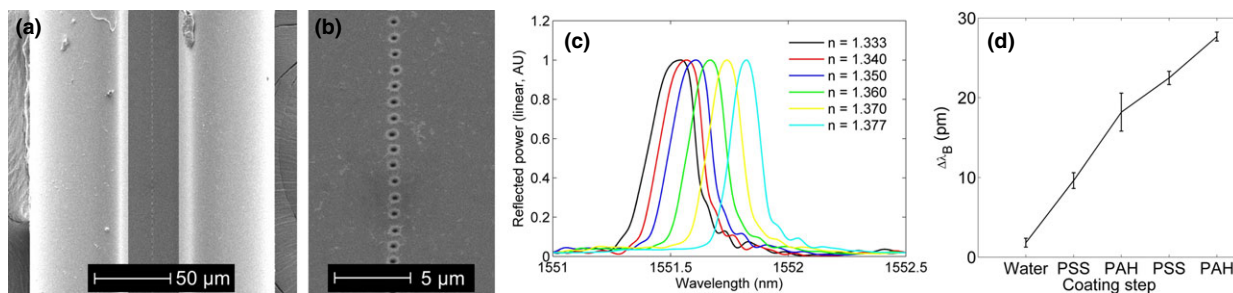


Fig. 5. (a, b) Scanning electron images of the ECMOF from Fig. 4(c) with femtosecond laser ablation gratings written on the exposed-core. (c) Shift in the reflected Bragg wavelength when the ECMOF is immersed into liquids of varying refractive index. (d) Shift in the Bragg wavelength as polyelectrolyte layers are coated onto the ECMOF.⁶⁸

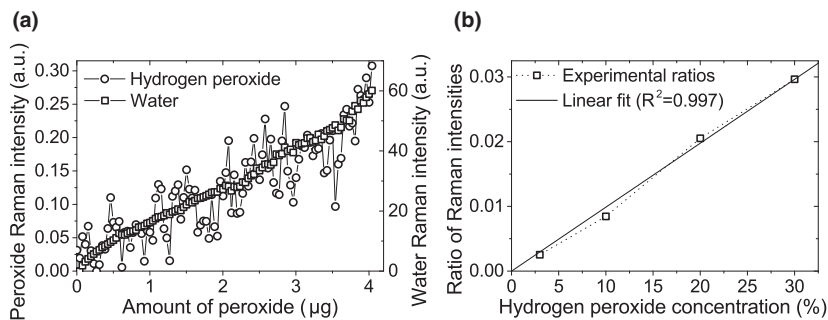


Fig. 6. (a) Experimental data showing the Raman signal intensity for hydrogen peroxide and water for an aqueous solution of hydrogen peroxide (b) correlation between the hydrogen peroxide concentration in water and the ratio between the Raman signal intensities.

sample volume (60 nL). The sensor was tested using hydrogen peroxide (H_2O_2), a key ingredient in making triacetone triperoxide (TATP), a difficult to detect home-made explosive, as well as using 1,4-dinitrobenzene (DNB), a member of the nitroaromatic family of explosives and a substitute molecule for 2,4,6-trinitrotoluene (TNT). In addition, using the solvent's Raman signature as a calibration standard in the same measurement, we were able to quantify the amount of explosive in the sample (Fig. 6b).

Background Raman signal from the solid core of SCMOFs can, however, hamper the detection limit of these optical fiber sensors. HCMOFs can overcome this issue, as the light is guided within the sample region itself, therefore maximizing the Raman signal.⁷³ These HCMOFs are time consuming to fabricate, as they rely on capillary stacking.^{74,75} Our work concentrated on single ring hollow core antiresonance reflection optical waveguiding fibers^{76,77} fabricated using the extrusion technique.⁷⁸ This simple fabrication process was used to fabricate a lead-silicate glass (Schott F2HT) preform

that was directly drawn to a single ring HCMOF (loss spectrum shown in Fig. 7a) with a core diameter of 47 μm , and a central ring diameter of 1.5 μm (Fig. 7a inset).

