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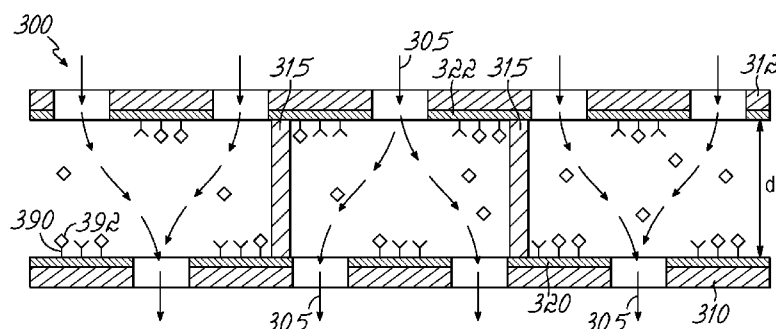


FIG. 3C

(57) Abstract: An electronic sweat sensor (300) includes a plurality of porous substrates (310, 312), each porous substrate (310, 312) having an electrically conductive surface (320, 322). The porous substrates (310, 312) have a generally planar surface. The generally planar surface may be adapted to be positioned on skin (12) generally coplanar with the skin. The electronic sweat sensor (300) further includes a porous spacer (315) layer defining a gap between at least two of the porous substrates (310, 312). When an analyte flow (305), which may be from skin (12), is moving perpendicular to the planar surface and through at least one of the porous substrates (310, 312), at least one of the conductive surfaces (320, 322) provides an electrical response to the presence of the analyte flow (305).

VERTICAL-FLOW ELECTRONIC BIO-CHEMICAL SENSING DEVICES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application relates to U.S. Provisional Application No. 62/003,715 and No. 62/003,692, both filed May 28, 2014, the disclosures of which are hereby incorporated by reference herein in its entirety.

BACKGROUND OF THE INVENTION

[0002] Numerous technologies have been developed to detect chemical solutes and various compounds (e.g., analytes) in the body. Many of these techniques measure impedance or charge transfer, or use techniques which benefit from closely spaced interdigitated electrodes. Fig. 1A shows a conventional impedance measuring, or impedance spectroscopy, device 100a used to detect chemical solutes and/or various compounds in the body. Sensing device 100a includes a first substrate 110, which may be made of glass or plastic for example, that carries pairs of interdigitated electrodes 120, 122 separated by a spacing or pitch ("d"). The pitch ("d") is typically made as small as possible, often only a few micrometers, to maximize the performance of the sensing device 100a. This creates challenges when integrating such technology with simple low-cost printed electronics or standard circuit board technology, which cannot achieve such finely patterned features. The sensing device 100a includes probes or biorecognition elements 190, which selectively capture analytes or biomarkers 192 in a horizontal flow of analytes 105. The horizontal flow of analytes 105 can be through a porous solid, gel, liquid gas, or other material suitable for transporting or permitting movement or transport of the analytes 192. Any method of transport for analytes is possible, including by diffusion, by advective flow in a fluid or gas, by iontophoresis, by electro-osmosis, or by other suitable techniques. As analytes 192 are captured onto probes 190, the measurement circuit 180 is able to detect charge transfer, changes in impedance, or other electrically measureable changes known by those skilled in the art that indicate the presence of analyte 192. These changes can even be used in some cases to measure the concentration of analyte 192 in flow 105. Two of several challenges of device 100a are the complexity of fabrication of the interdigitated electrodes 120, 122 and the low amount of diffusion or transport of analytes in flow 105 down to the probes 190, especially so at low analyte concentrations.

[0003] With reference to Fig. 1B, a prior art sensing device 100b is shown where the upper and lower walls, or any walls, of a microfluidic channel carry the sensing electrodes 120, 122. The channel and spacing between electrodes 120, 122 is defined by the spacing (“d”) between substrates 110, 112. All like numeral features provided and are similar to those described for Fig. 1. The device 100b allows a simple and reliable way to achieve closely spaced electrodes, which benefits numerous sensing modalities, and the flow of analytes 105 is always close to the probes 190 such that even at low concentrations of analytes 192 the analytes can more easily diffuse or transport to the probes 190. However, the configuration shown for device 100b will dramatically reduce the ease or rate of transport of flow of analytes 105, and in some cases, will be difficult to integrate with various complete bio or chemical sensor device designs.

[0004] Such devices require a sample to be introduced to a sensor surface or material. Often, the preferred requirements of sample introduction and of the sensor configuration are conflicting in one or more aspect, such that the performance of the device is reduced in one or more aspect. Furthermore, in many cases the fluid volume is very small, presenting unique challenges to the sensor configuration. In addition, the sensors themselves often require complicated configurations such as spaced electrodes to achieve greater performance.

[0005] What is needed are new devices and methods which can resolve one or more of the above challenges, and in particular, do so in a manner that is economical to manufacture. In particular, what is needed are better methods to efficiently introduce a sample close to the sensor surface, such that analyte diffusion is more rapidly completed from solution to the sensor.

SUMMARY OF THE INVENTION

[0006] The present invention provides electronic sweat sensors for sensing an analyte originating from skin or from another source where benefits of the present invention also apply. In one embodiment, an electronic sweat sensor includes at least one porous electrode providing an electrical response to the presence of an analyte. Said porous electrode has a generally planar surface and is adapted to be positioned on skin generally coplanar with said skin. The sensor further includes an analyte flow path from skin perpendicular to said planar surface and through said sensor. Said porous electrode provides a change in at least one electrical property in response to said analytes.

[0007] In one embodiment, an electronic sweat sensor includes a plurality of porous substrates, each porous substrate having an electrically conductive surface, said porous substrates having a generally planar surface and adapted to be positioned on skin generally coplanar with said skin. The sensor further includes a porous spacer layer defining a gap between at least two of said plurality of porous substrates and an analyte flow path from skin perpendicular to said planar surface and through at least one of said porous substrates. At least one of said conductive surfaces provides an electrical response to the presence of said analyte flow.

[0008] In one embodiment, an electronic sweat sensor includes at least one porous substrate having a first surface and a second surface, said second surface being opposite said first surface, said porous substrate having a generally planar surface and being adapted to be positioned on skin generally coplanar with said skin. The sensor further includes a first porous electrode layer adjacent to said first surface and a second porous electrode layer adjacent to said second surface. The sensor further includes an analyte flow path from skin perpendicular to said planar surface and through said at least one porous substrate. At least one of said first and second porous electrode layers provides an electrical response to the presence of an analyte.

[0009] In one embodiment, an electronic sweat sensor includes at least one porous substrate having an electrically conductive surface providing an electrical response to the presence of one or more analytes, said porous substrate having a generally planar surface and being adapted to be positioned on skin generally coplanar with said skin. The sensor further includes an analyte flow path through said sensor. Said at least one porous substrate is configured to confine an analyte flow such that said analyte flow is dominantly perpendicular to a planar surface of said porous substrate and through each porous substrate.

