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(54) MINIMALLY-INVASIVE SYSTEM AND METHOD FOR MONITORING ANALYTE LEVELS

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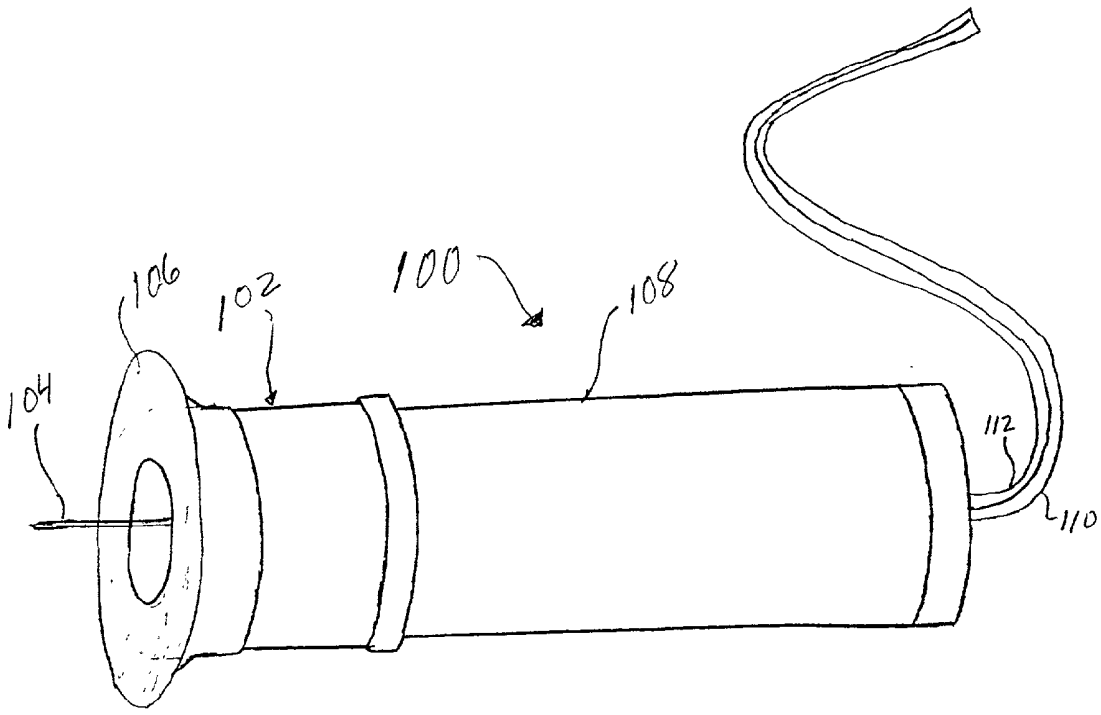
(57) **ABSTRACT**

A minimally-invasive analyte detecting device and method for using the same. The system and method employ a device having an active electrode optionally coated with a substance, and a counter-electrode that is configured at least partially surround the active electrode. The configuration of the auxiliary electrode and active electrode improves the current flow through the device and increases the sensitivity of the device. When the device is placed against the patient's skin, the active electrode is adapted to enter through the stratum corneum of a patient to a depth less than a depth in the dermis at which nerve endings reside. An electric potential is applied to the active electrode and the analyte level is determined based on the amount of current or charge flowing through the device.



