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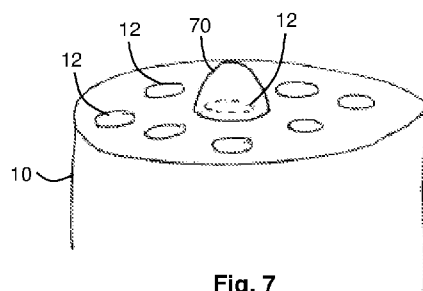


Fig. 7

(57) Abstract: A method for forming a sensing structure on a distal end of a mul-
ticore optical fibre, the method comprises contacting at least part of the distal end
of the multicore optical fibre with a polymerisation material, coupling light from
a light source to a proximal end of a selected one of the cores of the multicore op-
tical fibre, and photo-polymerising, using the light from the light source trans-
mitted through the selected core, a region of the polymerisation material adjacent to
a distal face of the selected core to form said sensing structure such that the sens-
ing structure substantially does not overlap any of the other cores of the multicore
optical fibre.



A sensing structure and method of forming a sensing structure

Field

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The present invention relates to a sensing structure, to a sensing probe comprising at least one sensing structure formed on an end of an optical fibre, and to a method of forming such a sensing probe and sensing structure.

10 Background

It has been proposed that real-time *in situ* measurements of the distal lung and of other anatomical regions may be obtained using an optical fibre probe that is formed by immobilizing molecules of a physiological sensor on the end of the optical fibre. The optical fibre probe may be inserted into the distal lung or other anatomical region, for example via the working channel of an endoscope. The physiological sensor may comprise, for example, a pH sensor.

One approach to immobilizing molecules of a physiological sensor on the end of an optical fibre involves coating nanoshells with the physiological sensor and physically affixing the nanoshells onto the end of the optical fibre. However, some methods of affixing nanoshells have been shown to be unsuccessful and/or unreliable.

A further approach to immobilizing molecules of a physiological sensor on the end of an optical fibre involves coating the distal tip of the optical fibre in a polymer in which molecules of the physiological sensor are embedded. The polymer may coat the entire distal end of the optical fibre. Polymerisation of the polymer may be initiated by light, for example by UV light.

30 Summary

In a first aspect of the invention, there is provided a method for forming a sensing structure on a distal end of a multicore optical fibre, the method comprising: contacting at least part of the distal end of the multicore optical fibre with a polymerisation material; coupling light from a light source to a proximal end of a selected one of the

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cores of the multicore optical fibre; and photo-polymerising, using the light from the light source transmitted through the selected core, a region of the polymerisation material adjacent to a distal face of the selected core to form said sensing structure such that the sensing structure substantially does not overlap any of the other cores of the multicore optical fibre.

Forming a sensing structure adjacent to a single core, where the sensing structure does not overlap other cores, may provide a robust sensing structure. The sensing structure may be less fragile or brittle and/or harder to displace than a sensing structure that overlaps other cores. The sensing structure may be individually addressable by excitation light when used for sensing. The sensing structure may provide a desired strength of signal when used for sensing.

The method may comprise controlling a parameter of the light source such that the sensing structure substantially does not overlap any of the other cores of the multicore optical fibre. The parameter of the light source may comprise at least one of power, intensity, duration of illumination. Light from the light source may be transmitted for a duration that is selected to form a sensing structure of a desired size.

A diameter of the selected core may be at least 5 μm , optionally at least 10 μm , further optionally at least 20 μm . A diameter of the sensing structure may be at least as large as a diameter of the selected core. The size of the sensing structure may determine a strength of signal provided by the sensing structure during sensing. When a sensing probe formed by the method is used for sensing, it may be easier to excite a larger core than a smaller core.

The light source may comprise a laser. The light source may be configured to provide coherent light. The light source may be configured to provide narrowband light. By using narrowband light, photo-bleaching of sensor molecules of the polymerisation material may be reduced or eliminated. Unwanted reactions of the polymerisation material may be reduced or eliminated.

A wavelength of the light source may comprise a wavelength of visible light. A wavelength of the light source may be between 400 nm and 700 nm, optionally between 400 nm and 550 nm, further optionally between 400 nm and 500 nm, further

optionally between 400 and 450 nm. A wavelength of the light source may be between 300 and 500 nm, optionally between 350 and 430 nm, further optionally between 350 nm and 420 nm. A wavelength of the light source may be above 400 nm. A wavelength of the light source may be below 700 nm, optionally below 550 nm, further optionally below 500 nm, further optionally below 450 nm.

A wavelength of the light source may be selected to be a wavelength that the selected core transmits well. A wavelength of the light source may be matched to an absorption wavelength of the polymerisation solution. The polymerisation solution may comprise a photo-initiator, and a wavelength of the light source may be matched to an absorption wavelength of the photo-initiator.

The sensing structure may comprise at least one of a pH sensor, a blood glucose sensor, an oxygen sensor, a carbon dioxide sensor. The sensing structure may comprise a physiological sensor configured to sense a physiological parameter. The physiological sensor may comprise at least one of fluorescein, a metal ligand complex, a boronic acid derivative. The physiological sensor may comprise a sensor configured for use in Raman spectroscopy and/or surface-enhanced Raman spectroscopy.

The physiological parameter may comprise at least one of a pH level, a blood glucose level, an oxygen level, an oxygen tension, a carbon dioxide level.

The method may further comprise forming a further sensing structure on a distal face of a further selected one of the cores of the multicore optical fibre by coupling light from the light source to a proximal end of the further selected core and photo-polymerising a region of polymerisation material adjacent to a distal face of the further selected core.

The sensing structure may comprise a first physiological sensor. The further sensing structure may comprise a second, different physiological sensor.

Different sensing structures on the same multicore optical fibre may be configured to sense different physiological parameters. Multiple parameters may be sensed using a single fibre optic probe.

The method may comprise forming an array of sensing structures at the distal end of a plurality of cores of the multicore optical fibre, wherein alternating sensing structures of the array are of different sensing structure types. The different sensing structure types may comprise different physiological sensors. The different sensing structure types may be configured to sense different physiological parameters. The different sensing structure types may be excitable by different frequencies of excitation light.

Alternating different sensing structure types may provide improved sensing performance. Alternating different sensing structure types may reduce cross-talk between adjacent sensing structures, when compared to adjacent sensing structures of the same type. If different sensing structure types are excitable by different frequencies of excitation light, then excitation light intended to excite one sensing structure may not excite adjacent sensing structures, even if it leaks from the intended core to an adjacent core.

The distal face of the selected core may be recessed with respect to a distal face of the multicore optical fibre. The sensing structure may be at least partially contained within a cavity formed by the recessing of the distal face of the selected core. By recessing the distal face of the selected core, and forming the sensing structure at least partially within a cavity formed by the recessing, the sensing structure may be better attached to the multicore optical fibre. It may be more difficult for the sensing structure to be mechanically removed.

The sensing structure may not protrude beyond the distal face of the multicore optical fibre. If the sensing structure does not protrude beyond the distal face of the multicore optical fibre, it may be difficult for the sensing structure to be removed mechanically. The positioning of the sensing structure may allow the end of the multicore optical fibre to be finished such that it presents a flat distal surface.

The distal face of the selected core may be recessed, optionally by etching of the selected core. The method may comprise recessing the distal face of the selected core, optionally by etching. The method may comprise etching the distal end of the multicore optical fibre before contacting the distal end of the multicore optical fibre with the polymerisation material. The etching may comprise preferentially etching at least

one core of the multicore optical fibre. The etching may comprise at least one of chemical etching, laser etching.

5 The method may comprise aligning light from the light source with the multicore optical fibre in dependence on an image formed by a camera positioned at the distal end of the multicore optical fibre, wherein the image is representative of light from the light source transmitted through one or more cores of the multicore optical fibre.

10 A power or intensity of light emitted by the light source during the aligning may be lower than a power or intensity of light emitted by the light source during photo-polymerisation. Using a lower power or intensity of light for alignment may allow accurate alignment of the light to be achieved. Using a lower power or intensity of light for alignment may allow alignment to be performed visually. Using a lower power or intensity of light for alignment may allow a good image to be formed by the camera.

15 A frequency of light emitted by the light source during the aligning may be the same as a frequency of light emitted by the light source during photo-polymerisation. A power or intensity of light emitted by the light source during the aligning may be substantially the same as a power or intensity of light emitted by the light source during photo-polymerisation.

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The method may further comprise preparing the distal end of the multicore optical fibre before contacting the at least part of the distal end of the multicore optical fibre with the polymerisation material. The preparing of the distal end of the multicore optical fibre may comprise polishing a face of the distal end of the multicore optical fibre. The preparing of the distal end of the multicore optical fibre may comprise coating the distal face of the selected core with a coating material, The coating material may comprise silane.

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30 In a second aspect of the invention, which may be provided independently, there is provided a method for forming a sensing structure on a distal end of a multicore optical fibre, the method comprising: contacting at least part of the distal end of the multicore optical fibre with a polymerisation material; coupling light from a light source to a proximal end of the multicore optical fibre; and photo-polymerising, using the light from the light source transmitted via one or more cores of the multicore optical fibre, a region

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of the polymerisation material adjacent to the distal end of the multicore optical fibre to form said sensing structure; wherein a distal face of at least one core of the multicore optical fibre is recessed with respect to a distal face of the multicore optical fibre to form at least one cavity and the sensing structure is at least partially contained within
5 said at least one cavity and/or at least partially fills said at least one cavity.

In a third aspect of the invention, which may be provided independently, there is provided an apparatus for forming a sensing structure on a multicore optical fibre, the apparatus comprising: a container for polymerisation material; means for receiving a
10 multicore optical fibre, arranged such that the multicore optical fibre is positionable such that at least part of a distal end of the multicore optical fibre is placeable in contact with polymerisation material when said polymerisation material is in the container; a light source; a controller for controlling operation of the light source; and a
15 positioner configured to position the light source relative to a proximal end of the multicore optical fibre such that light from the light source is coupled to a selected one of the cores of the multicore optical fibre; wherein the controller is configured to control the light source such that light from the light source, when coupled to the selected core, photo-polymerises a region of the polymerisation material adjacent to a distal face of
20 the selected core, thereby to form the sensing structure, wherein the forming of the sensing structure is such that the sensing structure substantially does not overlap any of the other cores of the multicore optical fibre.

