



(43) International Publication Date
13 March 2014 (13.03.2014)

(51) International Patent Classification:
G01N 27/327 (2006.01)

(21) International Application Number:
PCT/GB2012/052218

(22) International Filing Date:
7 September 2012 (07.09.2012)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant (for all designated States except US): **CILAG GMBH INTERNATIONAL** [CH/CH]; Landis +Gyr-Strasse 1, CH-6300 Zug (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SETFORD, Steven John** [GB/GB]; 6 Rose Street, Fortrose, Ross-shire IV10 8TN (GB). **SLOSS, Scott J.** [GB/GB]; 15 Cedarwood Avenue, Inverness IV2 6GW (GB).

(74) Agents: **BRUNNER, John Michael Owen** et al.; Carpmaels & Ransford, One Southampton Row, London WC1B 5HA (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: ELECTROCHEMICAL SENSORS AND A METHOD FOR THEIR MANUFACTURE

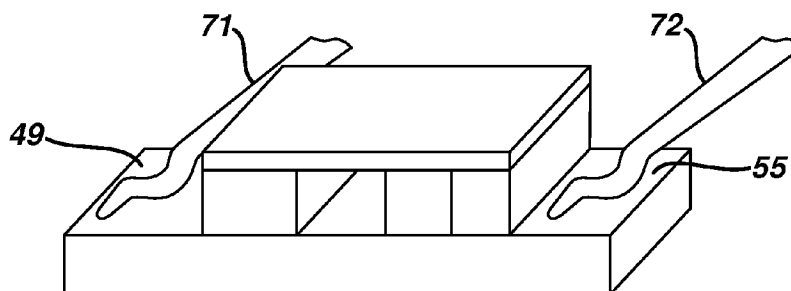


FIG. 4

(57) Abstract: The invention provides electrochemical-based modules useful for the determination of an analyte in a bodily fluid sample. The modules of the invention provide opposed electrodes, but the contact areas for making electrical contact between the electrodes and the analyte measurement device are coplanar.



ELECTROCHEMICAL SENSORS AND A METHOD FOR THEIR MANUFACTURE

Field of the Invention

[0001] The present invention relates to electrochemical sensors and methods for manufacturing the sensors. In particular, the invention relates to sensors with opposed electrodes, but coplanar contact points for purposes of electrical contact between the sensors and an analyte measurement device.

Background of the Invention

[0002] Methods and devices for the analyte detection and concentration measurement in a fluid sample are well known. For example, various devices and methods are known for determining glucose, ketone bodies, cholesterol, lipoproteins, triglycerides, acetaminophen or HbA1c concentrations in a sample of a bodily fluid such as urine, blood, plasma or interstitial fluid. Such determinations can be achieved using analytical test strips, based on, for example, visual, photometric or electrochemical techniques.

[0003] In an electrochemical technique, a fluid sample is placed into a sample chamber of an electrochemical cell of a sensor that includes at least a counter and working electrode. The analyte reacts with a redox reagent in the cell to form an oxidizable or reducible substance. The quantity of oxidizable or reducible substance may be electrochemically determined and related to the amount of the analyte present in the sample.

[0004] In the case of the measurement of glucose in a blood sample, the measurement may be based on the selective oxidation of glucose by means of an enzyme. For example, the enzyme glucose oxidase catalyzes the oxidation of glucose to gluconic acid by transfer of electrons from the glucose molecule to a prosthetic group embedded within the enzyme structure. This prosthetic group, now in a reduced state may be re-oxidized by addition of a suitable mediator which in turn assumes a reduced state. Conducting these reactions within an electrochemical cell with a test voltage applied between two

electrodes creates an output current by the electrochemical re-oxidation of the reduced mediator at the electrode surface. In an ideal environment, stoichiometric principles dictate that the amount of reduced mediator created during the enzymatic reaction is directly proportional to the amount of glucose present in the sample. Therefore, the test current generated is directly proportional to the concentration of glucose in the sample. The current generated may be detected by an analyte measurement device, such as a test meter, used in conjunction with the electrochemical cell or test strip and converted into a glucose concentration reading using an algorithm that relates the test current to a glucose concentration via a simple, mathematical relationship. Conventional electrochemical-based analytical test strips are described in, for example, U.S. Patent Nos. 6,179,979, 6,193,873, 6,284,125, 6,716,577, 6,749,887, 6,797,150, 6,863,801, 6,872,298, 7,045,046, 7,498,132, 7,846,312, 6,413,410 and 7,749,371 each of which is hereby incorporated in its entirety by reference.

[0005] Sensors for use in analyte testing, in which electrochemical cells are incorporated, typically use a carrier material to provide structural integrity and facilitate handling. The carrier materials may take any form, but typically are in the form of a test strip. The costs of sensor manufacture are related to the materials used and certain cost benefits accrue from reducing the quantities of specialized materials used in constructing the test strips, such as by using specialized materials in constructing only the electrochemical cell. However, manipulation of sensors that primarily constitute an electrochemical cell present challenges to end-users due to the resulting reduced size. Additionally, a small-sized strip or sensor increases the potential for contaminating the port of the meter, into which the sensor is placed, with the fluid being analyzed. Therefore, it is desirable for purposes of cost and manipulation to construct sensors having a reduced dimension wherein only the electrochemical cell component is made from specialized materials.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] Figure 1A is a top, plan view of an ECM of the invention.

[0007] Figure 1B is a top plan view of another embodiment of an ECM of the invention.

[0008] Figure 2A is a side view of the ECM of Figure 1A.

[0009] Figure 2B is an exploded view of the ECM of Fig. 2A.

[0010] Figure 3A is a side view of another embodiment of an ECM of the invention.

[0011] Figure 3B is an exploded view of the ECM of Fig. 3A.

[0012] Figure 4 is an elevated cross-section view of the ECM of Fig. 3A and electrical contact pins for an analyte measurement device.

[0013] Figures 5A through 5G depict various stages of production of one embodiment of an ECM of the invention.

[0014] Figures 6A through 6H depict various stages of production of a second embodiment of an ECM of the invention.

Detailed Description of the Invention

[0015] In general, the invention provides electrochemical-based sensors in the form of electrochemical modules (“ECMs”) useful for the determination of an analyte in a bodily fluid sample. The modules of the invention provide opposed electrodes, but the contact areas for making electrical contact between the electrodes and the analyte measurement device are coplanar. The modules of the invention are advantageous in that they are of a small size reducing manufacturing costs and facilitating incorporation of the ECMs into spools, cartridges or the like for purposes of feeding the ECMs into, or manipulating the ECMs within, an analyte measurement device, which eliminates the need for user

handling. Additionally, the ECMs of the invention may be conveniently manufactured using a continuous web-based process.

