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Pau et al.

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(45) **Date of Patent: Jun. 24, 2008**

(54) **MICROFLUIDIC SENSORS AND METHODS FOR MAKING THE SAME**

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(22) Filed: **Jan. 21, 2005**

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(51) **Int. Cl.**
G02B 6/00 (2006.01)
G01N 21/05 (2006.01)

(52) **U.S. Cl.** **385/12**; 385/14; 385/27; 385/39

(58) **Field of Classification Search** 385/12, 385/33, 13
See application file for complete search history.

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Primary Examiner—Tina M Wong

(57) **ABSTRACT**

Microfluidic optical sensor comprising: an optical waveguide capable of propagating light from an optical input port to an optical output port, the optical waveguide comprising an optical waveguide interaction region; a fluidic channel capable of conducting a fluid from a fluid input port to a fluid output port, the fluidic channel comprising a fluidic channel region; the fluidic channel region being separated from the optical waveguide interaction region by an interposed spacing material configured to transmit an evanescent field of the light through the spacing material between the optical waveguide interaction region and the fluidic channel region. Microfluidic optical sensor comprising an optical resonator. Methods for making microfluidic optical sensors.

21 Claims, 9 Drawing Sheets

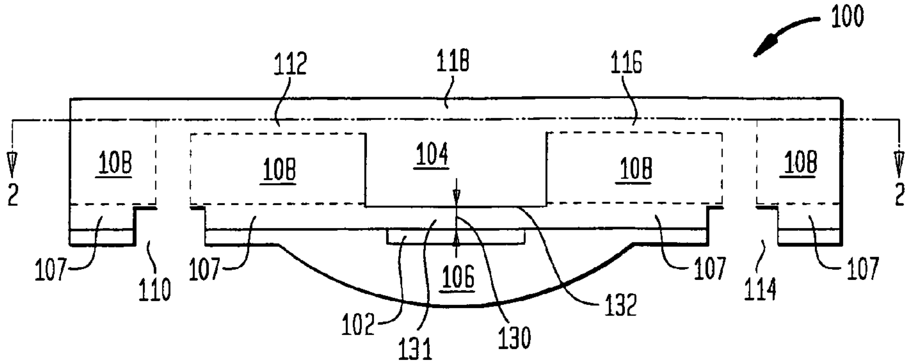

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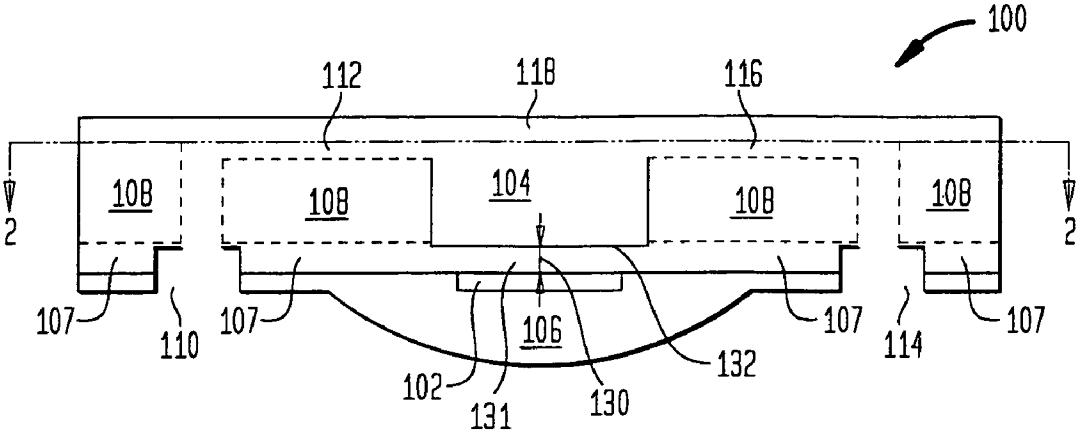
FIG. 1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112
118
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130
132

FIG. 2

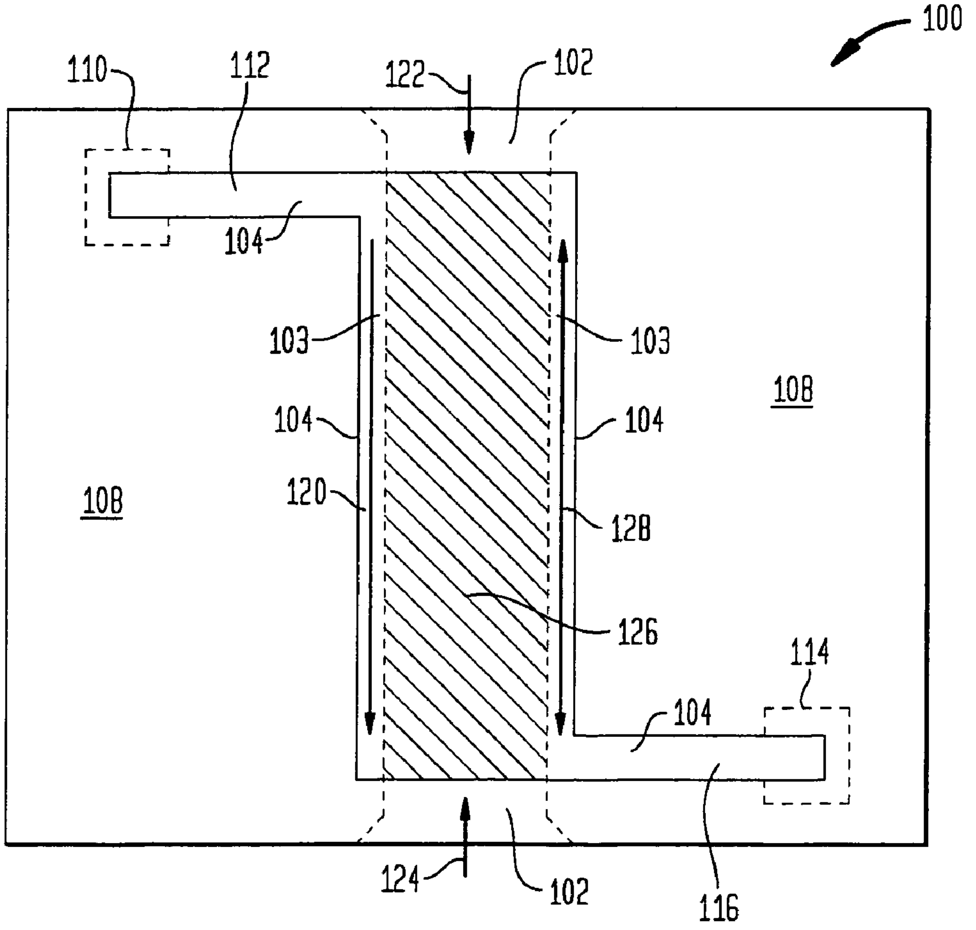
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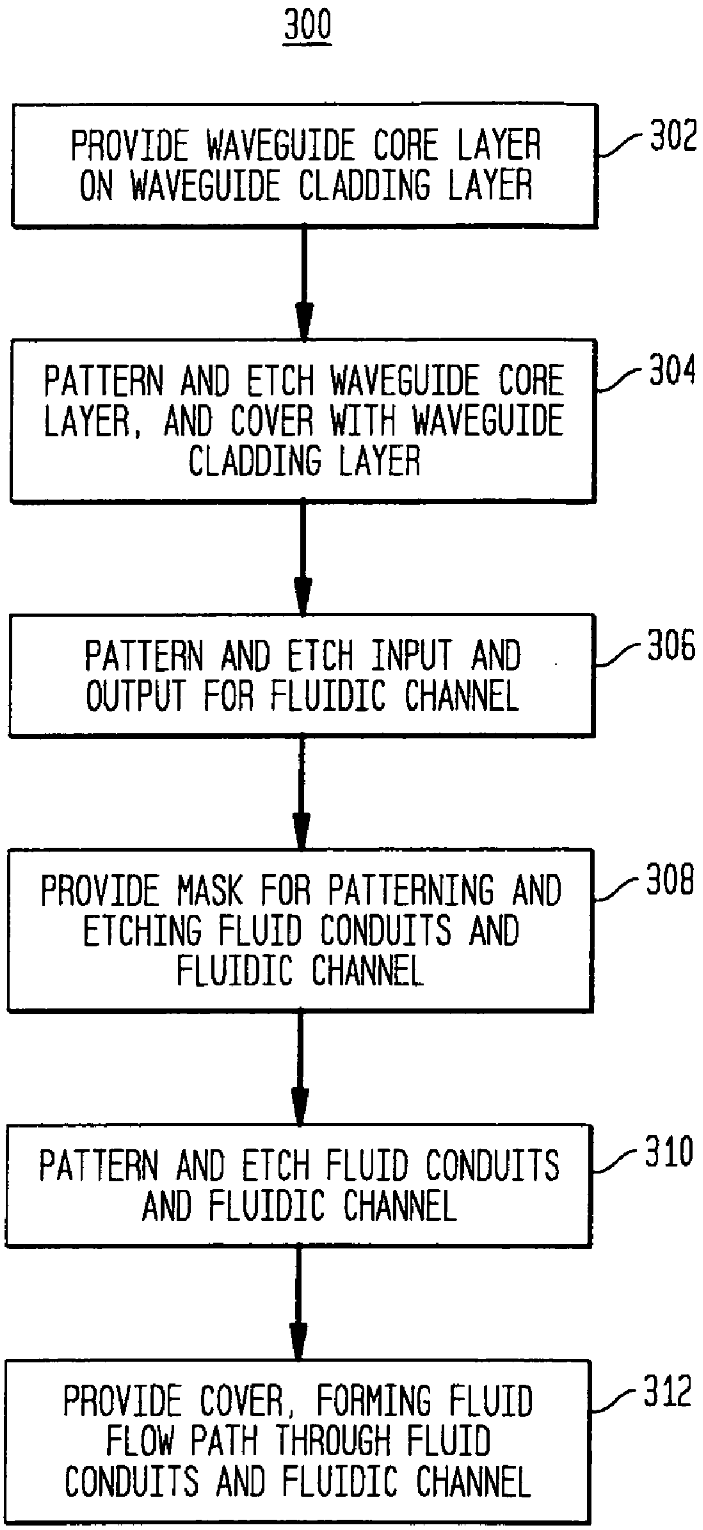
FIG. 3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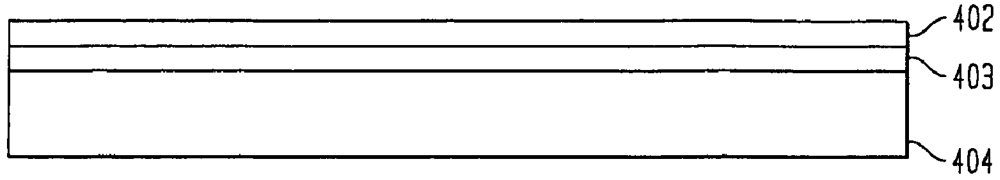
302
PATTERN AND ETCH WAVEGUIDE CORE LAYER, AND COVER WITH WAVEGUIDE CLADDING LAYER
304
PATTERN AND ETCH INPUT AND OUTPUT FOR FLUIDIC CHANNEL
306
PROVIDE MASK FOR PATTERNING AND ETCHING FLUID CONDUITS AND FLUIDIC CHANNEL
308
PATTERN AND ETCH FLUID CONDUITS AND FLUIDIC CHANNEL
310
PROVIDE COVER, FORMING FLUID FLOW PATH THROUGH FLUID CONDUITS AND FLUIDIC CHANNEL
312

