Abstract: This invention relates to a robust, microwave biosensor fabricated using MEMS fabrication techniques for highly sensitive and selective, rapid, label-free detection of biological or chemical substances. The biosensor subjected to this invention can be used for in-vitro, Point-of-care diagnostics which can have wide range of applications covering environmental monitoring, drug-discovery, disease diagnosis etc.
Microfluidic Channel Integrated Microwave MEMS Biosensor

Related Field of the Invention

This invention relates to a mechanically robust, microwave biosensor fabricated using MEMS fabrication techniques for highly sensitive and selective, rapid, label-free detection of biological or chemical substances. The biosensor subjected to this invention can be used for in-vitro, Point-of-care diagnostics which can have wide range of applications covering environmental monitoring, drug-discovery, disease diagnosis etc.

Background of the Invention (Prior Art)

In last decades, the field of biological and chemical sensors has gone through a significant growth, mainly due to the advancements in microfabrication technologies. The developed biosensors are mainly based on optical, mechanical and low-frequency electrochemical detection. Although they are quite effective, they have some drawbacks such as the use of optical markers [1].

Various studies in the genomics and proteomics field have shown that plenty of new biomarkers can significantly improve in-vitro, Point-of-Care (PoC) diagnostics [2] [3]. The biosensors developed for Point-of-Care diagnostic tools should satisfy the requirements which are real-time, rapid, and label-free with high-selectivity and sensitivity.

Current detection systems are based on fluorescence methods such as enzyme-linked immunoabsorbant assay (ELISA) which use labels to detect the binding of biomarkers to a biorecognition element. These method require heavy, expensive, optical devices and labeling of molecules. These bulky, costly and slow devices need a technical expert to operate and not suitable for in-vitro, Point-of-Care diagnostics which can be used for environmental monitoring or drug-discovery applications.

In [4], Li et al. presents a study which applies Distributed MEMS Transmission Lines (DMTLs) for biosensing applications. The flip-chip wafer bonding has been used to join two dies to form DMTL lines and the fluidic sample reservoir. The study investigates the effect of NaCl concentration on the dielectric constant by observing the change in insertion loss of solution-loaded DMTL structure. In a later study [5] and [6] by the same authors, organic...
(glucose solutions) and inorganic (NaCl solutions) substances are also detected using a
dielectric sensor which has been realized by bonding DMTL device with an acrylic fluidic
channel.

In common with this invention, these studies employs the detection method of
observing the changes in s-parameters in terms of both magnitude and frequency which is
attributed to the substances in the water.

The present invention differs from these studies in several ways. Firstly, in this
invention there is specific antibody-antigen binding events which provides the selectivity to
the sensor. Thus, the sensors presented in [1-3] are not specific the content of the fluid.
That is, the change in the s-parameters may be due to different substances in the fluid.
Secondly, by the way of this invention the sensitivity is enhanced by etching ground recesses
(108) instead of using periodic structures. This approach results in much simpler and
cheaper sensitivity enhancement. Lastly, the fluid in this invention interacts only in high-
dielectric-sensitive region (107) owing to the fabrication method which provides less RF loss
and ultra-high overall sensitivity.

In [7], Kim et al. demonstrates a transmission line as a bio-detection device based on
RF electric signals and MEMS. In this study, the researchers focuses on surface modification
from hydrophobic to hydrophilic of a benzocyclobutene (BCB) layer to detect Glucose oxidase
(GOx) as the biomolecule target.

Similarly in this document, they immobilizes poly dimethylallyl ammonium chloride
(PDAC) as the probe to which GOx is highly attractive. By this way, the selectivity is
provided. Again, they observe the changes in the microwave performance of the unloaded
transmission line due to the GOx molecules after cleaning to remove unexpected biomolecules. That is, the detection method relies on the changes in the microwave
properties of the transmission line itself rather than the fluid medium, which is the case in
this invention.

