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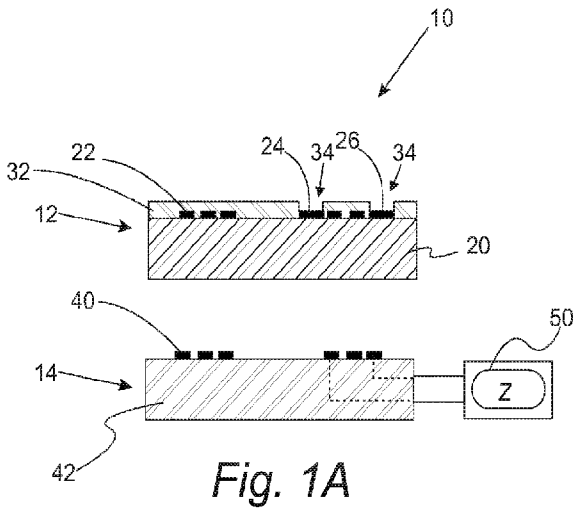


Fig. 1A

(57) Abstract: A sensor for measuring electrochemical impedance includes a primary circuit that includes a primary electrically conducting coil and a secondary circuit that includes a secondary electrically conducting coil. The primary electrically conducting coil is inductively coupled to the secondary circuit. During operation, the secondary electrically conductive couple has contact electrodes that contact a medium for which the impedance is to be measured. An alternating current source energizes the primary electrically conducting coil during impedance measurements.

WO 2017/210669 A1

METHOD FOR CONTACTLESS ELECTROCHEMICAL IMPEDANCE MEASUREMENT

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. provisional application Serial Nos. 62/345,263 filed June 3, 2016 and 62/345,757 filed June 4, 2016, the disclosures of which are hereby incorporated in their entirety by reference herein.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] The invention was made with Government support under Contract No. ECCS1231994 awarded by the National Science Foundation. The Government has certain rights to the invention.

TECHNICAL FIELD

[0003] In at least one aspect, the present invention is related to an apparatus for measuring electrochemical impedance.

BACKGROUND

[0004] Conductivity measurements are conventionally transmitted using a variety of techniques, with each making use of active circuitry such as microcontrollers, ASICs, or discrete components [1-6]. These components, along with an antenna or inductive coil, are typically soldered onto a printed circuit board (PCB). To mitigate cytotoxicity and the immune response, these electronics are typically encapsulated with biocompatible polymers such as Parylene C and PDMS [7-10]. However, the *in vivo* environment continues to pose a formidable challenge for the development of implantable microelectronic systems.

[0005] A variety of factors can induce sensor drift or failure. Water vapor and ion permeation create undesired paths for electric current and can alter critical bias voltages [11]. The inflammatory response to foreign bodies can subject the implant to a highly oxidative or acidic environment [12]. Blood flow and other involuntary movements can subject the implant to chronic and repeated mechanical strain. Such events can damage sensitive components or introduce errors in signal measurement and transmission.

[0006] The presence of the implant should also minimize harm to the host environment. The materials selected for the packaged device should be nontoxic and induce minimal immune response. The use of soft, flexible materials (i.e. those mechanically matching tissue properties) and elimination of sharp corners also serves to minimize damage to tissue [13]. Power requirements for electronics should be kept in check to minimize heating to safe levels.

[0007] To address these issues, an alternate approach would be the use of passive components. Currently, many methods exist to interrogate capacitive signals wirelessly, with notable examples of pressure, force, and strain measurement [13-15]. However, few attempts have been made to enable passive, wireless resistive measurement. One work incorporated a resistive strain gauge with a coil and capacitive element on a polyimide circuit board [16], but this was not intended for use in the wet, *in vivo* environment. Specifically, its coil and transduction elements were fabricated on a stiff substrate and the components are soldered together using non-biocompatible materials. A notable effort utilized eddy currents to passively and wirelessly determine conductivity and thickness of metallic layers [17]. This technique has a different purpose and is difficult to apply to *in vivo* measurements.

[0008] Accordingly, there is a need for improved method of making electrical conductivity and impedance measurements under wet and physiological conditions.

SUMMARY

[0009] The present invention solves one or more problems of the prior art, by providing in at least one embodiment a sensor for measuring electrochemical impedance of a medium. The sensor includes a primary circuit and a secondary circuit. The primary circuit includes a primary electrically conducting coil. The secondary circuit includes a first electrically insulating layer, a secondary

electrically conducting coil disposed over and contacting the first electrically insulating layer, a first metal contact electrode, a second metal contact electrode, and a second electrically insulating layer disposed over the secondary electrically conducting coil. The secondary electrically conducting coil includes a first end and a second end that are attached respectively to the first metal contact electrode and the second metal contact electrode. The second electrically insulating layer defining openings that expose the first metal contact electrode and the second metal contact electrode so that the medium for which measurement are performed can be contacted. The primary electrically conducting coil is inductively coupled to the secondary electrically conducting coil. During operation, an alternating current source energizes (e.g., applies an alternating current to) the primary electrically conducting coil during impedance measurements.

[0010] In another embodiment, a method for measuring electrochemical impedance using the sensor set forth herein is provided. The method includes a step of contacting the first metal contact electrode and the second metal contact electrode of the secondary circuit with a liquid medium for which an impedance is to be measured. The primary electrically conducting coil is positioned proximate to the secondary electrically conducting coil such that the primary electrically conducting coil is inductively coupled to the secondary electrically conducting coil. An alternating current is applied to the primary electrically conducting coil to perform an impedance measurement.

[0011] In still another embodiment, a method for forming the sensor for measuring electrochemical impedance set forth herein is provided. The method includes a step of coating a support substrate with a first electrically insulating layer. An optional adhesion layer and a first metal layer is patterned onto the first electrically insulating layer with the optional adhesion layer if present interposed between the first electrically insulating layer and the first metal layer. The optional adhesion layer and the first metal layer are patterned into a secondary electrically conducting coil with a first contact electrode and a second contact electrode. A second electrically insulating layer is deposited over secondary electrically conducting coil. The first contact electrode and a second contact electrode are then exposed by removing a portion of the second electrically insulating layer. Finally, the support substrate is separated from the first electrically insulating layer to release a secondary circuit.

[0012] Advantageously, the noncontact method and apparatus for measuring electrochemical conductivity of the present invention can be used in wet, ionic environments such as *in vivo* settings.

Chronic recording of physiological signals via the use of implanted sensors has been a long-standing goal for the medical and scientific community. Such sensors would enable continuous monitoring to facilitate greater understanding of disease progression as well as inform course of treatment. However, the *in vivo* environment poses a formidable challenge for the development of telemetry circuitry. The combination of the corrosive environment and constant movement can damage sensitive components or introduce errors in signal measurement and transmission. To minimize harm to the host environment, materials should be nontoxic and flexible. Power requirements should be kept in check to minimize heating to safe levels. Historically, wireless transmission of conductivity or resistivity has been limited to the use of active circuitry (i.e. microcontrollers, ASICs). This burdens system design by adding power constraints, thermal budget concerns, and bulk to the overall package. To address these concerns, the present invention introduces the use of reflected impedance across a pair of inductively coupled coils to achieve wireless resistive measurement. A variety of techniques based on electrochemical impedance measurement have been investigated (e.g. flow, pressure, or liquid volume sensing). This technique is widely applicable for resistive transduction and obviates the need for microcontrollers, discrete electronic components, and batteries. In addition, because of the thin film construction and simplicity, this method and sensing modality can be easily applied to a broad spectrum of applications.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] FIGURE 1A is an idealized schematic cross section of a sensor having a first circuit and a second circuit.

[0014] FIGURE 1B is a top view of the secondary circuit of Figure 1A.

[0015] FIGURE 1C is a top view of the primary circuit of Figure 1A.

[0016] FIGURE 2 is an idealized schematic of the sensor of Figures 1A-C in contact with a medium for performing impedance measurement thereof.

[0017] FIGURE 3: Schematic of reflected impedance principle, where Z_P represents the complex impedance of the primary circuit resistance and capacitance, L_P and L_S the inductances of coupled coils, and Z_S the complex impedance of the load on the secondary circuit. An AC source (LCR

meter) induces current within the secondary circuit across a pair of inductively coupled coils (mutual inductance M).