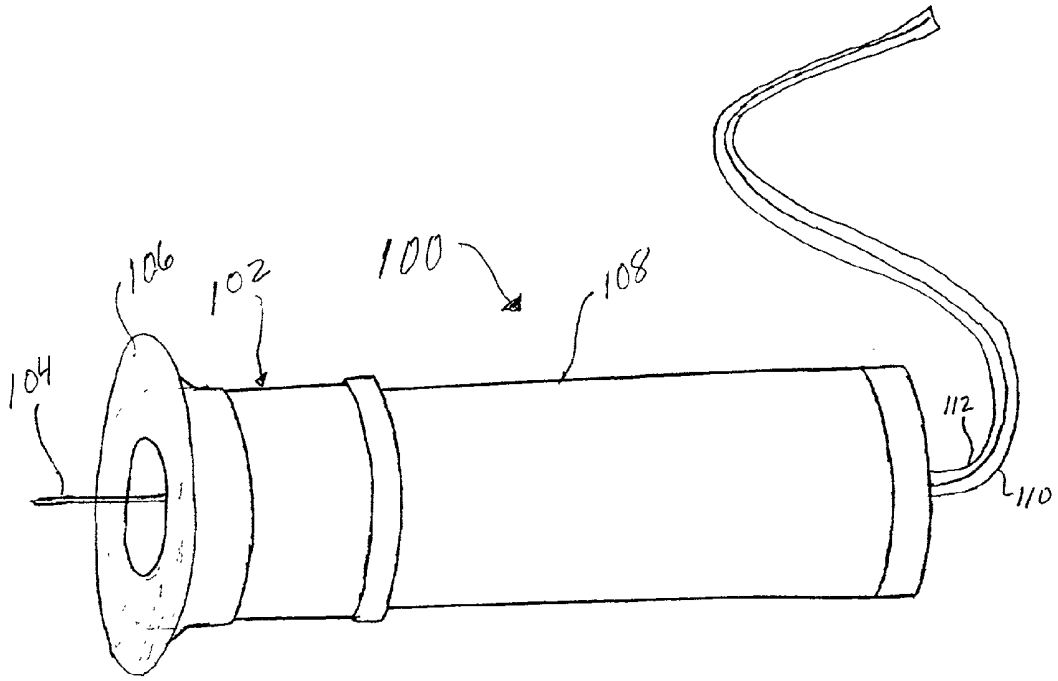


FIG. 1

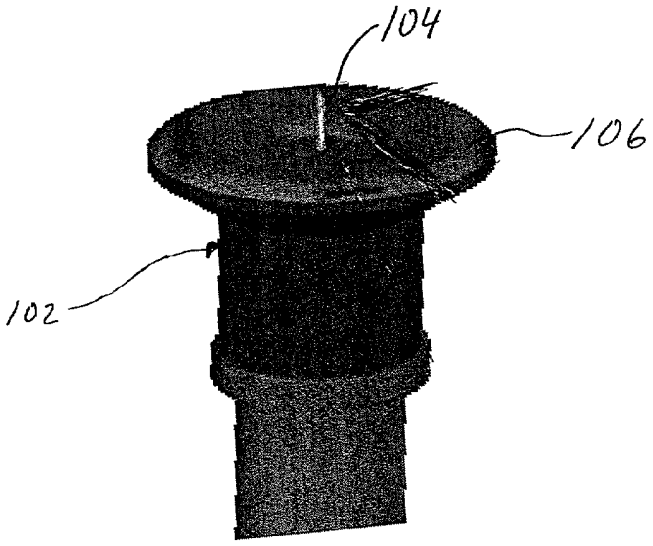


FIG. 2

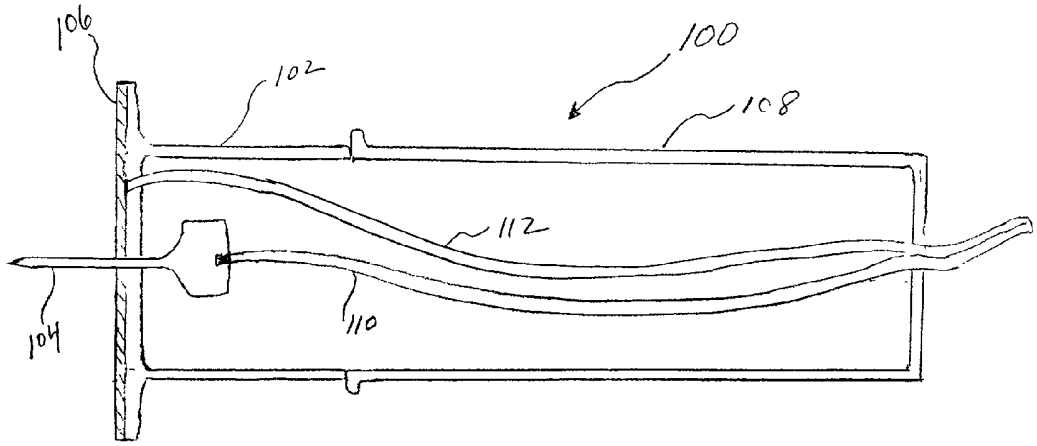

106
102
100
108
112
104
110

FIG. 3

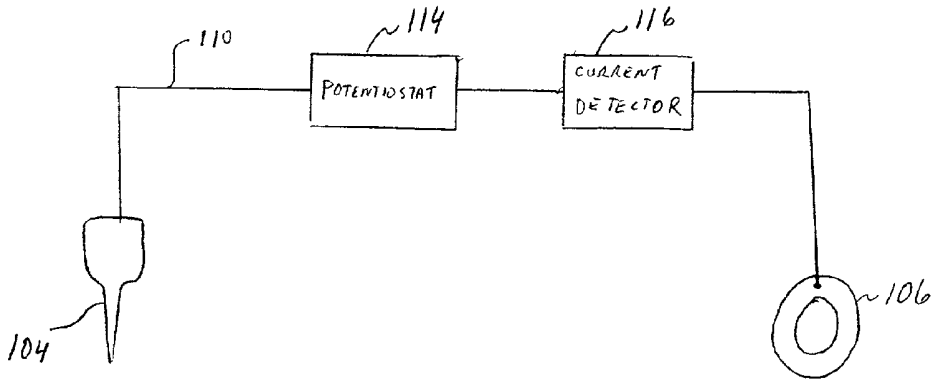

110
114
116
POTENTIOSTAT
CURRENT
DETECTOR
104
106

FIG. 4

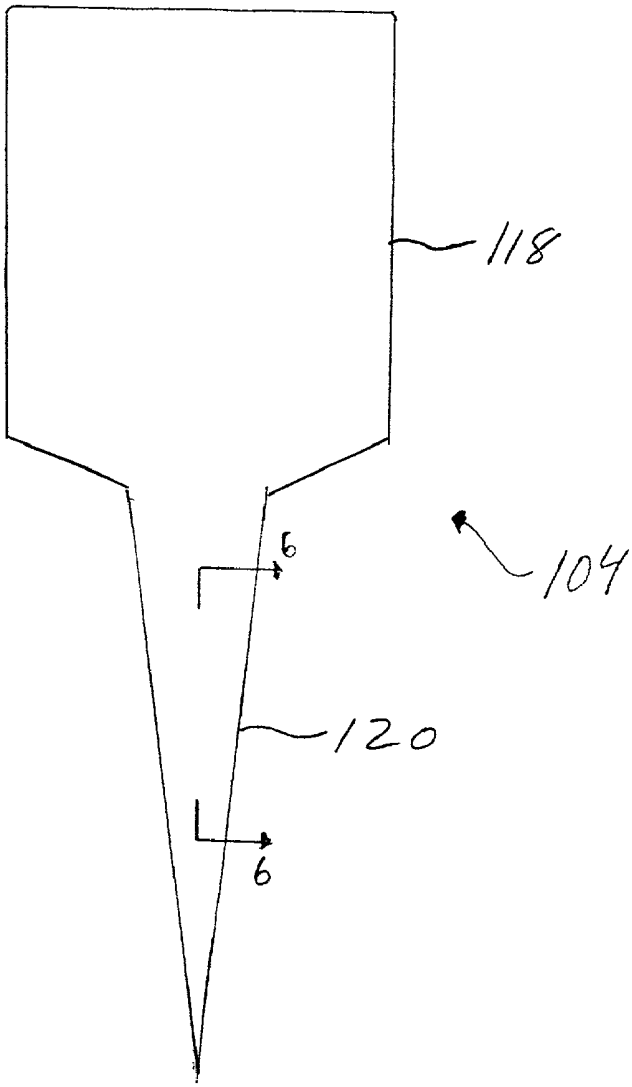