The present invention differs from this study in various aspects. First, the invention
integrates the microfluidic channel (106) into the transmission line structure to form a
dielectric-sensing capacitance and introduces extra inductances by ground recesses (108) to
create resonance. By this resonance, at a certain frequency the signal is totally lost and this
frequency shifts by the presence of the target biomolecule. Moreover, the microfluidic
channel is required for online, in-vitro detection of living microorganisms as they need to be
in an aqueous solution. It also allows to integrate the biosensor into a system operating autonomously or remote controlled. Lastly, by the way of invention the target biomolecules are concentrated in the high-sensitive region (107) under the microchannel cap (109) which significantly enhances the sensitivity.

A study on microwave and microfluidic sensor in [1] by Grenier et al. is presented. In this paper, it is described that the innovative, high-frequency (HV) based biological detection technique takes the advantage of both the label-free and contactless microwave/millimeter-wave detection and a microfluidic network.

The biological detection method presented in [1] is similar to the present invention in terms of the microfluidic channel and co-planar waveguide (CPW) structure accommodating the electromagnetic waves. Actually, there are some other studies such as [8], [9], [10] in the literature for permittivity measurements of biological substances.

However, none of these studies have a high-sensitivity, biomarker-specific detection region similar to (107) in this present invention. Note that by the way of this invention, the biological or chemical substances are specifically gathered and increased in number which significantly increases the sensitivity and provides lower detection limits.

A patent application [11] by Vasan et al. describes an RF MEMS biosensor for multiplexed label free detection. The biosensor in that invention is capable of sensing the presence of biomarkers by exploiting its mechanical and electrical characteristics. The antigen-antibody binding causes mechanical (membrane) deflections which changes the capacitance and so the electromagnetic response. They also observe the effect on return loss of the RF MEMS capacitor due to the bimolecular interactions between the target antigen and antibody molecules on the coplanar waveguide (CPW) surface. It is claimed that a new device is provided with RF MEMS structures integrated inside the microfluidic channels. The aim is to place the sensors in a matrix like structure for the detection of multiple biomarkers simultaneously.

The previous application can be seen to be similar to this invention in some points. Both inventions uses antibody-antigen interactions to make the biosensor specific to the biomarker of interest. One can also claim both inventions observe the changes in electromagnetic characteristics.
Although they have common sensor parts, they differ clearly from each other in the fundamentals of detection principle, read-out circuitry, microfabrication process flow and the integration of microfluidic and RF MEMS concepts.

First, it is crucially important that unlike [11], there is no mechanical change in this invention. Actually, there is no moving or deflecting parts in this invention. The detection principle is based on the change in dielectric properties which depends on the content of the fluid. The capacitance change is totally due to the presence of biomarkers which are captured by the immobilized antibodies. Again, the antibodies are not immobilized onto the membrane or the CPW surface as they are in [11]. On the contrary, there are only present under the microfluidic cap (109) not any other place. This confines the detection into the high sensitivity region (107) which significantly enhance the overall sensitivity.

Secondly, by this way of invention extra inductance is introduced by the ground recesses (108) and a resonance is obtained at a frequency with highly sensitive to the dielectric constant of the fluid medium. This frequency shifts depending on the quantity of the biomarkers present in the detection region (107). Note that this is totally different reading method from both observing the changes in time duration at the output of the multi-vibrator circuit and the RF loss based detection presented in [11]. This feature enables to observe the frequency shift directly using a network analyzer.

Another difference between the inventions is that they are the RF MEMS structures integrated inside the microfluidic channels in [5]. Nevertheless, the integration is done in reverse manner in this invention, that is, a microfluidic channel is integrated inside the microwave structures. This is achieved by exploiting a novel RF MEMS switch fabrication method in [12] for embedding a microchannel (106) into a RF MEMS capacitance for the first time. Thus, it is possible to create multiple detection regions like (107) for different biomarkers on the same microfluidic channel resulting in a high-throughput, simultaneous detection.