[0018] FIGURE 4: Equivalent single primary loop circuit with reflected impedance represented as Z_R. As shown in the equation on right, changes in electrochemical impedance (or Z_S in this case) are ultimately manifested as a change in Z_R with n^2 being the turns ratio.

[0019] FIGURE 5A is a schematic flowchart illustrating a method for forming the secondary circuit of the sensor for measuring electrochemical impedance.

[0020] FIGURE 5B is a schematic flowchart illustrating a method for forming the primary circuit of the sensor for measuring electrochemical impedance.

[0021] FIGURE 6: Overview of fabrication process. (i) Deposition of 10 μm thick Parylene C substrate. (ii) Patterning and deposition of Ti adhesion layer and Au. (iii) Deposition of 10 μm Parylene insulation layer, reactive ion etching (O_2) to expose electrode sites, release, and cutout from silicon substrate.

[0022] FIGURE 7: Photograph of microfabricated and released thin film Parylene C device held by forceps. Sixteen turn coil device shown. One, five, and six turn coils were also fabricated.

[0023] FIGURE 8: Inset of Figure 7; micrograph highlighting electrochemical impedance measurement electrodes (300 × 300 μm exposed area).

[0024] FIGURE 9: Secondary circuit schematic, which comprises of insulated Au coil and Randles circuit model of electrodes submersed in electrolyte.

[0025] FIGURE 10: Device under test (DUT) was placed within a Petri dish and submerged in PBS (phosphate buffered saline). Primary electrically conducting coil includes ferrite core to improve inductive coupling with thin film (secondary) coil. Not drawn to scale.

[0026] FIGURE 11: Frequency response of system comprising of the primary electrically conducting coil coupled with the DUT. The excitation signal on the LCR meter was set to 2.198 MHz (minimum system phase to bypass double layer capacitance C_{dl}) for subsequent testing.

[0027] FIGURE 12: Reflected impedance was observed to be inversely proportional to ionic concentration. Deionized water was used as a baseline reference and indicated using the arrow.

[0028] FIGURE 13: Electrochemical impedance of 1× PBS was observed to be inversely proportional to temperature.

[0029] FIGURE 14: Reflected impedance increased with coil misalignment across the range tested, but remained within 5% of baseline measurement.

DETAILED DESCRIPTION

[0030] Reference will now be made in detail to presently preferred compositions, embodiments and methods of the present invention, which constitute the best modes of practicing the invention presently known to the inventors. The Figures are not necessarily to scale. However, it is to be understood that the disclosed embodiments are merely exemplary of the invention that may be embodied in various and alternative forms. Therefore, specific details disclosed herein are not to be interpreted as limiting, but merely as a representative basis for any aspect of the invention and/or as a representative basis for teaching one skilled in the art to variously employ the present invention.

[0031] Except in the examples, or where otherwise expressly indicated, all numerical quantities in this description indicating amounts of material or conditions of reaction and/or use are to be understood as modified by the word "about" in describing the broadest scope of the invention. Practice within the numerical limits stated is generally preferred. Also, unless expressly stated to the contrary: percent, "parts of," and ratio values are by weight; the term "polymer" includes "oligomer," "copolymer," "terpolymer," irregular combinations of these, and the like; molecular weights provided for any polymers refers to weight average molecular weight unless otherwise indicated; the description of a group or class of materials as suitable or preferred for a given purpose in connection with the invention implies that mixtures of any two or more of the members of the group or class are equally suitable or preferred; description of constituents in chemical terms refers to the constituents at the time of addition to any combination specified in the description, and does not necessarily preclude chemical interactions among the constituents of a mixture once mixed; the first definition of an acronym or other abbreviation applies to all subsequent uses herein of the same abbreviation and applies mutatis mutandis to normal grammatical variations of the initially defined abbreviation; and,

unless expressly stated to the contrary, measurement of a property is determined by the same technique as previously or later referenced for the same property.

[0032] It is also to be understood that this invention is not limited to the specific embodiments and methods described below, as specific components and/or conditions may, of course, vary. Furthermore, the terminology used herein is used only for the purpose of describing particular embodiments of the present invention and is not intended to be limiting in any way.

[0033] It must also be noted that, as used in the specification and the appended claims, the singular form "a," "an," and "the" comprise plural referents unless the context clearly indicates otherwise. For example, reference to a component in the singular is intended to comprise a plurality of components.

[0034] The term "comprising" is synonymous with "including," "having," "containing," or "characterized by." These terms are inclusive and open-ended and do not exclude additional, unrecited elements or method steps.

[0035] The phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. When this phrase appears in a clause of the body of a claim, rather than immediately following the preamble, it limits only the element set forth in that clause; other elements are not excluded from the claim as a whole.

[0036] The phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps, plus those that do not materially affect the basic and novel characteristic(s) of the claimed subject matter.

[0037] The terms "comprising", "consisting of", and "consisting essentially of" can be alternatively used. When one of these three terms is used, the presently disclosed and claimed subject matter can include the use of either of the other two terms.

[0038] Abbreviation:

[0039] "PDMS" means polydimethoylsiloxane.

[0040] "PCB" means printed circuit board.

[0041] "PBS" means phosphate buffered saline.

[0042] "RF" means radio frequency.

[0043] With reference to Figures 1A-C, a sensor for measuring electrochemical impedance is provided. Figure 1A is an idealized schematic cross section of the sensor which has a primary circuit and a secondary circuit. Figure 1B is a top view of the secondary circuit. Figure 1C is a top view of the primary circuit. The sensing system 10 includes a secondary circuit 12 and a primary circuit 14. The secondary circuit 12 includes a first electrically insulating layer 20, a secondary electrically conducting coil 22 disposed over and contacting the first electrically insulating layer, and a pair of metal contact electrodes 24, 26. In a refinement, metal contact electrodes 24, 26 are separated by a distance of about 500 μm to 5000 μm. Typically, first electrically insulating layer 20 is a polymeric layer (e.g., poly(p-xylylene) polymers such as Parylene, PDMS, etc.). Secondary electrically conducting coil 22 includes a first end 28 and a second end 30 that are attached to contact electrodes 24, 26, respectively. Conveniently, secondary electrically conducting coil 22 is deposited as a spiraling metal layer onto first electrically insulating layer 20 along with contact electrodes 24, 26. In a refinement, the secondary electrically conducting coil has a spatial extent d_1 (i.e., outer diameter) from 1 to 20 centimeters.

[0044] A second electrically insulating layer 32 is disposed over and contacts secondary electrically conducting coil 22. Typically, second electrically insulating layer 32 is a polymeric layer (e.g., poly(p-xylylene) polymers such as Parylene, PDMS, etc.). Openings 34 and 36 in second electrically insulating layer 32 advantageously expose contact electrodes 24, 26 thereby allow these electrodes to contact a medium when measurements are made. In a refinement, these openings have a cross section from about 100 μm x 100 μm to about 600 μm x 600 μm. In another refinement, these openings have a cross sectional area from about 0.01 mm^2 to about 0.4 mm^2.

[0045] Primary circuit 14 includes a primary electrically conducting coil 40. In one refinement, primary circuit 14 includes electrically insulating substrate 42 over which primary electrically conducting coil 40 is positioned. Although virtually any coil arrangement may be used for primary circuit and primary electrically conducting coil 40, a construction similar to secondary circuit 12 is useful. In a refinement, the primary coil can be completely insulated in a manner similar to the secondary coil. Moreover, electrically conducting coil 40 does not have to be planar and can be a multi-layer coil (e.g., wound insulated wires).

[0046] Alternating current source 50 energizes the primary electrically conducting coil 40 by applying an alternating current thereto. In a refinement, alternating current source 50 is an impedance meter used to measure the impedance of primary electrically conducting coil 40 which is inductively coupled to secondary electrically conducting coil 22 as set forth below.

[0047] The size of the secondary electrically conducting coil 22 is maximized to optimize coupling with the primary electrically conducting coil 40. Coupling can also be improved by increasing the number of turns to capture increased magnetic flux. However, this can result in a large and unwieldy device footprint for implant applications. In a refinement, the number of windings in secondary electrically conducting coil 22 is from 1 to 50. In another refinement, the number of windings in secondary electrically conducting coil 22 is from 2 to 30. The present invention is not limited by the specific dimensions of the spirally metal layers forming secondary electrically conducting coil 22. However, metal layers having a thickness from about 300 angstroms to about 1 micron and widths from about 50 microns to 200 microns are found to be useful for secondary electrically conducting coil 22. Moreover, adjacent windings can be separated by distances of 50 microns to 300 microns.

