AN OPTICAL BIOSENSOR

FIELD OF INVENTION

The present invention relates broadly to an optical biosensor, to a holder for a sensor waveguide structure for an optical biosensor, to a method of assembling an optical biosensor, and to a method of biosensing.

BACKGROUND

Optical biosensors can enable a detection of changes of biological molecules, such as cells, proteins or metabolites from the body, via e.g. a change in the properties of light. Some common optical techniques include absorption, evanescent waves, fluorescence and surface plasmon resonance.

An example of an existing optical biosensor is the Biacore™ instruments from GE Life Sciences. It exploits the phenomenon of surface plasmon resonance (SPR) to detect molecular interactions, which enable researchers to study kinetics, affinity, specificity and concentrations of the molecules.

However, such systems typically include complicated optical components, a light source system and an optical detection system resulting in expensive and bulky equipment. For example, the Biacore™ instruments can measure about 154 centimetres (cm) x 79.3cm x 62.3cm and can weigh about 188 kilograms (kg). The smaller versions still measure around 59.6cm x 59.3cm x 56.3cm and weigh about 47kg. Thus, the size and weight of the system can significantly reduce its portability.

The prior art device also requires complex alignment systems to ensure proper and accurate alignment between the optical components. For example, the device has to ensure that light from a light emitting diode (LED), which can cover a fixed range of incident and reflected angles, is focused on a wedge on the sensor

surface through a semi-cylindrical glass prism. On the other side, the reflected output light beam coming out from the glass prism is required to focus onto an array of photodiodes. Further, the sensor chip is usually required to be placed against the semi-cylindrical glass prism, using a silicone opto-interface to ensure a good optical contact. The complexity of such alignment systems thus requires skilled personnel to operate and maintain. In addition, such complexities make miniaturization of the systems difficult.

Also, there could be a requirement for the re-alignment of the various optical components when the conventional system is moved or transported. This increases the need for skilled personnel to operate and maintain such systems.

Further, the optical components e.g. focusing lens, mirrors, assemblies and cylindrical prisms, used in the prior art systems are highly fragile and very delicate. In this regard, the conventional systems may be easily damaged during transportation, and reduces the portability of such devices.

A need therefore exists to provide a biosensor that seeks to address at least some of the above problems.

SUMMARY

In accordance with a first aspect of the present invention, there is provided an optical biosensor comprising: a sensor waveguide structure; an input waveguide structure; an output waveguide structure; and a holder for the sensor waveguide structure, the holder comprising means for aligning the sensor waveguide structure with the input waveguide structure and the output waveguide structure, for guiding a light signal from the input waveguide structure through the sensor waveguide structure and to the output waveguide structure.

The means for aligning may comprise alignment elements adapted for cooperating with alignment structures formed on the input waveguide structure, the output waveguide structure and the sensor waveguide structures respectively.

The alignment structures may be formed from a waveguide core material of the input, output, and sensor waveguide structures respectively.

The alignment structures may be formed during formation of a waveguide core from the waveguide core material.

The alignment structures may comprise one or more waveguide portions of one or more of the sensor waveguide structure, the input waveguide structure and the output waveguide structure.

The alignment structures may be formed during photolithography processing of the waveguide core material.

The means for aligning may comprise means for aligning respective top surfaces of the sensor waveguide structure, the input waveguide structure and the output waveguide structure for z-directional alignment.

The input waveguide structure may be adapted to be coupled to at least one light source and the output waveguide structure may be adapted to be coupled to at least one photo-detector.

The sensor waveguide structure may comprise a waveguide with one or more gaps along a light path direction of the waveguide, for immobilizing a sensing material.

A cross-section of the waveguide may increase along the light path direction.

The holder may be further configured to house the input and output waveguide structures.

The holder may be configured to be received in a housing together with the input and the output waveguide structures.

The holder may comprise visual indicators for confirming placement of the holder relative to the housing into which the holder may be receivable.

The input, sensor and output waveguide structures may comprise a plurality of waveguides, each of the waveguides configured for a respective wavelength of the light signal.

The holder may further comprise a port configured to receive a predetermined amount of the sample in a sensing region of the sensor waveguide.

The port may comprise retaining means for prevention of a spillage of the sample.

The holder may further comprise one or more vent holes for releasing air bubbles trapped in the sensing region.

The holder may further comprise means for alignment of the sensor waveguide structure with the holder.

The biosensor may further comprise an electronic module configured to receive a feedback signal indicative of the light signal from the input waveguide structure, and an output signal from the output waveguide structure.

The electronic module may comprise a processor adapted to control an intensity of the light signal based on the feedback signal and a reference value stored during an initialisation of the biosensor.

The electronic module may further comprise an interactive display controlled by the processor, for communication with a user.

The processor may be adapted to detect respective models and serial numbers of optical components associated with the input, sensor and output waveguide structures for controlling said optical components.

The biosensor may be configured for replaceably receiving the sensor waveguide structure, the input waveguide structure and the output waveguide structure respectively.

In accordance with a third aspect of the present invention, there is provided a method of assembling an optical biosensor, comprising the steps of:

providing a holder for a sensor waveguide structure for the optical biosensor, and

aligning the sensor waveguide structure with an input waveguide structure and an output waveguide structure of the biosensor using the holder for guiding a light signal from the input waveguide structure through the sensor waveguide structure and to the output waveguide structure.

The step of aligning the may comprise using co-operating alignment elements formed on the holder with alignment structures formed on the input waveguide structure, the output waveguide structure and the sensor waveguide structures respectively.

The alignment structures may be formed from a waveguide core material of the input, output, and sensor waveguide structures respectively.

The alignment structures may be formed during formation of a waveguide core from the waveguide core material.

The alignment structures may comprise one or more waveguide portions of one or more of the sensor waveguide structure, the input waveguide structure and the output waveguide structure.

The alignment structures may be formed during photolithography processing of the waveguide core material.

The method may further comprise aligning respective top surfaces of the sensor waveguide structure, the input waveguide structure and the output waveguide structure for z-directional alignment.

The method may further comprise using visual indicators for confirming placement of the holder relative to the housing into which the holder may be receivable.

The method may further comprise performing alignment of the sensor waveguide structure with the holder.

In accordance with a fourth aspect of the present invention, there is provided a method of biosensing, the method comprising using a biosensor as defined in the second aspect.

The method may further comprise receiving a feedback signal indicative of the light signal from the input waveguide structure, and an output signal from the output waveguide structure.