Another patent application [13] by Gurbuz et al. presents a biosensor implementation, rather than a discrete biosensor itself in this invention, wherein, input signals to the transceiver are target bio/chemical agents causing a change in the dielectric constant of the electrical device. The aim is to integrate it into the circuit of the transceiver in order to detect or estimate the type and amount of bio/chemical agents observing this change. In this biosensor implementation, they propose a circuit to which applied signals (voltage, current and pressure) are generated by biological or/and chemical agents such as
proteins, antibodies, antigens or chemical molecules. The implementation is to integrate an electrical device used for bio/chemical sensor into RF circuits such as RF power/low-noise amplifiers, Voltage controlled oscillators etc.

They exemplify the biosensor device used in the implementation as piezoelectric materials or inductors and capacitor combinations which converts bio/chemical agents/signals into their output signals. Again, it may be common in both inventions to utilization of specific antibodies similar to that in [5]. Nevertheless, the invention in [7] is related to the implementation of the biosensor into an RF circuit and there is no claim about how materials, liquids or biological/chemical interacts with the electromagnetic waves. In this invention, it is described that the microfluidic channel (106) is integrated into the microwave structure in which electromagnetic waves interacts with the materials and the performance is highly-sensitive to the content of the fluid. Unlike the biosensor implementation in [7], the novelty in this invention is about the detection principle of the biosensor that is the placement of antibodies inside the channel thanks to novel fabrication approach.

A device which is a combination of [1], [11] and [13] would be similar to this present invention. However, the fabrication method which enables embedding a microchannel of which inside is coated with antibodies into an RF/microwave structure and tunability for fluid would still be missing.

This present invention performs its function as different from prior devices; electromagnetic detection, no labeling or no moving parts, robustness and reliability.

As described above, the detection mechanism of the biosensor in this invention relies on electromagnetic wave-biomolecule interaction and the novel fabrication approach enable immobilizing antibodies and so antigens in the high-sensitive region. By this way, there is no labeling is required and no mechanical part exists resulting in robust, reliable and reproducible sensor structure. Moreover, the sensor can be mass-produced using MEMS fabrication methods with low-cost.

As both RF reading systems like network analyzer and microfluidic syringe pumps can be remote-controlled, the sensor can be used for real-time, online, remote monitoring of environment. Another advantage of this invention is that the sensor can be tuned for desired fluid such as water, milk, saliva, urine, blood or desired frequency by changing channel and recess geometry. It can also be customized for different biomarkers by changing the antibody to be immobilized.
Brief Description of the Invention:

The approach in this invention exploits the augmented interaction of biomarkers and radio frequency (RF) waves for the rapid, in-situ, highly sensitive and selective detection of biomarkers. By way of an untraditional, sacrificial-free MEMS fabrication of microfluidic channels integrated into microwave components, the detection region (107) is constrained to the volume only where the electric and magnetic fields are intense. By doing so, the biomarker-wave interaction and so the overall sensitivity is enhanced. This enhanced interaction is measured by measuring the change in the electromagnetic properties of the microwave components, such as frequency shift and/or amplitude change in the s-parameters. The selectivity of the biosensor is achieved through immobilizing antibodies specific to the biomarker of interest onto the inner wall of channels. Even without any bio-receptor element, this invention still can be used to detect anomalies in material content of the fluids which enables real-time monitoring. Moreover, fabricating multiple ground planes (103) and immobilizing various bio-receptor elements such as bacteria antibodies, multiplexed detection of different substances in the same fluid sample is also possible. Microwave and RF-waves stands for high-frequency electromagnetic waves from 300 MHz to 300 GHz.

Definition of the Figures

In order to explain the present invention in more detail, the following figures have been prepared and attached to the description. The list and the definition of the figures are given below.

**FIGURE 1** isometric view of the bottom and upper wafer before bonding

**FIGURE 2** isometric view of the biosensor after flip-chip bonding

**FIGURE 3** cross-sectional side view of the sensor when splits symmetrically on x-z plane

**FIGURE 4** cross-sectional front view (y-z plane) after the upper wafer is bonded

**FIGURE 5** top view of the biosensor when the microchannel cap is bonded

**FIGURE 6** symbolic representation of the CPW and the microchannel as integrated
**Definition of the Elements (Features/Components/Parts) on the Figures**

The definition of the features/components/parts that are covered in the figures that are prepared in order to explain the present invention better are separately numbered and given below.