FIG. 5

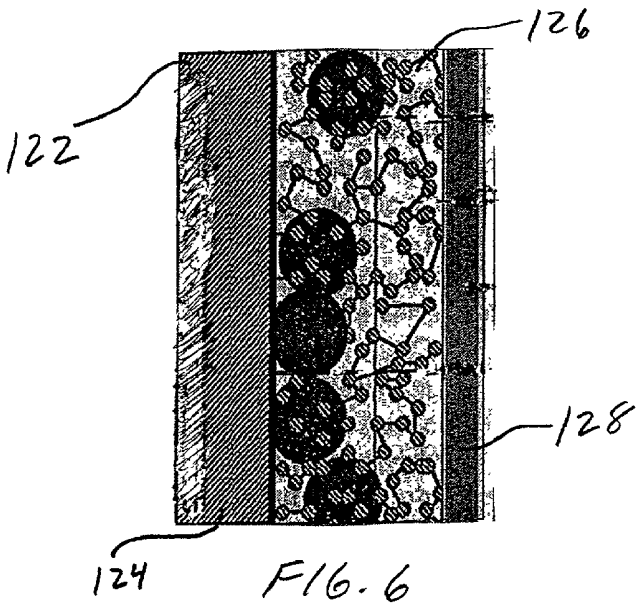


FIG. 6

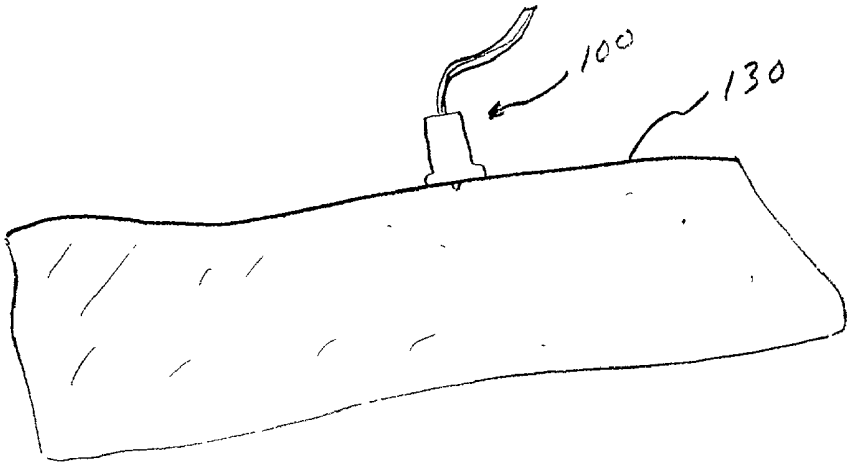

100
130

FIG. 7

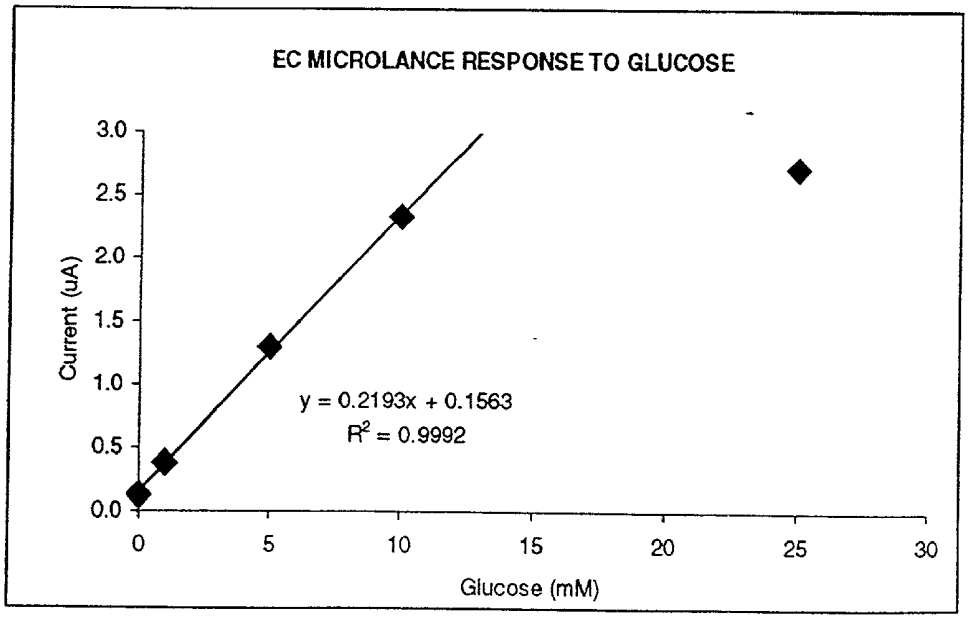

EC MICROLANCE RESPONSE TO GLUCOSE
Current (uA)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
y = 0.2193x + 0.1563
R2 = 0.9992
0
5
10
15
20
25
30
Glucose (mM)