The method may further comprise:

initialising the biosensor;

controlling an intensity of the light signal based on the feedback signal and a reference value stored during initialisation.

The method may further comprise communicating with a user via an interactive display controlled by the processor.

The method may further comprise detecting respective models and serial numbers of optical components associated with the input, sensor and output waveguide structures for controlling said optical components.

BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments of the invention will be better understood and readily apparent to one of ordinary skill in the art from the following written description, by way of example only, and in conjunction with the drawings, in which:

Figure 1a shows a block diagram illustrating an optical module according to an example embodiment of the present invention.

Figure 1b shows a block diagram illustrating an optical module according to an alternate embodiment.

Figures 2a and 2b shows an example implementation of the optical module 100 shown in Figure 1a.

Figures 3a and 3b show a block diagrams illustrating an internal top view of the optical module without the sensing module and with the sensing module mounted respectively according to an example embodiment.

Figures 4a and 4b show close-up perspective views of the optical module when the alignment element is not in operation (freed) and in operation (locked) respectively according to an example embodiment.

Figures 5a and 5b show side views of the alignment element when it is not in operation (freed) and in operation (locked) respectively according to an example embodiment.

Figure 6 shows a close-up top view of the sensing module according to an example embodiment.

Figure 7 shows a close-up top view of the sensing waveguide according to another example embodiment.

Figure 8 shows a block diagram illustrating the optical module according to another example embodiment.

Figure 9 shows a perspective view of the input chip, the sensing chip holder and the output chip according to an example embodiment.

Figures 10a – 10c show perspective views illustrating various stages of assembling the sensor chip with the chip holder to form the sensing module according to an example embodiment.

Figure 11 shows a perspective view illustrating how the sensing module comprising the chip holder, is positioned onto the input chip and output chip according to an example embodiment.

Figure 12a shows a top view of the input chip, output chip and the chip holder when in operation according to an example embodiment.

Figure 12b shows a cross-sectional view of the same configuration illustrated in Figure 12a about a line A-A.

Figure 13a shows a perspective view of the optical module in an example embodiment of the present invention.

Figure 13b shows the optical module of Figure 13a with the restraining lid closed.

Figure 13c shows a perspective view illustrating contact between restraining plungers and respective restraining wings according to an example embodiment.

Figure 13d shows the optical module of Figure 13a with the cover closed.

Figure 14 shows a block diagram illustrating an electronics module and its electrical connections with electrical components of an optical module according to an example embodiment.

Figure 15 shows a flow chart illustrating the initialization phase of the biosensor according to an example embodiment.

Figure 16 shows a flow chart illustrating a control process of the light source, performed by the MCU, according to an example embodiment.

Figure 17 shows a flow chart illustrating communication between the MCU and the touchscreen interface according to an example embodiment.

Figure 18a shows a block diagram illustrating an optical module according to another example embodiment.

Figure 18b shows a block diagram of a variation of the optical module of Figure 18a.

Figure 19 shows a block diagram illustrating an optical module according to another example embodiment.

Figure 20 shows a block diagram illustrating an optical module according to another example embodiment.

Figure 21 shows a block diagram illustrating an optical module according to another example embodiment.

Figure 22 shows a block diagram illustrating an optical module according to another example embodiment.

Figure 23 shows a block diagram illustrating an optical module according to another example embodiment.

Figure 24 shows a block diagram illustrating an optical module according to another example embodiment.

Figure 25 shows a schematic diagram illustrating a fabrication process of a sensing chip according to an example embodiment.

Figure 26 shows a flow chart illustrating a method of assembling an optical biosensor according to an example embodiment.

DETAILED DESCRIPTION

Embodiments of the present invention relate to a biosensor. The biosensor comprises an optical module comprising three main modular units, namely an input module, a sensing module and an output module. Each one of these modules may be replaceable to facilitate a different application of the biosensor. The biosensor according to embodiments of the present invention is based on strip optical polymer waveguides, wherein the detector is capable of detecting wavelengths and/or intensity of light which has passed through an analyte in a sample.

Figure 1a shows a block diagram illustrating an optical module 100 according to an example embodiment of the present invention. The optical module 100 comprises a housing 102, an input module 104, a sensing module 106, and an output module 108. The input module 104 comprises a light input source 110 and an input chip 105 which comprises an input waveguide 112. The sensing module 106 comprises a sensing chip 107 with a sensing waveguide 114, which may further comprise a gap 116. The sensing module 106 is capable of receiving a sample of e.g. an aqueous solution comprising an analyte. The output module 108 comprises an output chip 109 with an output waveguide 118, and a photodetector 120.

When in use, the light source 110 e.g. in the form of a narrowband light emitting diode (LED) or laser diode (LD), produces input light of a narrow emission spectrum (e.g. as illustrated by an intensity pulse in graph 130 in Figure 1). The input light is then guided from the light source 110 in the input module 104 to the sensing module 106, via the input waveguide 112 of the input chip 105. At the sensing module 106, the input light is received by the sensing waveguide 114 of the sensing chip 107. As the light from the input waveguide 112 passes through the

sensing waveguide 114, it interacts with the sample (not shown) causing a modulation in its properties such as absorption, polarization, etc. As an example, this modulation may be a change in absorption resulting in a change in the power transmitted to the output waveguide 118 (as illustrated by a lower intensity pulse in graph 132). This change in power due to absorption is proportional to the amount of analyte present in the sample. The output light is then guided to the output module 108, where it is received by the output waveguide 118 of the output chip 109. The output waveguide 118 then guides the output light to the photo detector 120.

In the example embodiment, the waveguide width in each segment is slightly larger than previous segment "upstream", such that width(112)<width(114 before gap)<width(114 after gap)<width(118).

In an alternate embodiment, instead of a light source, numeral 110 may be a light coupling structure which couples light from an external light source to the input waveguide 112 of the input chip 105. Similarly, the photodetector 120 may be a light coupling structure which couples light from the output waveguide 118 of the output chip 109 to an external photodetector.

The sensing module 106 of the example embodiments is replaceable such that the remainder of the components of the optical module 100 e.g. the input module 104 and the output module 108 can be reused. For example, the sensing module 106 can be removed from the optical module 100 where it can be washed or sterilized, such that any residue of the samples from a previous test are removed, before it is reused in the optical module 100. Alternatively, the low cost of fabricating a strip polymer waveguide-based sensing module can allow a new sensing module 106 to be used instead.