[0010] In one embodiment, an electronic sweat sensor includes at least one porous substrate having an electrically conductive surface, said porous substrate having a generally planar surface and being adapted to be positioned on skin generally coplanar with said skin and at least one iontophoresis electrode configured to cause an analyte flow. When said analyte flow is moving perpendicular to a planar surface of said porous substrate and through said sensor, said porous substrate provides an electrical response to the presence of said analyte.

[0011] In one embodiment, an electronic sweat sensor includes at least one porous substrate having an electrically conductive surface and being configured to provide an

electrical response to the presence of an analyte, said porous substrate having a generally planar surface and being adapted to be positioned on skin generally coplanar with said skin. The sensor further includes at least a first material for collecting an analyte diffusing through said skin, said first material having a lower concentration of said analyte than a concentration of said analyte in said skin, said at least one porous substrate being positioned between said skin and said first material. When an analyte flow diffusing through the skin perpendicular to a planar surface of said porous substrate is moving through said sensor, said porous substrate provides an electrical response to the presence of said analyte flow.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] The objects and advantages of the present invention will be further appreciated in light of the following detailed descriptions and drawings in which:

[0013] Fig. 1A is a schematic of a conventional sensing device.

[0014] Fig. 1B is a cross-sectional view of a conventional sensing device.

[0015] Fig. 2A is a cross-sectional view of a sensing device according to one embodiment of the present invention placed on skin.

[0016] Fig. 2B is a cross-sectional view of a sensing device according to one embodiment of the present invention incorporated into a lateral flow paper-microfluidic device.

[0017] Fig. 3A is a cross-sectional view of a sensing device according to one embodiment of the present invention.

[0018] Fig. 3B is a cross-sectional view of a portion of the sensing device of Fig. 3A showing a porous configuration.

[0019] Fig. 3C is a cross-sectional view of the sensing device of Fig. 3A showing an analyte flow.

[0020] Figs. 4A-C are cross-sectional views of sensing devices according to various embodiments of the present invention having different configurations.

[0021] Fig. 5A is a cross-sectional view of a sensing device according to one embodiment of the present invention placed on skin.

[0022] Fig. 5B is a cross-sectional view of the sensing device of Fig. 5A.

[0023] Fig. 5C is a cross-sectional view of a sensing device according to one embodiment of the present invention.

[0024] Fig. 6 is a cross-sectional view of a sensing device according to one embodiment of the present invention placed on skin.

DETAILED DESCRIPTION

[0025] The embodiments of the present invention described below are described primarily in terms of analytes transported in a fluid and applications such as wearable biomarker sensing device. However, the present invention is not so limited in application or functionality. The present invention applies to any electronic sensing modality that would benefit in at least one performance, cost or other valued metric for chemical or biomarker (i.e. analyte) sensing. The embodiments of the present invention discussed below are illustrated primarily focusing on the sensor devices themselves. For purposes of convenience, the descriptions may not include illustration or description of additional features or system-level components, software, batteries, or other components that may be needed for proper function that are obvious to those skilled in the art.

[0026] Aspects of the present invention apply to transport or flow of analytes through any material, including a porous solid, gel, liquid, gas, or other material suitable for transporting or permitting movement or transport of the analytes. Embodiments of the present invention may include any method of transport for analytes including, for example, diffusion, advective flow in a fluid or gas, iontophoresis, electro-osmosis, or other suitable techniques. The present invention contemplates any sensing modality or variation of embodiments of the present invention that benefit in performance, cost, convenience, sampling interval, longevity, limit of detection, specificity, ease of integration of additional features, ease of integration within a device, or any other aspect of bio or chemical sensing which can benefit from the embodiments of the present invention. Embodiments of the present invention will generally exhibit signal-to-noise advantages in sensors where a charge transfer between the electrode and solution occurs, including amperometric and impedance type sensing modalities and other sensing modalities which are known to benefit from use of interdigitated electrodes. Embodiments of the present invention will generally also allow sensors to stabilize more quickly, as the diffusive path length to the sensor surface is generally reduced.

[0027] Embodiments of the present invention may be advantageously integrated in a variety of applications, some of which are illustrated in Figs. 2A-2C. With reference to Fig. 2A, a porous sensing device 200a is shown which is laminated onto or placed adjacent to skin or tissue 12. Sensing device 200a uses absorbent or evaporative element 240 to transport sweat fluid or sweat analytes vertically in flow 205 from skin 12 through the porous sensing device 200a and onto element 240. Sensing device 200a is vertically porous and thin such that flow 205 occurs easily and quickly through sensing device 200a. Embodiments

discussed below include further details on the porosity of a sensing device. In this embodiment, there is very little dead volume of fluid created, and very little fluid is needed to allow sensing device 200a to function properly. Further, additional fluidic controls are not needed.

[0028] Fig. 2B shows a sensing device 200b incorporated into a lateral flow paper-microfluidic device. The lateral flow paper-microfluidic device includes a paper strip 250, which introduces fluid flow 205 through sensing device 200b, and a paper strip 260. The paper strip 250 introduces fluid flow 205 through the sensing device 200b, which is porous. The fluid flow 205 then passes to the paper strip 260, which carries fluid flow 205 away from sensing device 200b. In various embodiments, sensing devices 200b may be incorporated into lateral flow assay devices or simple flex electronic or wearable sensor devices, which must be thin and not made from rigid channel microfluidics.

[0029] With reference to Fig. 3A, a sensing device 300 includes substrates 310, 312 and spacer materials 315. Substrates 310, 312 may be, for example, porous membranes, porous films, meshes, or any other suitable porous material, such as commercial track-etch membranes. In the illustrated embodiment, substrates 310, 312 are coated with optional electrodes 320 and 322 and probes 390. Fig. 3B provides a top view of pores in substrate 310 and electrode 320. In embodiments where substrates 310 and 312 are electrically conductive themselves, a sensing device may exclude the optional electrodes 320, 322. In one embodiment, substrates 310, 312 are porous metal films or porous carbon fiber films and thereby provide electrically conductive surfaces. The porosity of the device 300 allows an analyte flow 305, which is shown in Fig. 3C in greater detail. Although not shown, substrate 310 has a first inner surface and a first outer surface. Further, substrate 312 includes a second inner surface and a second outer surface. Substrates 310, 312 overlie each other and are spaced a distance (“d”) apart, which may be roughly the distance between the first and second inner surfaces. Substrates 310, 312 may be spaced apart using spacer materials 315. The spacer materials 315 are porous and may be, for example, thin adhesives, spacer balls as are used in LCD displays, a photoresist, or an adhesive coated textile or mesh, among other materials. The spacers 115 are typically easy to fabricate, even down to only several micrometers across, using techniques known by those skilled in the art, and can regulate the spacing between the electrodes such that the impedance is adequately regular, predictable, and homogeneous. Sensing device 300 includes a variety of unique aspects and advantages. For instance, sensing device 300 is easily manufactured with a small electrode spacing (“d”)

and may have a thin and flexible construction. Sensing device 300 may be manufactured using low-cost fabrication methods such as roll-to-roll fabrication. Further, sensing device 300 can offer little resistance to fluid flow 305, and analytes 392 are brought into close proximity to probes 390 such that high performance sensing can be achieved for analytes at low concentrations and/or with low diffusivity. Another exemplary advantage is that the alignment of substrates 310, 312 is not required. Those skilled in the art may recognize further advantages. In another aspect of the present invention, the sensing device 300 could be used to provide detection by measurement of impedance, potential, current, frequency response, or other known methods of bio or chemical sensing technologies.