FIG. 4



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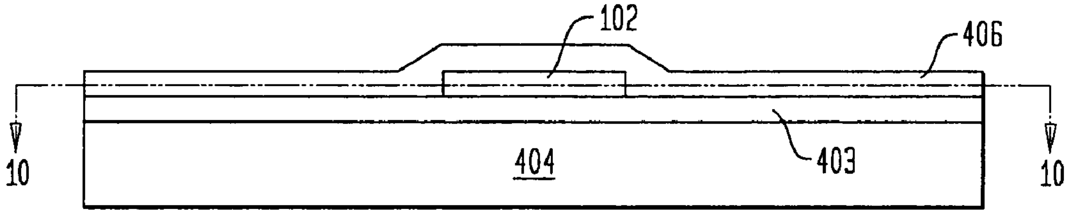

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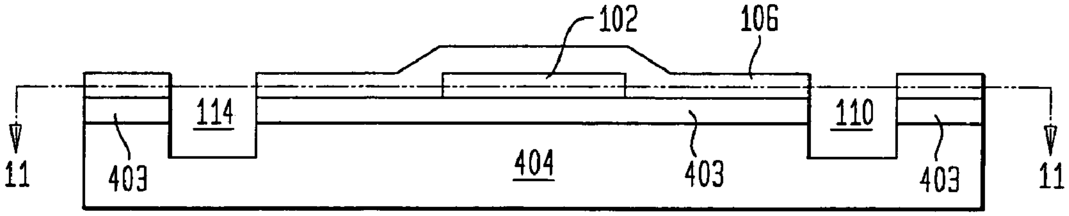


FIG. 7

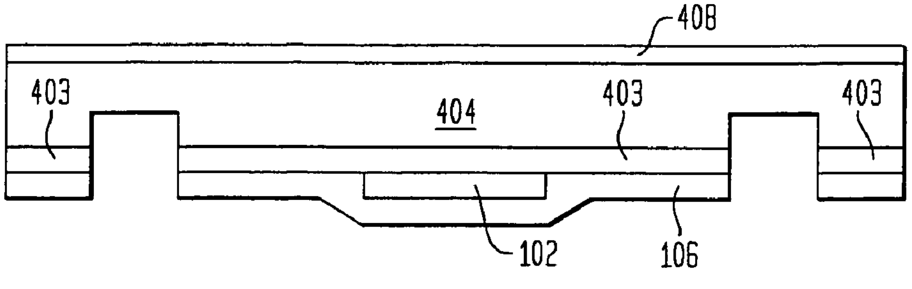
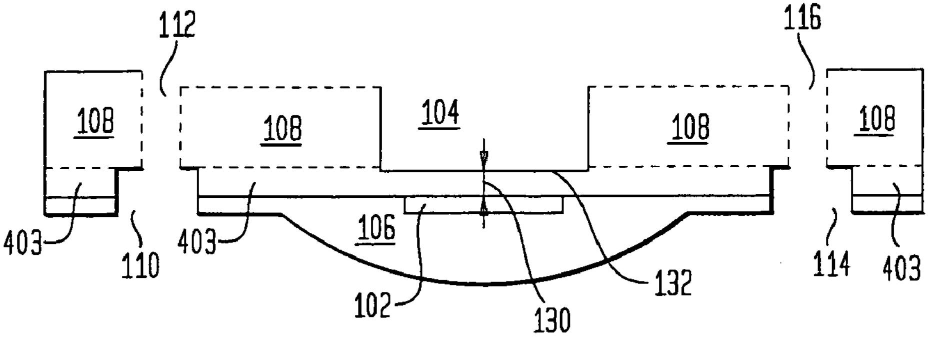


FIG. 8



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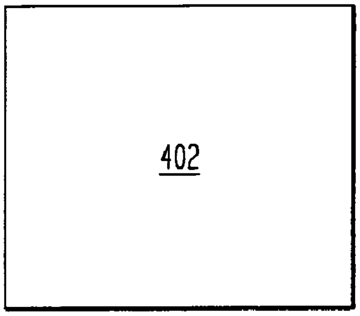
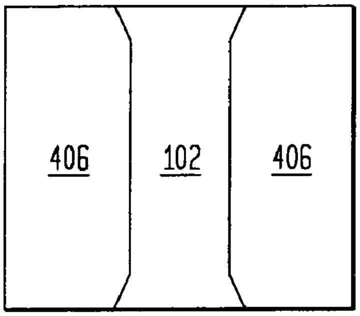


FIG. 10



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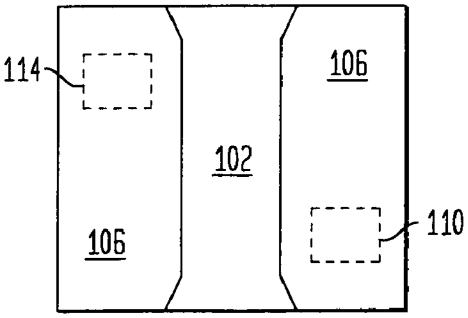

FIG. 12

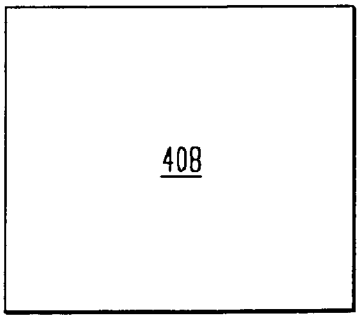

FIG. 13

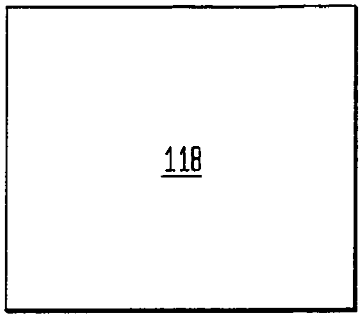

FIG. 16

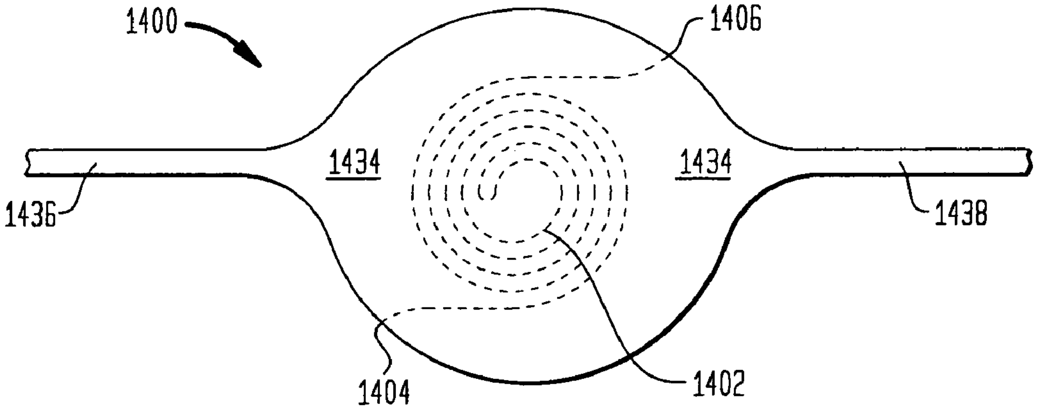

FIG. 14

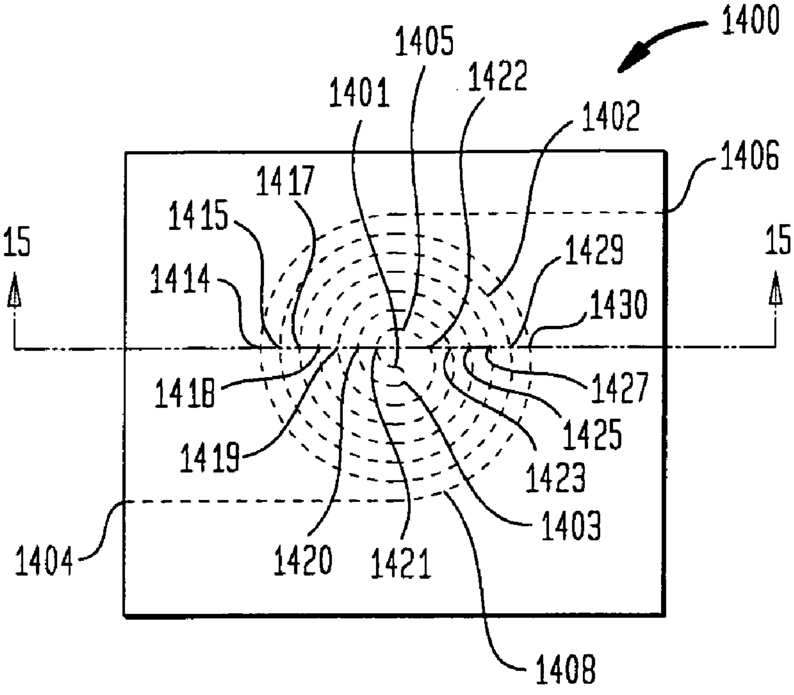
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FIG. 15