[0016] The invention provides ECMs comprising, consisting essentially of, and consisting of: a first substrate having a first conductive layer thereon and forming a first substrate-conductive layer assembly wherein the assembly has a first width and length; a second substrate having a second conductive layer thereon and forming a second substrate-conductive layer assembly wherein the assembly has a second width that is less than the first width and a second length that is substantially the same as the first length, the first and second conductive layers being in a facing relationship; a first and a second spacer disposed between the first and second assemblies and maintaining the assemblies in a spaced apart relationship; a chamber formed between the first and second assemblies and configured to receive a fluid sample, the chamber comprising a reagent capable of reacting with an analyte in the fluid sample; and a third spacer adjacent to one of the first or second spacers, a surface of the third spacer comprising a conductive layer that is in electrically conductive contact with the second conductive layer. In another embodiment, the invention provides ECMs comprising, consisting essentially of, and consisting of: a first substrate having a first conductive layer thereon, the first conductive layer comprising a first and second portion having a gap therebetween, the first substrate and first conductive layer forming a first substrate-conductive layer assembly wherein the assembly has a first width and length; a second substrate having a second conductive layer thereon and forming a second substrate-conductive layer assembly wherein the assembly has a second width that is less than the first width and a second length that is substantially the same as the first length wherein the first and second conductive layers are in a facing relationship; a first and a second spacer disposed between the first and second assemblies and maintaining the assemblies in a spaced apart relationship; a chamber formed between the first and second assemblies and configured to receive a fluid sample, wherein the chamber comprises a reagent capable of reacting with an analyte of the fluid sample; and an electrically conductive third spacer adjacent to one of the first or second spacers, wherein the third spacer is in contact with the gap and in

electrically conductive contact with the first and second conductive layers. Additionally, methods of manufacturing the ECM of the invention are provided.

[0017] Although the ECM of the invention may have a variety of shapes, it is preferred that the ECM be of a rectangular shape with the width (“W”) of the ECM being greater than the length (“L”) as shown in Figure 1A. However, as will be understood from the discussion below regarding contact areas between the ECM and the analyte measurement device with which the ECM will be used, other configurations are possible and within the scope of this invention, for example as shown in Figure 1B.

[0018] Referring to Figures 1A, 2A and 2B, ECM 10 is shown with a first substrate 11, which is composed of a non-conductive material. First conductive layer 12 is provided on one surface of substrate 11 and layer 12 and substrate 11 form a first substrate-conductive layer assembly 31. Second substrate 13 formed from a non-conductive material also is shown on one surface of which is provided second conductive layer 14. Second substrate 13 and second conductive layer 14 form second substrate-conductive layer assembly 32. First and second conductive materials 12 and 14 form the electrodes of the ECM and preferably extend across the entire width and length of the respective substrates on which they are provided. Preferably, and as shown, first and second conductive materials 12 and 14 are in a facing relationship. Also preferably, one of the substrate-conductive layer assemblies, as shown substrate 11 and conductive layer 12, has a width (“W₁”) that is greater than that (“W₂”) of the other substrate-conductive layer assembly. In the embodiment shown and preferably, the length (“L₁”) of the first substrate-conductive layer assembly is substantially the same as that (“L₂”) of the second substrate-conductive layer assembly.

[0019] Spacers 15 and 16, composed of non-conductive materials, are interposed between the facing surfaces of conductive layers 12 and 14 and serve to maintain the conductive materials in a spaced-apart relationship. Of note and preferably, is that one

spacer, spacer 15 as shown, has a width (“W₃”) greater than that (“W₄”) of the other spacer 16. The lengths of the spacers may be different, but preferably are the same. The spacers also define the sidewalls of a chamber 17, the top and bottom of which chamber are formed by the substrate-conductive layer assemblies. The chamber receives a fluid to be analyzed and, thus, the dimensions of the spacers must be selected so that the desired chamber size is obtained.

[0020] For convenience and purposes of orientation, the first substrate-conductive layer assembly 31 will be considered to be the bottom and the second substrate-conductive layer 32 will be considered to be the top of the ECM. However, these terms are not meant to limit these layers to a particular orientation.

[0021] As shown spacer 15 is preferably positioned so that its first latitudinal end 18 is positioned in substantial alignment with first latitudinal end 19 of the top substrate-conductive layer assembly 32. However, the latitudinal end 21 of second spacer 16 is positioned so that a gap is formed between it and latitudinal end 22 of the top substrate-conductive layer assembly 32. Immediately adjacent to latitudinal end 21 of spacer 16 is a third spacer 23. Preferably, there is substantially no gap between third spacer 23 and spacer 16. Spacer 23 is composed of a non-conductive material and has a third conductive layer 25 on one surface, which layer 25 faces and is in electrically conductive contact with second conductive layer 14. Third spacer 23 has a width (“W₅”) such that the latitudinal end 26 of third spacer 23 extends beyond the latitudinal end 21 of the top substrate-conductive layer assembly 32 and is preferably substantially aligned with latitudinal end 27 of the first substrate-conductive layer assembly 31.

[0022] Electrical contact between ECM 10 and an analyte measurement device, such as a meter, is provided for at the areas 28 and 29 of first conductive layer 12 and third conductive layer 18, respectively. Thus, areas 28 and 29 are sized and shaped so that the desired reliable, low-resistance contact may be made with the analyte measurement device.

[0023] The size and shape of the ECM 10 and its components may be varied to assume any desired configuration. For example, and as shown in Figure 1B, the ECM may assume a “t”-shaped configuration. In such a configuration, the width of the top and bottom substrate are as described for the ECM 10 of Figure 1A, but the top has an elongated length. One of ordinary skill in the art will recognize that the dimensions of the other components of the ECM of Figure 1B will be adjusted to achieve the desired result.

[0024] Preferably, however, the ECM is shaped substantially similar to Figure 1A and more preferably the width of ECM 10, at its widest portion, is about 3 mm to about 48 mm, and more preferably about 6 mm to about 10 mm, and the length is about 0.5 mm to about 20 mm, more preferably about 1 to 4 mm. The distance between the top conductive layer and the bottom conductive layer will vary depending on the desired chamber size. Preferably, the chamber is of a size such that the fluid volume the chamber may hold is from about 0.1 micro-liters to about 5 micro-liters, more preferably about 0.2 to about 3 micro-liters and most preferably about 0.2 to about 0.4 micro-liters. Preferably, the thicknesses of spacers 15 and 16 are suitable to achieve the desired chamber volume and more preferably may be about 1 microns to about 500 microns, yet more preferably 10 to about 400 microns, still more preferably about 25 to about 200 microns and most preferably about 50 to about 150 microns. The chamber aperture created by the spacers 15 and 16 may be of any desired dimension but preferably is between about 1.00 and about 1.75 mm.