[0030] A variety of analyte probes or electrical sensing methods are useful in embodiments of the present invention. By way of example, a probe or electrical sensing method may be an aptamer, redox couples, an antibody layer, an enzyme layer, or an ionophore membrane. Further, a surface that is selective in some way for sensing without a specific probe layer (e.g., stripping voltammetry) may be used. Generally, any surface that provides an electrical response to the presence of an analyte is adequate for use in embodiments of the present invention. Even surfaces that utilize an insulator on an electrically conductive surface, such as electrical capacitance or field-effect type sensors, are included since they also have an electrically conductive surface, and hence have an electrical response (be it direct or indirect) to the presence of said analyte.

[0031] Figs. 4A-4C illustrate various embodiments of the present invention having a sensing device including one or more substrates, electrodes, and probes in a variety of configurations. With reference to Fig. 4A, at least a portion of a sensing device 400a is shown, consisting of a porous substrate 410, electrodes 420, 422, and a coating or layer of probes for sensing 490. Similar to device 300a, device 400a includes advantageous the aspects of electrodes 420, 422 being in close proximity, the ease of the analyte flow 405, and the close proximity of the analytes (not shown) with probes 490. In one embodiment, electrodes 420, 422 may also coat the sides of the pores (not shown) in the substrate 410. Device 400a could be fabricated using several techniques, including angular vacuum metal deposition of a track-etch membrane with high-aspect ratio pores.

[0032] With reference to Fig. 4B, a portion of a sensing device 400b is shown. Sensing device 400b includes elements of device 400a and further includes an additional electrode 424 and substrate 412. The location of the probe layer 490 may be determined based on a variety of considerations. For example, the location of the probe layer 490 in device 400b

may have been determined because, in this embodiment, the probe layer 490 is easier to manufacture on the external surfaces of the substrate 410 of the device 400b. Those skilled in the art will recognize that a plurality of electrodes or arrangements are possible. Some sensing modalities require at least three electrodes: a reference electrode, a working electrode, and a counter electrode. In this regard, electrodes of device 400b could be any of these exemplary types of electrodes. Various embodiments of the present invention may include electrodes with or without probe layer 490.

[0033] With reference to Fig. 4C, a device 400C includes an electrode 420 on a porous substrate 410, and electrodes 422, 424 spaced apart from the porous substrate 410. Alternatively, in one embodiment, electrode 420 may also be porous. Porous electrodes may be, for example, a thin metal film that is porous or a fine metal wire mesh or a porous layer of carbon nanotubes. Utilizing porous electrodes may allow for a simpler manufacturing process.

[0034] With reference to Fig. 5A, a further embodiment of the present invention is shown as sensing device 500a is pressed onto skin 12. In another embodiment, sensing device 500a could be adhered to skin 12 with an adhesive (not shown). Sensing device 500a includes a wicking material 532 to collect sweat. The device 500a is able to confine fluid from sweat ducts 14 to horizontally confined locations in device 500a, for example as indicated by lines 507. This same configuration therefore confines analyte flow 505. The device 500a may further include elements for stimulating sweat by, for example, iontophoresis. In one embodiment where the device includes a sweat stimulant, such as pilocarpine, the flow 505 could also confine the iontophoresis of the sweat stimulant into just the sweat ducts 14 or dominantly in areas near the sweat ducts 14. Device 500a could achieve confinement of the flow 505 in several ways. In one embodiment, the space between two substrates by which device 500a is fabricated is sealed together with spacers that form a lattice of horizontally closed cells (e.g., a honeycomb lattice). In this embodiment, the spacers would form the sidewalls for each closed cell. In an advantageous aspect of the present invention, confining the horizontal flow reduces the overall sweat volume. Reducing the total volume of sweat needed to flow through or to the sensors may improve the sampling interval and/or may allow sensing at very low sweat rates. Some sensor types, such as impedance, amperometric, or others, require fluid to make an electrical contact between two electrodes. In embodiments where the sensor requires fluid to make electrical contact between two electrodes and where the sensor has a configuration similar to device 500a, the sensed signal would be limited to

where fresh sweat is flowing. In the other areas of the device where no sweat is present, the background signal would be very low due to much higher electrical impedance.

[0035] With reference to Fig. 5B, device 500b is shown as an exemplary configuration of device 500a of Fig. 5A. Device 500b includes porous layers 550, 552 and porous material 560. Layers 550, 552 include a substrate component and an electrode component, which could be an electrically conductive surface on the substrate component. Porous material 560 may act as a spacer layer. Sweat will flow vertically through device 500b, but the flow of the sweat horizontally through device 500b is restricted. The horizontal confinement of fluid is achieved by Laplace pressure and the fluid path (not shown) must be pressure permeated by pressure of sweat. This can be achieved by implementing materials for porous layers 550, 552 such that they are non-wicking to a fluid. In various embodiments, porous layers 550, 552 may be hydrophobic or only slightly hydrophilic. In one embodiment where porous layers 550, 552 are made of a polymer, and porous material 560 is made of a polymer with the same or similar wetting contact angle as the polymer of layers 550, 552, then a smaller pore diameter 562 compared to the pore diameter 564 would confine fluid flowing under pressure against device 500b, which would permeate device 500b substantially vertically.

[0036] With reference to Fig. 5C, one embodiment of the present invention includes porous layers 550, 552, 554, 556 and spacer layers 560 in a stacked configuration. In such an embodiment, numerous different types of sensors could be integrated in a single device and benefit from one or more advantages of the present invention.

[0037] With reference to Fig. 6, an embodiment of the present invention is shown which utilizes a device 600 including layers of hydrogels 615, an electrode 628, and porous sensor 602, which may be similar to one or more constructions according to embodiments of the present invention discussed above. Electrode 628 may provide an electric field to extract charged solutes or biomarkers by iontophoresis or indirectly by electro-osmotic flow of charged solutes, which drag non-charged solutes along with them. In this regard, device 600 is capable of sensing biomarkers or solutes extracted by electro-osmosis or reverse iontophoresis. Device 600 has a flow of analytes 607 through layers of hydrogels 615 and porous sensor 602. Porous sensor 602 may be constructed according to one or more aspects of the present invention. In one embodiment, for example, porous sensor 602 may be similar to device 300. This is an improvement over previous applications of electro-osmosis and iontophoresis that generally present analyte flow challenges in quickly drawing solutes to the sensor surface and also to the driving electrode for iontophoresis. An additional challenge is

also that solutes will build up or concentrate at the electrode driving the iontophoresis, which would contaminate the sensing of new solutes and/or could damage the sensor over time. In the device 600, such concentration of the solutes is not at the porous sensor 602 but instead at the electrode 628, which is further away and is utilized to drive the flow of at least one solute. Embodiments of the present invention are not limited to the illustrated arrangement. Those of ordinary skill in the art will recognize that other configurations and modes of analyte transport are possible.