FIG. 8

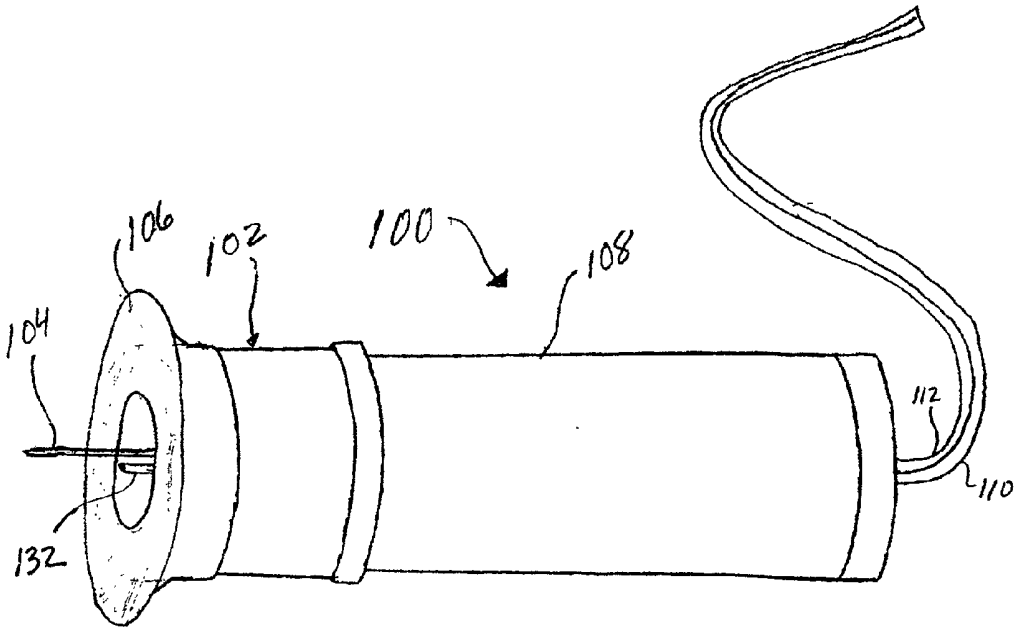


FIG. 9

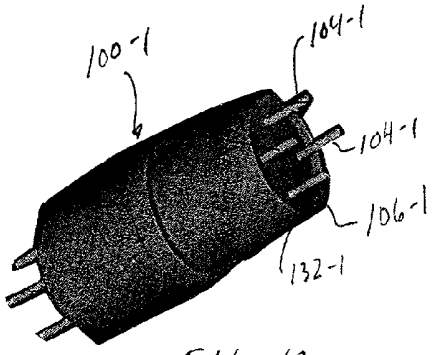


FIG. 10

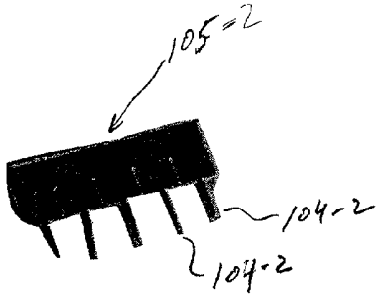


FIG. 11

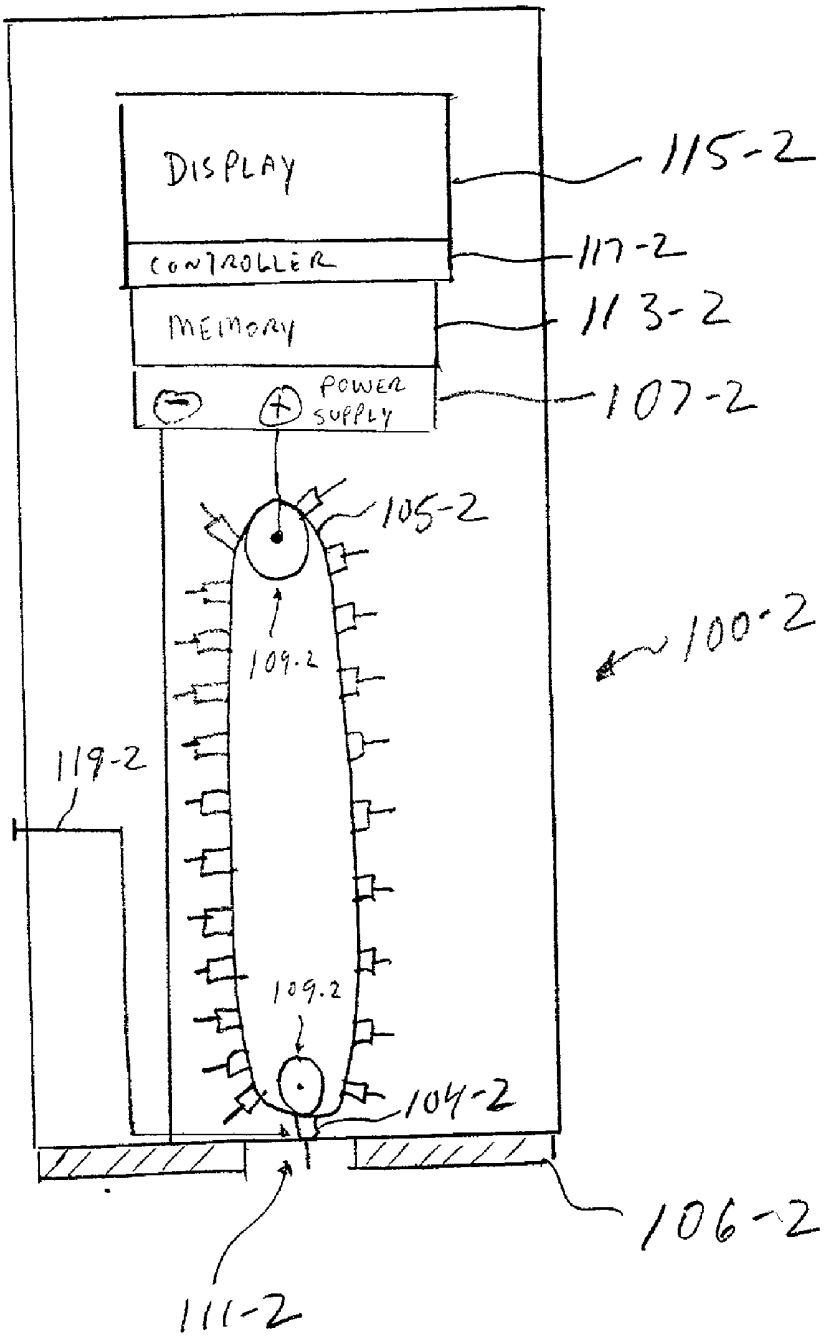

DISPLAY
115-2
CONTROLLER
117-2
MEMORY
113-2
POWER SUPPLY
107-2
105-2
109-2
100-2
119-2
109-2
104-2
106-2
111-2

FIG. 12

MINIMALLY-INVASIVE SYSTEM AND METHOD FOR MONITORING ANALYTE LEVELS

BACKGROUND THE INVENTION

[0001] 1. Field of the Invention

[0002] The present invention relates to a minimally-invasive system and method for monitoring analyte levels in a patient. More particularly, the present invention relates to a system and method employing a device which includes a micro probe functioning as an active electrode and a auxiliary electrode surrounding at least a portion of the active electrode, arranged to be placed against the skin of a patient to detect analyte levels in the patient with minimal pain and damage to the patient's skin.

[0003] 2. Description of the Related Art

[0004] People having diabetes must monitor their blood glucose level on a regular basis to assure that their blood glucose level remains within normal limits necessary to maintain a healthy living condition. Low glucose levels, known as hypoglycemia, can cause mental confusion and, in more extreme instances, coma and ultimately death. On the other hand, high blood glucose levels, known as hyperglycemia, can cause chronic symptoms such frequent urination and thirst, and if sustained over long periods of time, can result in damage to blood vessels, eyes, kidneys and other organs of the body.

[0005] Some people having mild diabetes can regulate their blood glucose levels through diet. However, people having moderate or severe forms of diabetes must take insulin to sustain acceptable blood glucose levels.