In a fourth aspect of the invention, which may be provided independently, there is provided a sensing probe comprising: a multicore optical fibre; and a sensing structure
25 formed on a distal end of the multicore optical fibre; wherein the sensing structure is adjacent to a distal face of a selected one of the cores of the multicore optical fibre and substantially does not overlap any of the other cores of the multicore optical fibre.

A diameter of the sensing structure may be less than an inter-core spacing of the cores
30 of the multicore optical fibre. A diameter of the sensing structure may be no more than twice a diameter of the selected core.

The sensing probe may comprise an array of sensing structures. Each sensing structure may be over a distal face of a respective core of the multicore optical fibre.

Each sensing structure may substantially not overlap any of the cores of the multicore optical fibre other than the core to which it is adjacent.

5 Sensing structures at the end of adjacent cores may be of different sensing structure types. The different sensing structure types may comprise different physiological sensors. The different sensing structure types may be configured to sense different physiological parameters. The different sensing structure types may be excitable by different frequencies of excitation light.

10 The sensing probe may provide a compact multi-functional probe suitable for use in sensing regions of the body, for example the distal lung. A size and/or flexibility of the sensing probe may facilitate access to a desired anatomical region.

15 The sensing structure may comprise a plurality of different materials. The different materials may be different fluorescent materials. The different materials may be excitable by different frequencies of excitation light.

20 The plurality of different materials may comprise a first material that is configured to sense a physiological parameter, and a second material that is not configured to sense the physiological parameter. Emission of light by the first material in response to excitation light may be sensitive to the physiological parameter. Emission of light by the second material in response to excitation light may be substantially insensitive to the physiological parameter. The second material may be used as a reference material when sensing the physiological parameter.

25 The physiological parameter may comprise at least one of a pH level, a blood glucose level, an oxygen level, an oxygen tension, a carbon dioxide level. The first material may comprise at least one of a pH sensor, a blood glucose sensor, an oxygen sensor, a carbon dioxide sensor.

30 There may be provided a method for forming a sensing structure on a distal end of a multicore optical fibre, the method comprising: contacting at least part of the distal end of the multicore optical fibre with a polymerisation material; coupling light from a light source to a proximal end of a selected one of the cores of the multicore optical fibre; and photo-polymerising, using the light from the light source transmitted through the
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selected core, a region of the polymerisation material adjacent to a distal face of the selected core to form said sensing structure, wherein said sensing structure comprises a first material that is configured to sense a physiological parameter and a second material that is substantially insensitive to the physiological parameter.

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There may be provided a sensing probe comprising: a multicore optical fibre; and a sensing structure formed on a distal end of the multicore optical fibre; wherein said sensing structure comprises a first material that is configured to sense a physiological parameter and a second material that is substantially insensitive to the physiological parameter.

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There may be provided a method for using the sensing probe as claimed or described herein, the method comprising: exciting the sensing structure by applying light from an excitation light source to the sensing structure; receiving a response signal from the sensing structure in response to the excitation; and analysing the response signal to determine a value for a physiological parameter.

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There may be provided a method or system substantially as described herein with reference to the accompanying drawings.

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Features in one aspect may be provided as features in any other aspect as appropriate. For example, features of a method may be provided as features of an apparatus and vice versa. Any feature or features in one aspect may be provided in combination with any suitable feature or features in any other aspect.

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Detailed description of embodiments

Embodiments of the invention are now described, by way of non-limiting example, and are illustrated in the following figures, in which:-

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Figure 1 is a schematic illustration of a multicore optical fibre;

Figure 2a is a schematic illustration of an optical apparatus configured for alignment of a light source with a core of a multicore fibre;

Figure 2b is a schematic illustration of an optical apparatus configured for photopolymerisation;

Figures 3a and 3b are schematic illustrations of an optical apparatus in accordance with an embodiment;

Figure 4 is a plot of laser spectra and photo-initiator absorbance;

Figure 5 is a flow chart illustrating in overview a method of an embodiment;

5 Figures 6a to 6f represent stages of immobilising polymer at the distal face of a non-etched optical fibre;

Figure 7 is a schematic illustration of a sensing structure formed on the distal face of a multicore fibre;

Figure 8 is a flow chart illustrating in overview a sensing method of an embodiment;

10 Figure 9 is a schematic illustration of a multicore fibre having alternating sensors on its multiple cores;

and

Figure 10a and 10b represent polymer immobilised inside an etched optical fibre.

15 Figure 1 schematically illustrates a multicore optical fibre 10 in accordance with an embodiment. The left side of Figure 1 illustrates a face of the multicore fibre 10. The multicore fibre 10 is a multimode fibre.

20 The multicore fibre 10 comprises a plurality of cores 12. Each core 12 is a light-transmitting portion of the multicore fibre 10. Each core 12 has a higher refractive index than a cladding 14 of the multicore fibre.

25 In the present embodiment, the multicore fibre 10 comprises nineteen cores 12. Each of the cores 12 is 20 μm in diameter. In other embodiments, any multicore optical fibre comprising any number and size of cores may be used. For example, the cores 12 may be smaller than 20 μm (for example 10 μm or 13 μm) or may be larger than 20 μm (for example, 50 μm or 100 μm).

30 In the present embodiment, the multicore fibre 10 is formed from pure silica with high-index Ge-doped silica regions forming each of the cores 12. A non-doped region of pure silica surrounding the cores 12 forms the cladding 14. The cladding 14 is surrounded by a coating 16. The coating 16 may comprise a biocompatible material. In other embodiments, the multicore fibre 10 may be formed of any suitable materials.

The right side of Figure 1 represents the propagation of light along a core 12 of the multicore fibre 10 by total internal reflection. The difference in refractive index between the core 12 and the cladding 14 allows light to travel along the core 12 by total internal reflection. The cladding 14 acts like a wall so that the light does not escape through the side walls of the multicore fibre 10.

Figure 2a is a schematic illustration of an optical apparatus in accordance with an embodiment. The optical apparatus comprises a light source 20, a single mode optical fibre 22, a first position adjuster 24, a first lens 26, a second lens 28, a second position adjuster 32, a multicore fibre 10, and a camera 34. In other embodiments, the apparatus may comprise additional components, components may be exchanged for different components, or certain components may be omitted.

The light source 20 comprises a laser configured to emit light at a wavelength of 405 nm. In other embodiments, any suitable light source may be used, for example any laser light source. The light source may provide coherent light. The light source may be narrowband. The light source may provide light of a specific wavelength. Any suitable wavelength may be used, for example any suitable wavelength of visible light.

A first end of the single mode optical fibre 22 is coupled to the light source 20. A second end of the single mode optical fibre 22 is held by the first position adjuster 24. In the present embodiment, the position of the first position adjuster 24 is fixed with respect to the laser light source. The first position adjuster 24 is not adjusted to align light from the light source 20 with the multicore fibre 10. In other embodiments, the first position adjuster 24 may be adjusted to align light from the light source 20 with the multicore fibre 10.

The single mode optical fibre 22 is configured to transmit a single wavelength of light (in this embodiment, 405 nm) from the light source 20 to the second end of the single mode optical fibre 22.

In use, light from the light source 20 is emitted from the second end of the single mode optical fibre 22 and passes through the first lens 26. A light path of the light is indicated in Figure 2a by dotted line 28. The light then passes through the second lens 30 and

into a proximal end of multicore fibre 10, which is held by the second position adjuster 32.

5 In further embodiments, the light from the single mode fibre 22 may be reflected by a mirror (not shown) into the proximal end of multicore fibre 10.

The second position adjuster 32 is operable to control a position of the proximal end of the multicore fibre 10. The second position adjuster 32 comprises controls in x, y and z, where z is a direction of travel of the light, and x and y are perpendicular to the z axis.
10 In other embodiments, any suitable position adjuster may be used. One or more position adjusters may be used to adjust a position of the multicore fibre 10, a position of the single mode fibre 22, or positions of both the multicore fibre 10 and the single mode fibre 22.

15 Light travels from the proximal end of the multicore fibre 10 down one or more cores of the multicore fibre 10. The camera 34 is positioned at the distal end of the multicore fibre 10. The camera 34 receives at least part of the light transmitted down the one or more cores and uses that light to form an image. In the present embodiment, the camera 34 is a compact CCD camera. In other embodiments, any suitable camera may
20 be used.

In the present embodiment, the camera 34 is connected to a display screen (not shown) on which a user may view the image formed by the camera 34. Any suitable display screen or other display device may be used, for example a computer screen.
25 The image may be enlarged to allow the user to distinguish individual cores of the multicore fibre 10.

The apparatus of Figure 2a is configured to allow the user to align light from the light source 20 with a single core of the multicore fibre 10, such that the light is primarily or
30 solely coupled to that core and not to other cores of the multicore fibre 10.

In use, the user may adjust the x and y position of the second position adjuster 32 to adjust a position of the light from the light source 20 on the proximal face of the multicore optical fibre 10. The user may adjust the z control of the second position
35 adjuster 32 to adjust a focus of the light.

As an example, the user may position the second position adjuster 32 at an initial position. At the initial position, light from the light source 20 may propagate through several of the cores 12 of the multicore optical fibre 10. The user may view the image from the camera 34 on the display screen and ascertain that the light is coupling to more than one core 12. The user may then adjust the second position adjuster 32 until the light couples to a single, selected core 12 of the multicore fibre 10.

In other embodiments, the image formed by the camera 34 may be analysed automatically and/or the second position adjuster 32 may operate automatically to align the light with the single core 12. A controller device (not shown) may analyse the camera image and move one or both of the position adjusters 24, 32 until the camera image shows that the light is coupled to a single selected core 12.

Figure 2b is a schematic illustration of a further configuration of the optical apparatus of Figure 2a. The apparatus comprises the light source 20, single mode optical fibre 22, first position adjuster 24, first lens 26, second lens 30, second position adjuster 32 and multicore fibre 10 as described above with reference to Figure 2a. However, the camera 34 is removed from the distal end of the multicore fibre 10. The distal end of the multicore fibre 10 is placed in a well-plate 40 containing a polymerisation solution, such that the polymerisation solution contacts some or all of the distal end of the multicore fibre 10. In further embodiment, at least part of the distal end of the multicore fibre 10 may be positioned in any suitable container containing any suitable polymerisation material.