[0038] In one aspect of the present invention, a sensing device senses diffusing analytes. Analytes and other solutes or molecules can passively diffuse through skin to the skin surface. As one example, alcohol appears at the skin surface approximately 30 minutes after oral ingestion. Solute can diffuse through skin, into and/or through sweat from wounds, cuts, or other pathways through skin. Diffusion is faster with a higher concentration gradient (i.e., greater change in concentration of the analyte over shorter distance it has to travel by diffusion). With further reference to Fig. 6, device 600 senses diffusing analytes. In this embodiment, the electrode 628 is removed and the gel 615 furthest away from the skin 12 would initially have low or zero concentration of the analyte or analytes to be sensed by porous sensor 602. For solutes in fluids such as water, oils, glycols, or other fluids or liquids, the porous sensor 602 could be filled with a fluid or gel to create a diffusion pathway through porous sensor 602. The gel 615 could be a hydrogel or a gel containing a liquid that increases skin permeability such as, for example, glycol. Advantages of using a porous sensor 602 according to an embodiment of the present invention in a device that senses diffusing analytes may include the following. Firstly, in an embodiment including a lateral flow or other flow technique across sensors (e.g., as shown in Figs. 1B or 2B), the diffusion pathway could be long (e.g., length of several mm or more), which reduces the concentration gradient of the analyte to be sensed. Secondly, the gel 615 furthest away from skin 12 could have a large volume (e.g., several mm thick) such that over time the gel 615 will maintain a low concentration of the analyte or analytes to be sensed by porous sensor 602. In this manner, gel 615 acts as a material into which an analyte can diffuse with a lesser concentration of the analyte than the analyte concentration found in skin. In an embodiment where the analyte is volatile (e.g., alcohol), the gel 615 furthest away from the skin 12 could be removed such that ambient air would represent the low concentration material to enable a direction of diffusion from skin to air. Thirdly, the device may further include advantageous aspects of the present invention described above, such as bringing analytes closer to the

sensing surface, which is important for sensing of very low concentration analytes. Those of ordinary skill in the art will recognize how to modify or configure the devices according to embodiments of the present invention so as to effectively operate in other applications.

[0039] The following examples are provided to help illustrate the present invention, and are not comprehensive or limiting in any manner.

[0040] EXAMPLE 1 – In one embodiment, a method of making a sensing device, such as a sensing device similar to device 300a, includes coating a first and a second polyimide track etch membrane with an electrode. The membrane may be, for example, one such as those manufactured by AR-Brown or IT4IP. The membranes have an initial thickness of 7.6, 13, or 25 μm , pore sizes of 100 nm, and a pore density of at least on average of one pore for every linear 5 μm . The coating may be a 10 nm coating of gold electrode. Adhesive spacer balls are then spray coated onto the gold coated side of the first prepared membranes. The first membrane is then dried of the solution used for the spray coating. The adhesive spacer balls may be from Sekisui Micropearl and have a diameter of about 5 μm , for example. The first and second prepared membranes are then adhered together with the gold-coated surfaces facing each other. To accomplish this, the first and second membranes may be hot-laminated at 140 °C, which activates the adhesive. One of several types of chemical or bio sensors can then be created through solution or chemical treatment of the gold surfaces. The treatments may typically be performed using a vacuum-degassing step to ensure solution treatment penetrates into the sandwiched structure of the two substrates. Lastly, a dilute solution of a water soluble polymer, such as Polyvinylpyrrolidone (PVP), is used to coat all surfaces of the film, again using vacuum for degassing, to create a sensing device which is hydrophilic (i.e., sweat wets through the device with no pressure required). The PVP coating process has been shown to be commercially viable for track-etch membranes down to even 10 nm pore sizes. If needed, one or more external surfaces of the resulting device can be cleaned of PVP if adhesion to another material or surface needs to be improved.

[0041] EXAMPLE 2 – In one embodiment, a sensing device includes two sheets of porous carbon paper, like those utilized in fuel cells, laminated on both sides of an ultrathin (e.g., 10 μm thick) sheet of porous paper or polymeric material. Other options include spacing materials used as spacers in electrolytic capacitors. The sensor is utilized for sensing chemistries and modalities known to work effectively with carbon electrodes.

[0042] EXAMPLE 3 – In one embodiment, a device of the present invention is created using aligned photolithographic methods. Using such a method would provide more homogenous electrical impedance and flow through the device.

[0043] This has been a description of the present invention along with a preferred method of practicing the present invention; however, the invention itself should only be defined by the appended claims.

WHAT IS CLAIMED IS:

1. An electronic sweat sensor for sensing an analyte comprising:
at least one porous electrode providing an electrical response to the presence of an analyte;
said porous electrode having a generally planar surface, and
an analyte flow path perpendicular to said planar surface and through said sensor,
wherein said porous electrode provides a change in at least one electrical property in response to said analytes.
2. The electronic sweat sensor of claim 1, wherein said generally planar surface of said porous electrode is adapted to be positioned on skin generally coplanar with skin and said analyte flow path is from said skin.
3. An electronic sweat sensor comprising:
a plurality of porous substrates, each porous substrate having an electrically conductive surface, said porous substrates having a generally planar surface;
a porous spacer layer defining a gap between at least two of said plurality of porous substrates; and
an analyte flow path perpendicular to said planar surface and through at least one of said porous substrates, wherein at least one of said conductive surfaces provides an electrical response to the presence of said analyte flow.
4. The electronic sweat sensor of claim 3, wherein said generally planar surfaces of said porous substrates are adapted to be positioned on skin generally coplanar with said skin and said analyte flow path is from skin.
5. The electronic sweat sensor of claim 4, wherein an analyte flow of sweat is vertically confined in said analyte flow path above sweat ducts in said skin.
6. The electronic sweat sensor of claim 3, wherein said electric response is a change in charge transfer with said electrically conductive surface.

7. An electronic sweat sensor comprising:
- at least one porous substrate having a first surface and a second surface, said second surface being opposite said first surface, said porous substrate having a generally planar surface;
 - a first porous electrode layer adjacent to said first surface;
 - a second porous electrode layer adjacent to said second surface; and
 - an analyte flow path perpendicular to said planar surface and through said at least one porous substrate, wherein at least one of said first and second porous electrode layers provides an electrical response to the presence of an analyte.
8. The electronic sweat sensor of claim 7, wherein said generally planar surface of said porous electrode is adapted to be positioned on skin generally coplanar with skin and said analyte flow path is from skin.
9. An electronic sweat sensor comprising:
- at least one porous substrate having an electrically conductive surface providing an electrical response to the presence of one or more analytes;
 - said porous substrate having a generally planar surface and being adapted to be positioned on skin generally coplanar with said skin, and
 - an analyte flow path through said sensor, wherein said at least one porous substrate is configured to confine an analyte flow such that said analyte flow is dominantly perpendicular to a planar surface of said porous substrate and through each porous substrate.
10. The electronic sweat sensor of claim 9, wherein said generally planar surface of said porous substrate is adapted to be positioned on skin generally coplanar with skin and said analyte flow is from said skin.
11. The electronic sweat sensor of claim 9, wherein an analyte flow of sweat is vertically confined in said analyte flow path above sweat ducts in said skin.
12. The electronic sweat sensor of claim 9, wherein said sensor includes two of said porous substrates, said sensor further comprising:
- a porous spacer material for separating said two porous substrates.