[0048] Additional improvement in coupling between secondary electrically conducting coil 22 and primary electrically conducting coil 40 can be achieved using a ferrite core on the primary electrically conducting coil. In a refinement, the size and number of turns of the secondary electrically conducting coil are such that the inductance of secondary electrically conducting coil 22 is from 1 to 100 microhenries. Moreover, the size and number of turns of the secondary electrically conducting coil are advantageously such that the coupling coefficient is greater than 0.8. In a refinement, the coupling coefficient is from 0.8 to 1. In this context, the coupling coefficient is given by the following formula:

$$k = \frac{M}{\sqrt{L_1 L_2}}$$

where

k is the coupling coefficient,

M is the mutual inductance,

L_1 is the inductance of the primary electrically conducting coil, and

L_2 is the inductance of the secondary electrically conducting coil. Larger values of the coupling coefficient indicate stronger coupling.

[0049] Primary circuit 14 includes a primary electrically conducting coil 40. In one refinement, primary circuit 14 includes electrically insulating substrate 42 over which primary electrically conducting coil 40 is positioned. Although virtually any coil arrangement may be used for primary circuit and primary electrically conducting coil 40, a construction similar to secondary circuit 12 is useful. Therefore, primary electrically conducting coil 40 can include a spiraling metal layer and can have also a spatial extent d_2 (i.e., outer diameter) from 1 to 20 centimeters. Therefore, the number of windings in primary electrically conducting coil 40 can be from 1 to 50. In another refinement, the number of windings in primary electrically conducting coil 40 can be from 2 to 30. As set forth for the secondary electrically conductive coil, the present invention is not limited by the specific dimensions of the spirally metal layers in primary electrically conducting coil 40. However, metal layers having a thickness from about 300 angstroms to about 1 micron and widths from about 50 microns to 200 microns are found to be useful for primary electrically conducting coil 40. Moreover, adjacent windings can be separated by distances of 50 microns to 300 microns. In a refinement, primary electrically conducting coil 40 can also include contact tabs 43, 44 to assist in attaching a current source to the primary electrically conducting coil.

[0050] With reference to Figures 1A-C and 2, a method for measuring electrochemical impedance with the sensor set forth above is provided. Figure 2 is a schematic illustration showing the contacting of the sensor with a medium. First metal contact electrode 24 and the second metal contact electrode 26 of the secondary circuit 12 are exposed to and contacted with medium 52 (e.g., a liquid medium such as an aqueous medium) for which an impedance is to be measured. Primary electrically conducting coil 40 is positioned proximate to but spatially separated from secondary electrically conducting coil 22 such that primary electrically conducting coil 40 is inductively coupled to secondary electrically conducting coil 22. In this context, proximate to means that primary electrically conducting coil 40 is positioned within a distance d_3 of secondary electrically conducting coil 22 (i.e., between centers) such that the coupling is established (e.g., within 5 centimeters). As set forth above, alternating current source 50 energizes the primary electrically conducting coil 40 by applying an alternating current thereto.

[0051] Non-contact electrochemical impedance measurement is achieved by observing changes in reflected load across the pair of inductively coupled coils 22 and 40. The pair of inductively coupled coils as set forth above shares the properties of a transformer. An alternating current source (e.g. from impedance meter 50) induces a varying magnetic field in the primary electrically conducting coil, which then induces a varying electromotive force in the secondary electrically conducting coil (Figure 3). To simplify, an equivalent single loop model that lumps the secondary circuit into a complex impedance term may be utilized (Figure 4). Due to conservation of energy, a load that is attached to the secondary electrically conducting coil will result in an apparent load on the primary side, as represented in Figure 4 In this manner, changes in the secondary load may be reflected across the inductively coupled coils and measured as changes on the primary side [18].

[0052] In another embodiment, a method for forming a sensor for measuring electrochemical impedance is provided. As depicted in the flowchart of Figure 5A, a substrate 60 is coated with first electrically insulating layer 20 in step a). Virtually any material can be used for substrate 60 so long as ultimately polymeric layer 20 can be removed. A useful substrate is a silicon wafer. In a refinement, first electrically insulating layer 20 is a polymeric layer. Examples of materials for such a polymeric layer include, but are not limited to, poly(p-xylylene) polymers (e.g., Parylene), PDMS, and the like. In step b), an optional adhesion layer 62 and a metal layer 64 are patterned onto first electrically insulating layer 20 with the adhesion layer interposed between the polymeric layer 20 and the metal layer. In this regard, titanium is found to be a particularly useful material for the adhesion layer. Metal layer 64 can be formed from virtually any metal. For example, metal layer 64 can be gold, platinum, aluminum, copper, nickel, cobalt, stainless steel, and the like. Moreover, optional adhesion layer 62 and a metal layer 64 can be deposited by sputtering, evaporation, chemical vapor deposition, and the like. Patterning of metal layer 64 can be achieved with a mask during deposition or by etching after deposition. In particular, optional adhesion layer 62 and a metal layer 64 are patterned to form secondary electrically conducting coil 22. Contact electrodes 24, 26 are also patterned in this step. In step c), second electrically insulating layer 32 is deposited over and contacts secondary coil 22 as well as portion of first electrically insulating layer 20 that are not overcoated with optional adhesion layer 62 and a metal layer 64. Therefore, optional adhesion layer 62 and a metal layer 64 are embedded between first electrically insulating layer 20 and second electrically insulating layer 32. In step d), contact electrodes 24, 26 are exposed with dimensions as set forth above. In step e), substrate 60 is separated from secondary circuit 12. As depicted in Figure 5B, primary circuit 14 is formed by

patterning metal layer 70 onto electrically insulating substrate 42. As set forth above, metal layer 70 can be formed from virtually any metal. For example, metal layer 70 can be gold, platinum, aluminum, copper, nickel, cobalt, stainless steel, and the like and may include an optional adhesion layer. Moreover, metal layer 70 can be deposited by sputtering, evaporation, chemical vapor deposition, and the like. Patterning of metal layer 70 can be achieved with a mask during deposition or by etching after deposition.

[0053] Advantageously, the materials selected for use in the various embodiments have a proven track record for use within the *in vivo* environment. Thin film gold was used for the electrodes due to its inertness and its well-characterized electrochemical properties [19]. Electrode size and spacing were based on previous investigations on electrochemical impedance sensing [20]. The low resistivity of gold also serves advantageous for its use as a coil in RF applications. Parylene C was selected as the substrate and to encapsulate the electrodes and coil, due to its excellent insulation properties as well as its amenability to microfabrication processes [21].

[0054] The following examples illustrate the various embodiments of the present invention. Those skilled in the art will recognize many variations that are within the spirit of the present invention and scope of the claims.

[0055] The fabrication of this thin film polymer device was based on previously reported methods [20]. A pair of Au electrodes (2000 Å thick on 200 Å Ti adhesion layer, 300 μm × 300 μm, 500 μm - 5000 μm electrode-to-electrode spacing) attached to a planar coil (30 mm diameter, 1-16 turns) was patterned and electron beam evaporated onto a flexible Parylene C substrate (10 μm thick) (Figure 6). Following deposition of another 10 μm Parylene insulation layer, electrodes were exposed via O_2 plasma reactive ion etching (Technics RIE, 200 W, 150 mTorr) [22].

[0056] After cutout and release (Figures 7 and 8), the devices were placed in a polystyrene Petri dish and submerged in phosphate buffered saline (PBS) of various concentrations (0.5 - 10×, 8-150 mS/cm [23]) and temperatures (22°C - 65°C) to mimic a range of typical and abnormal *in vivo* conditions. Deionized water was used to establish a baseline impedance reference.