After filling with ethanol, spectra showed a 4 times increase in the intensity of the ethanol Raman spectrum when coupled into the core compared to the signal from the bulk ethanol (Fig. 7b). The combination of ease-of-fabrication and enhanced Raman sensing performance highlights the potential of extruded single ring HCMOFs as Raman sensors.⁷⁹

Conclusion

Optical fiber sensors have emerged as a very promising category of devices due to the combination of attractive physical properties, ease of integration with existing optical sources and detectors and the large number of compatible sensing modalities. Lowering the detection limits for analytes of interest and increasing the selectivity

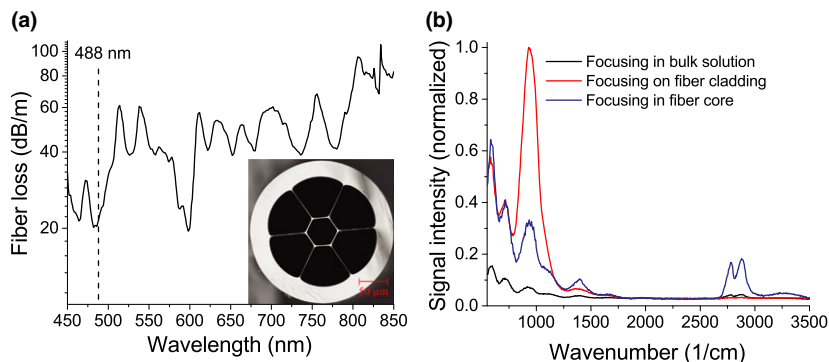


Fig. 7. (a) Optical loss from an extruded single ring HCMOF, highlighting the excitation wavelength used for Raman experiments. The inset shows a scanning electron microscope image of a cross section of the fiber.⁷⁹ (b) Raman signal of ethanol collected with the excitation light coupled in a bulk quantity of solution, on the fiber cladding and finally in the core of the optical fiber.

of optical fiber sensors are the main challenges for deploying these sensors in real-world applications.

In this work, we have demonstrated the use of MOFs in a diverse range of sensing applications to answer these challenges. MOFs have unique optical and physical properties that can be tailored by controlling the fiber geometry during fabrication, allowing for control over the light–matter interaction. The structural geometries of SCMOFs or HCMOFs enable interaction between light and analyte along the entire length of the fiber, allowing for measurements to be performed on small sample volumes with lower detection limits.

The use of label-free techniques such as WGM/SPR, Bragg gratings or Raman, as well as surface attachment methods for fluorescence-based sensing enables these sensors to be used without perturbing the sample. Lower detection limits can be aided by self-referencing methods that reduce the effect of fluctuations in the performance of the sensors at small signal levels and offer the potential for quantification of analytes in a sample. This makes MOF-based sensors particularly useful for measurements of low concentrations of analytes in small volumes of sensitive biological samples and has the potential to enable nondestructive *in vivo* or *in vitro* measurements in real time.

Acknowledgments

The authors would like to acknowledge funding support from the Centre for Nanoscale Biophotonics, through Australian Research Council (ARC) CE140100003, and ARC support through FL130100044, FS100

100039 and FS100200009 and LP110200736. Tanya Monro acknowledges the support of an ARC Georgina Sweet Laureate Fellowship. Stephen Warren-Smith is supported by the European Commission through the Seventh Framework Programme (FP7), PIIF-GA-2013-623248.

This work was performed in part at the OptoFab node of the Australian National Fabrication Facility utilizing Commonwealth and South Australian State Government funding. The authors acknowledge Peter Henry and Alastair Dowler for their contribution to the fiber drawing, and the Australian Defence Science and Technology Organisation (under the Signatures, Materials and Energy Corporate Enabling Research Program) for support of the suspended and exposed core silica fiber development at The University of Adelaide.

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