13. The electronic sweat sensor of claim 9, wherein said sensor includes at least three porous substrates, said sensor further comprising:
a plurality of porous spacer materials for separating each of said porous substrates from the other of said porous substrates.
14. An electronic sweat sensor comprising:
at least one porous substrate having an electrically conductive surface, said porous substrate having a generally planar surface and being adapted to be positioned on skin generally coplanar with said skin; and
at least one iontophoresis electrode configured to cause an analyte flow;
wherein, when said analyte flow is moving perpendicular to a planar surface of said porous substrate and through said sensor, said porous substrate provides an electrical response to the presence of said analyte.
15. An electronic sweat sensor comprising:
at least one porous substrate having an electrically conductive surface and being configured to provide an electrical response to the presence of an analyte, said porous substrate having a generally planar surface and being adapted to be positioned on skin generally coplanar with said skin; and
at least a first material for collecting an analyte diffusing through said skin, said first material having a lower concentration of said analyte than a concentration of said analyte in said skin, said at least one porous substrate being positioned between said skin and said first material;
wherein, when an analyte flow diffusing through the skin perpendicular to a planar surface of said porous substrate is moving through said sensor, said porous substrate provides an electrical response to the presence of said analyte flow.
16. The electronic sweat sensor of claim 15, wherein said first material includes a liquid.
17. The electronic sweat sensor of claim 15, wherein said first material includes a hydrogel.

18. The electronic sweat sensor of claim 15, further comprising:

a second material being positioned between said skin and said porous substrate when said sensor is placed on said skin, said second material including a component that increases skin permeability, said component being transferable to said skin when said sensor is placed on said skin.