The polymerisation solution comprises molecules of a physiological sensor. The physiological sensor may also be referred to as an indicator.

In the present embodiment, the physiological sensor is a fluorescent chemical physiological sensor that is configured to sense pH. In other embodiments, any physiological sensor may be used, for example any fluorescent chemical physiological sensor or any non-fluorescent physiological sensor (for example a Raman spectroscopy or surface-enhanced Raman spectroscopy sensor). The physiological sensor may be configured to sense any suitable physiological parameter, for example pH, oxygen tension, carbon dioxide level or glucose level. In some embodiments, the

polymerisation material may comprise molecules of more than one physiological sensor, for example molecules of different physiological sensors configured to sense different physiological parameters.

5 In the present embodiment, the polymerisation solution comprises two types of monomer, a photo-initiator, and a solvent. The first type of monomer is a fluorescent monomer, which in the present embodiment is fluorescein o-methacrylate. The fluorescent monomer is configured to act as a pH sensor. The second type of monomer is a cross-linker, which in the present embodiment is poly(ethylene glycol) diacrylate
10 (PEG diacrylate). In the present embodiment, the photo-initiator is diphenyl(2,4,5-trimethylbenzoyl) phosphine oxide (TPO) and the solvent is N,N-dimethylacetamide (DMA). In other embodiments, any suitable polymerisation material that is capable of being photo-polymerised may be used.

15 In some embodiments, the polymerisation material comprises a fluorescent physiological sensor that is configured to sense oxygen. The physiological sensor may comprise a metal ligand complex, for example ruthenium (II) tris(pyridine). The physiological sensor may comprise a metalloporphyrin, for example a platinum porphyrin. In some embodiments, the polymerisation material comprises a fluorescent
20 physiological sensor that is configured to sense glucose. The physiological sensor may comprise a boronic acid derivative.

The photo-initiator may be any photo-initiator that is configured to initiate polymerisation of the monomers when activated with light from the light source 20.

25 In the present embodiment, the photo-initiator is configured to initiate polymerisation when activated with light between 350 and 420 nm. In other embodiments, different wavelengths of light may be used. In some circumstances, photo-polymerisation may occur more quickly when light of a lower wavelength is used.

30 Figure 4 shows plots of laser spectra of a 405 nm laser (line 45) and of a 520 nm laser (line 46). Figure 4 also shows the photo-initiator absorbance of TPO (line 47).

35 A wavelength of the light source 20 may be chosen to be a wavelength that is efficiently transmitted by the cores of the multicore optical fibre 10. For example, the

wavelength may be chosen to avoid certain ultraviolet frequencies that may be transmitted poorly by the cores 12 of the multicore optical fibre 10.

5 In use, light from light source 20 passes through the single mode optical fibre 22 and lenses 26, 30 and into the multicore optical fibre 10. The light passes through one or more of the cores 12 of the multicore fibre 10 into the polymerisation solution. For example, if the second position adjuster 32 has been positioned to couple the light into a single core 12, the light passes through that single core 12 into the polymerisation solution. The light is configured to initiate photo-polymerisation of the polymerisation
10 solution. If light is transmitted through a single core 12, the light may initiate photo-polymerisation in a region of the polymerisation solution that is adjacent to the distal end of that single core.

15 Figure 5 is a flow chart showing in overview a method for forming sensing regions on the distal end of a multicore fibre 10, in accordance with an embodiment.

At stage 50 of the process of Figure 5, the distal face of the multicore fibre 10 is prepared by polishing the distal face and coating at least part of the distal face with silane. Coating the distal face with silane may enable polymer to become covalently
20 attached to the distal face when photo-polymerisation is performed at stage 56 of Figure 5. In other embodiments, any method may be used to activate a distal face of one or more cores such that a polymer may become covalently attached the distal face of the one or more cores.

25 In other embodiments, any suitable method of preparing the distal face of the multicore fibre 10 is used. Any suitable alternative or additional coating may be used. In further embodiments, stage 50 is omitted.

30 At stage 52, the multicore fibre 10 having a prepared distal face is positioned according to the configuration of Figure 2a, such that light from the light source 20 is incident on the proximal face of multicore fibre 10, and the camera 34 is arranged to receive light emitted at the distal end of multicore fibre 10.

35 The light source 20 is configured to provide light having a first power or intensity. The first power or intensity may be a low power or intensity.

In an experiment, the results of which are shown in Figure 6, the method of Figure 5 was used with a fluorescent monomer which was not pH-sensitive, to provide a proof of concept of the photo-polymerisation method. In the experiment, the light source 20 was
5 a 520 nm laser and the first power was less than 0.1 μ W.

The first power or intensity may be a lower power or intensity than is later used to initiate photo-polymerisation of the polymerisation solution. In the experiment, a light power used to initiate photo-polymerisation at stage 56 of Figure 5 was approximately
10 4 mW. The lower power of light may be used to obtain a good laser-core coupling. The lower power of light may be used to observe how good a coupling has been achieved.

The first, lower power or intensity may be suitable for imaging by the camera 34. At a high power, the display may be saturated with light, and the user may be unable to see
15 the cores.

In other embodiments, the first power or intensity may be substantially the same as the second power or intensity. For example, in some embodiments the photo-initiator may be capable of being photo-polymerised by a low light power, which may also be
20 suitable for use in coupling to the camera.

Light from a laser light source may be more coherent than light from some other light sources. The light may travel in phase. Therefore the light may be brighter than light from some other sources and may be focused to a small spot. A laser may have a
25 specific wavelength.

In the experiment using the method of Figure 5, the wavelength of the laser was 520 nm. In some embodiments, the wavelength of the laser is 405 nm. The laser wavelength may be selected to match a photo-initiator. In other embodiments, a
30 different laser wavelength may be selected, for example to match a different photo-initiator.

A user aligns the apparatus by moving the second position adjuster 32 (for example, by moving the x, y and/or z controls of the second position adjuster 32) to a position such
35 that light from light source 20 couples with a selected single core 12 of the multicore

5 fibre 10, and substantially does not couple with the other cores 12 of the multicore fibre 10. The camera 34 is used to check the coupling of light to the selected single core 12 of the fibre. The user may determine that the light has coupled into the selected single core 12 by monitoring the display screen. In other embodiments, the alignment of the apparatus may be performed automatically.

Figure 6a to 6f show images from the experiment described above, in which a 520 nm laser was used for photo-polymerisation.

10 Figure 6a shows an example of an image from the camera 34 as viewed on the display screen. Most of the cores 12 appear on the image as dark circles. However, one core 12 (identified on Figure 6a as core 12A) appears as a single bright spot. This indicates that the light from the light source 12 is coupled solely or primarily into core 12A. If a good coupling is achieved to core 12A, a high proportion of the light may pass down
15 core 12A. A better coupling may result in a higher proportion of the light passing down core 12A.

At stage 54, the user removes the camera 34 from the distal end of the multicore fibre 10. The user dips the distal end of the multicore fibre 10 into a well-plate 40 containing
20 polymerisation solution for photo-polymerisation of monomer (thereby changing the apparatus from the configuration of Figure 2a to the configuration of Figure 2b).

The polymerisation solution used in the experiment comprised a fluorescent monomer, a further monomer (for cross-linking) and a solvent.

25 The user does not change the position of either of the position adjusters 24, 32 or of the proximal end of the multicore fibre 10. Therefore, the configuration of the apparatus remains such that light from the light source will couple into a single core 12 of the multicore fibre 10.

30 The user may turn off the light source 20 while removing the camera 34 and placing the distal end of the multicore fibre 10 in the well-plate 40 containing the polymerisation solution.

At stage 56, the selected single core 12 (which in the example of Figure 6a is core 12A) is illuminated by light from the light source 20, the light from the light source 20 having a second power or intensity which is higher than the power or intensity used in the coupling of stage 52. For example, the user may switch the light source back on, and adjust the light source to provide light of the second power or intensity. In the experiment, the second power was approximately 4 mW.

The second power or intensity is selected to be high enough to cause photo-polymerisation of the polymerisation solution.

Since only the selected single core 12 is illuminated, photo-polymerisation occurs preferentially in a region adjacent to the distal face of the selected single core 12, forming a region of polymer at the distal face of the selected single core. Polymerisation starts close to the distal surface of the selected single core 12, and a region of polymer then grows from the distal surface of the selected single core 12 outwards. The speed of the growth of the polymer region may be dependent on the power or intensity of the light source, the concentration of the polymer solution, and/or a duration of illumination.

Light having a single wavelength is used for the photo-polymerisation. If a broader spectrum of light including multiple wavelengths were to be used for photo-polymerisation, in some circumstances indicators may be photo-bleached and/or different, unwanted reactions may be initiated.

At stage 58, illumination ceases and the region of polymer stops growing. In some embodiments, illumination ceases because the user turns off the light source 20. In other embodiments, the light source 20 may be turned off automatically, for example when a predetermined duration of illumination has been reached.

A duration of illumination may be chosen to result in a region of polymer of a desired size. A shorter duration of illumination may result in a smaller region of polymer. A longer duration of illumination may result in a larger region of polymer. In the present embodiment, a duration of illumination is chosen such that the region of polymer does not grow large enough to encroach on any adjacent core. For example a diameter of

the region of polymer may be less than an inter-core spacing of the cores of the multicore fibre 10.

5 The distal end of the multicore fibre 10 is removed from the polymerisation solution and polymerisation solution that has not been photo-polymerised is removed. In the present embodiment, once the distal end of the multicore fibre 10 is removed from the polymerisation solution, it is left to dry for a while then is rinsed with distilled water. In other embodiments, any suitable cleaning material may be used. The distal end of the multicore fibre 10 may be treated in any suitable way, for example by performing any
10 suitable cleaning process and/or applying any suitable coating.

The region of polymer that was formed at stage 54 may be referred to as a sensing structure or sensing region. In some embodiments, the region of polymer may be referred to as a polymer cone.
15

In some embodiments, the sensing structure is configured for sensing pH. In other embodiments, the sensing structure may be configured to sense any suitable physiological parameter.

20 Figure 6b shows an image of the distal end of the multicore fibre 10 after a region of polymer has been formed at the distal end of the core 12A. The region of polymer is confined to an area of the distal face adjacent to the selected single core 12A. The polymerisation solution was illuminated for around 20 minutes to form the region of polymer adjacent to core 12A. In other embodiments, longer or shorter illumination
25 times may be used.