Further, the sensing module 106 can comprise a sensing chip 107 having a sensing waveguide 114 of a design catered for a specific application using a respective sensing mechanism. For example, in the example embodiment shown in Figure 1a, the sensing waveguide 114 is of a gap structure wherein light power is changed as it passes through the sample. The sensing waveguide 114 can have different structures in alternate embodiments.

For example, Figure 1b shows a block diagram illustrating an optical module 100b comprising a sensing module 106b, which relies on Surface Plasmon Resonance (SPR) techniques according to an alternate embodiment. Here, the sensing chip 107b comprises a sensing waveguide 114b designed with a portion where its surface is coated with a metal coating 122 (e.g. gold or silver). The input light is reflected off the waveguide portion with the coating 122 at an angle which can sufficiently excite a surface plasmon wave. This excitation can result in a reduction in the power transmitted to the output waveguide. It will be appreciated that other waveguide designs for the sensing modules may be implemented according to the sensing mechanism requirements.

Therefore, a change in the sensing module 106 can allow the biosensor to be converted e.g. from a primarily absorption-based sensing application, to another SPR-based application. The optical module 100 can therefore be a platform for a variety of optical waveguide-based biosensor applications, due to its modular structure.

Figures 2a and 2b shows an example implementation of the optical module 100 shown in Figure 1a. As shown in Figures 2a and 2b, optical module 200 comprises a housing 202 and a replaceable sensing module 206. Figure 2a shows the replaceable sensing module 206 after it has been removed from the optical module 200, while Figure 2b shows the replaceable sensing module 206 housed within the optical module 200. The input and output modules are not visible in Figures 2a and 2b as they are hidden by the housing 202. Typically, the optical module 200 measures about 7.5cm x 4cm x 1.2 cm. The housing 202 in this embodiment functions as a holder for the sensing module 206, as well as for the input and output modules.

Figure 3a and 3b shows an internal top view of the optical module 200 of Figure 2. Figure 3a shows an example embodiment without sensing module 306, while Figure 3b shows the example embodiment with the sensing module 306 included in the housing 202. In this example embodiment, input module 304 and output module 308 are fixed to the housing 202, while the sensing module 306 is

replaceable. The sensing module 306 comprises a sensing chip 307 with a sensing waveguide 314 which includes a gap 316. A first light coupling structure 310 couples light from a light source (not shown) disposed above the light coupling structure 310, into the input waveguide 312 of the input chip 305. Similarly, a second light coupling structure 320 couples light from the output waveguide 318 of the output chip 309 into a photo-detector (not shown) disposed above the second light coupling structure 320.

The input module 304, sensing module 306 and output module 308 each comprises an alignment structure 324, 326 and 328 respectively. As illustrated in Figures 3a and 3b, the alignment structures 324, 326 and 328 comprise protuberances 334, 336 and 338 made of the waveguide core material, with hollow indentations 344, 346 and 348.

Returning to Figures 2a and 2b, the sensor housing 202 further comprises an alignment element 250, for locking the replaceable sensor module 306 (Figure 3b) in place, and to improve alignment between the input waveguide 312, the sensing waveguide 314 and the output waveguide 318. The alignment element 250 (Figure 2a and 2b) further comprises a body, e.g. a rigid bar, which is shaped to cooperate with the alignment structures 324, 326 and 328 (Figure 3).

Figure 4a shows a close up view of the optical module 200 (Figure 2), where the locking alignment element 250 is not in operation (freed). Figure 4b shows a close up view of the optical module 200, where the locking alignment element 250 is in operation (locked). The alignment element 250 comprises a rigid body with protrusions 254, 256 and 258 which respectively fit snugly into the hollow indentations 344, 346 and 348 of the alignment structures 324, 326 and 328.

Figure 5a shows a side view of the alignment element 250 when it is not in operation and free from the alignment structures 324, 326 and 328. Figure 5b shows the side view of the alignment element 250 when it is in locking operation with the alignment structures 324, 326 and 328. Structurally, the alignment structures 324, 326 and 328 are made of the waveguide core material, and they rest on an undercladding layer and a substrate. This layered structure is identical to that of the

input, sensing and output waveguides. In an example embodiment, the alignment structures 324, 326 and 328 are made of the same material as the input, sensing and output waveguides' core material and made from the same photolithography process using the same photomask. Therefore, their relative positions can be precisely controlled and aligning the alignment structures would similarly align the respective input waveguide 312, sensing waveguide 314 and output waveguide 318.

In the example embodiment illustrated in Figures 2 to 5, during operation, the gap 316 maybe immobilized with bio-receptors. The bio-receptors may then interact with particular constituents in the aqueous sample solution, which causes changes in the light power. Some of these changes may be caused by e.g. light absorption or light scattering as a result of the bio-reaction.

In example embodiments, to further enhance interaction between the aqueous solution and the bio-receptors immobilized on the surface of the input, sensing and output waveguides, the input, sensing and output waveguides can have various dimensions and shapes to increase the efficiency of light coupling and thus sensitivity. For example, as illustrated in Figure 6, the waveguide is of increasing surface area as it progresses from the input waveguide 604 to the output waveguide 608. In addition, as illustrated in Figure 7, the sensing waveguide 706 may have multiple segments to increase the total surface area on which the bio-receptors may be immobilized on to increase the efficiency of light coupling and thus sensitivity.

Figure 8 shows an interior top view of an optical module 800 according to another example embodiment of the present invention. In this example embodiment, the input module 804 and output module 808 are fixed to the housing 802 of the optical module 800, while the sensing module 806 is replaceable. The sensing module 806 comprises a sensing chip 807 with a sensing waveguide 814. The sensing waveguide 814 comprises a gap 816 which can contain the sample (not shown). The gap 816 is defined by a rim 817 made of the core waveguide material, and the sensing waveguide 814. Input light is guided from the light source 810 via the input waveguide 812 of the input chip 805 to the sensing waveguide portion 814a. Similarly, output light from the sensing waveguide portion 814b is guided via the output waveguide 818 of the output chip 809 into a photo-detector 820.

In this example embodiment, the replaceable sensing module 806 further comprises a sensing chip holder, which can accommodate or hold the sensor chip 807. Figure 9 shows a perspective view of the input chip 805, the sensing chip holder 950 and the output chip 809 according to an example embodiment. The sensing chip 807 (Figure 8) is not visible as it is housed within the sensing chip holder 950. Alignment of the sensing module 806 with the input module 804 and output module 808 (Figure 8) is achieved via the sensing chip holder 950. The sensing module 806 is first aligned with and held within the sensing chip holder 950. Next, the sensing chip holder 950 is aligned with the input chip 805 and output chip 809 of the input and output modules 804 and 808 respectively.