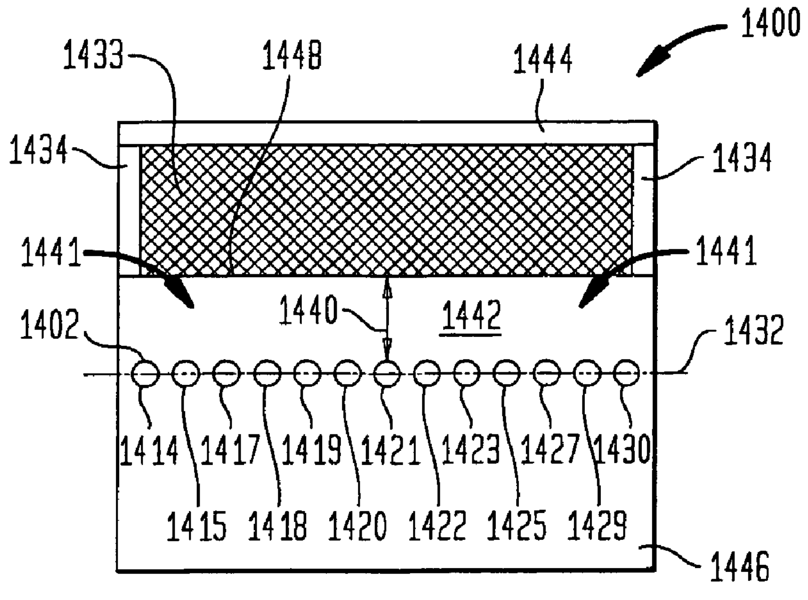
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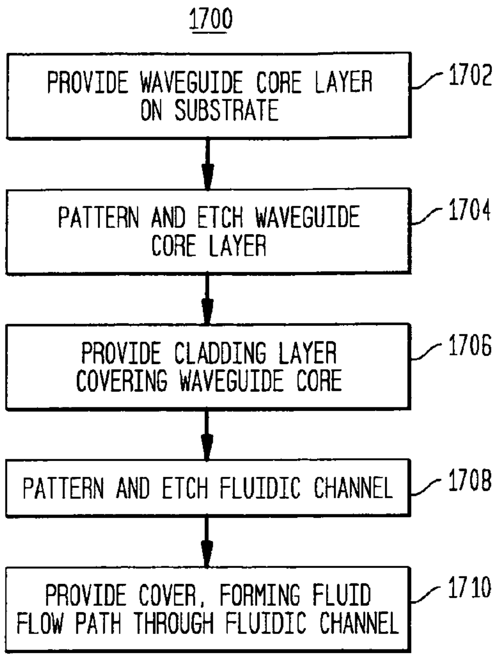
FIG. 17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PROVIDE WAVEGUIDE CORE LAYER ON SUBSTRATE
1702
PATTERN AND ETCH WAVEGUIDE CORE LAYER
1704
PROVIDE CLADDING LAYER COVERING WAVEGUIDE CORE
1706
PATTERN AND ETCH FLUIDIC CHANNEL
1708
PROVIDE COVER, FORMING FLUID FLOW PATH THROUGH FLUIDIC CHANNEL
1710

FIG. 18

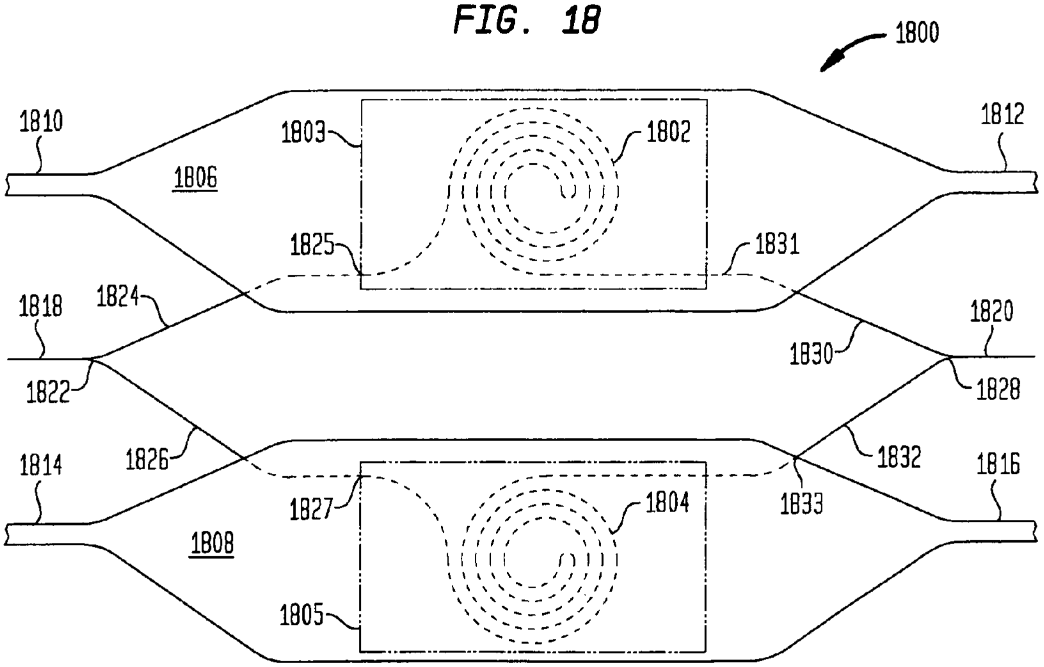
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FIG. 19

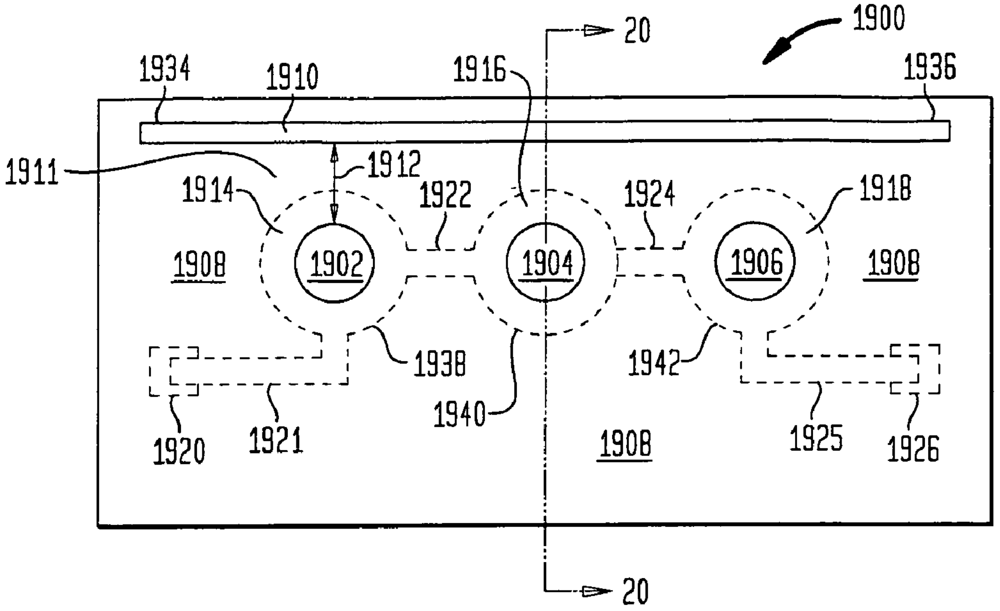
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FIG. 20