Figure 7 is a schematic illustration of a multicore fibre 10 having a plurality of cores 12 (for clarity, fewer than nineteen cores 12 are illustrated). A sensing structure 70 (which may be referred to as a polymer cone) has been formed on the distal end of one of the
30 cores 12 using the method of Figure 5.

At stage 60 of the process of Figure 5, the process of stages 52 to 58 is repeated for further cores 12 of the multicore fibre 10.

The camera 34 is placed at the distal end of multicore fibre 10 (on which one sensing structure has already been formed). Low-power light from the light source 20 is aligned with a second selected single core 12 of the multicore fibre 10 by moving the second position adjuster 32. The distal end of the multicore fibre 10 is then placed in polymerisation solution. In the present embodiment, the polymerisation solution used for further cores 12 of the multicore fibre 10 has the same constituents as the polymerisation solution used for the first selected single core 12. In other embodiments, different polymerisation solutions may be used.

The second single core 12 is illuminated with high-power light from the light source 20 to initiate photo-polymerisation. Illumination ceases when an appropriate size of polymer region has been created at the distal face of the second single core 12. The size of the polymer region may be dependent on a concentration of the polymerisation solution, a time of illumination and/or a power of the light source 20.

In the present embodiment, the size of the sensing structure formed on the second core 12 is larger than the size of the sensing structure formed on the first core 12. In other embodiments, the size of the sensing structures may be the same, or the second sensing structure may be smaller than the first sensing structure.

The process of stages 52 to 58 may be repeated for any suitable number of cores, for example for each of the nineteen cores 12 of the multicore fibre 10 of the present embodiment.

Figure 6c shows an image from the camera 34 in which a second single core (indicated as core 12B) of the multicore fibre 10 of Figure 6a and 6b is illuminated. Core 12B appears as a bright spot on the image. Figure 6d shows an image of the distal end of the multicore fibre 10 after a region of polymer has been formed at the distal end of the core 12A and a further region of polymer has been formed at the distal end of the core 12B. The polymer regions are discrete and do not touch each other.

Figure 6e shows an image from the camera 34 in which a second single core (indicated as core 12B) of the multicore fibre 10 of Figure 6a to 6d is illuminated. Figure 6f shows an image of the distal end of the multicore fibre 10 after a region of polymer has been formed at the distal end of the core 12A and further regions of polymer have been

formed at the distal end of cores 12B and 12C. In the experiment of Figures 6a to 6f, the photo-polymerisation process was repeated for each of cores 12A, 12B and 12C and then stopped at the third core (core 12C).

5 Figure 6f shows the three polymer cones at cores 12A, 12B and 12C fluorescent under green excitation light. The three bright spots in Figure 6f correspond to, from left to right, the polymer cone at core 12A, the polymer cone at core 12B, and the polymer cone at core 12C. In the experiment of Figures 6a to 6f, the polymer cones increase in size from core 12A to core 12C. In other embodiments, the polymer cones may be of
10 the same size, or may decrease in size.

In some embodiments performed using the method of Figure 5, light is singly coupled to one core of a multicore fibre 10. Illumination of individual cores within a multi-core fibre is used to provide localised photo-polymerisation of fluorescent chemical sensors
15 onto the ends of individual cores. The laser light source 20 that is used for photo-polymerisation is aligned visually using the camera 34 before power or intensity is increased to a level suitable for photo-polymerisation.

A light source 20 of very low power is used to obtain a good coupling between light and the selected core. The coupling is monitored by the compact camera 34 at the distal end. Once coupled, the distal tip is put in a well-plate 40 containing monomers and a photo-initiator for photo-polymerisation. Monomers are photo-polymerised at the same core 12 to which light was coupled. A polymer is formed at the irradiated core 12 thus
20 creating a discrete sensing core.

25 Each sensing structure formed by the method of Figure 5 may be restricted to a respective area around the distal end of a single core. The polymer may be stopped from spreading onto other cores. If the polymer were to spread too much, it may become easily displaced, fragile and/or brittle. By restricting each sensing structure to the vicinity of a single core, the sensing structures may be more robust, less fragile or
30 brittle and/or harder to displace than if they were to extend across multiple cores.

If the sensing structures are to be used in the body, it may be important that the sensing structures are robust. In some circumstances, the formation of sensing

structures as described with reference to Figure 5 may provide better adherence than some known methods of immobilising a physiological sensor.

5 Illumination of a single core may allow polymerisation to be initiated at the tip of that single core without initiating polymerisation on other areas of the distal surface of the multicore fibre 10.

10 The formation of sensing structures on individual cores 12 of the multicore fibre 10, where each sensing structure does not extend across other cores 12 of the multicore fibre 10, may allow the structures to be individually addressed when used for sensing. In some circumstances, improved sensing may be provided by such individually addressable sensors.

15 The multicore fibre 10 on which one or more sensing structures have been formed may be used as a sensing probe. In one embodiment, a sensing probe comprises a nineteen-core multicore fibre 10. On the distal end of the multicore fibre 10, a respective discrete sensing structure has been formed for each of the nineteen cores. Each sensing structure is restricted to an area around the distal end of its respective core and does not overlap any of the other cores. The sensing structures are spatially
20 separated. In some embodiments, the sensing structures are of the same or similar size. In other embodiments, different sensing structures may be of different sizes. For example, different sensing structures may be formed using different illumination times.

25 Figure 8 is a flow chart illustrating in overview a method of operation of a sensing probe comprising a plurality of sensing structures.

30 At stage 80, the distal end of the sensing probe is introduced into the distal lung, for example via the working channel of an endoscope. In further embodiments, the sensing probe may be introduced into any suitable environment to be sensed, for example any suitable anatomical region.

35 At stage 82, an excitation laser is focused on the proximal end of a selected one of the cores of the sensing probe. In other embodiments, any suitable excitation light source may be used. Excitation light travels down the selected core and excites physiological sensor molecules in the sensing structure associated with the selected core. The

sensor molecules fluoresce in response to the excitation light. Properties of the fluorescence of the sensor molecules (for example, a fluorescence intensity) depend on a physiological property of the environment of the sensing structure.

5 In one embodiment, the physiological sensor is a pH sensor, and the fluorescence of the physiological sensor is in dependence on the pH of the environment of the sensing region, for example the pH of a part of the distal lung into which the sensing probe is inserted.

10 At stage 84, a response signal comprising fluorescent light from the sensing structure is returned to the proximal end of the optical fibre (for example, to the proximal end of the selected core) and is detected by a detector, for example a camera or spectrometer.

15 In an embodiment, light from the excitation laser is reflected from a filter into the multicore fibre 10. The filter is configured to pass the response signal while filtering out light of the excitation wavelength. The filter may prevent excitation light from passing into the detector during the fluorescence measurement.

20 In an embodiment, substantially the same optical apparatus may be used for photopolymerisation as is used for fluorescence measurement. For example, the same lenses and position adjusters may be used.

At stage 86, the detector or a further analysis device analyses the response signal to
25 determine a value for the pH of the part of the distal lung into which the sensing probe is inserted.

At stage 88, the excitation laser is focused on a different single core of the sensing probe to excite a sensing structure associated with that core and to obtain a response
30 signal that is representative of pH. The excitation laser may be focused on each of the sensing structures in turn.

In the method of Figure 8, the physiological sensor is a fluorescent sensor. In other embodiments, any suitable sensor may be used. The sensor may be any sensor that
35 returns a response signal when excited by an excitation light source, where the

response signal is capable of being analysed to provide information about a physiological parameter. In some embodiments, the sensor may be a non-fluorescent sensor, for example a sensor that, on excitation by an appropriate wavelength of excitation light, may provide a signal that may be used for Raman spectroscopy or surface-enhanced Raman spectroscopy (SERS).

In the sensing probe of Figure 8, the sensing structures are each confined to the vicinity of a respective core by controlling the growth of polymer when the sensing structures are formed. By controlling the size of a sensing structure (for example, the size of a polymer cone) a strength of the response signal received from that sensing structure on excitation may be controlled. A large sensing structure may produce a larger response signal since it includes more of the physiological sensor. In some circumstances, a larger sensing structure may provide a signal more quickly and/or with less photo-bleaching than a smaller sensing structure.

However, if the polymer were to spread across multiple cores and/or the cladding, it may lead to light returning through multiple cores rather than just one core. It may then be more difficult to obtain a good signal from the sensing structure. In some circumstances, significant core-to-core coupling may occur. In some embodiments, a size of the sensing structure is selected to provide a strong response signal without significant core-to-core coupling.

The size of response signal received may be dependent on a size of the core. If a sensing structure were to be formed on a single very small core (for example a core of an imaging fibre which may have several thousand cores), that sensing structure may return a very small response signal that may have large errors. Furthermore, in some circumstances the physiological sensor molecules in that sensing structure may be readily photo-bleached since they may be present in very small quantities.

In some examples of an imaging fibre having a very large number of cores, a scanning method may be used in which a laser moves across all the cores. Such a scanning system may provide low average laser power. It may be difficult to polymerise on a single core of a fibre having thousands of small cores. It may be difficult to interrogate a single core of such a fibre in a defined (one-by-one) manner.

Fibres with more than one core may experience some coupling of light between the cores. In some circumstances, the coupling between cores may be worse if the cores are close together, similar in size, and/or small. For example, there may be large core-to-core coupling in multiple small core fibres such as imaging fibres, because the cores are packed close together. The light may spill out from one core into adjacent cores (and beyond) at significant levels. In some circumstances, such core-to-core coupling may be less with larger cores. For example, in some larger cores there may be a greater spacing between cores.

5 A nineteen-core optical fibre or other fibre having a larger core size (for example, a core size of at least 10 μm) and/or a smaller number of cores (for example, less than 100 cores) may make it practical for single cores to be illuminated with a high-intensity laser beam. It may be easier and more defined to focus an excitation laser on a single large (for example, $>10\text{ }\mu\text{m}$) core than on the end of a high density multicore fibre. A
10 focused excitation laser may allow more light to excite the fluorescent indicators.