1. Substrate Wafer
2. Signal trace
3. Ground planes
4. Fluid Inlet
5. Fluid Outlet
6. MicroChannel bed
7. Detection region
8. Recesses
9. MicroChannel cap
10. Upper Wafer

101 - Substrate Wafer

Substrate wafer can be made of various microfabrication materials such as glass, quartz, silicon etc. It has a thickness of around 500 µm as the standard. It can be etched using suitable etchant to form the microchannel.

102 - Signal trace

Signal trace is the conductor in the middle in which the electromagnetic waves propagate. It can be made of metals such as gold, aluminum. The gold is often preferred due to its being chemically inert and low-loss in terms of electromagnetics. Still, the aluminum can be used as it is cheaper compared to gold.

103 - Ground planes

Two conductor planes, at the left and right side of the signal trace, are the ground planes which allow the electromagnetic waves to propagate forming co-planar waveguide (CPW) structure.

Note that the width of the signal trace (W) and the gap size between the signal trace and the ground planes (G) are the critical parameters that defines the characteristic impedance of the waveguide and so the propagation velocity.
104 - Fluid Inlet

It is a fluidic input port which connects the fluid cable to the microchannel enabling the fluid of interest enters and moves into the channel without significant leakage.

105 - Fluid Outlet

The fluid outlet is the part where the fluid leaves the microchannel.

106 - Microchannel bed

The bottom and side walls are formed by etching the glass substrate. Then, some region(s) are gold electroplated and shaped to create CPW structure. The microchannel has a rectangular cross-section and straight for this example but it can be designed with other geometries.

107 - Microchannel cap

The cap of the microchannel is a gold layer which encloses the channel and connects two ground planes like a bridge. It can be fabricated using different methods, using sacrificial layer, molding techniques or flip-chip bonding. In this invention, the flip-chip bonding technique is used as it allows sacrificial-free approach and provides mechanical strength. In order to do this, a gold layer is electroplated onto another substrate wafer (110).

108 - Detection region

Detection region is the region where the sensing event takes place resulting in a change in the device characteristics. In this invention, detection region is selected to be where the electromagnetic performance of the device is most sensitive to material properties, especially dielectric properties of the fluid. Thus, bio-receptor elements, antibodies as an example, are to be immobilized onto this region.

109 - Recesses

Recesses are to introduce extra inductance to create an LC resonance in the frequency band of interest. They can be used to shift the resonance frequency down if needed. The geometry of this recesses can be altered to adjust the resonance frequency for different fluids and biomarkers of interest. Recesses can be either on ground plane (103) or on signal trace (102).

110 - Upper Wafer
This is another wafer on which the microchannel cap (109) is formed. This wafer is again
can be glass, quartz, silicon etc. For this example, another glass wafer is preferred as using
the same material provides mechanical stability.

**Detailed Description of The Invention**

This invention consists of two integrated parts as shown in Figure 4. They are a coplanar waveguide (CPW) structure in which the radio-frequency waves propagate and a microfluidic channel that the fluid of interest flows through.

The conductor used for the signal trace (102), the ground planes (103) and the microchannel cap (109) can be any conductor such as gold, copper, aluminum or tungsten with adequate RF properties. Gold is preferred here for its superior RF performance, inertness and that it is easy to immobilize antibodies on it. The substrates for bottom and upper wafer can be made of various substances such as glass, silicon, quartz etc. In this example, glass is chosen as it is low loss in microwave frequencies, low-cost and mechanically strong.

Antibodies are to be chosen for their specificity to the antigens (i.e. biomarkers, biological or chemical substances) of interest.

A commercially available substrate wafer (101), which can be made of various microfabrication materials such as glass, quartz, silicon etc. It has a thickness of around 500 µm as the standard. It can be etched using suitable etchant to form the microchannel.