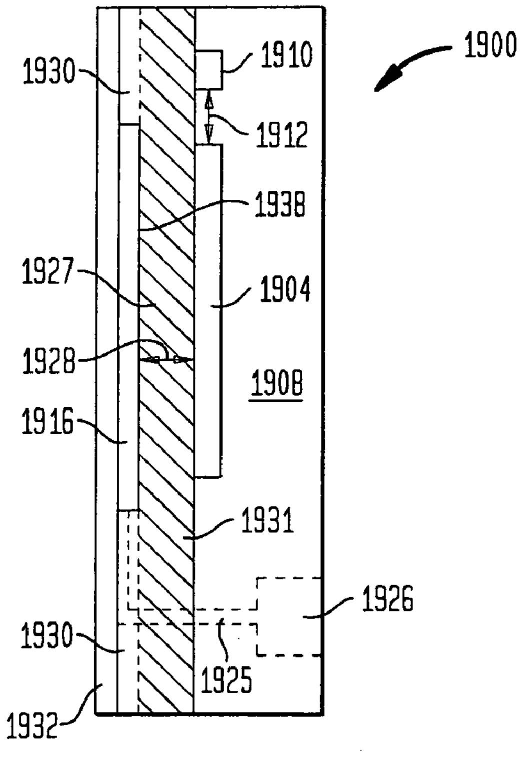
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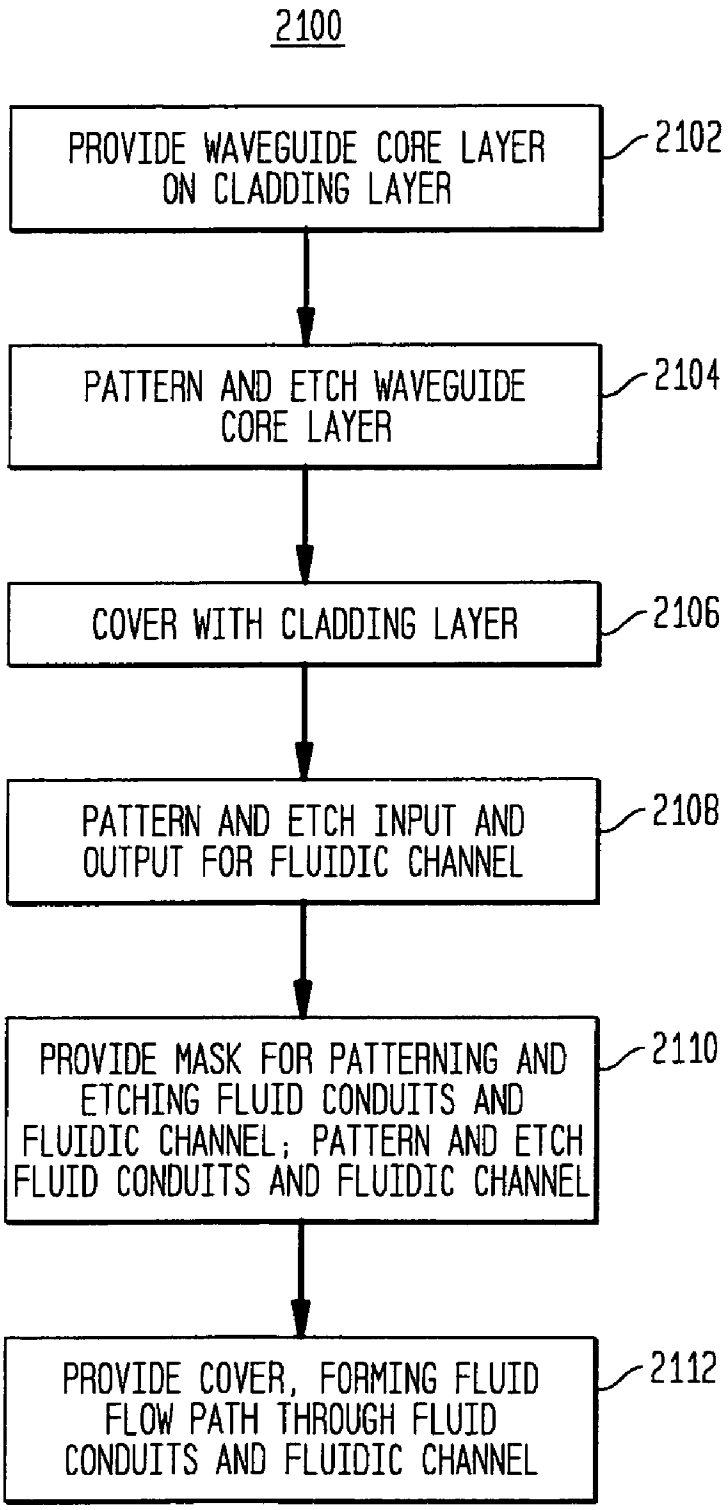
FIG. 21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PROVIDE WAVEGUIDE CORE LAYER ON CLADDING LAYER
2102
PATTERN AND ETCH WAVEGUIDE CORE LAYER
2104
COVER WITH CLADDING LAYER
2106
PATTERN AND ETCH INPUT AND OUTPUT FOR FLUIDIC CHANNEL
2108
PROVIDE MASK FOR PATTERNING AND ETCHING FLUID CONDUITS AND FLUIDIC CHANNEL; PATTERN AND ETCH FLUID CONDUITS AND FLUIDIC CHANNEL
2110
PROVIDE COVER, FORMING FLUID FLOW PATH THROUGH FLUID CONDUITS AND FLUIDIC CHANNEL
2112

MICROFLUIDIC SENSORS AND METHODS FOR MAKING THE SAME

FIELD OF THE INVENTION

The present invention relates to the field of microfluidic sensors and to methods for making such sensors.

BACKGROUND OF THE INVENTION

Microfluidic sensors have been fabricated in order to optically analyze small samples of fluids. For example, sensors have been made comprising a cuvette having optically neutral walls in which a small sample of a fluid to be analyzed is placed, and then a light beam is directed through the cuvette so that properties of the fluid such as the optical refraction, absorption and transmission characteristics can be detected by analysis of the transmitted and emitted light. Since the cuvettes are relatively small in order to place a small fluid sample in position for passage therethrough of a light beam, the path length of the light beam through the fluid in the cuvette is short. Moreover, the diameter of the light beam is generally small, so that the interaction cross-section between the fluid and the light beam also is accordingly small. Hence, in order to obtain a sufficiently strong signal for analysis, such systems typically cause the light beam to make a series of passes through the cuvette before the beam is directed into instrumentation for detecting refraction, absorption and transmission. Such systems are necessarily complex, and may therefore be both cumbersome and delicate. Further microfluidic sensors have been fabricated which comprise planar microfluidic channels incorporated into a microchip. However, the inefficiencies of multiple required passes of an analytical light beam through such microfluidic channels still remain.

SUMMARY OF THE INVENTION

There is a continuing need for microfluidic sensors that facilitate the efficient analysis of small volumes of fluids. Among the desired features in such sensors are elimination of the need for light beams to make multiple passes through an analyte fluid, integration of microfluidic channels and optical analysis into a single microchip, and robust, lightweight construction.

In one embodiment according to the present invention, a microfluidic optical sensor is provided, comprising: an optical waveguide extending between an optical input port and an optical output port, said optical waveguide being capable of propagating light from said optical input port to said optical output port, said optical waveguide comprising an optical waveguide interaction region; a fluidic channel extending between a fluid input port and a fluid output port, said fluidic channel being capable of conducting a fluid from said fluid input port to said fluid output port, said fluidic channel comprising a fluidic channel region; said fluidic channel region being separated from said optical waveguide interaction region by an interposed spacing material having a thickness; said thickness being configured to transmit an evanescent field of said light through said spacing material between said optical waveguide interaction region and said fluidic channel region.

In another embodiment according to the present invention, a microfluidic optical sensor is provided, comprising: an optical waveguide extending between an optical input port and an optical output port, said optical waveguide being capable of propagating light from said optical input port to said optical output port; a fluidic channel extending between a fluid input port and a fluid output port, said fluidic channel being capable of conducting a fluid from said fluid input port to said fluid output port; an optical resonator separated from said optical waveguide by a first spacing material having a first thickness between the optical resonator and the optical waveguide; said first thickness being configured to transmit an evanescent field of said light through the first spacing material between said optical waveguide and said optical resonator; said fluidic channel comprising a fluidic cavity region separated from said optical resonator by a second spacing material having a second thickness between the fluidic cavity region and the optical resonator; said second thickness being configured to transmit an evanescent field of light through the second spacing material between said optical resonator and said fluidic cavity region.

In a further embodiment according to the present invention, a method of making a microfluidic optical sensor is provided, comprising the steps of: providing an optical waveguide extending between an optical input port and an optical output port, said optical waveguide being capable of propagating light from said optical input port to said optical output port, said optical waveguide comprising an optical waveguide interaction region; providing a fluidic channel extending between a fluid input port and a fluid output port, said fluidic channel being capable of conducting a fluid from said fluid input port to said fluid output port, said fluidic channel comprising a fluidic channel region; providing a spacing material, having a thickness, interposed between said fluidic channel region and said optical waveguide interaction region; and configuring said thickness to transmit an evanescent field of said light through said spacing material between said optical waveguide interaction region and said fluidic channel region.

In an additional embodiment according to the present invention, a method of making a microfluidic optical sensor is provided, comprising the steps of: providing an optical waveguide extending between an optical input port and an optical output port, said optical waveguide being capable of propagating light from said optical input port to said optical output port; providing a fluidic channel extending between a fluid input port and a fluid output port, said fluidic channel being capable of conducting a fluid from said fluid input port to said fluid output port, said fluidic channel comprising a fluidic cavity region; providing an optical resonator separated from said optical waveguide by a first spacing material having a first thickness between the optical resonator and the optical waveguide; configuring said first thickness to transmit an evanescent field of said light through the first spacing material between said optical waveguide and said optical resonator; providing a second spacing material having a second thickness separating said fluidic cavity region and said optical resonator; and configuring said second thickness to transmit an evanescent field of light through the second spacing material between said optical resonator and said fluidic cavity region.

A more complete understanding of the present invention, as well as other features and advantages of the invention, will be apparent from the following detailed description and the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** shows a cross-sectional side view of an exemplary microfluidic optical sensor according to the present invention;

FIG. **2** shows a cross-sectional top view of the microfluidic optical sensor of FIG. **1**;

FIG. **3** shows the steps of an exemplary process for fabrication of the microfluidic optical sensor shown in FIGS. **1** and **2**;

FIGS. **4-8** show cross-sectional side views of a microfluidic optical sensor according to the present invention during various steps of its fabrication according to the process shown in FIG. **3**;

FIGS. **9-13** show top views of a microfluidic optical sensor according to the present invention during various steps of its fabrication according to the process shown in FIG. **3**;

FIG. **14** shows a cross-sectional top view of a microfluidic optical sensor according to the present invention;

FIG. **15** shows a cross-sectional side view of the microfluidic optical sensor of FIG. **14**;

FIG. **16** shows a further cross-sectional top view of the microfluidic optical sensor of FIG. **14**;

FIG. **17** shows the steps of a process for fabrication of the microfluidic optical sensor shown in FIG. **14**;

FIG. **18** shows a cross-sectional top view of a microfluidic optical sensor according to the present invention;

FIG. **19** shows a cross-sectional top view of a microfluidic optical sensor according to the present invention;

FIG. **20** shows a cross sectional side view of the microfluidic optical sensor shown in FIG. **19**; and

FIG. **21** shows the steps of an exemplary process for fabrication of the microfluidic optical sensor shown in FIG. **19**.

DETAILED DESCRIPTION

The present invention will now be described more fully with reference to the accompanying drawings, in which several presently preferred embodiments of the invention are shown. This invention may, however, be embodied in various forms and should not be construed as being limited to the embodiments set forth herein.