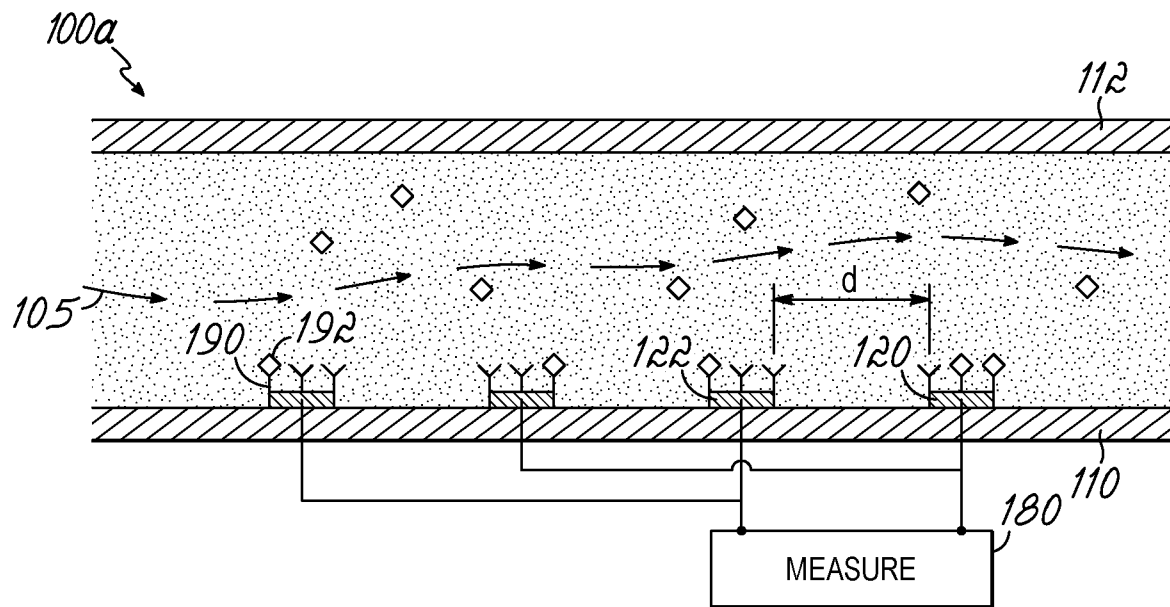


FIG. 1A
PRIOR ART

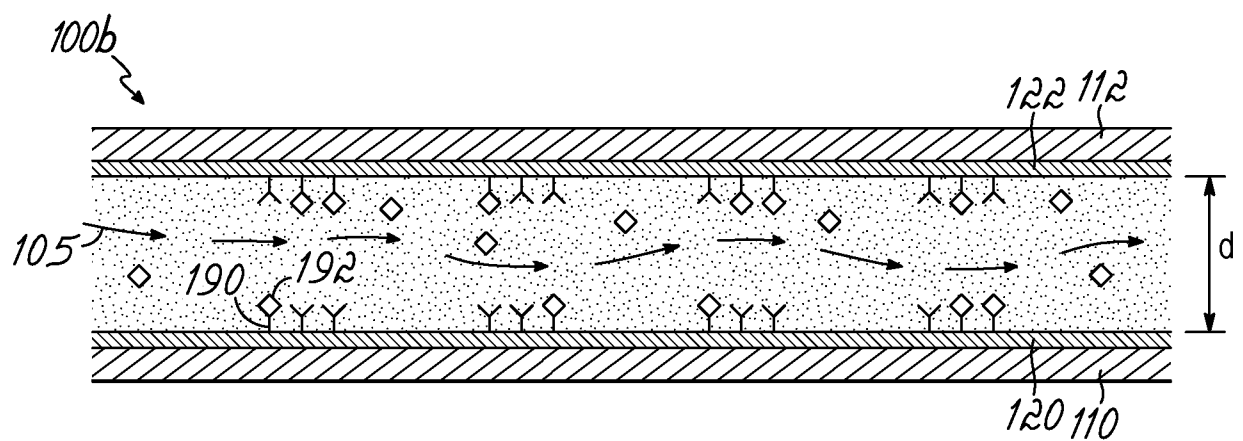


FIG. 1B
PRIOR ART

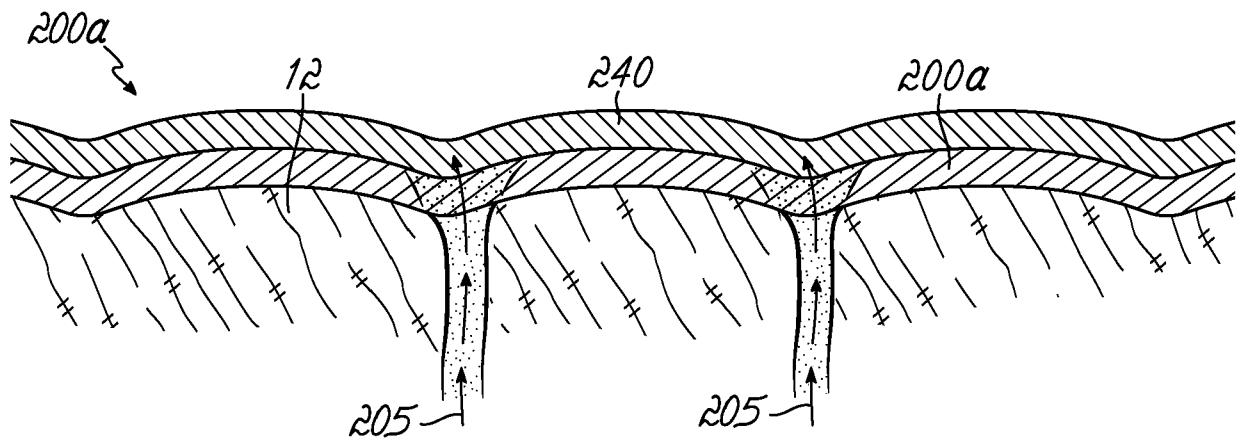


FIG. 2A

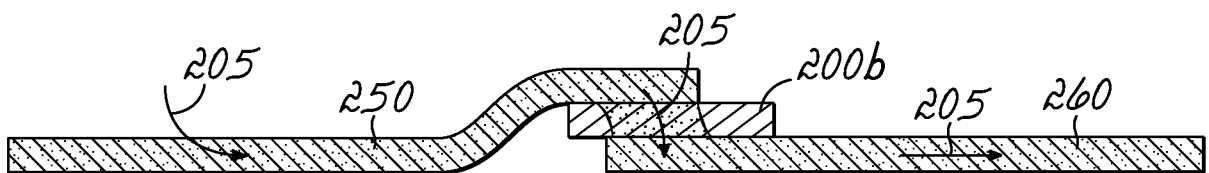


FIG. 2B

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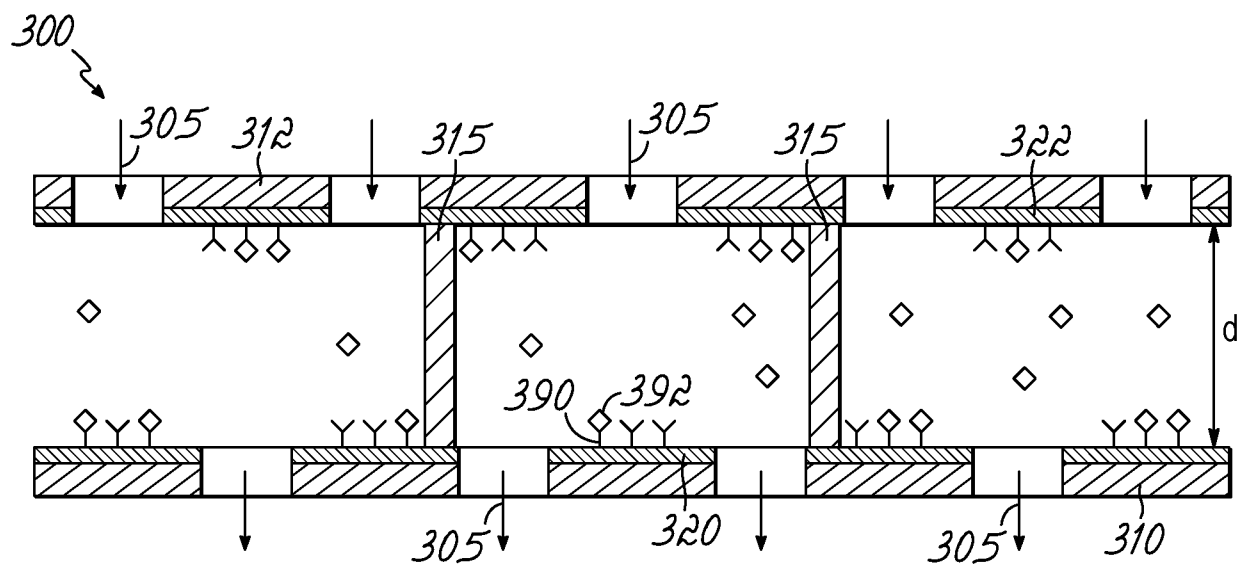