Figures 10a – 10c show perspective views illustrating various stages of assembling the sensor chip 807 (Figure 8) with the chip holder 950 (Figure 9) to form the sensing module 806 according to an example embodiment. Here, each of Figures 10a-c shows an isometric bottom view of the chip holder 950. With reference to Figure 10a, the sensor chip 807 comprises the sensing waveguide portions 814a and 814b, and the sensing gap 816. In addition, the sensor chip 807 further comprises alignment features e.g. 1002a and 1002b, which are made of the same waveguide core material as the sensing waveguide portions 814a and 814b, and thus have the same thickness as the waveguide portions 814a and 814b. The portions of the sensor chip 807 made of the waveguide core material, are shaded grey in the illustration of the waveguide sensor chip 807 as shown in Figure 10a. The chip holder 950 comprises receiving means, e.g. in the form of a chip receiving section 1004, to receive the waveguide sensor chip 807. In the example embodiment, the chip receiving section 1004 of the chip holder 950 is indented or sunken such that the protrusions on the sensor chip 807, as a result of the waveguide core material, matches that of the receiving section 1004 (shaded grey) in the chip holder 950. This can then allow the sensor chip 807 to fit into the chip holder 950, as shown in Figure 10b. Preferably, the receiving section 1004 of the chip holder 950 and the protrusions on the sensor chip 807 are shaped such that the sensor chip 807 may be placed in the receiving section 1004 in only one particular orientation. This can ensure that the chip 807 is always placed correctly, relative to the chip holder 950. For example, as shown in Figure 10c, the output sensing

waveguide portion 814b is wider than the input sensing waveguide portion 814a. Accordingly, the receiving section 1004 is dimensioned such that it can correctly receive the sensor chip 807 in only one orientation.

The chip holder 950 further comprises a hinged flap 1006, which can be arranged to secure the chip 807 against the receiving section 1004 of the chip holder 950. Figures 10a and 10b show the flap 1006 in the open state, while figure 10c shows the flap 1006 in a closed state. The flap 1006 has a hinged end 1008 and a locking end 1010. The hinged end 1008 is secured to the main body of the chip holder 950, while the locking end 1010 is rotatable about the hinged end 1008. The locking end 1010 further comprises an engaging means, e.g. a hook 1012, for engaging with an e.g. groove or catch 1014 located at the main body of the chip holder 950. The flap 1006 further comprises a convex surface 1016 for ensuring better contact between the flap 1006 and the sensor chip 807. In combination, the sensor chip 807 can be securely locked against the chip holder 950, when the flap 1006 is in the closed position. In particular, the sensing waveguide portions 814a and 814b are aligned against the receiving section 1004.

As shown in Figures 10a-c, the sensing chip 807 does not fully cover the indented receiving section 1004. The remaining uncovered portions 1004a and 1004b of the indented receiving section 1004 are shaped such that they are capable of respectively engaging with the input waveguide 812 of the input chip 804 and output waveguide 818 of the output chip 808 (Figure 8). As such, in alternate embodiments, the numerals 1004a and 1004b may be referred to as alignment grooves.

Figure 11 shows a perspective view illustrating how the sensing module 806 comprising the chip holder 950, is positioned onto the input chip 805 and output chip 809 according to an example embodiment. Figure 8 illustrates the relative positions of the sensing module 806 with the input chip 805 and output chip 809 when the biosensor 800 is in use. The sensing chip 807 is not clearly visible in this figure as it is held within the chip holder 950, behind the hinged flap 1006.

As described earlier, the alignment groove 1004a of the chip holder 950 is shaped to engage an end portion 812a of the input waveguide 812 of the input chip 805. Similarly, the alignment groove 1004b is shaped to engage an end portion 818a of the output waveguide 818 of the output chip 809. In the example embodiment, the chip holder 950 is further provided with additional grooves 1102a and 1102b, which can respectively engage alignment protrusions 1104a and 1104b, formed on the input and output chips 805, 809. The alignment protrusions 1104a and 1104b are made of the same waveguide core material and fabricated from the same photolithography process using the same photomask as the input and output waveguides 812, 818.

When in operation, i.e. when the chip holder 950 is engaged with the input and output chips 805 and 809 (e.g. as shown in Figure 9), the chip holder 950 rests on the input and output chips 805, 809. Specifically, the alignment grooves 1004a, 1004b and additional grooves 1102a, 1102b, rest on the end portions 812a, 818a and alignment protrusions 1104a, 1104b respectively.

The chip holder 950 is further provided with alignment keys 952a-e, projecting from the sides of the chip holder 950. The input chip 805 and output chip 809, comprises alignment structures 824 and 828 respectively, as described with respect to Figure 8. The alignment structures 824 and 828 comprise e.g. u-shaped brackets and are made of the waveguide core material and fabricated from the same photolithography process using the same photomask as the input and output waveguides 812, 818. In the example embodiment, alignment keys 952a, 952b and 952c fit into brackets 824a, 824b and 824c of the input chip respectively. Similarly, alignment keys 952d and 952e fit into brackets 828a and 828b of the output chip respectively. These brackets can help in the alignment of the sensing chip held 807 in the chip holder 950, with the input and output chips 805, 809, in the x-y directions.

Figure 12a shows a top view of the input chip 805, output chip 809 and the chip holder 950, when in operation, according to an example embodiment. The sensing chip is contained within the chip holder 950 and is not visible in Figure 12a. Figure 12b shows a cross-sectional view of the same configuration illustrated in Figure 12a about a line A-A. Groove 1102a of the chip holder 950 (not visible),

ensures that the top surface 1202 of the input waveguide 812 is aligned with the top surface 1204 of the sensing waveguide portion 814a. Similarly, Groove 1102b of the chip holder 950 (not visible), ensures that the top surface 1206 sensing waveguide portion 814b is aligned with the top surface 1208 of the output waveguide 818. The sensing waveguide comprises a gap 816, as previously discussed. In this regard, because the top surfaces of the waveguide portions are aligned, z-directional alignment of the input, output and sensing waveguides can be achieved.

Therefore, the chip holder 950 can provide alignment of the sensing chip 807 with the input and output chips 805 and 809, in all three physical dimensions.