The present invention provides microfluidic optical sensors and methods for making and using the same. The microfluidic optical sensors facilitate interaction between a fluid to be subjected to optical detection, and light that is employed in the detection. The microfluidic optical sensors provide a high level of interaction between the evanescent field of detector light and a small amount of analyte fluid. Hence, the microfluidic optical sensors provide high detection sensitivity. Small volumes of analyte fluids, as well as analyte fluids comprising small concentrations of target analytes, can thus be effectively analyzed by the microfluidic optical detectors.

FIG. **1** shows a cross-sectional side view of an exemplary microfluidic optical sensor **100** according to the present invention. The sensor **100** comprises an optical waveguide **102** integrated with a fluidic channel **104**. By "channel" is meant a cavity through which a fluid can pass. The cavity can be occupied, for example, by air, another gas, or a porous material. The optical waveguide **102** is bounded by a cladding layer **106** and a bottom cladding layer **107**, the bottom cladding layer **107** having an overlaying substrate **108**. A fluid input **110** communicates with fluidic channel **104** by a fluid conduit **112**. A fluid output **114** communicates with fluidic channel **104** by a fluid conduit **116**. A cover **118** is sealed to the substrate **108**, and forms a flow directing path for a fluid together with the fluid conduits **112** and **116** and the fluidic channel **104**.

FIG. **2** shows a cross-sectional top view of the microfluidic optical sensor **100** taken on line **2-2** shown in FIG. **1**. The sensor **100** comprises a fluidic channel **104** communicating with a fluid input **110** and a fluid output **114** by fluid conduits **112** and **116**, respectively. The fluidic channel **104** and the fluid conduits **112** and **116** are bounded by substrate **108**. The fluidic channel **104** overlies the optical waveguide **102** within an optical waveguide interaction region **126**.

The optical waveguide **102** is fabricated from a material having a relatively higher index of refraction that is suitable to serve as a waveguide core for the propagation of light. The term "light" means radiation having a wavelength or wavelengths in the infrared, visible, and/or ultraviolet spectra and suitable to propagate in the optical waveguide **102**. The term "optical" means "of or relating to light". The cladding layer **106**, the bottom cladding layer **107** and the substrate **108** are fabricated from a material or materials having a relatively lower index of refraction that is suitable to serve as a waveguide cladding to facilitate the propagation of the light in the optical waveguide **102**. The cover **118** is fabricated from a material that is suitable to be bonded to the substrate **108** and that is suitable, together with the substrate **108** and the bottom cladding layer **107**, for confining a fluid within the fluidic channel **104** and the fluid conduits **112** and **116**. In one embodiment, the optical waveguide **102** employed in the microfluidic optical sensors herein comprises silicon. In another embodiment, the cladding **106**, bottom cladding **107** and substrate **108** employed in the microfluidic optical sensors herein comprise silicon dioxide, silicon nitride, silicon oxynitride, ceramics, plastics, or quartz. Exemplary plastics include polydimethylsiloxane, polymethylmethacrylate, and poly(ethylene-terephthalate-glycol). The cover **118** and other layers herein to be bonded to substrates may, for example, comprise a borosilicate glass such as Pyrex 7740.

In operation, a fluid to be subjected to analysis is input into the microfluidic optical sensor **100** through the fluid input **110**. The fluid conduit **112** then carries the fluid into the fluidic channel **104**, where the fluid then generally proceeds in the direction of the arrow **120**. The fluid conduit **116** then carries the fluid to the fluid output **114**. The fluid is then collected for any desired post-analysis treatment or use. Light is propagated through the optical waveguide **102** in the general direction of arrow **122** or arrow **124**. In one embodiment, light is propagated in the general directions of both arrow **122** and arrow **124**. In any of these exemplary embodiments and in other exemplary embodiments discussed elsewhere in this specification, light that is propagated through the optical waveguide **102** makes only a single pass through the waveguide. In alternative embodiments, such light may make multiple passes through the optical waveguide **102**, but this practice generally is not required for effective, high sensitivity operation of the microfluidic optical sensor **100**.

As shown in FIG. **2**, a fluidic channel region **103** of the fluidic channel **104** overlies the optical waveguide **102** in the optical waveguide interaction region **126**. Light propagates in the optical waveguide **102** in the general direction of arrow **122** or arrow **124**. Both of arrows **122** and **124** are parallel with the general direction of arrow **120** indicating the general direction of flow of the fluid in the fluidic channel **104**. The light and fluid generally propagate, in the optical waveguide **102** and the fluidic channel **104** respectively, in either the same direction or a countercurrent direction over the distance indicated by the double-ended arrow **128** longitudinally traversing the optical waveguide interaction region **126**. In one embodiment, the linear distance **128** is up to about 10 centimeters (cm).

As shown in FIG. **1**, the optical waveguide **102** and the fluidic channel **104** are separated by a spacing layer **131** having a thickness **130** constituting a region of the cladding layer **107** in the optical waveguide interaction region **126**. The cladding layer **107** permits the evanescent field of light propagating in the optical waveguide **102** to penetrate to the substrate **108** and the fluidic channel **104** in the optical waveguide interaction region **126**. The thickness **130** is designed so that some of the evanescent field penetrates into the fluidic channel **104** within the optical waveguide interaction region **126**, where the light can interact with the surface **132** of the fluidic channel **104**. Light also interacts with fluid flowing in the fluidic channel **104**. The thickness **130** affects the extent to which the evanescent field interacts with the surface **132** and with the fluid in the fluidic channel **104**. If the thickness **130** is too great, the evanescent field will not reach the surface **132** nor interact with the fluid in the fluidic channel **104**. If the thickness **130** is too small, the propagation of the light in the optical waveguide **102** may be disturbed. In one embodiment, the thickness **130** is roughly equivalent to the wavelength of the light propagated in the optical waveguide **102**. The cross-sectional shape of the fluidic channel **104** desirably is compatible with the optical mode within the optical waveguide **102**. In an alternative embodiment, the bottom cladding layer **107** constitutes a region of the substrate **108**.

The refractive indices near the surface **132** are influenced by the nature of a fluid that is input through fluid input **110**, carried by the fluid conduit **112** into the fluidic channel **104**, withdrawn by fluid conduit **116** and then output through fluid output **114**. Hence, changes in such refractive indices cause changes in the light from the evanescent field that interacts with the surface **132** and with the fluid. These changes alter the optical path length and accordingly the phase of the light in the waveguide **102**.

Further, the optical absorption and transmission characteristics of the surface **132** and of fluid within the fluidic channel **104** are influenced by the nature of a fluid that is input through fluid input **110**, carried by the fluid conduit **112** into the fluidic channel **104**, withdrawn by fluid conduit **116** and output through fluid output **114**. Changes in such absorption and transmission accordingly change the wavelength spectrum of the light originating from the evanescent field that interacts with the surface **132** and with the fluid.

Light that is output from the microfluidic optical sensor in the direction **122** or **124**, including light that has interacted with the surface **132** and with fluid flowing in the fluidic channel **104**, can then be subjected to analysis for detection of phase changes, detection of polarization changes, detection of polarization mode dispersion changes, and detection of changes in the wavelength spectrum. In one embodiment, such light is input into a Mach-Zehnder interferometer for detection of phase changes induced by interaction of the evanescent field with the surface **132** and with fluid within the fluidic channel **104**. For example, a Mach-Zehnder interferometer can be integrated together with the microfluidic optical sensor **100** into a monolithic planar array comprising optical waveguide **102** bounded by cladding layer **106**, bottom cladding layer **107**, and substrate **108**. In a further embodiment, the microfluidic optical sensor **100** can itself be configured as a Mach-Zehnder interferometer. These integrated embodiments may provide for increased sensor accuracy, as all of the sensor components so integrated are subjected in a uniform manner to external stress such as temperature fluctuations. In another embodiment, light that is output from the microfluidic optical sensor **100** in the direction **122** or **124** can then be input into a spectrophotometer for detection of changes in the wavelength spectrum.

The nature of the fluid to be carried through the fluidic channel **104** for analysis by the microfluidic optical sensor **100** is a matter of the sensor operator's choice. For example, the fluid may be a liquid, a gas, a suspension of particles in a fluid, an emulsion, a solution, or a dispersion. The viscosity of the fluid desirably is suitable to facilitate flow of the fluid through the fluidic channel **104**. For example, if the fluid viscosity is too high, or if the size or concentration of particles or other solids in the fluid is too great, clogging may result or residue may be retained in the microfluidic optical sensor **100**. The fluid may be aqueous or nonaqueous, and organic or inorganic. The fluid may contain oligomers, polymers, or macromolecules. The fluid may contain biological analytes such as proteins, carbohydrates, fats, ribonucleic acids, bacteria, cells or viruses. The surface **132** can, if desired, be provided with a bound or otherwise fixed agent that will also selectively bind with components of or otherwise interact with the fluid carried in the fluidic channel **104**. For example, the surface **132** can be provided with bound antibodies adapted to selectively bind with and therefore enable detection of target antigens in the fluid. The target antigens can, for example, be tagged with a fluorescent, radioactive or chromophoric agent, so that the fluorescence, radioactivity or color change of antigens bound to the antibodies can be detected. Other biological and chemical binding regimes, such as proteins and protein receptors, or mutually-reactive chemical moieties, can also be used. Further, chemical and biological markers can be allowed to selectively bind or otherwise interact or react with components of a fluid to be analyzed, thus selectively changing the refractive index and light absorption profiles of the fluid itself.