[0057] The secondary circuit comprises of the Au planar coil (L = 11.1 μH, Q ~1.5 at 2.198 MHz) and electrodes submerged in electrolyte, which can be represented by the Randles circuit model (Figure 9). At resonant frequency, the reactance of the capacitive (C_{dl}) and inductive (thin film coil)

elements will be equal in magnitude but opposite in sign. The resulting reflected impedance consists of the remaining resistive element, which is the solution resistance (R_s). The Petri dish (0.8 mm thick base) was placed onto and concentrically aligned with the commercially available primary electrically conducting coil having a ferrite core (24 μH, Q = 180@125 kHz, Wurth Electronics, 50 mm diameter, 22 turns).

[0058] The primary electrically conducting coil was elevated (onto an additional Petri dish to prevent inadvertent coupling with the benchtop) and attached to an LCR meter (Hewlett Packard E4285A) (Figure 10), which provided the AC signal and recorded the reflected impedance. The optimal measurement frequency was determined to be 2.198 MHz (Q = 34.3, minimum phase, 1 V_{p-p}) to bypass the double layer capacitance (C_{dl}) in the Randles circuit (Figure 11) [24]. At this measurement frequency, the impedance is dominated by the solution resistance. Reproducibility of coil position was achieved by observing phase angle measurement and adjusting alignment until minimum phase (< ±1°) was attained. To assess misalignment performance, coil centers were translated up to 5 mm from initial alignment while measuring reflected impedance.

[0059] Reflected electrochemical impedance was measured from fabricated devices and utilized to transduce ionic concentration and temperature of the electrolyte into which the devices were submerged (Figure 12). The observed power draw at the primary electrically conducting coil was approximately 75 μW. Electrochemical impedance of ionic solutions has previously been shown with a direct wired measurement to be inversely proportional to temperature [25]. This relation was measured wirelessly using this reflected impedance method with 1× PBS across a range of different temperatures (Figure 13). Reflected impedance increased linearly with coil misalignment by approximately 1% per mm of coil center offset (Figure 14). The results were achieved with a 5 turn thin film coil, and preliminary results suggest that altering coil diameter and increasing turn count can reduce misalignment effects on baseline impedance measurement.

[0060] While exemplary embodiments are described above, it is not intended that these embodiments describe all possible forms of the invention. Rather, the words used in the specification are words of description rather than limitation, and it is understood that various changes may be made without departing from the spirit and scope of the invention. Additionally, the features of various implementing embodiments may be combined to form further embodiments of the invention.

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WHAT IS CLAIMED IS:

1. A sensor for measuring electrochemical impedance comprising:

a primary circuit that includes a primary electrically conducting coil;

a secondary circuit that includes a first electrically insulating layer, a secondary electrically conducting coil disposed over and contacting the first electrically insulating layer, a first metal contact electrode, a second metal contact electrode, and a second electrically insulating layer disposed over the secondary electrically conducting coil, the secondary electrically conducting coil including a first end and a second end that are attached respectively to the first metal contact electrode and the second metal contact electrode, the second electrically insulating layer defining openings that expose the first metal contact electrode and the second metal contact electrode, wherein the primary electrically conducting coil is inductively coupled to the secondary electrically conducting coil; and

an alternating current source energizing the primary electrically conducting coil during impedance measurements.

2. The sensor of claim 1 wherein during operation, the secondary circuit is positioned in a medium for which the electrical impedance is to be measured.

3. The sensor of claim 1 wherein the primary electrically conducting coil is positioned proximate to but spatially separated from the secondary electrically conducting coil.

4. The sensor of claim 1 wherein the primary electrically conducting coil is positioned within 5 centimeters from the secondary electrically conducting coil.

5. The sensor of claim 1 wherein the alternating current source is an impedance meter.

6. The sensor of claim 1 wherein the first electrically insulating layer is a polymeric substrate.

7. The sensor of claim 1 wherein the second electrically insulating layer is a polymeric layer.

8. The sensor of claim 1 wherein the secondary electrically conducting coil is deposited as a spiraling metal pattern onto the first electrically insulating layer.

9. The sensor of claim 1 wherein a coupling coefficient between the primary electrically conducting coil and the secondary electrically conducting coil is greater than or equal to 0.8.

10. The sensor of claim 1 wherein an inductance of the secondary electrically conducting coil is from 1 to 100 microhenries.

11. A method for measuring electrochemical impedance comprising:

providing a primary circuit that includes a primary electrically conducting coil;

providing a secondary circuit that includes a first electrically insulating layer, a secondary electrically conducting coil disposed over and contacting the first electrically insulating layer, a first metal contact electrode, a second metal contact electrode, and a second electrically insulating layer disposed over the secondary electrically conducting coil, the secondary electrically conducting coil including a first end and a second end that are attached respectively to the first metal contact electrode and the second metal contact electrode, the second electrically insulating layer defining openings that expose the first metal contact electrode and the second metal contact electrode,

contacting the first metal contact electrode and the second metal contact electrode of the secondary circuit with a liquid medium for which an impedance is to be measured;

positioning the primary electrically conducting coil proximate to the secondary electrically conducting coil such that the primary electrically conducting coil is inductively coupled to the secondary electrically conducting coil; and

applying an alternating current to the primary electrically conducting coil to perform an impedance measurement.

12. The method of claim 11 wherein the alternating current is applied from an impedance meter.

13. The method of claim 11 wherein the first electrically insulating layer is a polymeric substrate.

14. The method of claim 11 wherein the second electrically insulating layer is a polymeric layer.

15. The method of claim 11 wherein the secondary electrically conducting coil is deposited as a spiraling metal pattern onto the first electrically insulating layer.

16. The method of claim 11 wherein a coupling coefficient between the primary electrically conducting coil and the secondary electrically conducting coil is greater than or equal to 0.8.

17. The method of claim 11 wherein an inductance of the secondary electrically conducting coil is from 1 to 100 microhenries.

18. A method for forming a sensor for measuring electrochemical impedance comprises:

a) coating a support substrate with a first electrically insulating layer;

b) patterning an optional adhesion layer and a first metal layer onto the first electrically insulating layer with the optional adhesion layer if present interposed between the first electrically insulating layer and the first metal layer, the optional adhesion layer and the first metal layer being patterned into a secondary electrically conducting coil with a first contact electrode and a second contact electrode;

c) depositing a second electrically insulating layer over secondary electrically conducting coil;

d) exposing the first contact electrode and a second contact electrode; and

e) separating the support substrate from the first electrically insulating layer to release a secondary circuit.

19. The method of claim 18 further comprising forming a primary circuit by:

a') patterning a second metal layer onto an electrically insulating substrate.