[0006] Conventional methods of monitoring blood glucose levels directly monitor the concentration of glucose in a small sample of blood taken from the person. Accordingly, if the person wishes to test his or her blood glucose level, the person can use a small needle or lance to puncture, for example his or her fingertip and drain a droplet of blood into the sampling device. However, this invasive method is painful to the person. Moreover, precautions must be taken sterilize the area in which the puncture is made, as well as the puncturing instrument, so that a pathogen is not introduced into the person's bloodstream. These methods can also be somewhat messy and unsanitary, and somewhat time consuming.

[0007] As an alternative to the conventional invasive techniques, miniaturized glucose sensing needles have been developed over the past several years. These types of devices typically include a metal substrate with an enzyme as an active electrode and an adjacent metal substrate that serve as the return and reference electrodes. The enzyme, typically glucose oxidase, catalyzes the oxidation of glucose, and the byproducts of the reaction are measured electrochemically at the active electrode. The electrochemical measurement is affected by imposing an electrical potential between the active and the counter/reference (auxiliary) electrodes. At a particular potential, electric current begins to flow as a consequence of the chemical reaction at the electrodes. The current is related to the concentration of the electro-active species, which is in turn governed by the amount of glucose in the test medium. In the case of conventional glucose strips, the test medium is capillary blood; in the case of implantable electrodes, the medium is tissue.

[0008] These devices are typically macroscopic or, in other words, more than 200 microns in diameter and often a centimeter or more in length. Accordingly, these devices are invasive, because they can penetrate the skin up to one centimeter deep. Additionally, these devices typically employ conventional needles, wires and multi-layer plastic substrates which require complicated multi-step manufacturing processes that are both time consuming and expensive. Examples of known glucose sensing devices are described in U.S. Pat. Nos. 4,953,552, 5,680,858 and 5,820,570, and in PCT publication WO 98/46124.