[0025] Substrates 11 and 13 are of any size and shape that achieves the desired ECM configuration. The thickness of the substrates preferably are between about 50 microns to about 200 microns in thickness, preferably about 100 to about 175 microns. The substrates are composed of any suitable electrically-insulating, non-conducting material and, preferably, the material selected has a coefficient of thermal expansion sufficiently small so that the resulting substrate layers do not adversely affect the chamber volume.

Suitable materials include, for example, a nylon substrate, polycarbonate substrate, a polyimide substrate, a polyvinyl chloride substrate, a polyethylene substrate, a polypropylene substrate, a glycolated polyester substrate, a polyester substrate, ceramic, glass or the like and combinations thereof. The substrates are preferably formed of polyethylene terephthalate ("PET"). Optionally, the substrates may contain one or more fillers to control physical properties. The top substrate layer is preferably wholly or partially translucent or transparent, or includes a translucent or transparent window, so that filling of the strip chamber with the fluid to be analyzed may be seen by the user. Although, for the purpose of explanation only, ECM 10 has two conductive layers forming two electrodes, and one chamber therein the ECM may be designed to include any suitable number of electrodes, chambers and conductive layers.

[0026] First and second conductive layers 12 and 14 may be deposited on substrate 11 by any suitable deposition method including thin film deposition, sputtering, spray coating, electro-less plating, thermal evaporation, printing methods including screen printing, and the like and combinations thereof. Conductive layers 12 and 14 are formed from any suitable, electrically conductive material including, metals such as gold, palladium, platinum, tin-oxide, iridium, indium, and titanium-palladium alloys and non-metals including electrically carbon-based materials with or without electro-catalytic materials, graphene and the like and combinations thereof. Preferably, the material is a metal and more preferably, one of the conductive layers is formed of palladium and the other is formed of gold, and more preferably the conductive layer on which the reagent is deposited is gold and the other is palladium or both are gold. A preferred deposition method of these materials is by sputtering. The conductive layers may be of any suitable thickness. If a thick film is desired, the thickness typically will be about 5 to 20 mm. If a thin film is desired, the thickness will be about 10 to about 100 nanometers.

[0027] The reagent 24 as shown is disposed on one of the conductive layers, but may be disposed on multiple surfaces of the chamber. The reagent may cover an area of any desired dimensions, but in ECM 10 as shown in Figure 1A the reagent will have a width

of between about 1 and 4 mm and preferably about 2.25 to 3 mm, a length of about 2 to about 3.5 microns, and a height to about 2 to about 10 microns. The reagent may be any reagent useful in carrying out the analyte analysis desired and may be formed from various materials including mediators, enzymes and the like and combinations thereof. Preferably, the reagent will be of a formulation that is capable of recognizing one or more specific target analytes for example, a biological marker molecule in a fluid sample. Thus, the reagent may include enzyme such as redox enzyme and enzymes requiring co-factors for the oxidation or reduction of analyte species and more specifically may include glucose oxidase, glucose dehydrogenase ("GDH") containing a pyrroloquinone co-factor, GDH containing a nicotinamide adenine dinucleotide cofactor, or a GDH containing a flavin adenosine dinucleotide. Additionally, the reagent may include, antibodies, and other binding ligands such as receptors as well as species that facilitate electrochemical determination of the analytes including redox species, solubilization reagents, buffers, salts, wetting agents such as surfactants and other ionic and non-ionic species. A preferred reagent will contain reagents capable of determining metabolites such as glucose, lactate, ketone bodies, cholesterol and the like. An exemplary reagent formulation is described in U.S. Patent No. 7,291,256 incorporated in its entirety herein by reference. The reagent and be deposited by any convenient, known method including slot-coating, dispensing from the end of a tube, ink-jet printing, and screen-printing. Suitable exemplary processes are described in U.S. Patent Nos. 6,749,887; 6,676,995; and 6,830,934 all incorporated in their entireties herein by reference.

[0028] Spacers 15, 16 and 23 may be of any suitable thickness and typically will be between about 25 to about 200 microns in thickness, more preferably between about 70 and about 110 microns. The spacers may be formed from a suitable non-conductive material and preferably from such a material that exhibits a degree of flexibility suitable for use in web-based manufacturing. Suitable electrically resistive materials which may be preferred include materials such as polyesters, polystyrenes, polycarbonates, polyolefins, polyethylene terephthalate, glasses, ceramics, mixtures and the like and combinations thereof. Preferably, the material used is MELINEX®, available from Du

Pont, with double-sided coatings of a heat activated adhesive, more preferably with double-sided coating of ARCare™ 90503 available from Adhesives Research. A separate adhesive layer, preferably heat activated adhesive and more preferably ARCare™ 90503 may be applied to attach the spacer to the conductive layers.

[0029] Alternatively, the spacers may function as a double-sided adhesive to adhere the top and bottom surfaces of the spacers to the conductive material layers. Thus, the spacers may be formed of an electrically resistive material with an adhesive property. Suitable adhesives include, for example, heat activated adhesives, pressure sensitive adhesives, heat cured adhesives, chemically cured adhesives, hot melt adhesives, hot flow adhesives, and the like. Suitable adhesive include those described in U.S. Patent Application Serial No. 12/570,268 which is incorporated in its entirety herein by reference. Pressure sensitive adhesives may be preferred for use in certain embodiments where simplification of fabrication is desired, but the tackiness of pressure sensitive adhesives may result in fabrication tool gumming or product tackiness. In such embodiments, heat or chemically cured adhesives are generally preferred. Especially preferred are the heat-activated and heat-cured adhesives that can be conveniently activated at the appropriate time.

[0030] A hot melt adhesive, which is a solvent-free thermoplastic material that is solid at room temperature and is applied in molten form to a surface to which it adheres when cooled to a temperature below its melting point, may also be used. Polyester hot melt adhesives preferred, available, for example, from Bostik Corp. of Middleton, Massachusetts, are linear saturated polyester hot melts exhibiting melting points from about 65 °C up to about 220 °C. and range from completely amorphous to highly crystalline in nature. Polyamide (nylon) hot melt adhesives, available from Bostik, may also be used, including both dimer-acid and nylon-type polyamide adhesives. Suitable hot melt adhesive chemistries include ethyl vinyl acetate, polyethylene, and polypropylene.

[0031] Lamination techniques may also be used to bond the spacer layers to the conductive layers and suitable lamination techniques are described in U.S. Pat. No. 6,596,112 incorporated herein in its entirety by reference. In general, the layers to be laminated are placed adjacent to each other and heat is applied, whereby a bond between the layers is formed. Pressure may also be applied to aid in forming the bond.