20. The method of claim 18 wherein the support substrate is a silicon wafer.

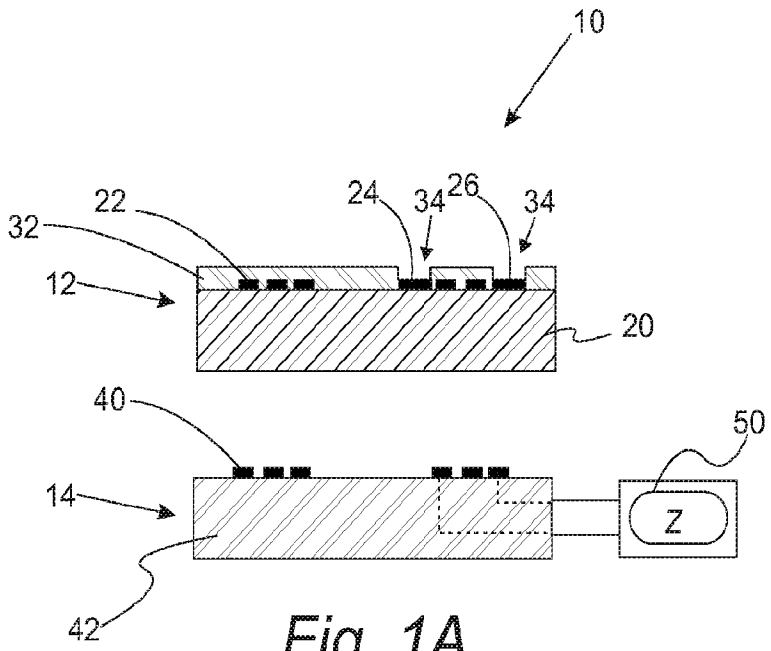


Fig. 1A

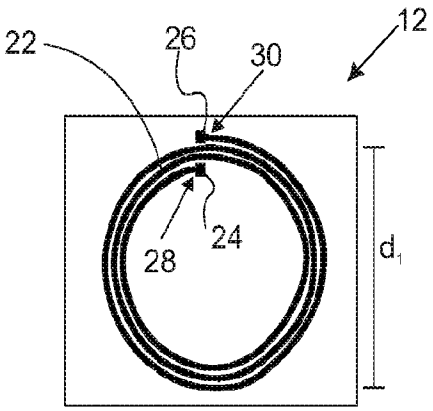


Fig. 1B

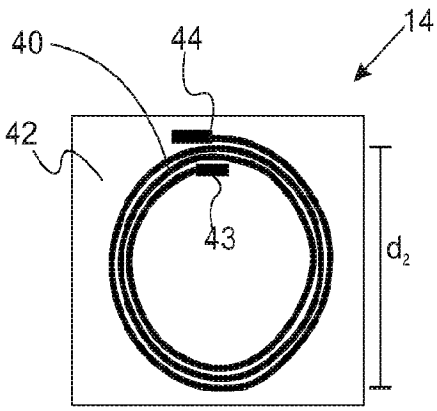


Fig. 1C

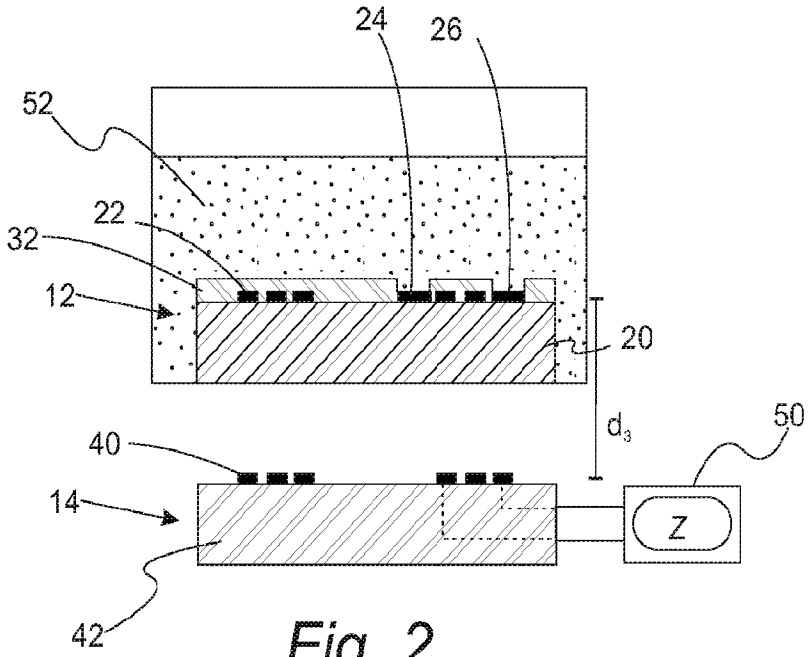


Fig. 2

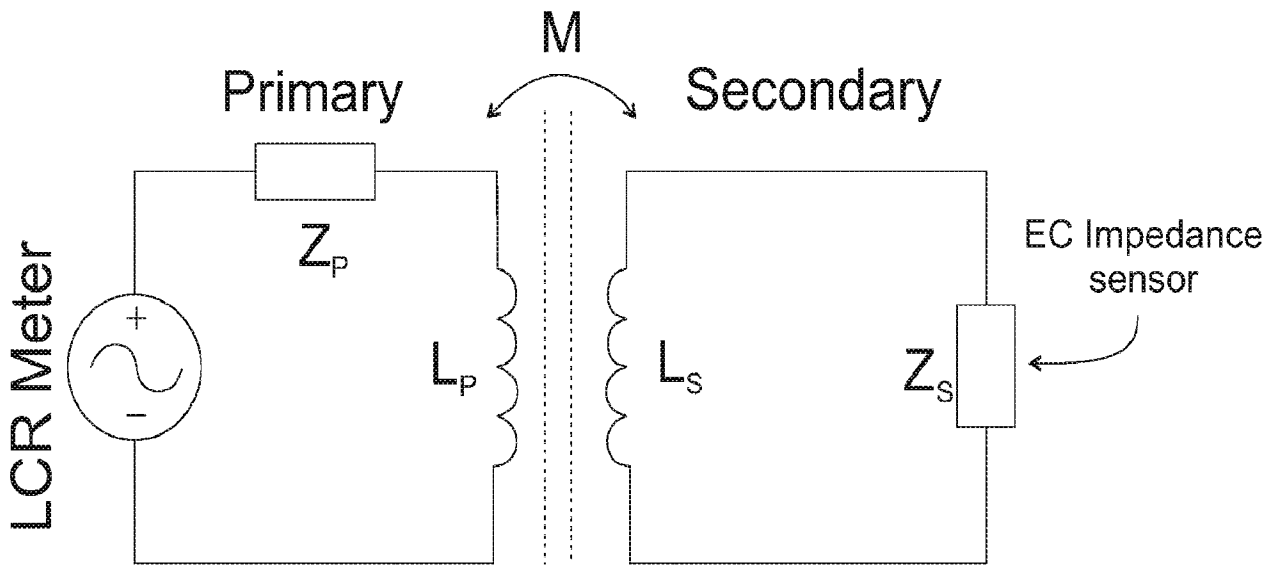
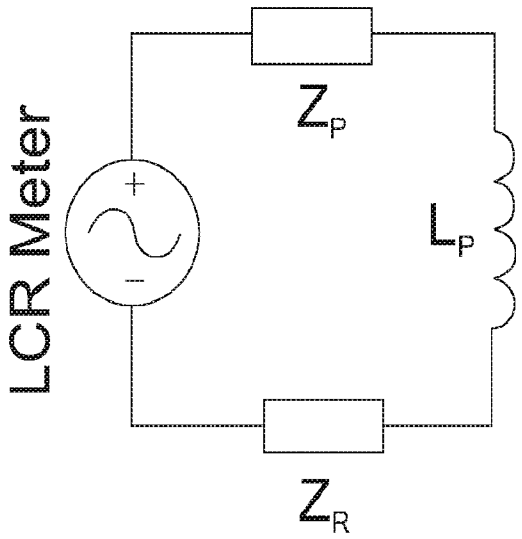