[0009] Maximizing the active electrode area increases the current response of the system. Especially in the case of the implantable system, the active electrode area is small—often ten-fold smaller than strip-based electrodes. Furthermore, the active and return/reference electrodes often share the same substrate—further limiting the available active area. One advantage of the invention described herein is that the return electrode is separated from the active electrode substrate and can be positioned on the surface of the skin, at least partially surrounding the minimally-invasive working electrode. This configuration allows maximum usage of the active electrode, and it permits the use of a large external return electrode. Both aspects improve the signal and performance of the system, while maintaining the small minimally invasive, pain-free format of the design.

[0010] Accordingly, a need exists for an improved minimally invasive system for monitoring analyte levels in patients.

SUMMARY OF THE INVENTION

[0011] The present invention relates to a system and method for detecting an analyte component, such as glucose, in a patient. The system and method employ a device comprising an active electrode optionally coated with a substance, such as glucose oxidase, and a counter-electrode that is configured to surround at least a portion of the active electrode. The configuration of the counter and active electrode improves the current flow through the device and increases the sensitivity of the device. When the device and method are used to detect the analyte of a patient, the active electrode may have a portion thereof adjacent to a substance, for example, glucose oxidase, and a length such that when the device is placed against the patient's skin, the active electrode is adapted to pass through the stratum corneum of the patient, preferably to a depth at which few nerve endings reside, to enable the analyte in the patient to be electrochemically detected, either directly or, for example, by reaction with a substance on the portion of the active electrode to produce an electrochemically detectable species. As stated above, the auxiliary electrode is configured to surround at least a portion of the active electrode, and is adapted to contact the patient's skin when the device is placed against the patient's skin. The active electrode extends beyond a base portion of the device to a length suitable to access the analyte, and the auxiliary electrode is coupled to a surface of the base portion proximate to that from which the active electrode extends. The active electrode is further adapted to have applied to its electric potential to measure a reaction between the analyte in the patient and the substance adjacent to the active electrode. The device can further include a reference electrode, disposed at a distance from the active electrode less than or

equal to a distance between the active electrode and any portion of the auxiliary electrode, or adjacent to the active electrode, or integral with the auxiliary electrode, so that the reference electrode acts as a reference potential for the electrical potential applied to the active electrode. The reference electrode can thus be used to compensate for changes in resistivity of the skin which can effect the accuracy of the device.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] These and other features and advantages of the present invention will be more readily appreciated from the following detailed description when read in conjunction with the appended drawings, in which:

[0013] **FIG. 1** illustrates an example of a analyte detecting device according to an embodiment of the present invention;

[0014] **FIG. 2** is a detailed view of the distal end of the analyte detecting device shown in **FIG. 1**;

[0015] **FIG. 3** is a cross-sectional view of the analyte detecting device shown in **FIG. 1**;

[0016] **FIG. 4** is an exemplary electrical schematic of the components employed in or used in conjunction with the analyte detecting device shown in **FIG. 1**;

[0017] **FIG. 5** is detailed view of an example of an active electrode employed in the analyte detecting device shown in **FIG. 1**;

[0018] **FIG. 6** is a detailed cross-sectional view of a portion of the active electrode shown in **FIG. 5**;

[0019] **FIG. 7** illustrates an example of the manner in which the analyte detecting device shown in **FIG. 1** is used on a patient;

[0020] **FIG. 8** is a graph showing an example of the relationship between current passing through the device shown in **FIG. 1** and the glucose concentration in the environment in which the active electrode is inserted;

[0021] **FIG. 9** illustrates an example of an analyte detecting device, as shown in **FIG. 1**, having a reference electrode;

[0022] **FIG. 10** is an example of an analyte detecting device according to another embodiment of the present invention;

[0023] **FIG. 11** is an example of a strip of active electrodes for the analyte detecting device according to a further embodiment of the present invention; and

[0024] **FIG. 12** illustrates a cross-sectional view of another example of a analyte detecting device as shown in **FIG. 1** modified to include an active electrode dispenser according to another embodiment of the present invention

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0025] FIGS. **1-6** illustrate an analyte detecting device **100** according to an embodiment of the present invention. As shown in **FIG. 1**, the device **100** includes a base portion **102** which employs an active electrode **104** and an auxiliary electrode and or in combination therewith, a reference electrode **106** which are described in more detail below. As used herein, the terms counter or reference electrode include combinations thereof as is known in the art. The base portion **102** is connected to a housing **108** that extends along the lengthwise direction of the device **100**. The base portion **102** and housing **108** can therefore act as the base of the device **100** that can be held during operation as described in more detail below. The base portion **102** can be fixed or pivotable with respect to the axis of active electrode **104** to any angle, by various means, for example, by constructing base portion **102** from an elastic material or providing a joint such that the active electrode can be inserted at a angle less than or about 90 degrees when the auxiliary electrode **106** is positioned substantially parallel and adjacent to the skin of a patient.