In embodiments described above, the same polymerisation material is used to form each of the polymer regions. Each polymer region comprises the same polymer and molecules of the same physiological sensor. In other embodiments, different
20 polymerisation materials may be used for different sensing structures. Different sensing structures may comprise different physiological sensors. Different sensing structures may be configured to sense different physiological parameters.

In some embodiments, different polymerisation solutions are used to form different
25 polymer regions. In some embodiments, the polymerisation solutions used to form sensing structures configured to sense different physiological parameters are photo-polymerised using the same frequency of light. In other embodiments, the polymerisation solutions are photo-polymerised using different frequencies of light. The light source may be configured to provide light of more than one frequency. For
30 example, the light source may comprise two or more lasers, each providing light of a different frequency.

A sensing probe may be developed that has discrete sensing cores, for example discrete sensing cores that are configured for sensing different physiological
35 parameters.

The ends of different individual cores of a multicore fibre may be coated with different sensors (for example, different fluorescent sensors) which may have different wavelengths, resulting in a multiplexed multicore fibre that may detect multiple physiological parameters (for example, pH, oxygen tension, carbon dioxide levels, or glucose levels). Different indicators with different excitation wavelengths may be used on the same optical fibre.

For example, in one embodiment a first sensing structure is formed on a first core of a multicore fibre 10 using a polymerisation solution comprising molecules of a first physiological sensor configured to sense pH, for example fluorescein. A second sensing structure is formed on a second core of the multicore fibre using a polymerisation solution comprising molecules of a second physiological sensor configured to sense glucose, for example a boronic acid derivative. Further sensing structures may also be formed.

The end of the multicore fibre 10 on which the first and second sensing structures are formed is inserted into the distal lung of a patient. The first sensing structure is excited with a first wavelength of excitation light to obtain a response signal which may be analysed to obtain a value for pH. The second sensing structure is excited with a second wavelength of excitation light to obtain a response signal which may be analysed to obtain a value for glucose level. The first and second sensing structures may be excited at the same time or sequentially. The first and second wavelengths of excitation light may be provided by one or more excitation light sources.

In other embodiments, the first and second physiological sensors may be excited by the same wavelength of excitation light. A single light source may be used to excite the first and second sensing structures. The first and second sensing structures may be excited at the same time or sequentially.

In some embodiments, the response signal from the second physiological sensor has a different frequency from the response signal from the first physiological sensors. The response signals can be differentiated by time (if the structures are excited at different times), by frequency and/or by position. In some embodiments, the response signals

from the different physiological sensors have the same or similar frequencies. The response signals may be differentiated by time and/or by position.

5 By providing multiple types of sensing structure on a single multicore fibre, each sensing structure comprising a different physiological sensor, a sensing probe may be formed that is capable of sensing multiple physiological parameters, for example sensing multiple physiological parameters simultaneously or near-simultaneously. It may be possible to measure different analytes at the same wavelength if using different sensors.

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A compact sensing probe may be produced that is capable of sensing several different physiological parameters. The sensing probe may be formed of a single multicore optical fibre. The small size of the sensing probe may be important when accessing regions such as the distal lung. If a flexible multicore fibre is used, the flexibility of the fibre may also help to facilitate access to such anatomical regions.

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The sensing probe may be described as a multiplexed optical sensor. Each core of the sensing probe may measure different physiological conditions, for example blood glucose concentration, oxygen, carbon dioxide, and blood pH. A small, compact and flexible multiplexed sensing system may be provided for continuous monitoring of physiological conditions.

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A number of physiological parameters within the distal lung (or other anatomical region) may be measured concurrently using a variety of chemical fluorescent sensors attached (via multiplexing) the end of an optical multicore fibre. The sensors may be securely attached in a multiplexed fashion by forming a plurality of polymer sensing structures as described above, each comprising a different physiological sensor.

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In some embodiments, different types of sensing structures having different physiological sensors are formed on alternating cores of the sensing probe. The different sensing structures may be distributed such that each sensing structure is adjacent to a sensing structure of a different type. For example, a sensing structure configured to sense pH may be formed on a first core, and sensing structures configured to sense glucose, oxygen, and carbon dioxide respectively may be formed on three cores adjacent to the first core.

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Figure 9 is a schematic illustration of one embodiment in which an array of sensing structures is formed on the distal end of a multicore fibre. Sensing structures having different physiological sensors are formed on alternating cores. Each core on which a sensing structure comprising a first physiological sensor (for example, a pH sensor) is formed is shaded with vertical lines. Each core on which a sensing structure comprising a second physiological sensor (for example, a glucose level sensor) is formed is shaded with vertical lines. Each core on which a sensing structure comprising a third physiological sensor (for example, an oxygen tension sensor) is formed is shaded with dots. The sensors are alternated such that no core has the same sensor as any of its neighbouring cores.

Alternating different types of sensing structure may reduce cross-talk between different cores of the optical fibre. For example, each different type of sensing structure may be excited by a different wavelength and/or may emit a response signal of a different wavelength. In some circumstances, excitation light leaking from a core to an adjacent core may not excite the sensing structure on that core.

In some embodiments, the distal surface of the multicore fibre 10 is etched before any sensing structures are formed on the distal surface. The etching process preferentially removes material from the distal end of the one or more cores, such that a distal surface of each core is recessed with respect to a distal surface of the multicore fibre, for example a distal surface of the cladding. Each recessed core forms a cavity on the distal surface of the multicore fibre, which may be referred to as a pit. The cavity may be a region from which material of the core has been removed by etching.

The etching may comprise any suitable etching method. The etching method may comprise chemical etching, for example etching using hydrogen fluoride (HF). The etching method may comprise laser etching, for example femtosecond laser etching. In some embodiments, etching may remove an approximately hemispherical portion of each core to form approximately hemispherical pits.

After etching, the distal surface of the multicore fibre may be prepared in any suitable manner. In some embodiments, a surface of each pit is activated such that a polymer

becomes covalently attached to the pit surface. For example, silane may be applied at least to a surface of each pit to aid adherence of the polymer.

5 The process of Figure 5 is performed to form sensing structures on each of one or more of the cores of the etched fibre. For each core, a region of polymerisation solution adjacent to the distal end of that core is photo-polymerised. The extent of the polymer region may be dependent on a time of illumination, a concentration of the polymer solution and/or a power or intensity of the light source 20.

10 Figure 10a and 10b shows sensing structures formed on an etched fibre surface. For fabricating the sensing structures shown in Figures 10a and 10b, the polymerisation solution comprised fluorescein o-methacrylate, poly(ethylene glycol) diacrylate (PEG diacrylate), diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (TPO) and N,N-dimethylacetamide (DMA).

15 A laser light source having a wavelength of 405 nm was used. A light power of around 10 to 50 μ W was used to couple the laser light source to a single core of the multicore fibre 10. A light power of around 100 μ W was used for photo-polymerisation. The working power for the photo-polymerisation was lower than the power used for a light source wavelength of 520 nm. The photo-polymerisation of each sensing structure took about 5 seconds.

20 It may be seen from Figure 4 (the graph of TPO absorbance and the laser spectra) that the photo-initiator, TPO, has higher absorbance at 405 nm than at 520 nm. The photo-initiator is more reactive at 405 nm than at 520 nm. Therefore a lower light power was used to initiate photo-polymerisation than was used with a 520 nm light source. A shorter duration of illumination was also used.

25 The 405 nm wavelength may efficiently activate the photo-initiator (TPO) in the polymerisation solution. The photo-initiator absorbs in the 405 nm region. In this embodiment, using a laser light source at 405 nm reduces the time of polymerisation when compared with a laser light source at 520 nm. Compared to the light power and time for the 405 nm light source, a 520 nm light source may use a much higher power and/or longer irradiation time to grow a single sensing structure using TPO as a photo-initiator.

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5 In some circumstances, a high power light source and/or long time of photo-polymerisation may result in the fluorescent compounds starting to photo-bleach. Using a light source of a wavelength that is more strongly absorbed by the photo-initiator may avoid or reduce photo-bleaching.

10 Figure 10a shows a plurality of cores 112. A sensing structure has been formed on the distal end of a selected core 112A. Figure 10b shows the same plurality of cores 112 after a further sensing structure has been formed on the distal end of a further selected core 112B. In the embodiment of Figure 10a and 10b, each selected core is illuminated for around 5 seconds to form the sensing structures. Two polymer cones are fabricated on the same fibre, one after the other.

15 When the multicore fibre of Figures 10a and 10b was exposed to relevant changes in pH discrete areas of fluorescence were clearly visible on the end of the multicore fibre, resulting in an optical signal that may be captured and analysed.

20 In some embodiments, the sensing structure may coat the pit at the distal end of the core without filling the pit. In some embodiments, the pit may be fully or partially filled with polymer, but the polymer may not extend outside the pit. For example, the polymer may not extend over the surface of the cladding 14 adjacent to the core 12. In some embodiments, the polymer may fill the pit and also extend outside the pit. For example, the polymer may fill the pit and also form an external polymer cone 70, for example as shown in Figure 7.

25 The use of etching may enable better attachment of indicators (physiological sensors). By etching the fibre to form pits and growing the polymer inside those pits, the polymer may adhere better than if the polymer were grown on a surface that is flush to the surface of the multicore fibre. The sensing structure may be less likely to detach from the end of the multicore fibre. The sensing structure may be more robust. For example, it may be less likely to be knocked off. A sensing structure that is fully contained within a pit may be difficult to mechanically remove.

35 Even for a sensing structure that extends beyond the extent of the pit, the part of the sensing structure that is inside the pit may form a firm connection to the multicore fibre,

which may be considered to be analogous to that of the root of a tooth. The sensing structure may therefore be difficult to mechanically remove.

5 In some circumstances, it may be easier to control the spatial extent of a sensing structure that is grown inside a pit than a sensing structure that is grown on a flush surface.

10 A depth of etching may be chosen to form a desired size of pit. A depth of etching may be controlled by a time of etching. A size of pit may correspond to a desired size of sensing structure, for example a size of sensing structure that will provide a desired signal strength.

15 If sensing structures are fully contained within pits, it may be possible to polish the end of the multicore fibre 10 to give a flat fibre end even when sensing structures are present. The flat end may be useful for clinical applications.