Fig. 3



$$Z_R = n^2 Z_S$$

Fig. 4

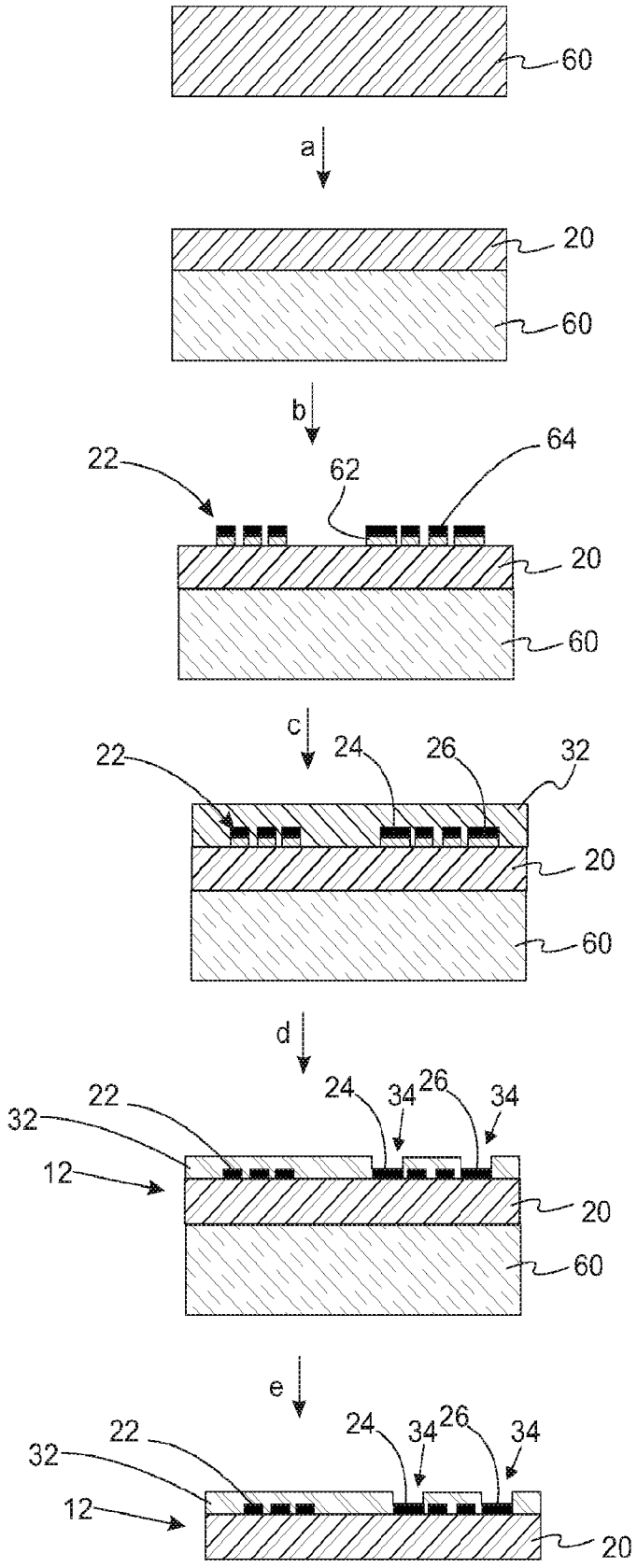

60
a
20
60
b
22
62
64
20
60
c
22
24
26
32
20
60
d
22
32
12
24
34
26
34
20
60
e
22
32
12
24
34
26
34
20