Returning to Figure 9, the chip holder 950 further comprises a handle 954, a sample delivery port 956 and a plurality of restraining wings 958a-d. The handle 954 facilitates easier handling of the disposable chip holder 950, given its small main body dimensions of about 2.4 cm x 1.3cm x 3.2 cm. The sample delivery port 956 is located directly above the sensing gap 816 and allows a user to introduce a measurement sample into the sensing gap 816 in the sensing waveguide 814 of the sensing chip 807 disposed within the chip holder 950 (Figure 8). In the example embodiment, the sample loading is performed by a pipette and, to prevent any possible spillage, the sample delivery port 956 is provided with a retaining means, e.g. in the form of a plurality of thin anti-spill flaps 960, which can serve to contain the sample fluid within the sample delivery port 956. In another example embodiment, the sample anti-spill flaps 960 may be replaced by a lipped surface, as the small volume of the sample may be held by e.g. surface tension with little spillage.

The chip holder 950 may also be provided with one or more vent holes, e.g. 962, which can allow air trapped in the sensing gap 816 of the sensing chip 807, to escape. Trapped air bubbles in the sensing gap can affect the readings of the optical based biosensor.

Figure 13a shows a perspective view of the optical module 800 in an example embodiment of the present invention. In this example embodiment, the input module 804 and output module 808 housed and fixed within the housing 802 of

the optical module 800. The sensing module 806 has been placed inside the housing 802. The housing 802 comprises a restraining lid 1302, for securing the sensing module 806 to the interior of the housing 802. The restraining lid 1302 comprises one or more restraining plungers 1304. When the restraining lid 1302 is in the closed position, the plungers 1304 push against the respective restraining wings e.g. 958 (Figure 11), and can serve to restrain movement of the sensing module 806 within the housing 802. Figure 13b shows the housing 802 with the restraining lid closed. Figure 13c shows the hidden interactions between the plungers 1304 on the restraining lid 1302 with the respective restraining wings 958. The optical module 800 measures about 57 x 76.2 x 33.4 millimetres (mm).

The housing 802 also comprises a cover 1306, which can close and thus serve to prevent stray light from entering the waveguides during measurement. The cover 1306 can be held securely in the restraining lid 1302 via a ball plunger 1308. Figure 13d shows the housing 802 with the cover 1306 and restraining lid 1302 closed, e.g. when measurements are being taken.

In an example embodiment, the total amount of the sample solution is determined by e.g. the gap 816 (Figure 8) and the chip holder 950 (Figure 9). In order to prevent any solution leakage, the top surface of the rim structure 817 (Figure 8) and the lower surface of the chip holder 950 are preferably in contact with one another.

The sensing region, e.g. the gap 816, can be filled by the capillary force of the sample solution. A hydrophilic material is preferred for the surface of the gap 816 in sensing chip 807 (Figure 8), and a hydrophobic material is preferred for the chip holder 950 to contain the fluid in the sensing gap 816.

In the example embodiment, the sensing chip 807 comprises sensing waveguide portions for guiding light to and from the sensing region. For example, the sensing region can be a gap structure designed to maximize the interaction of light with the desired analyte. The waveguide portions are also utilized to define a region for containing the bio-fluid (in conjunction with the chip holder 950) for

measurement purposes, and prevent the fluid from spilling over to either the input or output modules or to other undesired regions of the biosensor.

As described in example embodiments, the sensing waveguide structure (or sensing chip) sits snugly inside a chip holder which is used for delivering the fluid to the sensing region. The alignment is such that the top surface of the waveguide in the sensing region is in close contact with the chip holder. This allows the alignment of all the waveguide structures (input, output, and sensing chips) with the waveguide core's top surface as the alignment reference. Aligning the top surface has the added advantage of reduced power penalty due to waveguide core thickness variations which may arise in the sensing chip due to manufacturing tolerances. There are also certain lithographically defined structures on the input and output chips which can be used as alignment references for the sensing chip holder structure.

In the embodiments described with reference to Figures 8 to 13, the sensing module (sensing chip plus chip holder) has alignment keys on either side so that it can be aligned to the input and output waveguide chip through corresponding alignment locks. The number of alignment keys on either side of the chip holder is different and can serve as a visual indication to assist a user in avoiding any ambiguity when placing the sensing module within the separate housing in which the holder is receivable.

Procedure for dispensing fluid and measurement:

Step 1: The opto-fluidic chip is placed in between the input and output chips. (Figure 13a)

Step 2: The restraining lid is closed which secures the opto-fluidic chip by applying a controlled amount of force through ball plungers located on the restraining lid and on the casing. The liquid is dispensed into the sensing region via the sample delivery port, after the first flap is secured, for measurement. (Figure 13b, 13c)

Step 3: The cover is closed which prevents any stray light from entering the waveguides during measurement. This cover is held securely in the restraining lid through a ball plunger. (Figure 13d)

Step 4: After measurement is done, the arrangement is such that when the cover is lifted, it lifts the restraining lid as well. (Figure 13a)

In an example embodiment, the chip holder is made of polypropylene. Alternatively, any material with chemical resistance to the reagent used in the sensing application and has sufficient flexibility to provide for a hinged flap 1006, may be used The chipholder is also preferably transparent or translucent to enable the user to see the sample solution within the gap area.

With reference to Figure 8, the input module 804 may further comprise a feedback photo-detector 840, and the output module 808 may further comprise a background photo-detector 830. The background photo-detector 830 serves to measure a background noise reading, which is subtracted from the reading obtained by the measuring photo-detector 820. The feedback photo-detector 840 continuously measures the power of the light source 810 via the feedback waveguide 842 disposed within the input module 804. In the event that the light power has deviated from the required power, the feedback photo-detector 840 can serve to identify such scenarios and thus provide indications to adjust or replace the light source 810 accordingly. In other example embodiments, the feedback detector 840 may detect changes in the frequency of the input light.

In alternative example embodiments, the feedback waveguide may extend through the input, sensing and output modules, with the feedback photo-detector disposed within the output module, as illustrated in Figure 22a or 22b. Here, the waveguides from the light source 2210 branch out and end at the measuring photo-detector 2220 and feedback photo-detector 2240 respectively. A background photo-detector 2230 similar to that described with respect to Figure 8 is also provided. The example feedback waveguides illustrated in Figure 22a and 22b can better mimic the actual propagation of light through the various waveguide sections and can

therefore be better representations of the actual measured light by the photo-detector. The feedback waveguides may also comprise an air gap accordingly.