[0032] Third conductive layer 25 of third spacer 23 may be formed from the materials as disclosed above for conductive layers 12 and 14. Third conductive layer 25 preferably forms a reliable, low resistance interface with second conductive layer 14. The formation of such an interface provides an electrically conductive contact between layers 25 and 14 and may be accomplished by use of a suitable conductive adhesive as the third conductive layer or as a layer intermediate these surfaces. This intermediate layer may be applied by any suitable means including printing or applying it as a transfer adhesive. More preferably the conductive adhesive is either pressure or temperature activated. If it is printed the layer preferably is between about 5 to about 15 μm in thickness and if transferred on is between about 25 to about 50 μm thick. Alternatively, a reliable interface between conductive layers 25 and 14 is formed by using thermal lamination to provide a fused joint. As yet another alternative, the meter in which the ECM is used may include a contact that applies pressure to the top of substrate 13.

[0033] Referring to Figures 3 and 3B, another embodiment of the invention is shown. ECM 40 has a first substrate 41 with first conductive layer 42 is provided on one surface. First conductive layer 42 is composed of two portions 56 and 57 with a gap 54 therebetween that is sufficient to ensure that portions 56 and 57 are isolated from each other so that substantially no electrical conduction occurs between them. Gap 54 may be formed by any convenient method, but preferably is formed by laser ablation of first conductive layer 42. Second substrate 43 also is shown on one surface of which is provided second conductive layer 44, which conductive layer 44 preferably extends across the entire width and length of substrate 43. Preferably, and as shown, first and second conductive materials 42 and 44 are in a facing relationship. Also preferably, one

of the substrate-conductive layer assemblies, has a width that is greater than that of the other substrate-conductive layer assembly with the lengths being substantially the same.

[0034] Spacers 45 and 46, composed of non-conductive materials, are interposed between conductive layers 42 and 44. A chamber 47 is provided between spacers 45 and 46 and within the chamber is reagent 48. As shown spacer 45 is preferably positioned so that its first latitudinal end 62 is positioned in alignment with first latitudinal end 63 of the top substrate-conductive layer assembly 52. However, the latitudinal end 64 of second spacer 46 is positioned so that a gap is formed between it and latitudinal end 65 of the top substrate-conductive layer assembly 52. Immediately adjacent to latitudinal end 64 of spacer 46 is a third spacer 53 which is conductive. Preferably, there is substantially no gap between third spacer 53 and spacer 46.

[0035] Spacer 53 is composed of a suitable conductive material which is in electrically conductive contact with second conductive layer 44 as well as first conductive layer 42. For example, spacer 53 may be applied as a solid, semi-solid or liquid that solidifies *in-situ*. Exemplary materials include double-sided conductive tape such as 3M 9712 (125 microns), polyester mesh with acrylic adhesive and conductive carbon filler. Conductive spacer 53 has a width such that its latitudinal end 66 is substantially aligned with the latitudinal end 65 of the top substrate-conductive layer assembly 52.

[0036] Electrical contact between ECM 40 and an analyte measurement device, such as a meter, is provided for at areas 55 and 49 of first conductive layer 42. Thus, areas 55 and 49 are sized and shaped so that the desired reliable, low-resistance contact may be made with the analyte measurement device. Figure 4 depicts ECM and electrical contact pins 71 and 72 of an analyte measurement contacting areas 55 and 49 of ECM 40.

[0037] In use, an analyte measurement device will connect to the two electrical contact areas of the ECMs of the invention to form a complete circuit. In one embodiment, a circuit disposed in the measurement device can apply a test potential or current between

the two contact areas. In a fluid detection mode, the measurement device will apply a constant current of suitable amperage between the electrodes of the ECM. A fluid sample is delivered to the chamber of the ECM until the chamber is filled. When the fluid sample bridges the gap between the electrodes, the measurement device will measure a voltage decrease below a predetermined threshold resulting in initiation of analyte as described in U.S. patent No. 6,193,873 incorporated in its entirety herein by reference. Suitable analyte measurements devices include battery-powered, hand-held meters controlled by on-board micro-processors with circuitry for applying predetermined potentials.

[0038] Manufacture of the ECMs of the invention of the invention may be accomplished by any known method. Preferably, a continuous, web process is used for mass production of the ECMs One process is shown in Figures 5A through 5G. A metal, such as gold or palladium, is sputter-coated onto one surface of a web of a first substrate material, such as PET, that has a generally elongate, rectangular configuration to provide a conductive film as shown in Figure 5A. Multiple reagent stripes of the same or different material are dispensed onto portions of the conductive layer as shown in Figure 5B. Spacers, of unequal width, with or composed of adhesive layers covered by a release liner, are laminated on either side of the reagent as shown in Figure 5C. The latitudinal end of either spacer does not extend to the latitudinal end of the substrate-metal web. In Figure 5D is shown a third spacer, one surface of which is has been sputter-coated with a suitable conducting material such as gold, applied adjacent to the spacer that was previously applied and which has the smaller width. The third spacer is applied so that no electrical connection is established with the palladium or gold coated substrate. A second substrate, as seen in Figure 5E, the inner facing of which is gold coated, is then laminated onto the spacers. The three different tracks, A, B, and C, of ECMs shown in Figure 5 E may be separated by cutting length-wise along lines I and II to form single continuous tracks of ECMs as shown in Figure 5F. Each of the continuous tracks in then cut width-wise to form multiple, singulated ECMs as shown in Figure 5G. Alternatively, a continuous track may be scored width-wise, but not cut, so as to form a continuous

ribbon of ECMs each of which may, if required, be torn or cut along the score line for disposal after use.

[0039] Another process for manufacturing ECMs of the invention is shown in Figures 6A through 6 H. A conductive film is laminated onto a first substrate material, such as PET, that has a generally elongate, rectangular configuration to provide a conductive film as shown in Figure 6A. Multiple length-wise areas of the conductive surface are laser ablated to strip the conductive film from those areas as shown in Figure 6B. Multiple reagent strips of the same or different material are dispensed onto portions of the conductive layer as shown in Figure 6C. Non-conductive spacers, of unequal width, with or composed of adhesive layers covered by a release liner are laminated on either side of the reagent as shown in Figure 6D. A third conductive spacer is applied so as to overlay a portion of the gap formed by ablation in the first conductive layer as the conductive material of the first conductive layer, as shown in Figure 6E, to establish an electrical connection between the first and second conductive layers of the ECM. A second substrate, as seen in Figure 6F the inner facing surface of which is coated with an electrically conductive coating, is then laminated onto the spacers. The three different tracks, A, B, and C, of ECMs shown in Figure 6F may be separated by cutting length-wise along lines I and II to form single continuous tracks of ECMs as shown in Figure 6G. Each of the continuous tracks is then cut width-wise to form multiple, singulated ECMs as shown in Figure 6H.