Fig. 5A

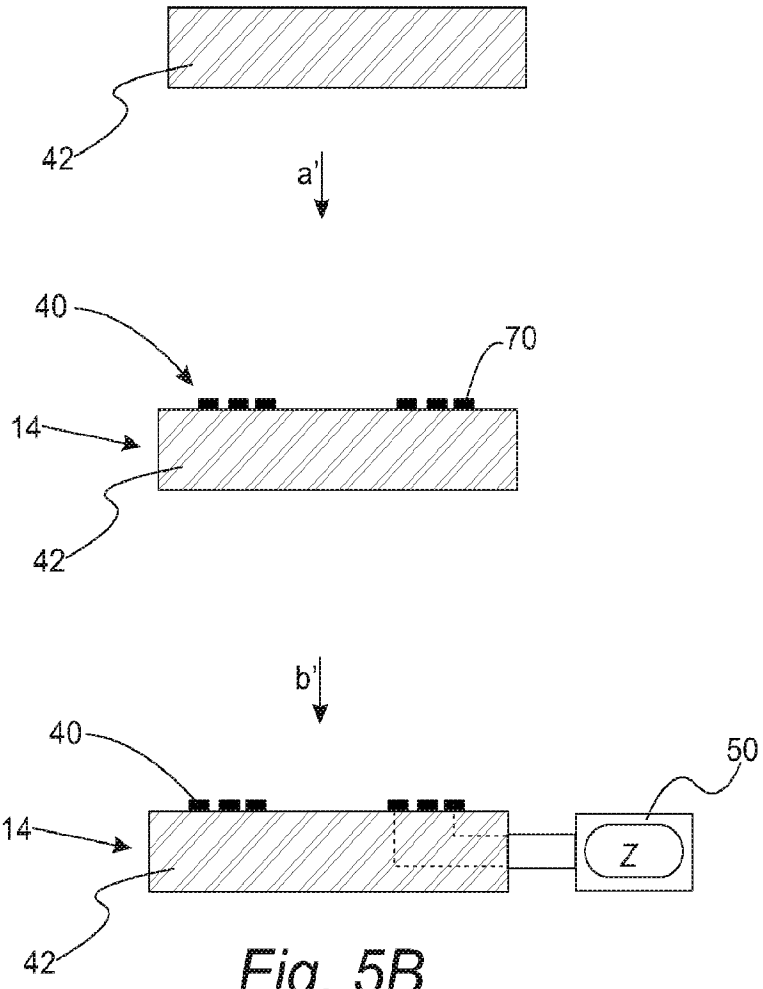


Fig. 5B

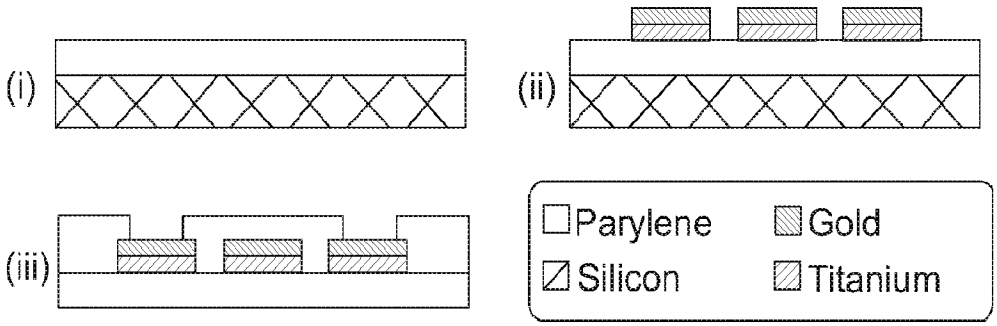


Fig. 6

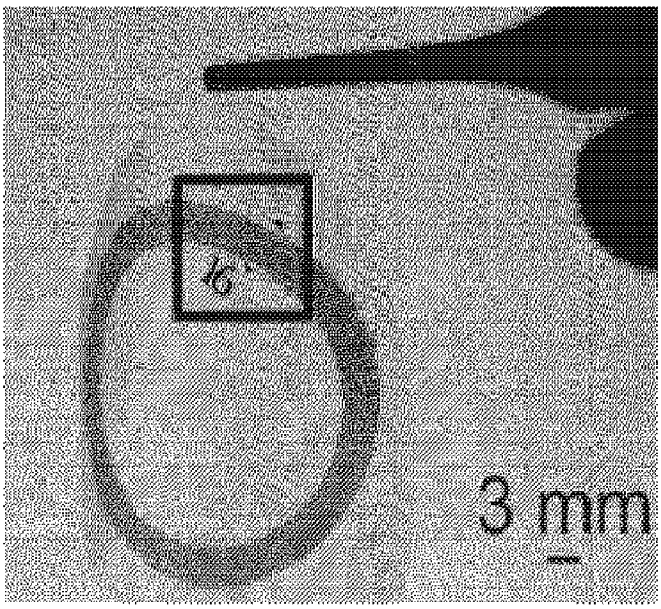


Fig. 7

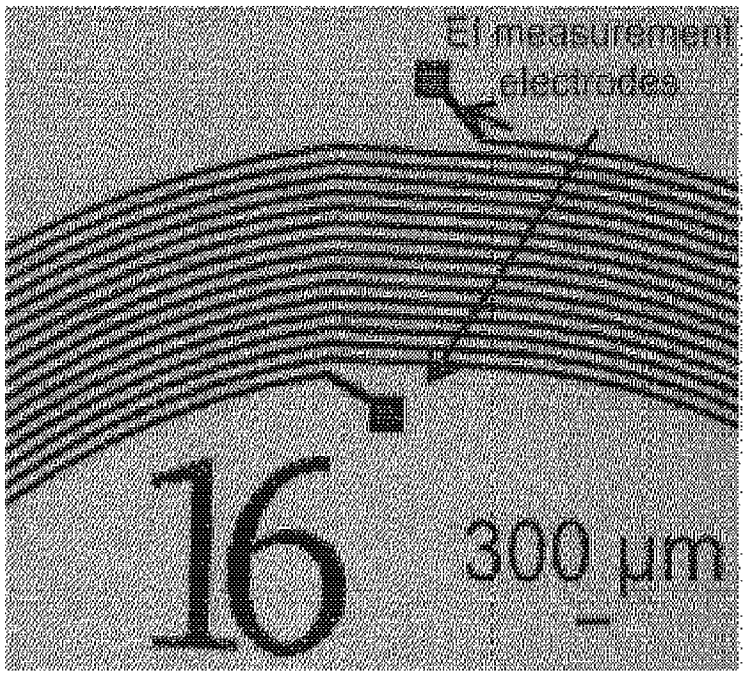

EI measurement
electrodes
16
300 μm

Fig. 8

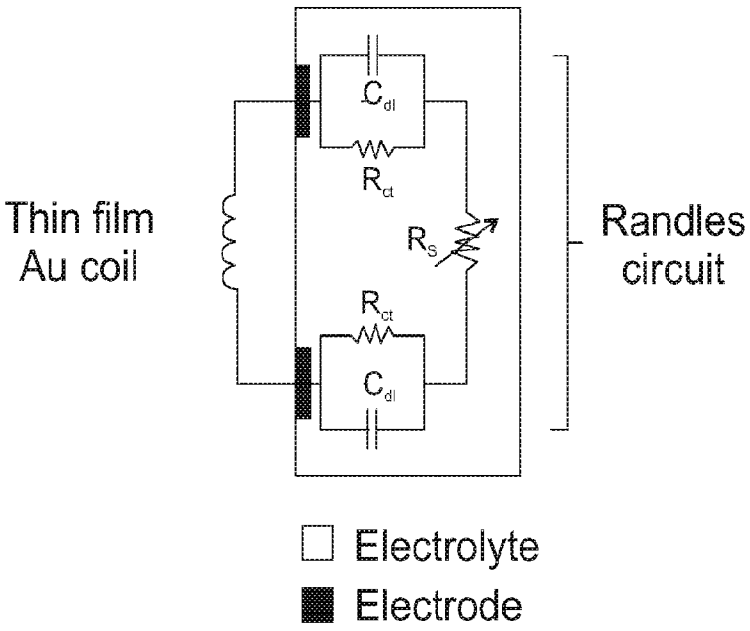

Thin film
Au coil
C_{dl}
R_{ct}
R_s
R_{ct}
C_{dl}
Randles
circuit
Electrolyte
Electrode

Fig. 9

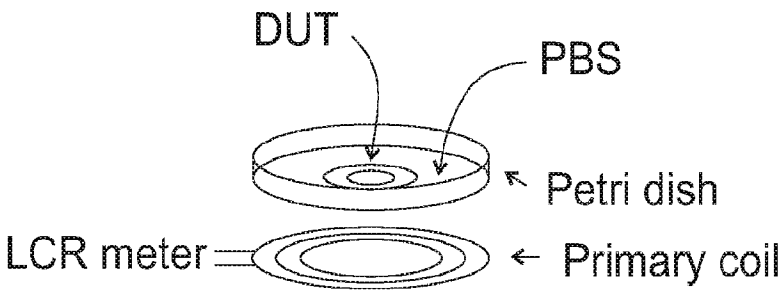


Fig. 10

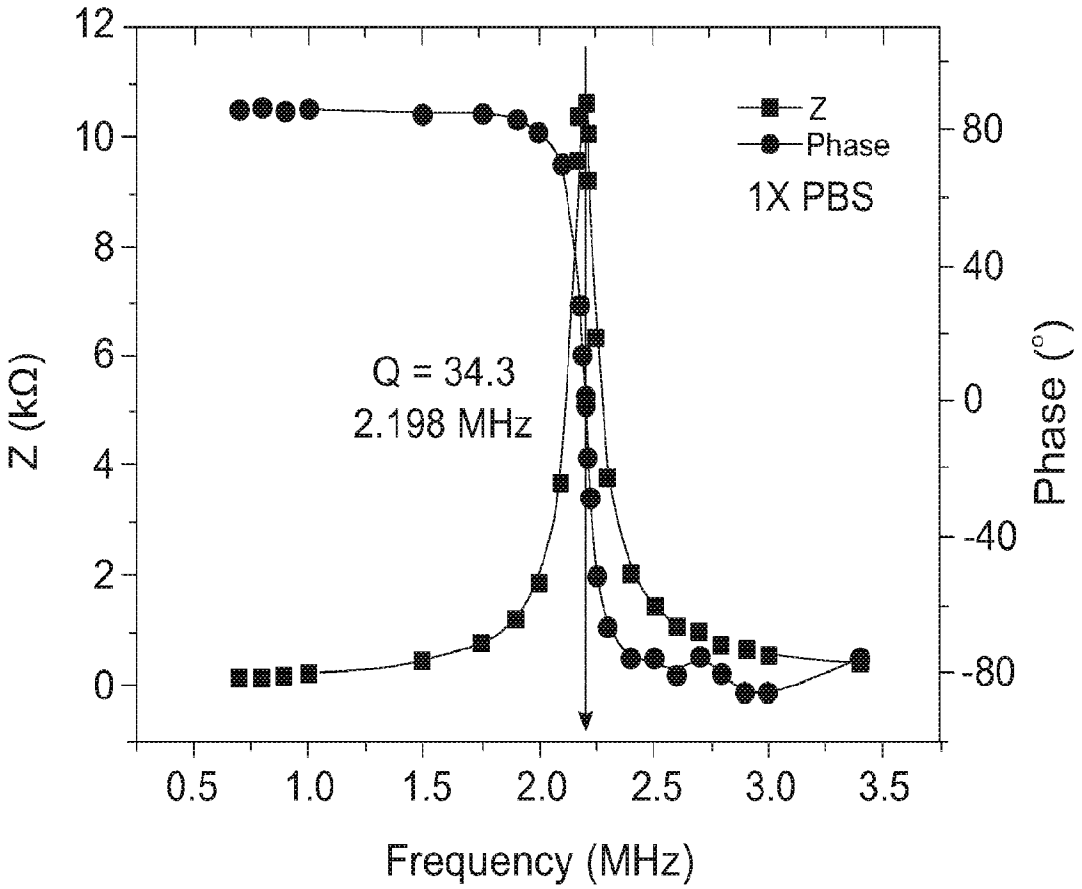

12
10
8
6
4
2
0
Z (kΩ)
80
40
0
-40
-80
Phase (°)
Z
Phase
1X PBS
Q = 34.3
2.198 MHz
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Frequency (MHz)

Fig. 11

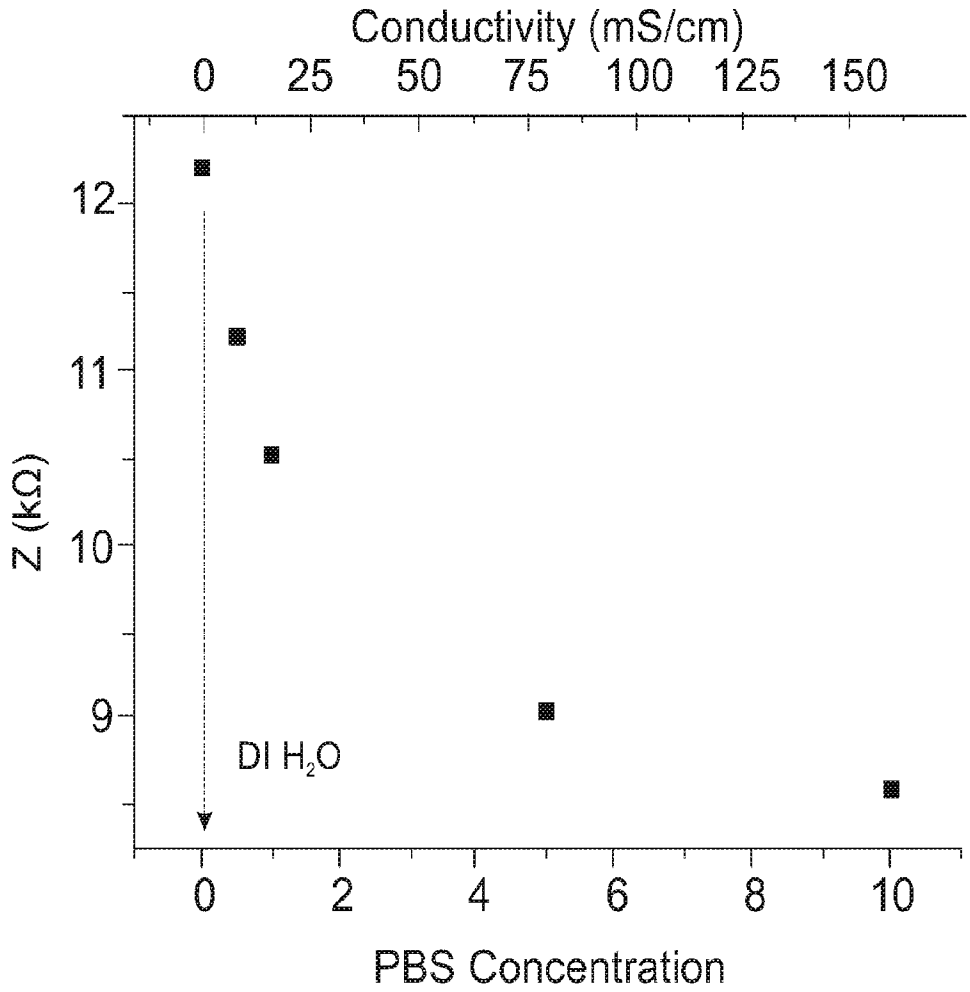

Conductivity (mS/cm)
0
25
50
75
100
125
150
12
11
10
9
Z (kΩ)
DI H2O
0
2
4
6
8
10
PBS Concentration