In this example substrate wafer (101), is glass. The microchannel bed (106) the bottom and side walls are formed by etching the glass substrate. Then, some regions (107) are gold electroplated and shaped to create CPW structure. The microchannel has a rectangular cross-section and straight for this example but it can be designed with other geometries.

The fluidic ports; fluid inlet (104) and fluid outlet (105) are formed by etching the substrate. Fluid inlet (104) is a fluidic input port which connects the fluid cable to the microchannel enabling the fluid of interest enters and moves into the channel without significant leakage and the fluid outlet (105) is the part where the fluid leaves the microchannel.

Then the conductor, which is gold in this case, is electroplated and shaped in order to form signal trace (102) and the ground planes (103) resulting in co-planar waveguide.
structure. Signal trace (102) is the conductor in the middle in which the electromagnetic waves propagate. It can be made of metals such as gold, aluminum. The gold is often preferred due to its being chemically inert and low-loss in terms of electromagnetics. Still, the aluminum can be used as it is cheaper compared to gold.

In addition to this, the ground planes (103) are ground recessed (108) to introduce extra inductance which can be adjusted by altering the geometrical parameters. The resulting structure is as presented in Figure 1.

The ground planes (103) which allow the electromagnetic waves to propagate forming co-planar waveguide (CPW) structure, are two conductor planes, at the left and right side of the signal trace (102).

Ground recesses (108) are to introduce extra inductance to create an LC resonance in the frequency band of interest. They can be used to shift the resonance frequency down if needed. The geometry of this recesses (108) can be altered to adjust the resonance frequency for different fluids and biomarkers of interest.

Detection region (107) is the place where the antibodies are immobilized and the antigen-antibody binding events occur. Actually, it is a part of microchannel where the bottom and side walls are formed by the signal trace. When the upper wall of the channel, i.e. cap (109), is formed to connect ground planes to each other, there is a parallel plate capacitor formed between the signal trace and the cap.

In this invention, a novel sacrificial-free microfabrication approach which has been previously used for RF-MEMS switches [12], is exploited for the first time to fabricate the microchannel embedded into the coplanar waveguide.

This approach uses wafer bonding techniques, gold-gold bonding in this example, to create a microchannel instead of using a sacrificial layer and removing it later. Thus, it is become possible to immobilize antibodies selectively in the microchannel either before or after the bonding process.

In this method, the biomarkers of interest (for example bacteria, protein, enzyme or DNA) are trapped by highly specific antibody-antigen binding in the detection region (107) where the sensitivity is maximum. By this novelty, the biomarkers are collected and their density is increased in only electromagnetically high-sensitive region. Then, their presence is detected by observing the change in the electromagnetic performance of the microwave
structure. The detection method using the change in microwave properties are already known. The novelty here is to make this change specific by immobilizing antibodies, not onto the conductors but into the channel thanks to the novel sacrificial-free microfabrication.

Another novelty is that etching ground recesses to create resonance with adjustable frequency and high quality factor increases the sensitivity and the usability of the sensor.

Thanks to the novel design, antibodies are immobilized between the signal (102) and the ground plane (103). Thus, it becomes possible that the biomarkers are trapped by highly specific antibody-antigen binding in the detection region (107).

By this way, the density of only the biomarker of interest is significantly increased and their existence is detected by observing the change in dielectric properties of the fluid.

**The Parts Interact To Make The Invention Work**

In this invention, the microchannel and the co-planar waveguide structure is fabricated with a novel, integrative, sacrificial-free approach using flip-chip bonding. By this way, the fluid in the channel is to be employed as the dielectric material between the signal trace and the microchannel cap (109) which connects the ground planes like a bridge. Thus, the signal is coupled to the ground through the fluid with a coupling coefficient. This coupling creates a capacitance which depends on the dielectric properties, and so the content of the fluid. Note that this coupling mainly occurs in the region (107) where the cap and the signal overlaps and the electromagnetic wave intensity is far higher here. Unlike many other devices in the literature [5],[6] and [7], by the way of this invention the microchannel is integrately fabricated into the RF device which eliminates extra fabrication steps, reduces cost and improves the performance providing flexibility in the design of detection region (107).