[0040] Preferably, the ECMs of the invention are not used in conjunction with a carrier. However, the ECMs may be incorporated with a carrier to provide additional structural integrity and facilitate handling. Suitable carriers are disclosed in U.S. Patent Application Serial No. 13/090,620 incorporated in its entirety herein by reference. Such a carrier may be formed from any suitable material and preferably is formed from inexpensive materials, such as plastic or cardboard, that are non-conductive and that do not chemically react the ECM over time.

What is claimed is:

1. An electrochemical module, comprising:

a first substrate having a first conductive layer thereon and forming a first substrate-conductive layer assembly wherein the assembly has a first width and a first length;

a second substrate having a second conductive layer thereon and forming a second substrate-conductive layer assembly wherein the assembly has a second width that is less than the first width and a second length that is substantially the same as the first length wherein the first and second conductive layers are in a facing relationship;

a first and a second spacer disposed between the first and second assemblies and maintaining the assemblies in a spaced apart relationship;

a chamber formed between the first and second assemblies and configured to receive a fluid sample, wherein the chamber comprises a reagent capable of reacting with an analyte in the fluid sample; and

and a third spacer adjacent to one of the first or second spacers, a surface of the third spacer comprising a conductive layer that is in electrically conductive contact with the second conductive layer.

2. The module of claim 1, wherein the first width is about 3 mm to about 48 mm, and more preferably about 6 mm to about 10 mm, and the first length is about 0.5 mm to about 20 mm, more preferably about 1 to 4 mm.

3. The module of claim 1 or 2, wherein the chamber comprises a size such that the fluid volume within the chamber is from about 0.1 micro-liters to about 5 micro-liters.

4. The module of claim 1, wherein the first and second conductive layers comprise a metal selected from the group consisting of gold, palladium, platinum, tin-oxide, iridium, indium, titanium-palladium alloys, and combinations thereof.

5. The module of claim 4, wherein the first and second conductive layers comprise the same metal.

6. The module of claim 1, wherein one of the first and second conductive layers comprises palladium and one of the first and second conductive layers comprises gold.

7. The module of claim 1, wherein the first and second conductive layers comprise a non-metal selected from the group consisting of carbon-based materials, carbon-based materials with electro-catalytic materials, graphene, and combinations thereof.

8. An electrochemical module, comprising

a first substrate having a first conductive layer thereon, the first conductive layer comprising a first and second portion having a gap therebetween, the first substrate and first conductive layer forming a first substrate-conductive layer assembly wherein the assembly has a first width and a first length;

a second substrate having a second conductive layer thereon and forming a second substrate-conductive layer assembly wherein the assembly has a second width that is less than the first width and a second length that is substantially the same as the first length wherein the first and second conductive layers are in a facing relationship;

a first and a second spacer disposed between the first and second assemblies and maintaining the assemblies in a spaced apart relationship;

a chamber formed between the first and second assemblies and configured to receive a fluid sample, wherein the chamber comprises a reagent capable of reacting with an analyte in the fluid sample; and

an electrically conductive third spacer adjacent to one of the first or second spacers, wherein the third spacer is in contact with at least a portion of the gap and in electrically conductive contact with the first and second conductive layers.

9. The module of claim 8, wherein the first width is about 3 mm to about 48 mm, and more preferably about 6 mm to about 10 mm, and the first length is about 0.5 mm to about 20 mm, more preferably about 1 to 4 mm.

10. The module of claim 8 or 9, wherein the chamber comprises a size such that the fluid volume within the chamber is from about 0.1 micro-liters to about 5 micro-liters.

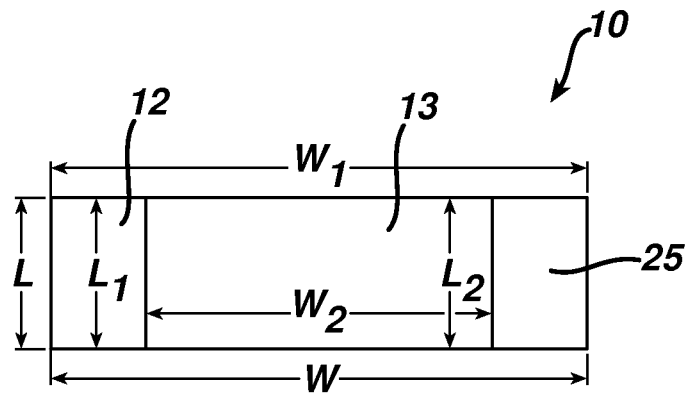
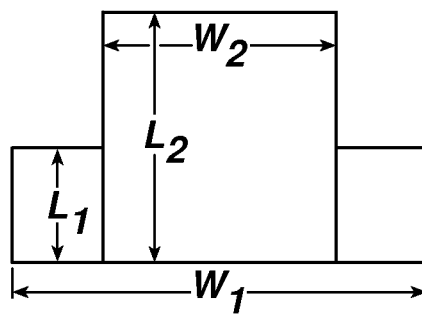
11. The module of claim 8, wherein the first and second conductive layers comprise a metal selected from the group consisting of gold, palladium, platinum, tin-oxide, iridium, indium, titanium-palladium alloys, and combinations thereof.

12. The module of claim 11, wherein the first and second conductive layers comprise the same metal.

13. The module of claim 8, wherein one of the first and second conductive layers comprises palladium and one of the first and second conductive layers comprises gold.

14. The module of claim 8, wherein the first and second conductive layers comprise a non-metal selected from the group consisting of carbon-based materials, carbon-based materials with electro-catalytic materials, graphene, and combinations thereof.