FIG. 3A

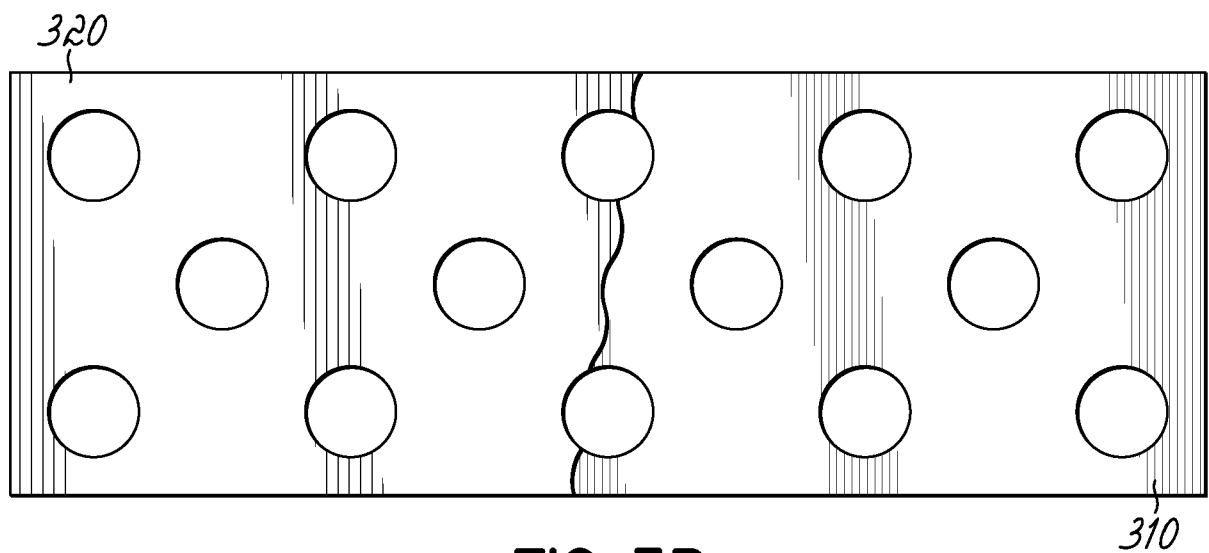


FIG. 3B

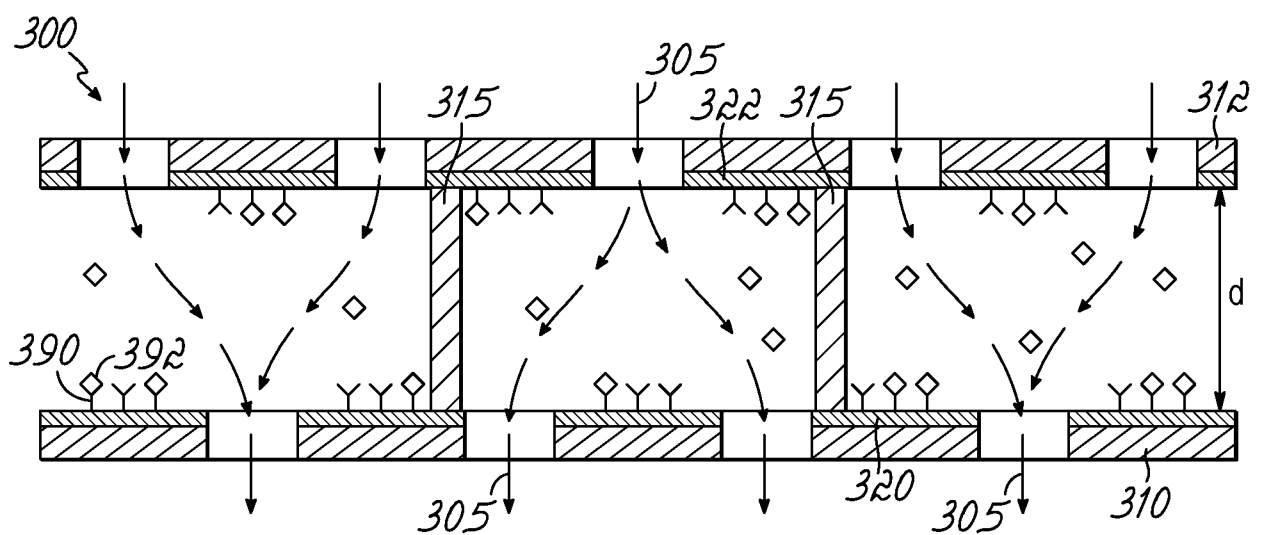


FIG. 3C

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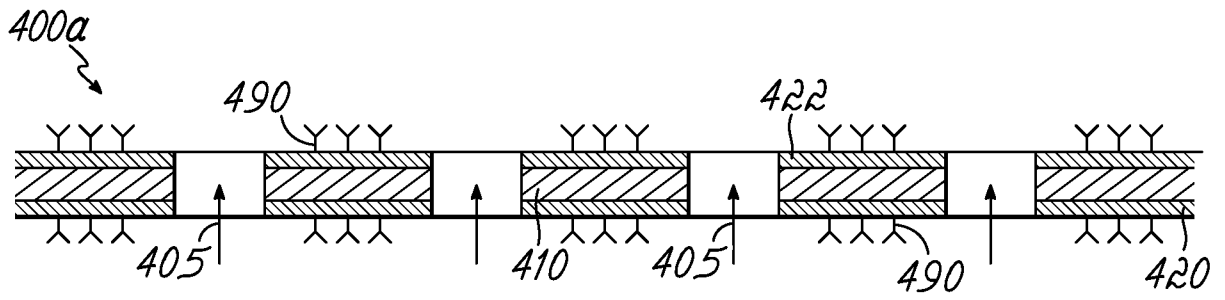