20 In some embodiments, sensing structures are formed which extend over multiple etched cores. In one embodiment, a group of adjacent cores of the multicore fibre is illuminated by light source 20, causing a region of polymer adjacent to group of adjacent cores, and extending over the distal ends of the group of cores, to polymerise. In another embodiment, a region of polymer is polymerised by an external light source that does not illuminate one or more of the cores of the multicore fibre. By providing an etched surface, a region of polymer that extends over multiple cores may be more stable than if it were formed on a non-etched surface.

25 In embodiments above, a pH-sensitive fluorescent monomer is added to the polymerisation solution. A sensing structure is formed by polymerisation of the pH-sensitive monomer. The sensing structure therefore comprises a pH-sensing fluorescent material.

30 In further embodiments, two different fluorescent monomers are included in the polymerisation solution. One of the fluorescent monomers is a pH-sensitive dye and the other of the fluorescent monomers is a reference dye that is not pH-sensitive. The polymerisation solution comprises the two different fluorescent monomers, a further monomer (as a polymer backbone or cross-linker), a photo-initiator and a solvent. In

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other embodiments, the polymerisation solution may comprise any suitable components in addition to the two different fluorescent monomers.

5 In some embodiments, the pH-sensitive monomer is as described above, for example, with reference to Figures 2a and 2b. The reference monomer is a rhodamine monomer (for example, Acryloxyethyl thiocarbamoyl Rhodamine B) or a porphyrins-based monomer (for example, meso-Tetra[4-(allyloxy)phenyl] porphine chloride).

10 The two fluorescent monomers are photo-polymerised together on the same core to form a sensing structure comprising a pH-sensitive fluorescent material and a reference fluorescent material that is not pH-sensitive.

In use, the sensing structure is excited by excitation light. The pH-sensitive fluorescent material and the reference fluorescent material each fluoresce.

15 A response signal comprising fluorescent light from the sensing structure is detected by a detector, for example a camera or spectrometer. The fluorescent light from the sensing structure comprises fluorescent light from both the pH-sensitive fluorescent material and the reference fluorescent material. An amount of light from the pH-sensitive fluorescent material is compared to an amount of light from the reference fluorescent material to obtain a ratiometric measurement of pH (for example, by calculating a ratio of light received from the pH-sensitive fluorescent material to light received from the reference fluorescent material). Since the reference fluorescent material is not sensitive to pH, the ratiometric measurement changes with pH.

25 Performing a ratiometric analysis using two different fluorescent materials in a single sensing structure may result in a more accurate measurement of pH. The use of a ratiometric analysis may result in more robust sensors.

30 Sensing of the distal lung is described above. In other embodiments, different anatomical regions may be sensed using a sensing probe comprising one or more sensing structures formed at the end of individual cores of the sensing probe. For example, a sensing probe may be used to analyse circulating blood. A sensing probe may be used to sense any anatomical region that is capable of being accessed via an endoscope, for example the bronchus, gastrointestinal tract, or urinary tract. Sensing

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may be performed on any suitable human or animal subject. Sensing may be performed for any suitable medical or veterinary application.

5 It may be understood that the present invention has been described above purely by way of example, and that modifications of detail can be made within the scope of the invention.

Each feature disclosed in the description and (where appropriate) the claims and drawings may be provided independently or in any appropriate combination.

10

CLAIMS:

1. A method for forming a sensing structure on a distal end of a multicore optical fibre, the method comprising:
 - 5 contacting at least part of the distal end of the multicore optical fibre with a polymerisation material;
 coupling light from a light source to a proximal end of a selected one of the cores of the multicore optical fibre; and
 photo-polymerising, using the light from the light source transmitted through the
10 selected core, a region of the polymerisation material adjacent to a distal face of the selected core to form said sensing structure such that the sensing structure substantially does not overlap any of the other cores of the multicore optical fibre.
2. A method according to Claim 1, comprising controlling a parameter of the light
15 source such that the sensing structure substantially does not overlap any of the other cores of the multicore optical fibre.
3. A method according to claim 1 or 2, where the distal face of the selected core is recessed.
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4. A method according to any preceding claim, comprising etching the distal end of the multicore optical fibre before contacting the distal end of the multicore optical fibre with the polymerisation material, the etching comprising preferentially etching at least one core of the multicore optical fibre.
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5. A method according to Claim 4, wherein the etching comprises at least one of chemical etching, laser etching.
6. A method according to any preceding claim, wherein a diameter of the selected
30 core is at least 5 μm , optionally at least 10 μm , further optionally at least 20 μm .
7. A method according to any preceding claim, wherein the light source comprises a laser.

8. A method according to any preceding claim, wherein a wavelength of the light source comprises a wavelength of visible light, optionally wherein a wavelength of the light source is between 400 nm and 550 nm.

5 9. A method according to any preceding claim, wherein the sensing structure comprises at least one of a pH sensor, a blood glucose sensor, an oxygen sensor, a carbon dioxide sensor.

10 10. A method according to any preceding claim, further comprising forming a further sensing structure on a distal face of a further selected one of the cores of the multicore optical fibre by coupling light from the light source to a proximal end of the further selected core and photo-polymerising a region of polymerisation material adjacent to a distal face of the further selected core.

15 11. A method according to Claim 10, wherein the sensing structure comprises a first physiological sensor and the further sensing structure comprises a second, different physiological sensor.

20 12. A method according to any preceding claim, comprising forming an array of sensing structures at the distal end of a plurality of cores of the multicore optical fibre, wherein alternating sensing structures of the array are of different sensing structure types.

25 13. A method according to Claim 12, wherein the different sensing structure types comprise different physiological sensors.

14. A method according to Claim 12 or Claim 13, wherein the different sensing structure types are configured to sense different physiological parameters.

30 15. A method according to any of Claims 12 to 14, wherein the different sensing structure types are excitable by different frequencies of excitation light.

16. A method according to any preceding claim, wherein the distal face of the selected core is recessed with respect to a distal face of the multicore optical fibre.

17. A method according to Claim 16, wherein the sensing structure is at least partially contained within a cavity formed by the recessing of the distal face of the selected core.

5 18. A method according to Claim 16 or Claim 17, wherein the sensing structure does not protrude beyond the distal face of the multicore optical fibre.

10 19. A method according to any preceding claim, comprising aligning light from the light source with the multicore optical fibre in dependence on an image formed by a camera positioned at the distal end of the multicore optical fibre, wherein the image is representative of light from the light source transmitted through one or more cores of the multicore optical fibre.

15 20. A method according to Claim 19, wherein a power or intensity of light emitted by the light source during the aligning is lower than a power or intensity of light emitted by the light source during photo-polymerisation.

20 21. A method according to Claim 19 or Claim 20, wherein a frequency of light emitted by the light source during the aligning is the same as a frequency of light emitted by the light source during photo-polymerisation.

25 22. A method according to any preceding claim, further comprising preparing the distal end of the multicore optical fibre before contacting the at least part of the distal end of the multicore optical fibre with the polymerisation material, the preparing comprising at least one of:

- a) polishing a face of the distal end of the multicore optical fibre;
- b) coating the distal face of the selected core with a coating material, optionally wherein the coating material comprises silane.

30 23. A method for forming a sensing structure on a distal end of a multicore optical fibre, the method comprising:

contacting at least part of the distal end of the multicore optical fibre with a polymerisation material;

coupling light from a light source to a proximal end of the multicore optical fibre;

35 and

photo-polymerising, using the light from the light source transmitted via one or more cores of the multicore optical fibre, a region of the polymerisation material adjacent to the distal end of the multicore optical fibre to form said sensing structure;

5 wherein a distal face of at least one core of the multicore optical fibre is recessed with respect to a distal face of the multicore optical fibre to form at least one cavity and the sensing structure is at least partially contained within said at least one cavity.

24. An apparatus for forming a sensing structure on a multicore optical fibre, the
10 apparatus comprising:

a container for polymerisation material;

means for receiving a multicore optical fibre, arranged such that the multicore optical fibre is positionable such that at least part of a distal end of the multicore optical fibre is placeable in contact with polymerisation material when said polymerisation
15 material is in the container;

a light source;

a controller for controlling operation of the light source and

a positioner configured to position the light source relative to a proximal end of the multicore optical fibre such that light from the light source is coupled to a selected
20 one of the cores of the multicore optical fibre;

wherein the controller is configured to control the light source such that light from the light source, when coupled to the selected core, photo-polymerises a region of the polymerisation material adjacent to a distal face of the selected core, thereby to form the sensing structure, wherein the forming of the sensing structure is such that the
25 sensing structure substantially does not overlap any of the other cores of the multicore optical fibre.

25. A sensing probe comprising:

a multicore optical fibre; and

30 a sensing structure formed on a distal end of the multicore optical fibre;

wherein the sensing structure is over a distal face of a selected one of the cores of the multicore optical fibre and substantially does not overlap any of the other cores of the multicore optical fibre.

26. A method according to Claim 25, wherein a diameter of the sensing structure is less than an inter-core spacing of the cores of the multicore optical fibre.

5 27. A method according to Claim 25 or Claim 26, wherein a diameter of the sensing structure is no more than twice a diameter of the selected core.

10 28. A probe according to any of Claims 25 to 27, comprising an array of sensing structures, wherein each sensing structure is adjacent to a distal face of a respective core of the multicore optical fibre.

29. A probe according to Claim 28, wherein sensing structures at the end of adjacent cores are of different sensing structure types, wherein at least one of:
a) the different sensing structure types comprise different physiological sensors;
b) the different sensing structure types are configured to sense different physiological parameters;
15 c) the different sensing structure types are excitable by different frequencies of excitation light.

20 30. A method for using the sensing probe of any of Claims 25 to 29, the method comprising:
exciting the sensing structure by applying light from an excitation light source to the sensing structure;
receiving a response signal from the sensing structure in response to the excitation; and
25 analysing the response signal to determine a value for a physiological parameter.