In embodiments of the biosensor, the optical module as described in Figures 1-13 is coupled to an electronics module. Figure 14 shows a block diagram illustrating an electronics module 1404 and its electrical connections with electrical components of an optical module 1402 according to an example embodiment. The electrical components of the optical module 1402 include a light source 1410, a sensing photo-detector (PD1) 1420, a background photo-detector (PD2) 1430 and a feedback photo-detector (PD3) 1440. The optical module 1402 may also be provided with one or more thermocouples 1450 to determine the internal temperature of the optical module 1402. In the example embodiment, the thermocouple 1450 is positioned such that it is directly below the sensing region of the sensing chip, such that it measures the temperature where the interactions of the light with the sample take place.

In an example implementation, the electronics module measures about 109 x 76.2 x 25.4mm. The electronics module 1404 comprises a subtraction circuit 1460, an analogue to digital converter (ADC) 1462, a micro-controller unit (MCU) 1464, a memory unit 1466 and an interactive display, e.g. in the form of a touch screen panel 1468. The subtraction circuit 1460 receives the analogue outputs of PD1 1420 and PD2 1430, and subtracts the reading of PD2 1430 from the reading of PD1 1420. As explained earlier, the subtraction allows the removal or reduction of the background noise. The subtracted analogue value is then passed on to the ADC 1462. The reading of PD3 1440 is passed on directly to the ADC 1462. In the example embodiment, no subtraction of background noise is performed to the reading of PD3 1440, as the background noise measured by PD2 1430 is representative only of the output module. In an alternative embodiment, the subtraction of background noise may also be performed on the reading of PD3 1440.

In the example embodiment, the ADC 1462 receives the difference between the readings of PD1 1420 and PD2 1430, and the reading of PD3 1440. The ADC 1462 digitizes the readings for the MCU 1464, which then processes the signals accordingly. The non-volatile data is stored in the memory unit 1466 comprising e.g.

Electrically Erasable Programmable Read-Only Memory (EEPROM), which may be accessed by the MCU 1464.

The digitized reading from PD3 1440, e.g. PD3_V, may be used to control the power of the light source, e.g. by adjusting the current through the light source 1410. This is achieved in the example embodiment through a constant current source 1470 and a digital resistor 1472, as shown in Figure 14.

In addition, there may be situations where good alignment of the input, sensing and output chips result in a large proportion of light incident onto PD1 1420, causing PD1 1420 to be saturated, during the initialization phase. In this regard, the light intensity has to be calibrated to a value within an optimum range to which PD1 1420 and PD3 1440 may function correctly. For example, assuming PD1 1420 is capable of a detection range of about 1-2 Volts (V), with the targeted initialisation voltage of about 1.5V. With good alignment, the PD1 1420 may experience saturation, as a large proportion of light from the LED light source 1410 propagates through the input, sensing and output waveguides and are incident on PD1 1420. Alternatively, in an embodiment with fixed input and output chips and a replaceable sensing chip, the sensing chip may have a larger core waveguide thickness than the input and output chips. This can similarly increase the light propagation, thus saturating PD1 1420. In those situations, the MCU 1464 of the example embodiments can adjust the digital resistor 1472 to lower the current powering the light source 1410. In other situations where the light power incident on PD1 1420 is poor, e.g. where alignment is poor or where the core sensing waveguide thickness of the sensing chip is low, the MCU 1464 can increase the current powering the light source 1410.

Figure 15 shows a flow chart 1500 illustrating the initialisation phase, where the MCU 1464 (Figure 14) seeks to adjust LED intensity to match the targeted detected intensity at PD1 1420 according to an example embodiment. The MCU 1464 first determines if the reading of PD1 1420 is in the targeted range (as illustrated by step 1502). If so, the reading of PD3 1440, is stored as the reference voltage Ref_PD3_V in the memory unit 1466 (as illustrated by step 1504). This value will be used for future LED intensity control purposes. If the MCU 1464 determines

that the reading of PD1 1420 is not in the targeted range, the intensity is controlled by e.g. adjusting the resistance of the digital resistor, until the reading of PD1 1420 is in the targeted ranges (as illustrated by steps 1506, 1508 and 1510).

In the example embodiment, the readings obtained by PD3 1440 are not amplified and do not saturate. As such, there is no need to cater for a saturated PD3 1440. It will be appreciated that control mechanisms to ensure that PD3 1440 is not saturated may be implemented in alternate embodiments to ensure that the stored reference value of PD3 1440 is correct.

Figure 16 shows a flow chart 1600 illustrating a control process of the light source 1410, performed by the MCU 1464, according to an example embodiment. The MCU 1464 first retrieves a desired reference voltage Ref_PD3_V (Figure 15) from the memory unit 1466 (as illustrated by step 1602). This desired reference value may be stored during an initialization phase where the initial reading of PD3_V is read and stored in the memory unit 1466, before the sample is loaded into the sensor. Next, the voltage value PD3_V is read from the PD3 1440 (step 1604). The voltage value PD3_V is monitored and adjusted continuously based on the reference value Ref_PD3_V, as illustrated by steps 1606 and 1608. For example, if the reference value Ref_PD3_V is greater than PD3_V, the LED intensity is increased by 1 level (step 1610), the voltage value PD3_V is read again (step 1612) and compared against the reference value Ref_PD3_V (step 1614). This is repeated until the reference value Ref_PD3_V is no longer greater than PD3_V. Steps 1616, 1618 and 1620 describe a similar loop if the reference value Ref_PD3_V is lower than the reading PD3_V. In the example embodiment, PD3_V is monitored and adjusted every second by default. However, the interval of successive monitoring and adjustments can be configured by the user according to specific requirements.

Figure 17 shows a flow chart 1700 illustrating communication between the MCU 1464 and the touchscreen interface 1464 (Figure 14) according to an example embodiment. At steps 1702, 1704, the touchscreen waits for a command from the MCU 1464. If a command is received from the MCU 1464, at step 1706, the command header is checked. If the command is unknown, the touchscreen is reset (step 1708). If the command is known, it is checked against a command library at

step (step 1710) to determine the information to be displayed. At step 1712, the information (e.g. in the form of an image) is displayed to the user. At step 1714, the touchscreen detect the user's response, e.g. through touch status. If there is a response from the user, at step 1716, a signal reporting the position of touch is sent back to the MCU 1464.