FIG. 4A

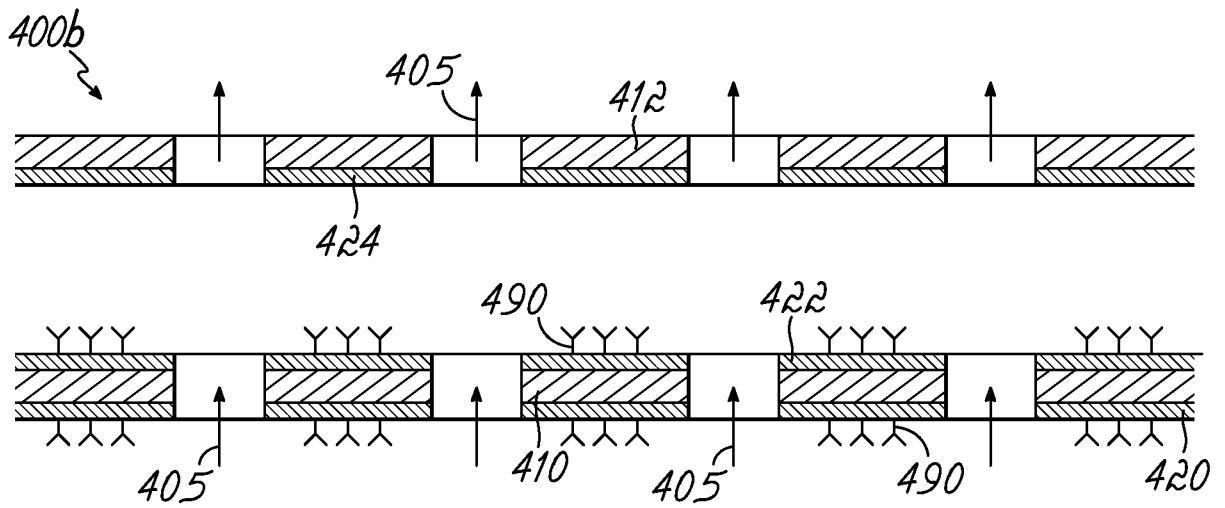


FIG. 4B

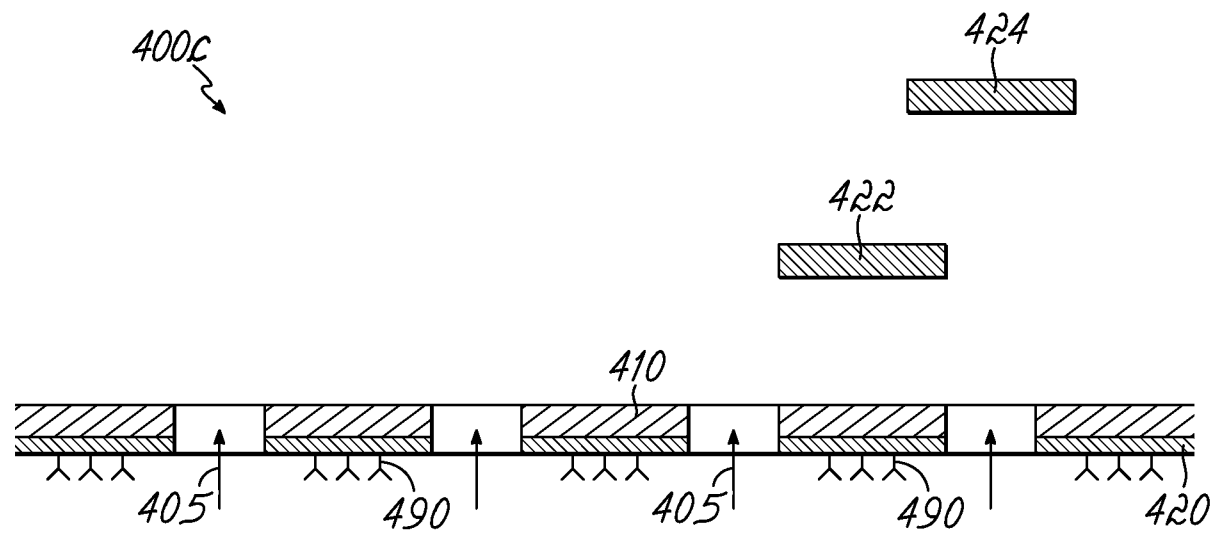


FIG. 4C

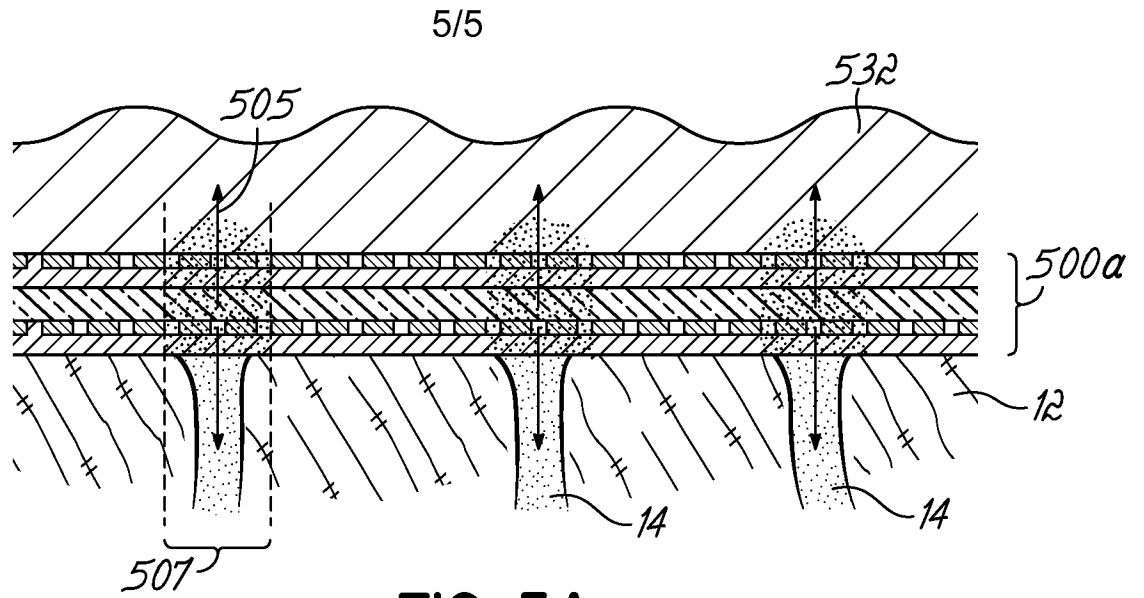


FIG. 5A

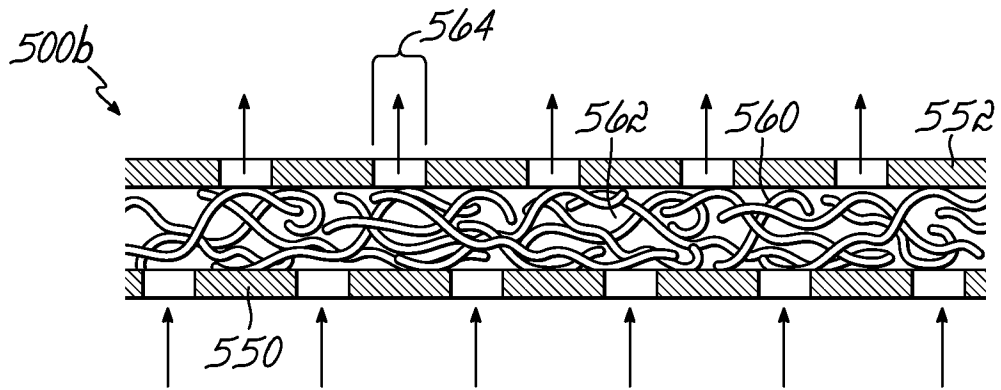


FIG. 5B



FIG. 5C

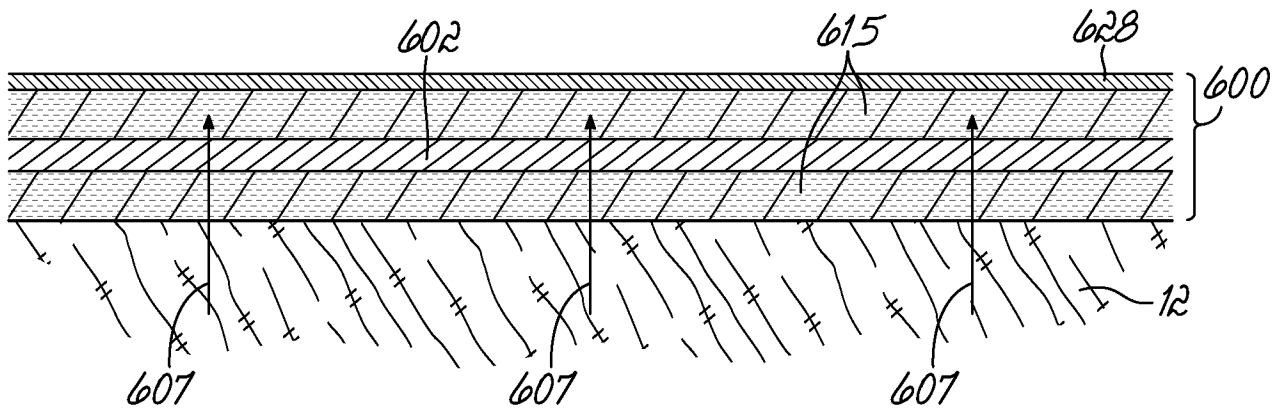


FIG. 6

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2015/032830

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/00 (2015.01)

CPC - A61B 5/4266 (2015.04)

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)

IPC(8) - A61B 5/00; G01N 27/26, G01N 27/333 (2015.01)

USPC - 204/403.06, 204/403.12, 204/412; 604/20

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

CPC - A61B 5/4266; G01N 27/26, G01N 27/333 (2015.04) (keyword delimited)

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

PatFt, AppFt, Orbit, Google Scholar

Search terms used: sweat sensor, sensor, analyte, porous electrode, conductive, electrode, iontophoresis electrode, porous spacer, porous, spacer

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010/0044224 A1 (KATAKY) 25 February 2010 (25.02.2010) entire document	9-11, 15-18
Y		1-8, 12-14
Y	US 7,813,780 B2 (SHAH et al) 12 October 2010 (12.10.2010) entire document	1, 2, 7, 8
Y	US 7,959,791 B2 (KJAER et al) 14 June 2011 (14.06.2011) entire document	3-6, 12, 13
Y	US 6,269,265 B1 (ANDERSON) 31 July 2001 (31.07.2001) entire document	14
A	US 2008/0045816 A1 (JANG et al) 21 February 2008 (21.02.2008) entire document	1-18
P, A	US 2015/0112165 A1 (UNIVERSITY OF CINCINNATI) 23 April 2015 (23.04.2015) entire document	1-18
P, A	US 2015/0112164 A1 (UNIVERSITY OF CINCINNATI) 23 April 2015 (23.04.2015) entire document	1-18

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

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"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

27 July 2015

Date of mailing of the international search report

14 AUG 2015

Name and mailing address of the ISA/

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