FIG. **3** shows the steps of an exemplary process **300** that is suitable for fabrication of the microfluidic optical sensor **100**. FIGS. **4-8** together with FIG. **1** show cross-sectional side views and FIGS. **9-13** together with FIG. **2** show top views of the microfluidic optical sensor **100** during various steps of its fabrication according to the exemplary process **300** shown in FIG. **3**. Referring to FIG. **3**, in step **302** a waveguide core layer **402** having a relatively higher refractive index is provided on a waveguide cladding layer **404** having a relatively lower refractive index as shown in cross-sectional side view in FIG. **4** and top view in FIG. **9**. In one embodiment, step **302** comprises the provision of a bottom cladding layer **403** interposed between the layers **402** and **404**. The bottom cladding layer serves to define and permit precise control over the thickness **130** discussed earlier, and also serves as an etch stop for the preparation of the fluidic channel as also discussed below. In step **304** the waveguide core layer **402** is patterned and etched to form the optical waveguide **102** and is covered with a waveguide cladding layer **406** having a relatively lower refractive index as shown in cross-sectional side and top views in FIGS. **5** and **10** respectively, the latter figure being taken on line **10-10** shown in FIG. **5**. In step **306**, fluid input **110** and fluid output **114** are patterned and etched as shown in cross-sectional side view in FIG. **6** and top view in FIG. **11**, the latter figure being taken on line **11-11** shown in FIG. **6**. Formation of cladding layer **106** is also thus completed. In step **308**, the backside of the cladding layer **404** opposite to that on which the optical waveguide **102** is formed, is then provided with a masking layer **408** suitable for subsequent patterning and etching of such surface to form the fluid conduits **112** and **116** and the fluidic channel **104**, as shown in cross-sectional side view in FIG. **7** and in top view in FIG. **12**. In step **310**, the masking layer **408** is patterned, etched and then removed, to form the fluid conduit **112**, fluidic channel **104**, and fluid conduit **116**, as shown in cross-sectional FIGS. **8** and **2**, and fabrication of the substrate **108** is completed. The bottom cladding layer **403** serves as an etch stop in formation of the fluidic channel **104**, terminating the etching at the surface **132**. Hence, the bottom cladding layer **403** also effectively defines and controls the distance **130**. In step **312**, as shown in cross-sectional side view in FIG. **1** and top view in FIG. **13**, a cover **118** is sealed to the substrate **108**, forming a flow directing path for a fluid together with the fluid conduits **112** and **116** and the fluidic channel **104**.

The exemplary steps of FIG. **3** can be carried out, for example, using semiconductor chip fabrication processes adapted to the materials selected for making the microfluidic optical sensor **100** as earlier discussed. The steps of FIG. **3** are merely exemplary, and it is to be understood that such steps can readily be carried out in different manners or orders. It is further understood that the various elements of the microfluidic optical sensor **100** can be built up, patterned and etched by using analogous steps carried out in analogous process routines, or otherwise fabricated, in order to produce the same or a similar device structure. Background information is provided in Verpoorte, Elizabeth, et al., "Microfluidics Meets MEMS," *Proceedings of the IEEE*, Vol. 91, No. 6, June 2003, pp. 930-948, the entirety of which is hereby incorporated herein by reference.

FIG. **14** shows a cross-sectional top view of an exemplary microfluidic optical sensor **1400** according to the present invention. The sensor **1400** comprises an optical waveguide **1402** in the form of a spiral doubled over upon itself. The optical waveguide **1402** comprises a first end **1404** and a second end **1406**. In this exemplary embodiment, the first end **1404** serves as an optical input and the second end **1406** serves as an optical output. The first end **1404** and the second end **1406** together form an outermost double loop **1408** of the optical waveguide **1402**, and take the form of smooth curves without any sharp directional changes in order to avoid undue attenuation of light propagating in the optical waveguide **1402**. The outermost double loop **1408** leads continuously inward toward the center **1401** of the spiral of the optical waveguide **1402**, through a plurality of inner loops having successively smaller diameters, terminating in an S-shaped link **1403** between the portions of an innermost double loop respectively connected to the first end **1404** and the second end **1406**. In one embodiment, the length of the path along the optical waveguide **1402** between the first end **1404** and the second end **1406** is up to about 0.2 meter. In another embodiment, the length of the path along the optical waveguide **1402** between the first end **1404** and the second end **1406** is up to about two (2) meters. As the path length increases, so does the sensitivity of the microfluidic optical detector **100**. In one embodiment, the diameter of the outermost double loop **1408** is within a range of between about one and about five cm, and the diameter of the innermost double loop **1405** is within a range of between about one and about ten millimeters (mm).

FIG. **15** shows a cross-sectional side view of the microfluidic optical sensor **1400** taken on line **15-15** shown in FIG. **14**. Portions **1414**, **1415**, **1417**, **1418**, **1419**, **1420**, **1421**, **1422**, **1423**, **1425**, **1427**, **1429**, and **1430** of the optical waveguide **1402**, visible in both FIGS. **14** and **15**, are in a spaced apart arrangement in a plane indicated by line **1432**, collectively forming an optical waveguide interaction region **1441**. FIG. **16** shows a further top cross-sectional view of the microfluidic optical sensor **1400**. The spiral of the optical waveguide **1402** is integrated with and overlaid by a fluidic channel region **1433** constituting a portion of a fluidic channel **1434** having an input **1436** and an output **1438**. The fluidic channel **1434** is overlaid by a cover **1444**. Referring to FIG. **15**, the fluidic channel **1434** is spaced apart from the plane **1432** of the optical waveguide **1402** by a cladding layer **1442** at a distance **1440**. The spiral of the optical waveguide **1402** is underlaid by a substrate **1446**.

The optical waveguide **1402** is fabricated from a material having a relatively higher index of refraction that is suitable to serve as a waveguide core for the propagation of light. The cladding layer **1442** and the substrate **1446** are fabricated from materials having relatively lower indices of refraction that are suitable to serve as waveguide claddings to facilitate the propagation of light in the optical waveguide **1402**. The cover **1444** is fabricated from a material that is suitable to be bonded to the cladding layer **1442** and that is suitable, together with the cladding layer **1442**, for confining a fluid within the fluidic channel **1434**.

In operation, a fluid to be subjected to analysis is input into the microfluidic optical sensor **1400** through the fluid input **1436**. The fluid fills the fluidic channel **1434** and is then carried to the fluid output **1438**. The fluid is then collected for any desired post-analysis treatment or use. Light is propagated through the optical waveguide **1402** from the first end **1404** to the second end **1406**. In one alternative embodiment, light is propagated through the optical waveguide **1402** from the second end **1406** to the first end **1404**. In another alternative embodiment, light is propagated both from the first end **1404** to the second end **1406**, and from the second end **1406** to the first end **1404**. In a further alternative embodiment, **1436** serves as the fluid output, and **1438** serves as the fluid input.

As shown in FIG. **16**, the fluidic channel **1434** overlies the optical waveguide **1402**. Light propagates in the optical waveguide **1402** in the general direction from the first end **1404** to the second end **1406**. As shown in FIG. **15**, the optical waveguide **1402** and the fluidic channel **1434** are separated at a distance **1440** by a spacing layer constituted by the cladding layer **1442**. The cladding layer **1442** is thin enough across the distance **1440** to permit the evanescent field of light in the optical waveguide interaction region **1441** of the optical waveguide **1402** to penetrate into the fluidic channel region **1443** of the fluidic channel **1434**. There, the light can interact with the surface **1448** of the fluidic channel **1434** and the fluid flowing in the fluidic channel **1434**. This light can be analyzed in a manner analogous to that discussed above in connection with the microfluidic optical sensor **100**. The interaction path length through the optical waveguide **1402** is approximately given by the formula $L_i=2\pi Nr$, where N is the number of single loops (each double loop constituting two single loops) and r is the mean radius of the outermost loop **1408**.

FIG. **17** shows the steps of an exemplary process **1700** that is suitable for fabrication of the microfluidic optical sensor **1400**. In step **1702** a waveguide core layer having a relatively higher refractive index is provided on a substrate **1446** having a relatively lower refractive index as shown in FIG. **15**. In step **1704** the waveguide core layer is patterned and etched to form the optical waveguide **1402** as shown in FIGS. **14** and **15**. In step **1706** the optical waveguide **1402** is covered with a waveguide cladding layer **1442** having a relatively lower refractive index as shown in FIG. **15**. In step **1708**, the fluidic channel **1434** is patterned and etched into the waveguide cladding layer **1442** as shown in FIGS. **15** and **16**. In step **1710**, as shown in FIG. **15**, a cover **1444** is sealed to the cladding layer **1442**, forming a flow directing path for a fluid together with the fluidic channel **1434**. The exemplary steps of FIG. **17** can be carried out, for example, using semiconductor chip fabrication processes adapted to the materials selected for making the microfluidic optical sensors as earlier discussed. The steps of FIG. **17** are merely exemplary, and it is to be understood that such steps can readily be carried out in different manners and orders, and that the various elements of the microfluidic optical sensor **1400** can be built up, patterned and etched, or otherwise fabricated, by using analogous steps carried out in analogous process routines in order to produce the same or a similar device structure.

FIG. **18** shows a cross-sectional top view of an exemplary microfluidic optical sensor **1800** according to the present invention. The sensor **1800** comprises two spiral optical waveguides **1802** and **1804**, each doubled over onto itself in the same manner as discussed above in connection with the optical waveguide **1402** shown in FIG. **14**. As shown in FIG. **18**, the fluidic channel **1806** overlies the optical waveguide **1802**, and the fluidic channel **1808** overlies the optical waveguide **1804**. Each of the spiral optical waveguides **1802** and **1804** is incorporated into a structure analogous to that discussed above in connection with FIGS. **14** and **15**, facilitating analogous interaction of evanescent field light with the respective fluidic channels **1806** and **1808**. Fluidic channel **1806** comprises input port **1810**, and output port **1812**. Fluidic channel **1808** comprises input port **1814**, and output port **1816**. Desirably, fluidic channel **1806** has a flow channel slightly larger than and approximating the perimeter of spiral optical waveguide **1802** as shown within the region **1803**. Desirably, fluidic channel **1808** has a flow channel slightly larger than and approximating the perimeter of spiral optical waveguide **1804** as shown within the region **1805**. The sensor **1800** further comprises an optical waveguide input **1818**, and an optical waveguide output **1820**. An optical splitter **1822** provides two waveguide outputs from the optical waveguide input **1818**. Waveguide **1824** connects one of such waveguide outputs to an input **1825** to spiral optical waveguide **1802**, and waveguide **1826** connects the other of such waveguide outputs to an input **1827** to spiral optical waveguide **1804**. An optical coupler **1828** combines two optical inputs into optical waveguide output **1820**. Optical waveguide **1830** connects an output **1831** from spiral waveguide **1802** to one of such optical inputs. Optical waveguide **1832** connects an output **1833** from spiral waveguide **1804** to the other of such optical inputs.