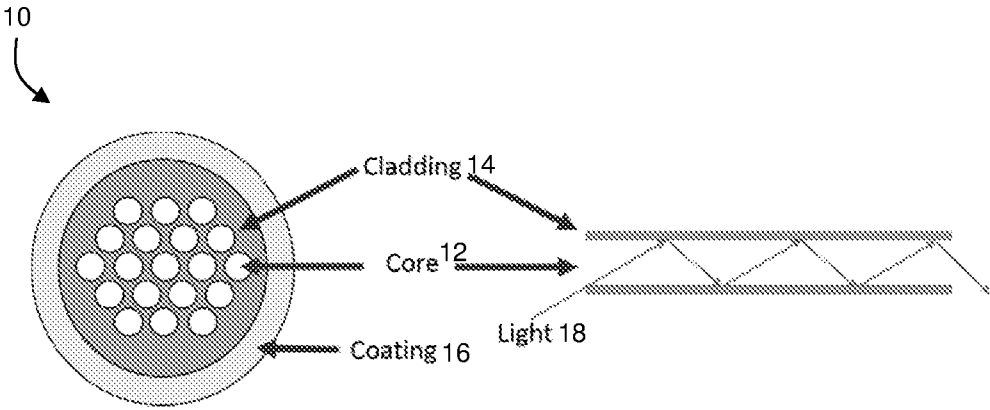


Fig. 1

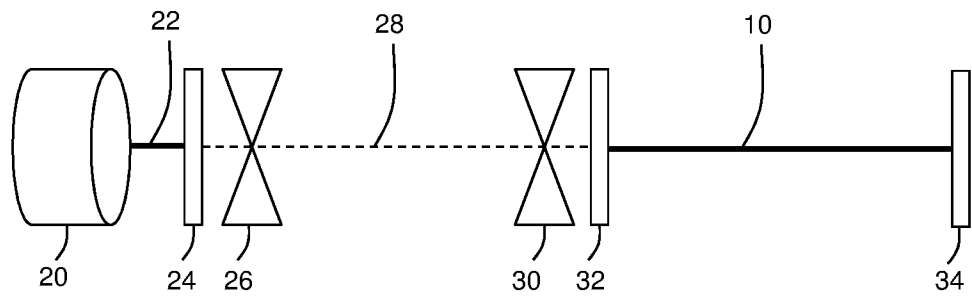


Fig. 2a

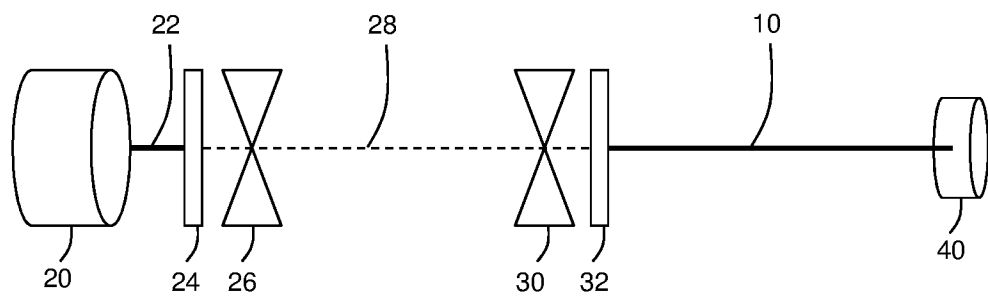


Fig. 2b

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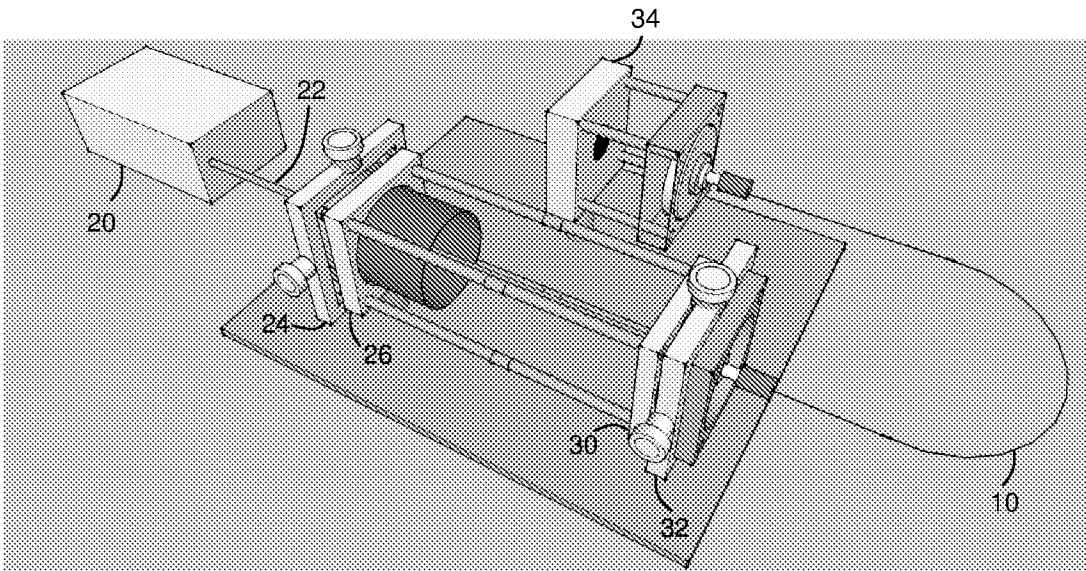


Fig. 3a

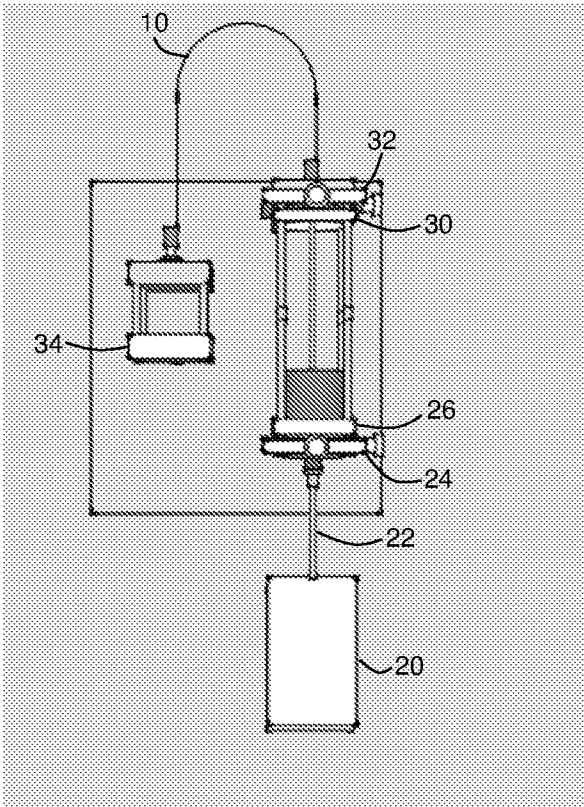


Fig. 3b

4/9

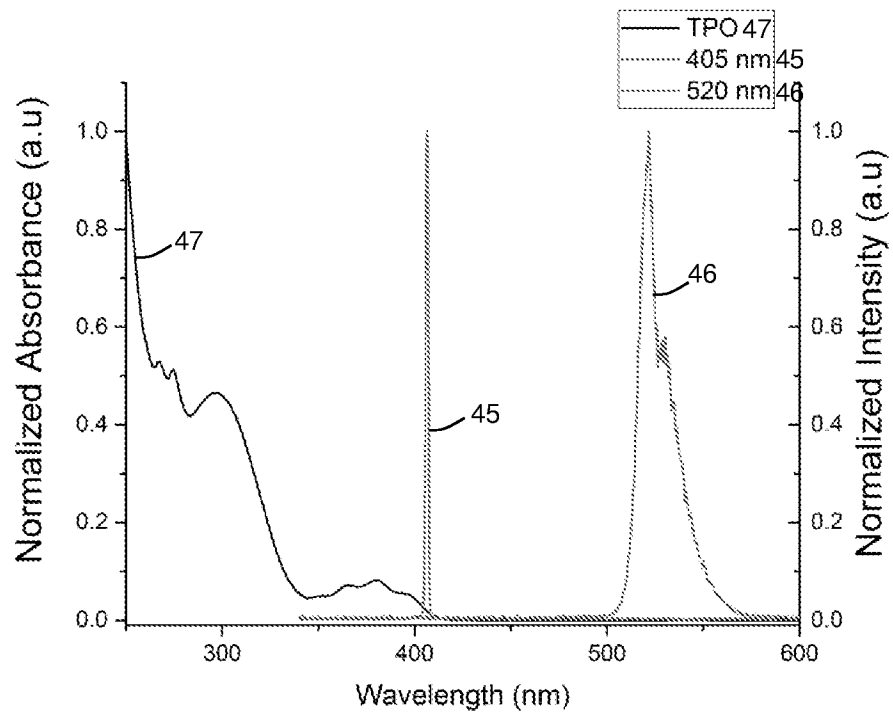
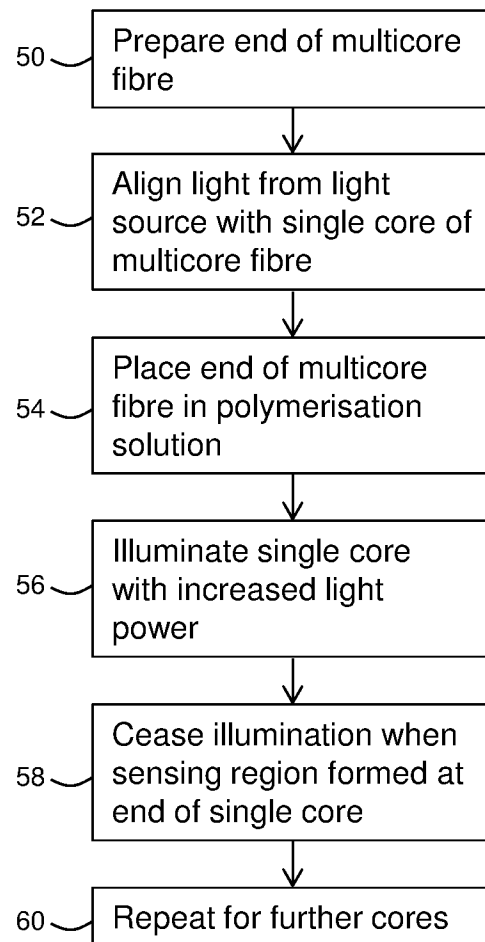