1/6

**FIG. 1A****FIG. 1B**

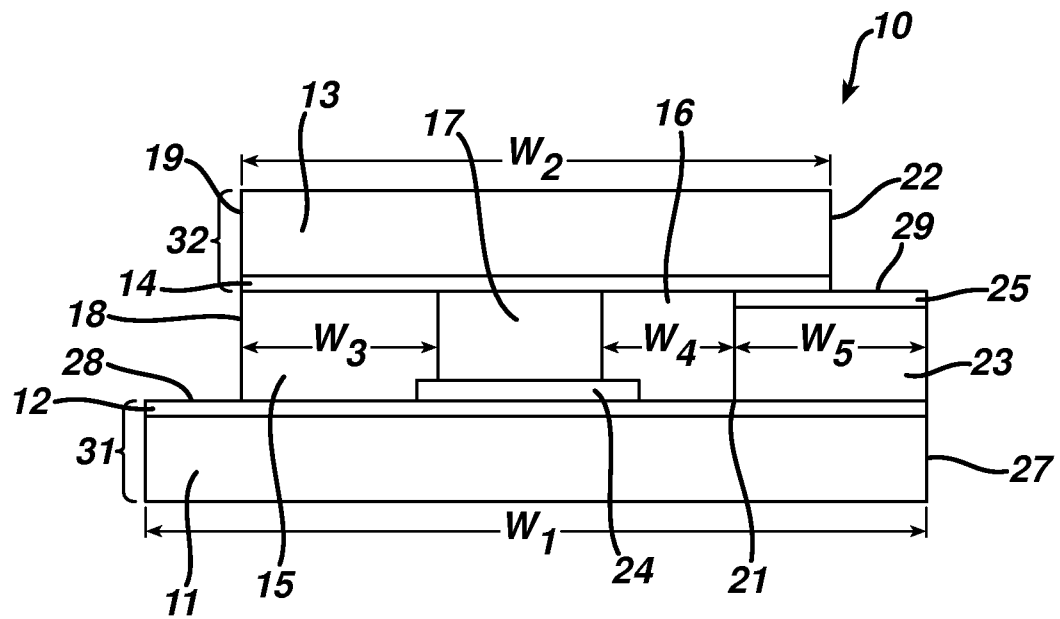


FIG. 2A

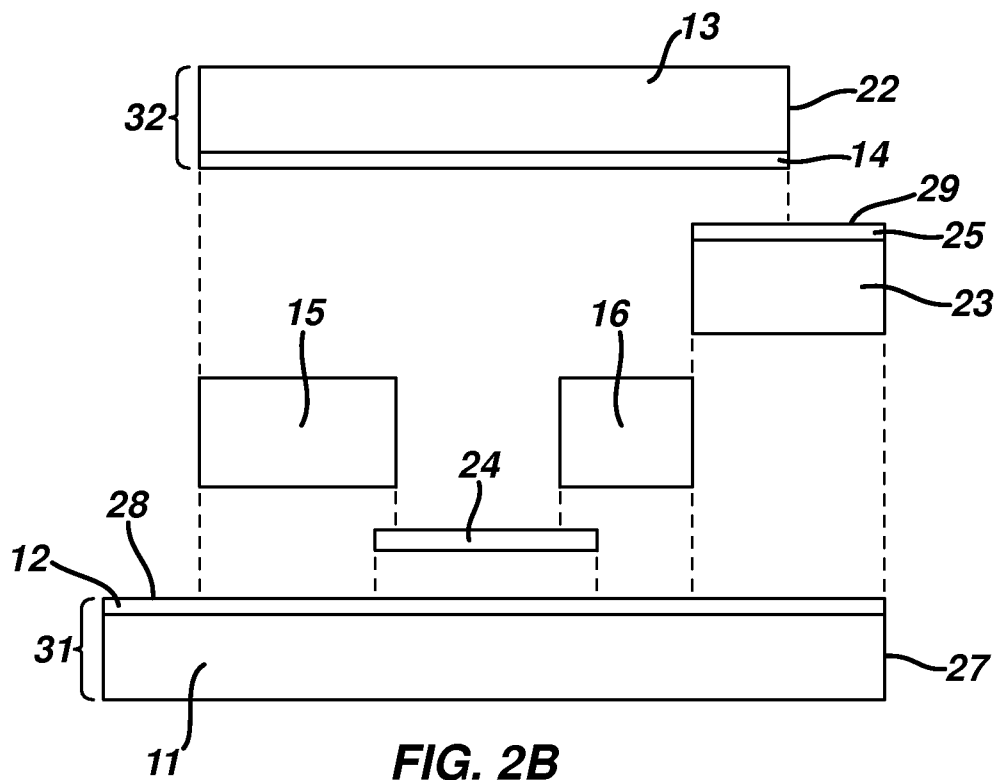


FIG. 2B

3/6

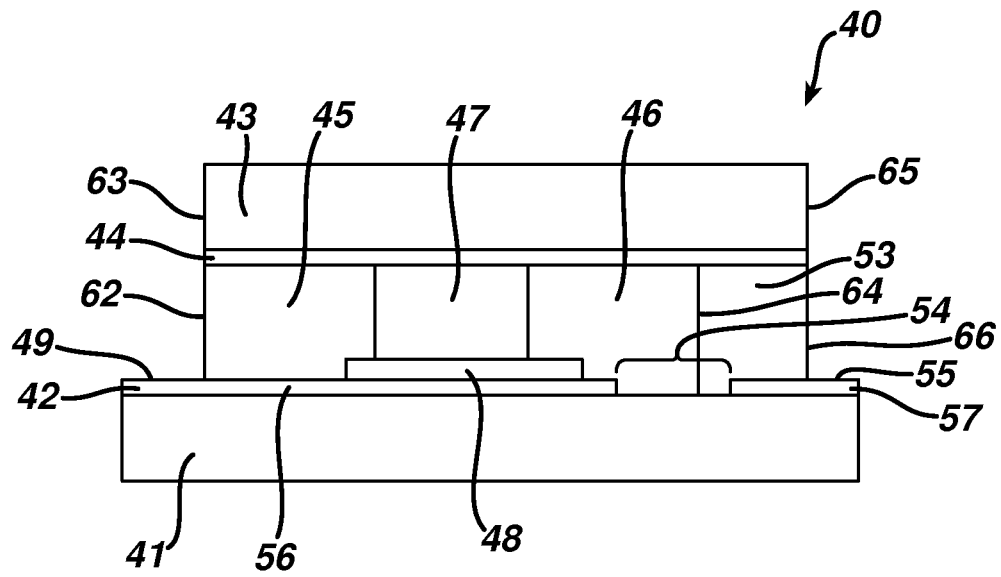


FIG. 3A

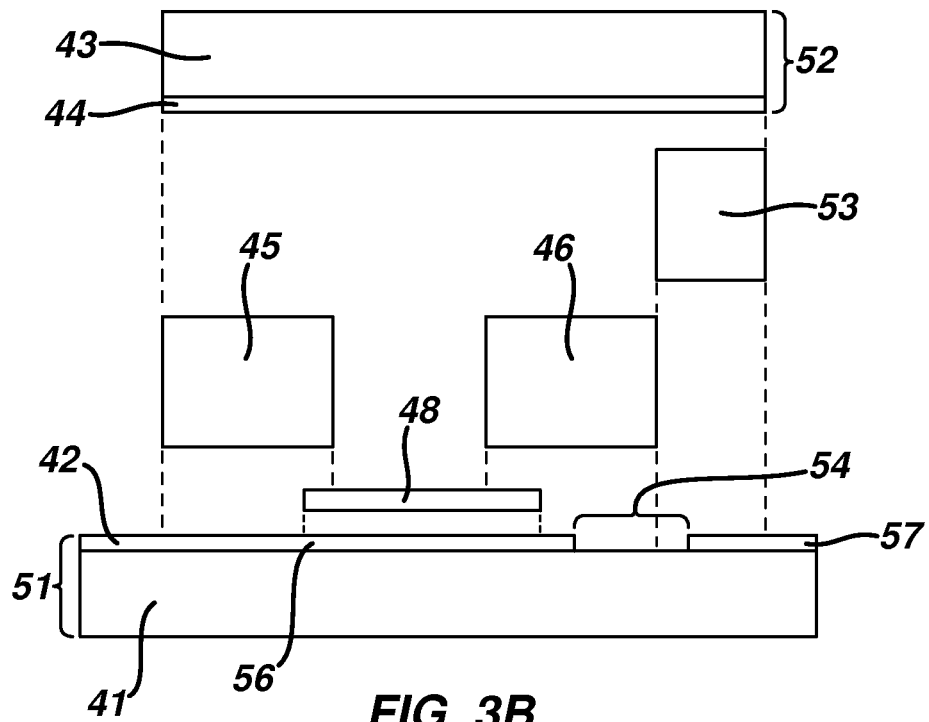


FIG. 3B

4/6

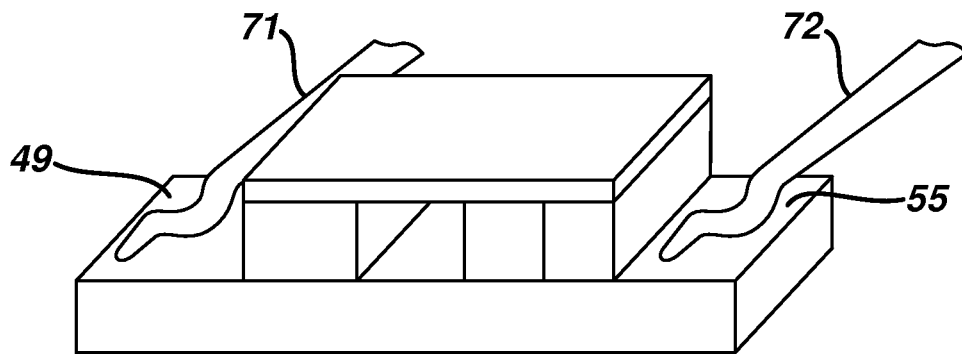


FIG. 4

5/6

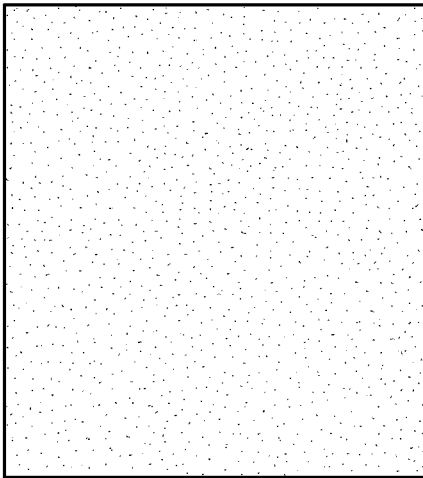


FIG. 5A

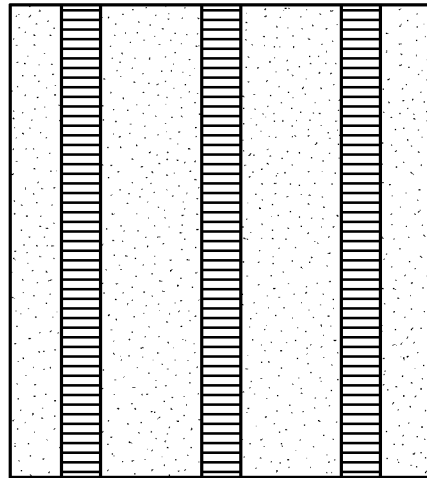


FIG. 5B

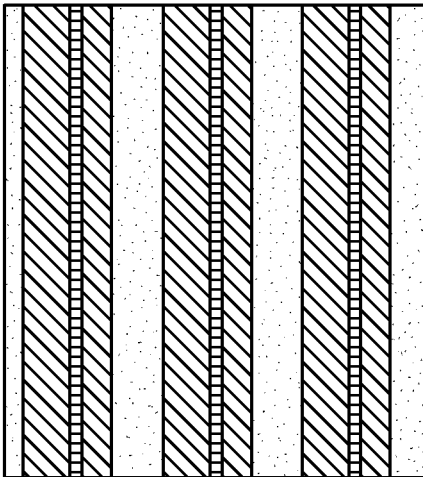


FIG. 5C

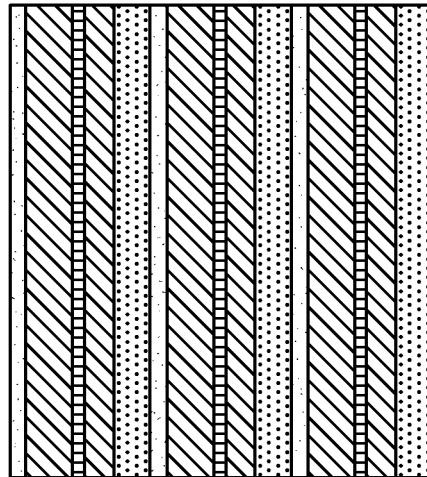


FIG. 5D

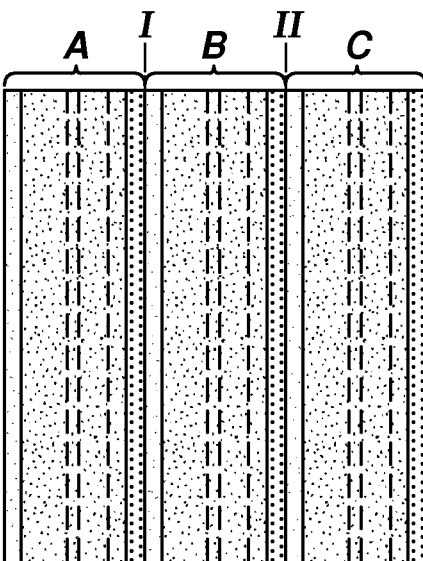


FIG. 5E

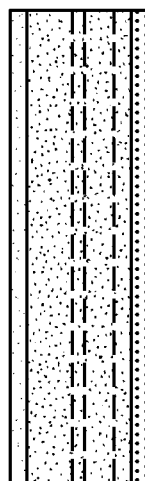


FIG. 5F



FIG. 5G

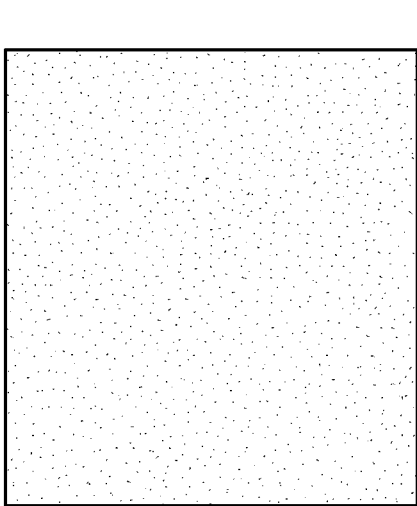


FIG. 6A

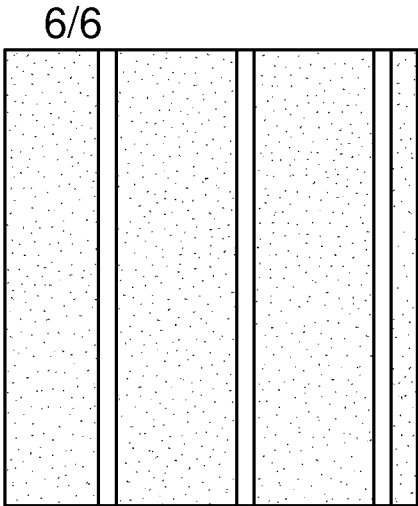


FIG. 6B

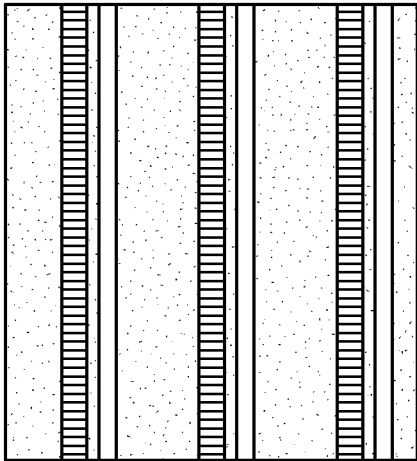


FIG. 6C

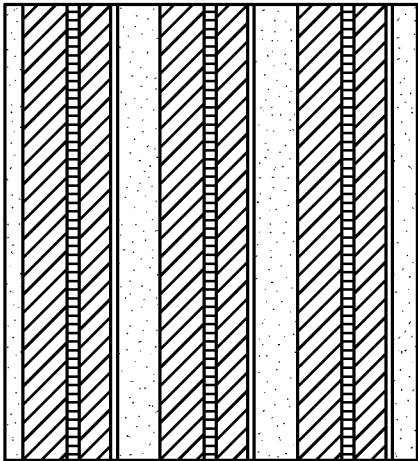


FIG. 6D

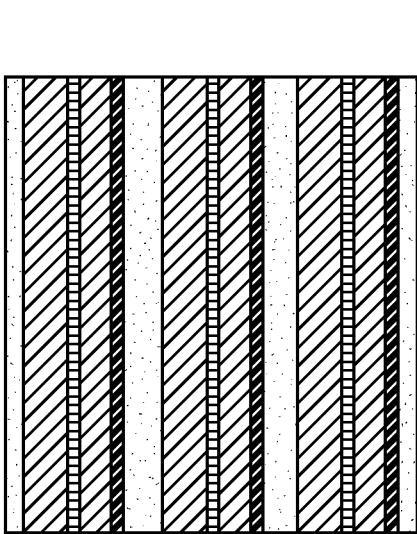


FIG. 6E

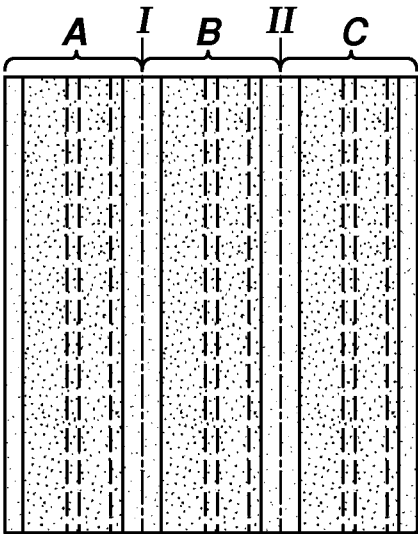


FIG. 6F

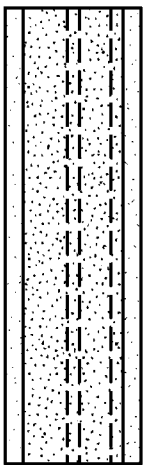


FIG. 6G



FIG. 6H

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2012/052218

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N27/327