During the fabrication of co-planar waveguide, recesses are etched into the ground plane to introduce inductance. This inductance, together with the capacitance created in the detection region (107), results in a resonator structure. The frequency of this resonance can be shifted down to lower frequencies (below 18 GHz) since high-frequency components (over 26 GHz) and measurements setups are expensive in both size and cost.

By the way of sacrificial-free approach, it is possible to functionalize the region (107) selectively. In here, immobilizing antibodies only onto this region is preferred. Thus, it allows to capture and keep the biomarkers, which is bacteria for this example, in the detection
region (107) where the coupling is highly sensitive to the changes in the content of the fluid. In the detection region the bacteria are selectively collected and increased in number owing to the specificity of the antibodies. Moreover, the volume of the fluid in this region is small enough so that the density of the bacteria becomes significantly large to change the dielectric properties of the fluid. This change shifts the resonant frequency of the LC resonator structure.

Antibodies are immobilized between the signal and ground planes (103) not onto them. This enables us both to detect the existence of the bacteria by observing the electromagnetic changes and to confine the detection into where the sensitivity is maximum.

Recesses (108) etched into ground planes (103) is another preferred embodiment to introduce inductance. Thus, there is an LC resonance, together with the capacitance, which has a tunable frequency by adjusting the recess geometry. With this tunability, the steepness of the frequency dip is increased resulting in higher sensitivity.

If the antibodies are not immobilized between the signal and the ground, the change in the electromagnetic performance would not be due to the bacteria content in the fluid. If the detection region (107) is not constrained into small volume, then the density of bacteria may not be enough to change the electromagnetic properties of the fluid. If the ground recesses (108) are not etched, the invention would still work but the frequency dip would be at much higher frequencies and it would be needed that much more expensive tools are used to measure as indicated before.

The microchannel height at the detection region (107) must be small enough that the density of biological substance (bacteria in this example) is large to change the dielectric constant and the coupling ratio.

The inner surface of the signal trace (102) and the microchannel cap (109) will be selectively coated by antibodies to create an antigen-specific, electromagnetically-high-sensitive detection region (107). This coating is better to be uniform for more precise results. Moreover, the antigens are to bind to these antibodies and stay in the detection region (107).

The device subjected to this invention can be used to detect anomalies in fluidics without any receptor element. In this case, the permittivity of the fluid of interest can be observed in real-time. This data can be subjected to temperature compensation and natural variations can be eliminated using historical data as shown in [14]. Hence, a wide range of
changes in material properties can be detected. This kind of sensors can be used for non-specific real-time environmental monitoring and early warning systems.

If the sensor is expected to be specific for substances, then bio/chemical receptor elements are immobilized onto the detection region (107) before wafer bonding. Other than the antibodies given as an example in this invention, these receptor elements can also be compromised of any combination of biological or chemical molecule such as DNA, imiRNA, enzymes, proteins, chemical molecules, ATP etc.

**Structural Alternatives**

The tunability of the resonance frequency can be provided using different design and methods such as etching recesses in signal line rather than the ground plane or connecting a distributed or lumped inductor. Moreover, the recesses and so the extra inductance can be eliminated however the resonance only due to the microchannel cap (109) itself would be at much higher frequencies which requires expensive reading devices and systems.

The frequency spectrum of the electromagnetic waves interacted with the sample of interest can be extended to higher frequencies than radio-frequencies. For example, the frequency used for the detection of dielectric properties can be higher than 300 GHz placing in infrared region of the electromagnetic spectrum.

The upper wafer (110) can be removed after flip-chip bonding and overall top surface of the biosensor can be exposed to deposition for sealing. Or, alternatively, it remains for mechanical robustness and the gaps between non-contacting signal and ground planes can be sealed only.

The upper wafer (110) is another wafer on which the microchannel cap (109) is formed. This wafer is again can be glass, quartz, silicon etc. For this example, another glass wafer is preferred as using the same material provides mechanical stability.