It will be appreciated that the MCU 1464 may be programmed to cater for specific applications. For example, the screen can prompt the user to e.g. load the sensing module, change the sensing module after a first test. The user may also be prompted to key in a sensing module reference number, such that readings from a particular sensing module may be referenced accordingly. In such an example embodiment, the memory unit 1466 stores the sensing module reference number as well as the associated reading of the light power changes for future retrieval. The MCU 1464 may also be programmed to perform calculations, such as the comparison or determination of ratios between two separate readings.

The MCU 1464 may also be able to recognize the model and serial number of the optical module. With the model number, the MCU 1464 can determine the applications/tests which are executable for a particular optical module. For example, as illustrated in the example embodiments in e.g. Figures 8-13, the model number of the optical module may indicate to the MCU 1464 that the output module of the optical module comprises a photo-detector. Thus, the MCU 1464 may then present the user with tests which measure the light power, and be able to configure the photo-detectors accordingly.

In contrast, suppose the model number of the optical module indicates that the optical module has a fixed output module comprising a spectrometer instead. The MCU 1464 may then be programmed to allow the user to select particular tests/applications which detect changes in the wavelength of light. Figures 18a and 18b illustrate such an example embodiment. The optical module 1800 comprises respective fixed input and output modules 1804, 1808. In contrast with the narrowband light source 110 of Figure 1, a light source 1810 of the input module 1804 comprises a broad band light source which allows the transmission of a broad spectrum of light (as illustrated by graph 1830). Further, instead of a narrowband

photodetector 120, the output module 1808 of the optical module 1800 comprises a spectrometer 1808. Thus, in addition to the detection of light power, the optical module 1800 can detect the wavelength of the light. In this regard, wavelength changes in the output light can be detected. Figure 18a shows a gap-based replaceable sensing module 1806 similar to the one illustrated in Figure 1a. Figure 18b shows a SPR-based replaceable sensing module 1806b similar to the one illustrated in Figure 1b. Similar to the optical module of Figure 1, the optical module 1800 of Figure 18a also comprises a housing 1802, while the input module 1804, sensing module 1806 and output module 1808 each comprise a respective waveguide 1812, 1814 and 1818. The sensing waveguide 1814 comprises a gap 1816. In Figure 18b, the sensing waveguide 1814b of the sensing module 1806b comprises a metal layer 1822.

It will be appreciated that the modular nature of the input and output modules according to the example embodiments can allow any one of the input and output modules to be replaceable as well. For example, as illustrated in Figure 19, the output module 1808 of the optical module 1800 illustrated in Figure 18a has been replaced by an output module 1908. The output module 1908 comprises a more cost effective photo-detector instead of a spectrometer. In such an embodiment, the replaceable sensing module 1906 further comprises a filter 1922, disposed on the sensing waveguide 1914, to filter the frequency spectrum of light. Thus, while the light from the light source 1910 of the input module 1904 has a broadband spectrum (as illustrated by graph 1930), the light received at the sensing region 1916 and at the photo-detector 1920 has a narrowband spectrum (as illustrated by graphs 1931 and 1932). In other example embodiments, the filter 1922 may be disposed in the output waveguide 1918 of the output module 1908 or in the input waveguide 1912 of the input module 1904. Further, in such an embodiment, the replaceable input or output modules may also be provided with model and serial numbers, for the MCU to appropriately determine the available tests/applications.

Figure 20 shows a block diagram illustrating an optical module 2000 according to another example embodiment. In this embodiment, the optical module 2000 comprises a housing 1902 and a fixed input module 1904 comprising a light source 1910 and input waveguide 1912 similar to the one illustrated in Figure 19.

The optical module 2000 further comprises a multi-channel sensing and output waveguides to allow for the detection of e.g. three different light-sample interactions. In contrast to the output module 1908, the output module 2008 comprises a plurality of output waveguides, e.g. 2018a-c respectively coupled to a plurality of photodetectors, e.g. 2020a-c. Similarly, light from the input waveguide 1910 may be split into a plurality of sensing waveguide 2014a-c in the replaceable sensing module 2006, each sensing waveguide being provided with a sensing gap. Each of the sensing waveguides 2014a-c are further disposed with a respective filter 2022a-c, each filter allowing a different narrow band of light through (as illustrated by graphs 2030, 2031 and 2032 respectively. In this regard, the same sample can be tested for light power changes of different wavelengths of light, e.g. λ_1, λ_2, λ_3, such that different analytes may be detected for at the same time.

In an alternative embodiment, the splitting of light from a single waveguide into a plurality of waveguides may be achieved at the input module 1904 instead.

Figure 21 shows a block diagram illustrating an optical module 2100, with a plurality of light inputs, according to an example embodiment. For example, here a plurality of light sources 2110a-c are used to provide input light of different wavelengths λ_1, λ_2, λ_3 respectively. At the output module, a plurality of photo-detectors 2120a-c are used to detect light signals having the respective wavelengths.

Figure 23 shows a block diagram illustrating an optical module 2300, with a plurality of light inputs of different wavelengths λ_1, λ_2, λ_3 being utilized in a time domain multiplexing scheme. Each respective light source 2310a-c is ON only at a particular time instant with all the other light sources being OFF. The detection circuit 2320 is then synchronized with the time sequence of the input light sources so that at any one instant of time, only light from a specific light source with the specific wavelength is being interrogated.

Figure 24 shows a block diagram illustrating an optical module 2400, with a plurality of light inputs of different wavelengths λ_1, λ_2, λ_3 being utilized in a frequency domain multiplexing scheme. Each respective light source 2410a-c's power output at

the detector 2420 is modulated at a specific frequency f_1, f_2, f_3 by modulating the applied current to each light source. The signal detected by the detector 2420 is demodulated at the frequency corresponding to the respective light source.

Figure 25 shows a schematic diagram illustrating a fabrication process of a sensing chip according to an example embodiment. The same fabrication process may be similarly applied to the input and output chips accordingly. First, a bottom cladding material is disposed onto a substrate 2502 by using the conventional film fabrication method to form a bottom cladding layer 2504. Next, a photo-pattern-able core material is disposed onto the bottom cladding layer 2504 by using film fabrication methods to form the core layer 2506a. Next, the photo-pattern-able core layer 2506a is exposed to UV light through photomask to form a waveguide core 2506b. Further, the unexposed core layer is removed by a developer solution.

Figure 26 shows a flow chart 2600 illustrating a method of assembling an optical biosensor according to an example embodiment. At step 2602, a holder for a sensor waveguide structure for the optical biosensor is provided. At step 2604, the sensor waveguide structure is aligned with an input waveguide structure and an output waveguide structure of the biosensor using the holder for guiding a light signal from the input waveguide structure through the sensor waveguide structure and to the output waveguide structure.