[0026] As shown in exemplary FIGS. **1-3** the active electrode **104** may be located along the axial center or substantially along the axial center of the device **100**. Also, an auxiliary electrode **106**, which may be circular or substantially circular, extends entirely around the active electrode **104**. Active electrode may alternatively be automatically or manually extendable from the base portion **102** either manually or by mechanical means to insert at least a portion of active electrode **104** through the stratum corneum at any angle greater than zero up to about 90 degrees relative to the surface of the skin to which it is applied. The auxiliary electrode **106** can be made entirely of, or be combinations thereof, of any suitable base material, either conductive or non-conductive, such a silicon, plastic, or a metal, or optionally a non-conductive material coated with a conductive material, such as gold, platinum, graphite, palladium, or the like, including thin metal foils or films or metal foils or films supported on plastic, paper, or other flexible material. The auxiliary electrode **106** can extend around the entire circumference of the base portion **102** of the device **100** as shown in **FIGS. 1 and 2**, or can extend along any suitable portion of the circumference of the base portion **102** so as to encircle the active electrode **104** either entirely or partially. The auxiliary electrode **106** can also be divided into several semi-circular or arcuate shapes. Alternatively, the auxiliary electrode **106** need not be circular, but can be any suitable shape such as square, rectangular, oval, or can be any suitable pattern of electrodes. Furthermore, the auxiliary electrode **106** can be configured as to contain adjacent to at least a portion of the surface, a conductive gel material or any other suitable conductive material or device. Auxiliary electrode **106** can be of suitable construction to provide for conforming closely and or securely to the skin, including the use of adhesive means generally know in the art. Auxiliary electrode **106** can also include an abrasive surface which can slightly abrade the surface of the patient's skin, as well as the stratum corneum, to thus establish better electrical contact with the patient. Furthermore, the auxiliary electrode **106** can be configured to be minimally invasive to the patient's skin as is the active electrode **104**.

[0027] An exemplary device is shown in **FIG. 3**, whereby the active electrode **104** may be coupled to a conductor **110** that extends along the hollow interiors of the base portion **102** and housing **108** of the device **100**, while auxiliary electrode **106** is coupled to a conductor **112** that also extends along the hollow interiors of the base portion **102** and housing **108** of the device **100**. Alternatively, the base portion **102** and housing **108** of the device **100** may be flat or of open-structure to lie substantially flat. Conductors **110** or **112** are electrically insulated from each other. An exemplary device, as illustrated schematically in **FIG. 4**, has the active electrode **104** and the counter-electrode **106** coupled

to a voltage generating device, such as a potentiostat **114**, and a current detector **116**, the purposes of which are described in more detail below.

[**0028**] As shown in **FIG. 5**, the active electrode **104** can have a tab portion **118** and a probe portion **120**. In this example, the tab portion **118** can be square-shaped or substantially square-shaped having a width of 1 mm or about 1 mm and a length of 1 mm or about 1 mm. The probe portion **120** can have a length ranging from at or about 20 μm to at or about 5000 μm. However, the length of the probe portion **120** is preferably small, for example, at or about 100-2000 μm, so as to be minimally invasive when inserted in the patient's skin as described in more detail below. In addition, the diameter of the tip of probe **120** is substantially small, for example 100-250 μm or less. Also, the active electrode **104** need not have the configuration shown in **FIG. 5**, but rather, can be shaped as a needle, microlance, microneedle, or have any other suitable shape to provide access through the stratum corneum.

[**0029**] Furthermore, the active electrode **104** can be disposable, that is, used once and replaced with another fresh active electrode **104**. In other words, the active electrode **104** can be removably coupled to the conductor via, for example, a socket arrangement (not shown) so that after use, the active electrode **104** can be removed from the device **100** by hand or through the use of an instrument, and discarded. Alternatively, the device **100** can be configured with an ejection tool (not shown) which ejects the active electrode **104**. Once the used active electrode **104** has been removed or ejected, another active electrode **104** can be inserted into the device **100**.

[**0030**] Also, as discussed in more detail below with regard to **FIGS. 11 and 12**, the device **100** can be configured with a supply of active electrodes **104**, which can be selectably fed to an active location such as that shown in **FIG. 1**, and then discarded after use. Likewise, the auxiliary electrode **106** can be reusable or disposable. In addition, the device **100** can be configured with a retractable mechanism (not shown) that can be controlled to extend the active electrode **104** from the distal end of the device **100** so that the active electrode **104** can enter the patient's stratum corneum when the distal end of the device is placed against the patient's skin as can be appreciated by one skilled in the art. The retractable mechanism can further be controlled to retract the active electrode **104** back into an opening in the distal end of the device **100** after use. Alternatively, the retractable mechanism can be configured as an ejection mechanism to eject the active electrode **104** after use so that a fresh active electrode **104** can be installed.

[**0031**] **FIG. 6** is a cross-sectional view of a portion of an exemplary probe portion **120** of the active electrode **104** as shown in **FIG. 5**. As illustrated, the probe portion **120** is made of a base material **122**, such a silicon substrate, stainless steel, plastic, or any other suitable material. The base material **122** is coated with a conductor, such as platinum, gold, graphite, palladium, or any other suitable material **124**. For example, the base material **122** can be sputter-coated with platinum to form the conductive layer **124**. A substance **126** adjacent to at least a portion of **124**, for example, glucose oxidase containing layer **126**, is applied to the conductive layer **124** in an immobilization matrix as illustrated. For example, the glucose oxidase can be dissolved in aqueous media and dispensed onto conductive layer **124** followed by exposure to glutaraldehyde solution, and allow to dry. Upon drying, the glucose oxidase enzyme becomes cross-linked on the surface of the base material **122**. Or the enzyme can be immobilized by spin coating an aqueous solution of enzyme and a UV crosslinkable polyvinyl alcohol modified polymer. An interference film **128** can then be applied over the glucose oxidase layer **126** as shown. Glucose oxidase enzyme immobilization methods and interference films for reducing extraneous signal from electro-active species found in biological fluids are well known in the art. Additionally, mediators can be included in the layer **126** as is known in the art.