ADD.

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/015292 A1 (AGAMATRIX INC [US]; IYENGAR SRIDHAR [US]) 29 January 2009 (2009-01-29)	1-5,8-12
Y	page 4, paragraph 1 - page 9, paragraph 1; figures 1-13	6,7,13, 14
Y	----- US 7 749 371 B2 (GUO SHERRY [US] ET AL) 6 July 2010 (2010-07-06) cited in the application column 4, lines 44-57; figures 1-4	6,7,13, 14
X	----- WO 2010/095787 A1 (ALL MEDICUS CO LTD [KR]; AHN YON CHAN [KR]; PARK MI SUK [KR]; CHA MIN) 26 August 2010 (2010-08-26) paragraphs [0102] - [0110]; figure 8 ----- -/-	1,8



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

29 May 2013

Date of mailing of the international search report

06/06/2013

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Lazar, Zala

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2012/052218

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/056345 A1 (I SENS INC [KR]; CUI GANG [CN]; KIM JU-YONG [KR]; KIM MOON-HWAN [KR];) 10 July 2003 (2003-07-10) page 8, line 6 - page 12, line 25; figure 3 -----	1-3, 7-10,14

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2012/052218

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009015292	A1	29-01-2009	
		AU 2008279043 A1	29-01-2009
		CA 2697164 A1	29-01-2009
		CN 101779120 A	14-07-2010
		EP 2176651 A1	21-04-2010
		KR 20100066449 A	17-06-2010
		US 2009026074 A1	29-01-2009
		WO 2009015292 A1	29-01-2009

US 7749371	B2	06-07-2010	
		CN 1975403 A	06-06-2007
		EP 1770396 A2	04-04-2007
		EP 2278330 A2	26-01-2011
		EP 2280276 A2	02-02-2011
		JP 4964552 B2	04-07-2012
		JP 4988059 B2	01-08-2012
		JP 2007108171 A	26-04-2007
		JP 2012008151 A	12-01-2012
		US 2007074977 A1	05-04-2007
		US 2010270178 A1	28-10-2010

WO 2010095787	A1	26-08-2010	
		EP 2324345 A1	25-05-2011
		KR 100918027 B1	18-09-2009
		US 2012142117 A1	07-06-2012
		WO 2010095787 A1	26-08-2010

WO 03056345	A1	10-07-2003	
		AT 452985 T	15-01-2010
		AU 2002251574 A1	15-07-2003
		CN 1514937 A	21-07-2004
		DK 1342093 T3	29-03-2010
		EP 1342093 A1	10-09-2003
		ES 2334893 T3	17-03-2010
		JP 3948627 B2	25-07-2007
		JP 2005513508 A	12-05-2005
		KR 20030054204 A	02-07-2003
		PT 1342093 E	01-02-2010
		US 2004045821 A1	11-03-2004
		WO 03056345 A1	10-07-2003