Fig. 12

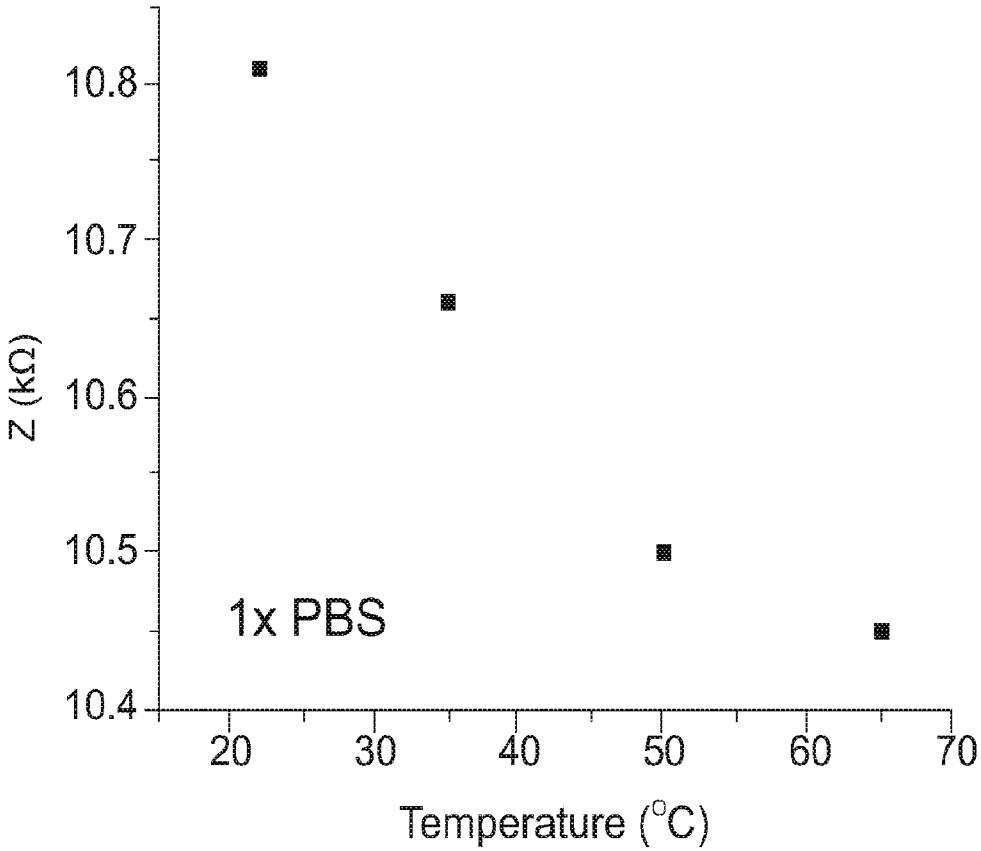


Fig. 13

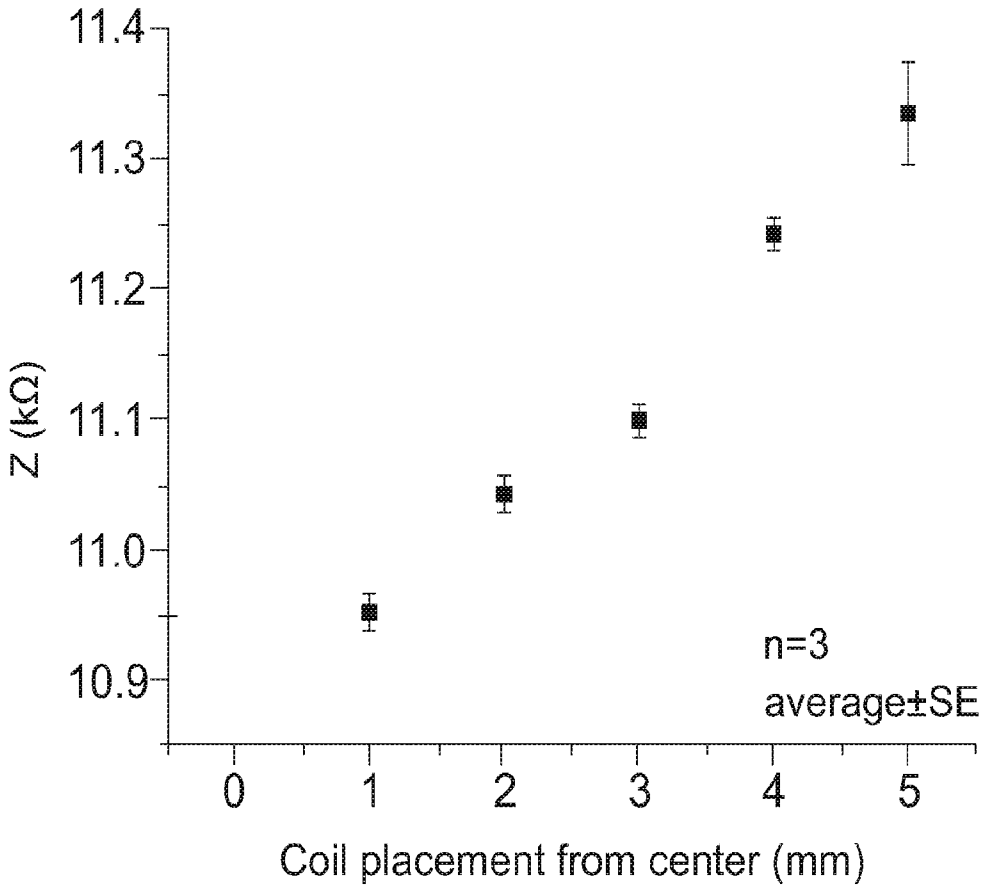

11.4
11.3
11.2
11.1
11.0
10.9
Z (kΩ)
n=3
average±SE
0
1
2
3
4
5
Coil placement from center (mm)

Fig. 14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/035877

A. CLASSIFICATION OF SUBJECT MATTER

G01N 17/02(2006.01)i, G01N 33/28(2006.01)i

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 17/02; G01K 7/24; A61B 5/145; G01N 27/30; H05K 3/30; A61F 13/42; G01N 27/02; A61B 5/1473; H02J 7/02; G01N 33/28

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: impedance, detect, measure, noncontact, electrode, coil, electrochemical, substrate, resistive, strain, medium, implant, device and polymeric

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2015-0053575 A1 (UNIVERSITY OF MANITOBA) 26 February 2015 See paragraphs [0062], [0092]-[0113] and figures 1, 5-8, 12.	1-20
Y	US 2014-0336485 A1 (CALIFORNIA INSTITUTE OF TECHNOLOGY) 13 November 2014 See paragraphs [0045]-[0061], [0095] and figures 3A-3B, 6, 19.	1-20
A	US 2014-0176063 A1 (MILUX HOLDING S.A.) 26 June 2014 See paragraphs [0012]-[0019] and figure 1.	1-20
A	US 2013-0131618 A1 (ABRAHAM et al.) 23 May 2013 See paragraphs [0021]-[0024] and figures 1-2.	1-20
A	US 2014-0002111 A1 (POTYRAILO et al.) 02 January 2014 See paragraphs [0054]-[0055] and figure 1.	1-20

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

☒ See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 August 2017 (25.08.2017)	**25 August 2017 (25.08.2017)**

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LEE, Hun Gil
Telephone No. +82-42-481-8525

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/US2017/035877

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Information on patent family members

International application No.

PCT/US2017/035877

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