In operation of the sensor **1800**, a fluid containing components to be analyzed is carried through fluidic channel **1806**, from input port **1810** to output port **1812**. A reference fluid is carried through fluidic channel **1808**, from input port **1814** to output port **1816**. Light is input at port **1818** and split into two portions by optical splitter **1822**. Optical waveguide **1824** carries one of such portions to the input **1825** to spiral **1802**. Optical waveguide **1826** carries the other of such portions to the input **1827** to spiral **1804**. Optical waveguide **1830** carries light from the output **1834** from spiral **1802** to an input to coupler **1828**. Optical waveguide **1832** carries light from the output **1833** from spiral **1804** to the other input to coupler **1828**. Thus, the microfluidic optical sensor **1800** can be operated as a Mach-Zehnder interferometer in order to detect a relative phase shift between the two optical arms of the interferometer generated at optical waveguides **1824** and **1826**, as induced by the nature of a fluid being analyzed by the sensor **1800**. A phase change in the light output on optical waveguide **1820** is indicative of the refractive index of the analyte fluid passed through fluidic channel **1806**.

In an alternative embodiment, the spiral **1804** and the fluidic channel **1808** are omitted. In this embodiment, waveguides **1826** and **1832** are directly connected together to create a waveguide path having a defined length between the optical splitter **1822** and optical coupler **1828**. The length of such waveguide path can be selected to generate, for example, a fixed phase shift. In a further embodiment, the spiral **1804** is included, and the fluidic channel **1808** is omitted. In this latter embodiment, a long optical path through the spiral **1804** between waveguides **1826** and **1832** is created. The length of such waveguide path can be selected to serve, for example, as a fixed control or otherwise result in desired interferometer performance.

FIG. **19** shows a cross-sectional top view of an exemplary microfluidic optical sensor **1900** according to the present invention. The microfluidic optical sensor **1900** comprises a plurality of optical resonators **1902**, **1904**, and **1906** having a disc shape or other desired shape, fabricated from a material suitable for forming an optical waveguide core and having a relatively higher refractive index than the surrounding matrix. In particular, the optical resonators **1902-1906** are bounded by a cladding layer **1908** having a relatively lower refractive index. An optical waveguide **1910** is integrated with and spaced apart from the optical resonators by a spacing layer **1911** constituting a region of the cladding layer **1908**, at a minimum distance **1912**. A fluidic channel comprising a plurality of fluidic channel regions **1914**, **1916** and **1918** having perimeters generally corresponding to but slightly larger than those of the optical resonators **1902**, **1904** and **1906**, respectively, is integrated with and underlies such optical resonators. In one embodiment,.the perimeters of the fluidic channel regions **1914**, **1916** and **1918** are defined by average diameters within a range of between about 0.1 mm and about 1 mm. In another embodiment, the diameters of the fluidic channel regions **1914**, **1916** and **1918** are up to about ten microns. Further embodiments have other diameters within a range between about ten microns and about 0.1 mm. A fluid input **1920** enables injection of a fluid into the fluidic channel region **1914** through a fluid conduit **1921**. A fluid conduit **1922** enables fluid to be conveyed from the fluidic channel region **1914** into the fluidic channel region **1916**. A fluid conduit **1924** enables fluid to be conveyed from the fluidic channel region **1916** into the fluidic channel region **1918**. A fluid output **1926** enables ejection of a fluid through a fluid conduit **1925** from the fluidic channel region **1918**. FIG. **20** shows a cross sectional side view of the microfluidic optical sensor **1900** taken on line **20-20** shown in FIG. **19**. The fluidic channel region **1916** is shown adjacent to the optical resonator **1904**, spaced apart by a distance **1928**. The fluidic channel regions **1914**, **1916** and **1918** are bounded by the substrate **1930** also underlying the optical waveguide **1910** and the optical resonator **1904**. FIG. **20** shows the optical waveguide **1910** and the optical resonator **1904** spaced apart from the fluidic channel region **1916** by a spacing layer **1927** constituting a region of the substrate **1930** by the distance **1912**. The spacing layer **1927** can alternatively be constituted by a bottom cladding layer **1931** interposed between the cladding layer **1908** and the substrate **1930**. A cover layer **1932** is positioned adjacent to the substrate **1930**, and also forms a flow-directing path for a fluid together with the fluid conduits **1921**, **1922**, **1924** and **1925**, and the fluidic channel regions **1914**, **1916** and **1918**.

In operation, fluid is input by the fluid input **1920** through fluid conduit **1921** into fluidic channel region **1914**. The fluid then successively flows by fluid conduit **1922** into fluidic channel region **1916**, and by fluid conduit **1924** into fluidic channel region **1918**. The fluid is then output through fluid conduit **1925** to the fluid output **1926** and collected for any desired post-analysis treatment or use. Light is input into the optical waveguide **1910** from the optical input point **1934**. As the light propagates in the optical waveguide **1910** toward the optical output point **1936**, the cladding layer **1908** permits the evanescent field of light in the optical waveguide **1910** to couple across the distance **1912** into the optical resonators **1902**, **1904**, and **1906**, each of which constitutes an optical waveguide interaction region. As the light resonates in the optical resonators **1902**, **1904** and **1906**, the substrate **1930** permits a portion of an evanescent field of the light in the optical resonators **1902**, **1904** and **1906** to penetrate across the distance **1928** to the surfaces **1938**, **1940** and **1942** of the fluidic channel regions **1914**, **1916** and **1918**, respectively. The evanescent field of such light can interact with the surfaces **1938**, **1940** and **1942** as well as with fluid flowing within the fluidic channel regions **1914**, **1916** and **1918**. The interaction path within each of the fluidic channel regions **1914**, **1916** and **1918** can be approximately expressed by the formula, $L_i = c\tau_c = \lambda Q/2\pi$, where τ_c is the channel region lifetime, c is the speed of light, and Q is a unitless quality factor indicative of the light reflective capability of the perimeters of the optical resonators **1902**, **1904** and **1906**. A high Q corresponds to a highly confining optical cavity where light bounces inside the cavity many times before exiting. Typical values of high Q are within a range of between about 10^4 and about 10^6. Light from the waveguide **1910** as output at point **1936** including light that has interacted with the surfaces **1938**, **1940** and **1942** and with fluid flowing in the fluidic channel regions **1914**, **1916** and **1918** can then be subjected to analysis for detection of phase changes, and changes in the wavelength spectrum, in the same manner as earlier discussed.

In one embodiment comprising optical resonators **1902**, **1904** and **1906**, the microfluidic optical sensor **1900** has a relatively small bandwidth, for example within a range of between about 1.0 nanometer (nm) and 0.1 nm, and is accordingly equipped with a narrow linewidth stabilized laser light source. In general, microfluidic optical sensors that do not incorporate resonators may have a relatively large bandwidth, on the order of about 100 nm, and therefore may be more practical to implement because they may not need a narrow linewidth stabilized laser source.

The optical waveguide **1910** and the optical resonators **1902**, **1904** and **1906** are fabricated from materials having relatively higher indices of refraction that are suitable to serve as waveguide cores for the propagation of light. The cladding layer **1908**, the cladding layer **1931** and the substrate **1930** are fabricated from materials having relatively lower indices of refraction that are suitable to serve as waveguide claddings to facilitate the propagation of light at wavelengths that propagate in optical waveguide **1910**. The cover **1932** is fabricated from a material that is suitable to be bonded to the substrate **1930** and that is suitable, together with the substrate **1930** and the cladding layer **1931**, for confining a fluid within the fluidic channel regions **1914**, **1916** and **1918**, and the fluid conduits **1921**, **1922**, **1924** and **1925**.

FIG. **21** shows the steps of an exemplary process **2100** that is suitable for fabrication of the microfluidic optical sensor **1900**. In step **2102** a waveguide core layer having a relatively higher refractive index is provided on a waveguide cladding layer having a relatively lower refractive index, which may include an interposed bottom cladding layer as earlier discussed. In step **2104** the waveguide core layer is patterned and etched to form the optical waveguide **1910** and the optical resonators **1902**, **1904** and **1906**. In step **2106** the optical waveguide **1910** and the optical resonators **1902**, **1904** and **1906** are covered with a waveguide cladding layer **1908** having a relatively lower refractive index as shown in FIG. **20**. In step **2108**, the liquid input **1920** and the liquid output **1926** are patterned and etched into the waveguide cladding layer **1908** as shown in FIGS. **19** and **20**. In step **2110**, the substrate **1930** is patterned and etched to form the fluidic channel regions **1914**, **1916** and **1918**, and the fluid conduits **1921**, **1922**, **1924** and **1925** as shown in FIGS. **19** and **20**. In step **2112** as shown in FIG. **20**, a cover **1932** is sealed to the substrate **1930**, forming a flow directing path for a fluid together with the fluidic channel regions **1914**, **1916** and **1918**, and the fluid conduits **1921**, **1922**, **1924** and **1925**. The exemplary steps of FIG. **21** can be carried out, for example, using semiconductor chip fabrication processes adapted to the materials selected for making the microfluidic optical sensor as earlier discussed. The steps of FIG. **21** are merely exemplary, and it is to be understood that such steps can readily be carried out in different manners and orders, and that the various elements of the microfluidic optical sensor **1900** can be built up, patterned and etched, or otherwise fabricated, by using analogous steps carried out in analogous process routines in order to produce the same or a similar device structure.