The inlet-outlet ports (104, 105) for microfluidics and the path the fluid flows can be physically changed, for example in geometry, or chemically for hydrophobicity. Barriers can also be introduced into microfluidic channel for filtering purposes.

The bottom and up wafer can be bonded with any techniques. Here, for example, gold-gold thermo-compression bonding is exploited.
It is possible to modify the sensor for multiplexed detection with multiple detection region (107) and immobilizing bio-receptor elements onto each other for various substances. As a significant advantage, this multiplexed sensors can be fabricated integratedly with the same microchannel (106) at a single fabrication step. Thus, the fluid sample flowing through the microchannel (106) can be investigated for different bio/chemical substances (bacteria, viruses etc.)

References


CLAI MS

1. RF sensor characterized in comprising;
   a) Substrate wafer (101) from etchable material, containing
      • wave guide, which includes at least one ground plane (103) and at least one signal trace (102)
      • microchannel bed (106), embedded into wave guide,
      • detection region (107), located where the electromagnetic response of the sensor is the most sensitive to the material properties, especially dielectric properties, of the fluid and
   b) Upper wafer (110) containing microchannel cap (109) layer to form a parallel plate capacitor formed between the signal trace (102) and the microchannel cap (109).

2. Sensor according to claim 1 where etchable material is glass, quartz or silicon.

3. Sensor according to claim 1 where signal trace is made up of conductor material.

4. Sensor according to claim 3 where signal trace (102) is made of metal.

5. Sensor according to claim 1 where signal trace (102) is made of gold or aluminum.

6. Sensor according to claim 1 where signal trace (102) is made of gold.

7. Sensor according to claim 1 where ground planes (103) are placed on both sides of signal trace (102).

8. Sensor according to claim 1 where biomarkers are immobilized on detection region (107).

9. Sensor according to claim 8 where biomarkers are antibody, bacteria, protein, enzyme or DNA.

10. Sensor according to claim 1 which further comprises recesses (108) either on ground plane (103) or on signal trace (102) to introduce extra inductance.
Figure 6

- Fluid Input
- Microchannel
- Detection region
- Co-planar Waveguide
- RF Input
- RF Output
- Fluid Output
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

<table>
<thead>
<tr>
<th>INV.</th>
<th>G91N27/22</th>
<th>G01N27/327</th>
</tr>
</thead>
</table>

According to International Patent Classification (IPC) or to both national classification and IPC.

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

- G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
</table>

X Further documents are listed in the continuation of Box C.

* Special categories of cited documents:
- A: document defining the general state of the art which is not considered to be of particular relevance
- E: earlier invention or patent published on or after the international filing date
- L: document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another invention or other special reason (as specified)
- O: document referring to an oral disclosure, use, exhibition or other means
- P: document published prior to the international filing date but later than the priority date claimed
- T: later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- X: document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- Y: document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- Z: document member of the same patent family

Date of the actual completion of the international search

4 May 2016

Date of mailing of the international search report

13/05/2016

Name and mailing address of the ISA/

European Patent Office, P.B. 5618 PatentDAO 2 NL-2280 HV Rijswijk
Tel. (31-70) 340-2040, Fax (31-70) 340-3048

Authorized officer

Lazar, Zala
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patent document cited in search report</td>
<td>Publication date</td>
<td>Patent family member(s)</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>-----------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>WO 2006104902 Al</td>
<td>05-10-2006</td>
<td>CN 101171509 A</td>
</tr>
<tr>
<td>EP 1861701 Al</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JP 5154400 B2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JP 2008534930 A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KR 20080002874 A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US 2010066389 Al</td>
<td>18-03-2010</td>
<td></td>
</tr>
<tr>
<td>WO 2006104902 Al</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US 2014011697 Al</td>
<td>09-01-2014</td>
<td>NON E</td>
</tr>
<tr>
<td>US 2013302843 Al</td>
<td></td>
<td>US 2013302843 Al</td>
</tr>
<tr>
<td>US 2016033435 Al</td>
<td></td>
<td>US 2016033435 Al</td>
</tr>
</tbody>
</table>