Fig. 4

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**Fig. 5**

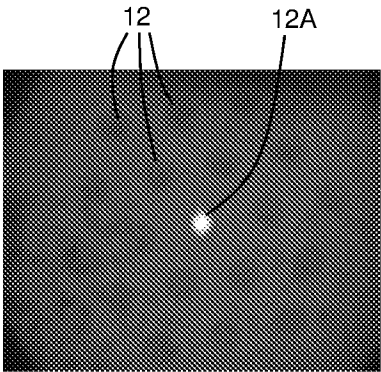


Fig. 6a

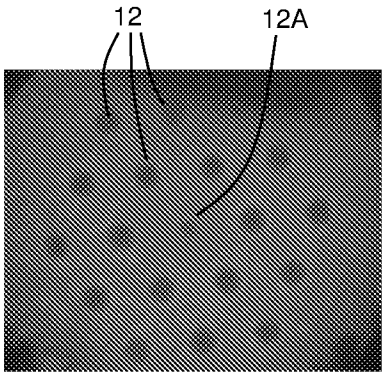


Fig. 6b

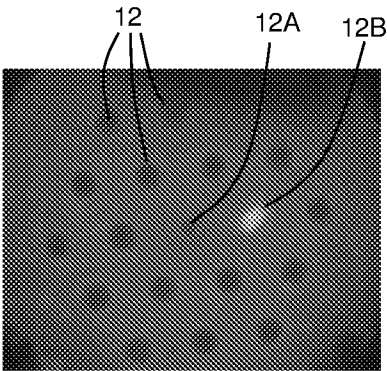


Fig. 6c

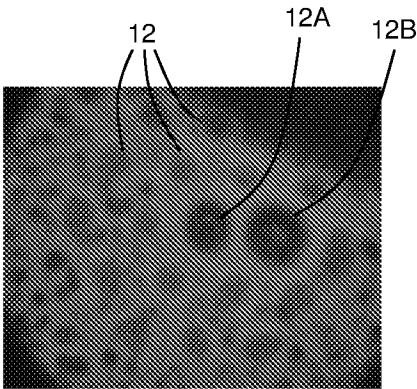


Fig. 6d

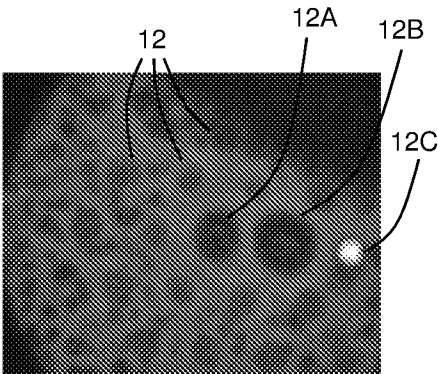


Fig. 6e

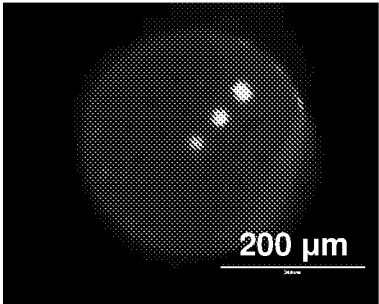


Fig. 6f

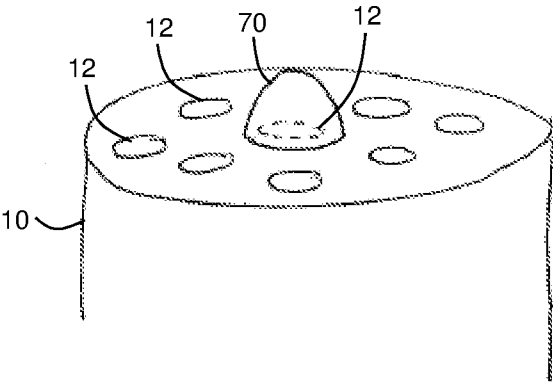
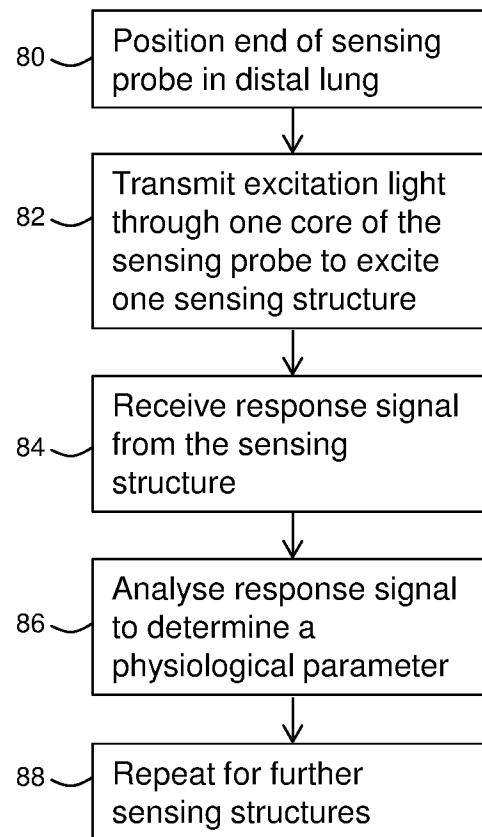


Fig. 7

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**Fig. 8**

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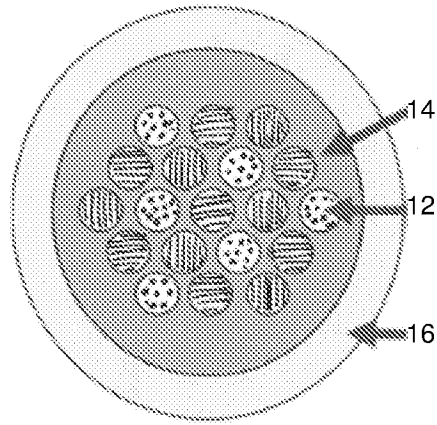


Fig. 9

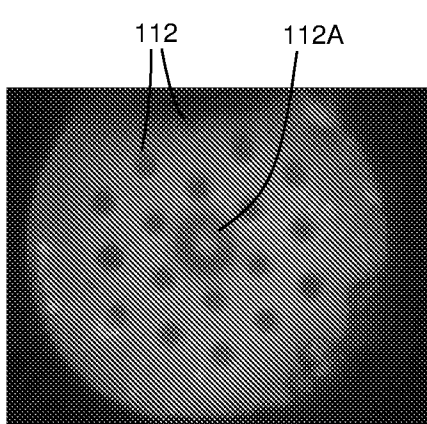


Fig. 10a

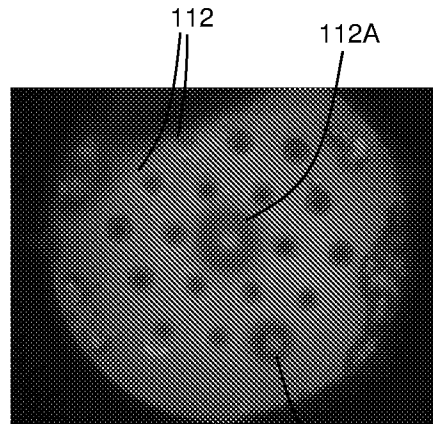


Fig. 10b

112B

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2017/051497

A. CLASSIFICATION OF SUBJECT MATTER		
INV.	G02B6/24	G02B6/02 A61B5/00 A61B5/145 A61B5/1455
	G02B23/24	
ADD.	G02B6/26	
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) G02B A61B		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YADONG ZHAO ET AL: "In Situ Fiber-Optic Oxygen Consumption Measurements from a Working Mouse Heart", ANALYTICAL CHEMISTRY, vol. 71, no. 17, 1 September 1999 (1999-09-01), pages 3887-3893, XP055396850, US ISSN: 0003-2700, DOI: 10.1021/ac9903003 abstract page 3887, column 2, line 33 - page 3888, column 1, line 8 page 3888, column 2, line 9 - line 28 page 3888, column 2, line 54 - page 3889, column 1, line 12 page 3890, column 2, line 6 - line 34; figure 2 ----- -/--	1-22, 24-30
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 9 August 2017		Date of mailing of the international search report 17/10/2017
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Mouget, Mathilde

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2017/051497

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2013/202263 A1 (PLAIN JEROME [FR] ET AL) 8 August 2013 (2013-08-08) paragraph [0029] - paragraph [0031] paragraph [0043] - paragraph [0047]; figure 1 -----	1-22, 24-30
A	CHRISTIANE MUNKHOLM ET AL: "Polymer modification of fiber optic chemical sensors as a method of enhancing fluorescence signal for pH measurement", ANALYTICAL CHEMISTRY, vol. 58, no. 7, 22 June 1986 (1986-06-22), pages 1427-1430, XP055396825, US ISSN: 0003-2700, DOI: 10.1021/ac00298a034 abstract page 1427, column 2, line 17 - line 26 page 1428, column 2, line 15 - page 1429, column 1, line 2 page 1429, column 1, line 42 - page 1429, column 2, line 4; figures 1, 2 -----	1-22, 24-30
A	SONG A ET AL: "HIGH-PERFORMANCE FIBER-OPTIC PH MICROSENSORS FOR PRACTICAL PHYSIOLOGICAL MEASUREMENTS USING A DUAL-EMISSION SENSITIVE DYE", ANALYTICAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 69, no. 5, 1 March 1997 (1997-03-01), pages 863-867, XP000686373, ISSN: 0003-2700, DOI: 10.1021/AC960917+ abstract page 864, column 2, line 12 - line 40 -----	1-22, 24-30
A	US 5 627 922 A (KOPELMAN RAOUL [US] ET AL) 6 May 1997 (1997-05-06) column 2, line 17 - line 37 column 3, line 4 - line 7 column 3, line 64 - column 4, line 66; figure 4 -----	1-22, 24-30

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2017/051497

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-22, 24-30

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-22, 24-30

Method for forming a sensing structure on one of the cores on the distal end of a multicore optical fiber such that the sensing structure does not overlap with the other cores.

2. claim: 23

Method for forming a sensing structure on at least one of the cores on the distal end of a multicore optical fiber wherein the distal face of said at least one core is recessed with respect to the overall distal face of the fiber

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2017/051497

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
US 2013202263	A1	08-08-2013	CN	102918439 A		06-02-2013
			EP	2553508 A1		06-02-2013
			FR	2958414 A1		07-10-2011
			JP	2013527934 A		04-07-2013
			US	2013202263 A1		08-08-2013
			WO	2011124803 A1		13-10-2011

US 5627922	A	06-05-1997	US	5361314 A		01-11-1994
			US	5627922 A		06-05-1997
			WO	9406040 A1		17-03-1994