The microfluidic optical sensors can, for example, be incorporated into systems comprising further elements. For example, such sensors can be incorporated into monolithic planar systems formed on microchips in order to facilitate further processing of the light and of the fluid as discussed herein.

While the present invention has been disclosed in a presently preferred context, it will be recognized that the present teachings may be adapted to a variety of contexts consistent with this disclosure and the claims that follow. For example, the optical and fluid paths shown in FIG. **2** can have the same or different lengths, such lengths being chosen in the fabricator's discretion, and do not have to be mutually parallel or coextensive. Input and output conduits can be located in positions other than as shown in FIGS. **1** and **2**. Microfluidic optical sensors similar to that shown in FIGS. **1** and **2** but comprising multiple waveguides and/or fluidic channels, which may or may not be mutually coextensive and aligned together in a sandwich, can be constructed. For example, the optical waveguide **102** can be sandwiched between two fluidic channels **104**. For example, the spiral waveguide **1402** shown in FIG. **14** can be of any desired circumference and length, and can be arranged in a format other than the spiral doubled upon itself as shown in the figure, so long as the waveguide **1402** does not have sharp turns causing excessive optical attenuation and so long as it can be practically fabricated. The fluidic channel **1434** desirably overlays or underlays the entire footprint of the spiral as shown in FIGS. **14-16**, but this is not essential. In an alternative embodiment, the spiral waveguide **1402** is sandwiched between two fluidic channels **1434**. A further embodiment may comprise multiple spiral waveguides **1402** and/or multiple fluidic channels, which may or may not be mutually coextensive and aligned together in a sandwich. For example, the spiral waveguides **1802** and **1804** shown in FIG. **18** can each independently be varied in the same manner as discussed with reference to the spiral waveguide **1402** of FIG. **14**, and any desired number of such spirals can be arranged in a desired layout on one or more mutually overlaid layers in an array device. The corresponding fluidic channels can be arranged in corresponding variations, provided that the desired overlapping of evanescent optical fields with adjacent fluidic channels is obtained. Further for example, the optical resonators shown in FIGS. **19** and **20** may be varied in circumference, shape, thickness and numbers as desired. Additional waveguides can be positioned within the microfluidic optical sensors to provide evanescent field interactions with the optical resonators. In an alternative embodiment, the exemplary optical resonator **1904** is sandwiched between fluidic channel regions **1916**; and optical resonators **1902** and **1906** are likewise sandwiched. A further embodiment may comprise multiple optical resonators **1904** and/or multiple fluidic channel regions, which may or may not be mutually coextensive and be aligned together in a sandwich.

We claim:

1. A microfluidic optical sensor, comprising:

an optical waveguide extending between an optical input port and an optical output port, said optical waveguide being capable of propagating light from said optical input port to said optical output port, said optical waveguide comprising an optical waveguide interaction region that comprises an optical waveguide loop;

a fluidic channel extending between a fluid input port and a fluid output port, said fluidic channel being capable of conducting a fluid from said fluid input port to said fluid output port, said fluidic channel comprising a fluidic channel region;

said fluidic channel region being aligned in a sandwich with said optical waveguide interaction region and separated from said optical waveguide interaction region by an interposed spacing material having a thickness;

said thickness being configured to enable transmission of an evanescent field of light through said spacing material between said optical waveguide interaction region and said fluidic channel region.

2. The microfluidic optical sensor of claim **1**, in which said fluidic channel region and said optical waveguide interaction region are substantially mutually parallel over a distance.

3. The micro fluidic optical sensor of claim **1**, in which said fluidic channel region has a first width dimension transverse to a direction of flow of a fluid from said fluid input port to said fluid output port, and in which said optical waveguide interaction region has a second width dimension transverse to a direction of propagation of light from said optical input port to said optical output port, said first width dimension being at least about as large as said second width dimension.

4. The microfluidic optical sensor of claim **3**, in which said first width dimension is greater than said second width dimension.

5. The microfluidic optical sensor of claim **1**, comprising a second fluidic channel extending between a second fluid input port and a second fluid output port, said second fluidic channel being capable of conducting a fluid from said second fluid input port to said second fluid output port, said second fluidic channel comprising a second fluidic channel region, said second fluidic channel region being aligned in a sandwich with said optical waveguide interaction region and separated from said optical waveguide interaction region by an interposed second spacing material having a second thickness configured to enable transmission of an evanescent field of light through said second spacing material between said optical waveguide interaction region and said second fluidic channel region.

6. The microfluidic optical sensor of claim **1**, comprising an optical waveguide interaction region comprising a plurality of optical waveguide loops which are mutually nested to form a spiral having a circumference formed by an outermost optical waveguide loop.

7. The microfluidic optical sensor of claim **1**, in which said fluidic channel region has a width dimension transverse to a direction of flow of a fluid from said fluid input port to said fluid output port, said width dimension being at least about as large as a circumference formed by an outermost optical waveguide loop.

8. The microfluidic optical sensor of claim **7**, in which said width dimension is greater than said circumference.

9. The microfluidic optical sensor of claim **1**, comprising a plurality of fluidic channel regions of said fluidic channel separated from a respective plurality of optical waveguide interaction regions by interposed spacing layers.

10. The microfluidic optical sensor of claim **1**, further comprising a second optical waveguide extending between a second optical input port and a second optical output port, said second optical waveguide being capable of propagating light from said second optical input port to said second optical output port, said second optical waveguide comprising a second optical waveguide interaction region that comprises a second optical waveguide loop.

11. A microfluidic optical sensor, comprising:

an optical waveguide extending between an optical input port and an optical output port, said optical waveguide being capable of propagating light from said optical input port to said optical output port;

a fluidic channel extending between a fluid input port and a fluid output port, said fluidic channel being capable of conducting a fluid from said fluid input port to said fluid output port;

an optical resonator separated from said optical waveguide by a first spacing material having a first thickness between the optical resonator and the optical waveguide;

said first thickness being configured to enable transmission of an evanescent field of light through the first spacing material between said optical waveguide and said optical resonator;

said fluidic channel comprising a fluidic cavity region separated from said optical resonator by a second spacing material having a second thickness between the fluidic cavity region and the optical resonator;

said second thickness being configured to enable transmission of an evanescent field of light through the second spacing material between said optical resonator and said fluidic cavity region.

12. The microfluidic optical sensor of claim **11**, comprising a plurality of optical resonators.

13. The microfluidic optical sensor of claim **11**, where the optical resonator includes a perimeter configured to cause multiple reflections of light.

14. The microfluidic optical sensor of claim **11**, in which:

said optical resonator comprises a first circumference;

said fluidic channel region comprises a second circumference; and

said second circumference is at least about as large as said first circumference.

15. The microfluidic optical sensor of claim **11**, further comprising a second fluidic channel extending between a second fluid input port and a second fluid output port, said second fluidic channel being capable of conducting a fluid from said second fluid input port to said second fluid output port, said second fluidic channel comprising a second fluidic cavity region separated from said optical resonator by a third spacing material having a third thickness between said second fluidic cavity region and said optical resonator, said third thickness enabling transmission of an evanescent field of light through said third spacing material between said optical resonator and said second fluidic cavity region.

16. A method of making a microfluidic optical sensor, comprising the steps of:

forming an optical waveguide extending between an optical input port and an optical output port, said optical waveguide being capable of propagating light from said optical input port to said optical output port, said optical waveguide comprising an optical waveguide interaction region that comprises an optical waveguide loop;

forming a fluidic channel extending between a fluid input port and a fluid output port, said fluidic channel being capable of conducting a fluid from said fluid input port to said fluid output port, said fluidic channel comprising a fluidic channel region;

wherein said fluidic channel region and said optical waveguide interaction region are aligned in a sandwich and a spacing material, having a thickness, is interposed between said fluidic channel region and said optical waveguide interaction region; and wherein said thickness is configured to enable transmission of an evanescent field of light through said spacing material between said optical waveguide interaction region and said fluidic channel region.

17. The method of claim **16**, comprising the steps of:

forming a fluidic channel region having a first width dimension transverse to a direction of flow of a fluid from said fluid input port to said fluid output port;

wherein the optical waveguide interaction region has a second width dimension transverse to a direction of propagation of light from said optical input port to said optical output port, said first width dimension being at least about as large as said second width dimension.

18. The method of claim **16**, wherein forming an optical waveguide includes forming an optical waveguide interaction region comprising a plurality of optical waveguide loops which are mutually nested to form a spiral having a circumference formed by an outermost optical waveguide loop.

19. A method of making a microfluidic optical sensor, comprising the steps of:

forming an optical waveguide extending between an optical input port and an optical output port, said optical waveguide being capable of propagating light from said optical input port to said optical output port;

forming a fluidic channel extending between a fluid input port and a fluid output port, said fluidic channel being capable of conducting a fluid from said fluid input port to said fluid output port, said fluidic channel comprising a fluidic cavity region;

forming an optical resonator separated from said optical waveguide by a first spacing material having a first thickness between the optical resonator and the optical waveguide;

wherein said first thickness enables transmission of an evanescent field of light through the first spacing material between said optical waveguide and said optical resonator;

wherein a second spacing material having a second thickness separates said fluidic cavity region and said optical resonator, said second thickness enabling transmission of an evanescent field of light through the second spacing material between said optical resonator and said fluidic cavity region.

20. The method of claim **19** wherein forming an optical resonator includes forming an optical resonator that comprises a first circumference; and

wherein forming a fluidic channel includes forming a fluidic channel region that comprises a second circumference; said second circumference being at least about as large as said first circumference.

21. The method of claim **19**, further comprising the steps of:

forming a plurality of optical resonators, said plurality of optical resonators being separated from said optical waveguide by a first spacing material having a first thickness between the optical resonators and the optical waveguide, said first thickness enabling transmission of an evanescent field of light through the first spacing material between said optical waveguide and said optical resonators; and

wherein a second spacing material having a second thickness separates said fluidic cavity region and said optical resonator, said second thickness enabling transmission of an evanescent field of light through the second spacing material between said optical resonators and said fluidic cavity region.

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