The biosensor according to the example embodiments is advantageously compact and easy to manufacture and assemble. Preferably, the biosensor can be re-configured and/or re-used by replacing the relevant input/sensing/output modules depending on the application. Further, the alignment parts advantageously ensure that the waveguide sections are properly aligned in all 3 physical dimensions such that performance is maintained even if a module is replaced.

It will be appreciated by a person skilled in the art that numerous variations and/or modifications may be made to the present invention as shown in the specific embodiments without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to be considered in all respects to be illustrative and not restrictive.

CLAIMS

1. An optical biosensor comprising:

a sensor waveguide structure;

an input waveguide structure;

an output waveguide structure; and

a holder for the sensor waveguide structure, the holder comprising

means for aligning the sensor waveguide structure with the input waveguide structure and the output waveguide structure, for guiding a light signal from the input waveguide structure through the sensor waveguide structure and to the output waveguide structure,

wherein the means for aligning comprises alignment elements adapted for co-operating with alignment structures formed on the input waveguide structure, the output waveguide structure and the sensor waveguide structures respectively, and

wherein the means for aligning comprises means for aligning respective top surfaces of the sensor waveguide structure, the input waveguide structure and the output waveguide structure for z-directional alignment.

2. The biosensor as claimed in claim 1, wherein the alignment structures are formed from a waveguide core material of the input, output, and sensor waveguide structures respectively.

3. The biosensor as claimed in claim 2, wherein the alignment structures are formed during formation of a waveguide core from the waveguide core material.

4. The biosensor as claimed in claim 3, wherein the alignment structures comprise one or more waveguide portions of one or more of the sensor waveguide structure, the input waveguide structure and the output waveguide structure.

5. The biosensor as claimed in claims 3 or 4, wherein the alignment structures are formed during photolithography processing of the waveguide core material.

6. The biosensor as claimed in any one of the preceding claims, wherein the input waveguide structure is adapted to be coupled to at least one light source

and the output waveguide structure is adapted to be coupled to at least one photo-detector.

7. The biosensor as claimed in any one of the preceding claims, wherein the sensor waveguide structure comprises a waveguide with one or more gaps along a light path direction of the waveguide, for immobilizing a sensing material.

8. The biosensor as claimed in claim 7, wherein a cross-section of the waveguide increases along the light path direction.

9. The biosensor as claimed in any one of the preceding claims, wherein the holder is further configured to house the input and output waveguide structures.

10. The biosensor as claimed in any one of claims 1 to 8, wherein the holder is configured to be received in a housing together with the input and the output waveguide structures.

11. The biosensor as claimed in claim 10, wherein the holder further comprises visual indicators for confirming placement of the holder relative to the housing into which the holder is receivable.

12. The biosensor as claimed in any one of the preceding claims, wherein the input, sensor and output waveguide structures comprise a plurality of waveguides, each of the waveguides configured for a respective wavelength of the light signal.

13. The biosensor as claimed in any one of the preceding claims, wherein the holder further comprises a port configured to receive a predetermined amount of the sample in a sensing region of the sensor waveguide.

14. The biosensor as claimed in claim 13, wherein the port comprises retaining means for prevention of a spillage of the sample.

15. The biosensor as claimed in claim 13, wherein the holder further comprises one or more vent holes for releasing air bubbles trapped in the sensing region.

16. The biosensor as claimed in any one of the preceding claims, wherein the holder further comprises means for alignment of the sensor wave guide structure with the holder.

17. The biosensor as claimed in claim 1, further comprising an electronic module configured to receive a feedback signal indicative of the light signal from the input waveguide structure, and an output signal from the output waveguide structure.

18. The biosensor as claimed in claim 17, wherein the electronic module comprises a processor adapted to control an intensity of the light signal based on the feedback signal and a reference value stored during an initialisation of the biosensor.

19. The biosensor as claimed in claim 18, wherein the electronic module further comprises an interactive display controlled by the processor, for communication with a user.

20. The biosensor as claimed in claims 18 or 19, wherein the processor is adapted to detect respective models and serial numbers of optical components associated with the input, sensor and output waveguide structures for controlling said optical components.

21. The biosensor as claimed in any preceding claim, configured for replaceably receiving the sensor waveguide structure, the input waveguide structure and the output waveguide structure respectively.

22. A method of assembling an optical biosensor, comprising the steps of:

providing a holder for a sensor waveguide structure for the optical biosensor, and

aligning the sensor waveguide structure with an input waveguide structure and an output waveguide structure of the biosensor using the holder for guiding a light signal from the input waveguide structure through the sensor waveguide structure and to the output waveguide structure,

wherein the step of aligning comprises using co-operating alignment elements formed on the holder with alignment structures formed on the input

waveguide structure, the output waveguide structure and the sensor waveguide structures respectively, and

wherein the method further comprises aligning respective top surfaces of the sensor waveguide structure, the input waveguide structure and the output waveguide structure for z-directional alignment.

23. The method as claimed in claim 22, wherein the alignment structures are formed from a waveguide core material of the input, output, and sensor waveguide structures respectively.

24. The method as claimed in claim 23, wherein the alignment structures are formed during formation of a waveguide core from the waveguide core material.

25. The method as claimed in claim 24, wherein the alignment structures comprise one or more waveguide portions of one or more of the sensor waveguide structure, the input waveguide structure and the output waveguide structure.

26. The method as claimed in claim 24 or 25, wherein the alignment structures are formed during photolithography processing of the waveguide core material.

27. The method as claimed in any one of claims 22 to 26, further comprising using visual indicators for confirming placement of the holder relative to the housing into which the holder is receivable.

28. The method as claimed in any one of claims 22 to 27, further comprising performing alignment of the sensor waveguide structure with the holder.

29. A method of biosensing, the method comprising using a biosensor as claimed in claim 1.

30. The method as claimed in claim 29, further comprising receiving a feedback signal indicative of the light signal from the input waveguide structure, and an output signal from the output waveguide structure.

31. The method as claimed in claim 30, further comprising:

initialising the biosensor;

controlling an intensity of the light signal based on the feedback signal and a reference value stored during initialisation.

32. The method as claimed in claim 31, further comprising communicating with a user via an interactive display controlled by the processor.

33. The method as claimed in claims 31 or 32, further comprising detecting respective models and serial numbers of optical components associated with the input, sensor and output waveguide structures for controlling said optical components.