[**0032**] It is also noted that the active electrode **104** can be coated with differed types or combinations of enzymes, such as glucose oxidase, dehydrogenase, lactate dehydrogenase, and so on, and can use non-enzymatic molecular recognition chemicals capable of redox chemistry, otherwise known as electrochemically responsive receptors, to detect different types of components in the patient, all of which are known in the art. It is also noted that the active electrode **104** can be substantially free of any substance or enzyme as taught by Jung, S. K. et al., *Analytical Chemistry,* 71: 3642-3649 (1999); Gorski et al., *J. Electroanalytical Chem.* 425 (1-2): 191-199 (1997); and Zen et al., *Analyst,* 125 (12): 2169-2172 (2000), the entire contents of each being incorporated herein by reference.

[**0033**] For example, the device **100** can be used to measure electrochemically active components such as electrolytes, oxygen, nitric oxide, lactate, insulin, neurotransmitters, drugs, and other analytes in the patient's body, as well as other characteristics such as the pH level in the patient's blood, the patient's temperature, resistance of the patient's skin, and so on. The reaction that occurs on the active electrode **104** can thus be a direct measure of electro-active species such as oxygen, nitric oxide, and so on, or the reaction can rely on enzymes to enable electrochemical detection such as glucose oxidase, glucose dehydrogenase, lactate dehydrogenase, as discussed above. It is understood that the term analyte includes electrochemically active species present in the patient as well as electrochemically active reaction products or by-products of species present in the patient with substances in layer **126**. Also, the device **100** can be configured with many types of materials, such as metals, ceramics, or plastics, and the electronics shown in **FIG. 4** can be integrated into the device **100**, if desired. Additionally, device **100** can be integrated with any drug delivery device. Drug delivery devices include infusion, pump, transdermal, syringe, gas-assisted particle injectors, electroporation, intra- and interdermal injection devices for introducing liquid, particles, suspensions, emulsions, nanoparticles, micelles, liposomes and the like. Additionally, device **100** can be integrated with any drug delivery device to provide "closed-loop" control of monitoring and delivery of drugs, nucleic acids, or proteins.

[**0034**] The operation of the device **100** will now be described. As shown in **FIG. 7**, when the device **100** is used to detect the analyte of interest in the patient, the active electrode **104** and auxiliary electrode **106** can be brought into contact with the surface of a patient's skin **130**, such as the surface of the patient's arm. By extending active electrode **104** from the base portion **102** either with mild pressure or by way of mechanical means, the active elec-

trode **104** will pass through the stratum corneum of the patient's skin **130**, while the auxiliary electrode **106** will rest on the surface of the patient's skin **130**. It is noted that since the length of the active electrode **104** is small, for example 100-2000 μm, the active electrode **104** will only penetrate minimally into the patent's skin **130**, and will reduce or eliminate substantially the tendency of the patient to bleed, nor will it contact the nerve endings in the patient's skin **130** to cause the patient discomfort. In an alternative embodiment, a plurality of active electrodes **104** are provided suitable for indexing sequentially within the base portion **102** and auxiliary electrode **106** for use followed by storage of used active electrodes for ease and save disposal thereof. Indexing of the plurality of electrodes is achieved using mechanical means suitable for such manipulation as known in the art.

[**0035**] Once through the stratum corneum, the active electrode **104** or the substance adjacent thereto electrochemically interacts with analyte in the tissue, or blood or interstitial fluid thus providing a detectable signal. For example, when the substance is glucose oxidase and the analyte is glucose, when the device **100** is placed against the skin and active electrode **100** is passed through the stratum corneum to a depth sufficient to access the analyte, the following electrochemical reaction occurs:

$$\text{Glucose} + H_2O + 1/2\,O_2 \xrightarrow{\text{Glucose Oxidase}} \text{Gluconic acid} + H_2O_2$$

[**0036**] As can be appreciated by one skilled in the art, in accordance with the above reaction, oxygen is converted to hydrogen peroxide (H_2O_2) in the absence of mediators. The potentiostat **114** (see **FIG. 4**) can then be controlled to apply a potential to the active electrode **104** to place the active electrode **104** at an effective electric potential relative to the electrical potential of the patient's skin and preferably relative to the electrical potential of the auxiliary electrode **106**. By effective electric potential, it is understood to mean a potential suitable to oxidize any or all of the electrochemically active analyte or species, for example, hydrogen peroxide generated by the glucose-glucose oxidase reaction set forth above, and induce a measurable electrical current to flow through the device **100** and, in particular, through the patient's skin **130** between the active electrode **104** and auxiliary electrode **106**. The effective electric potential, as is known in the art, is dependent on the metal substrate **124** chosen. The applied effective potential may be applied in a variety of ways as required by the specific application, including but not limited to ramped, stepped, pulsed, programmed pulse, and combinations thereof.

[**0037**] The magnitude of this current is related to the concentration of glucose in the patient. As shown, for example, in the graph of **FIG. 8**, the magnitude of current increases as the glucose level increases. Current detector **116** can monitor the current that is flowing thought the device **100**. The current detector can be coupled to a controller (not shown), such as a microcomputer, which interprets the current in accordance with the graph shown in **FIG. 8** to determine glucose level in the patient's blood. The detector can be configured as is known in the art to measure current or charge directly, or derivatives thereof.

[**0038**] It is further noted that variations in the condition of the patient's skin **130** can possibly affect the accuracy of the readings, because such variations can alter the level of current flow. As discussed in the example above, the active electrode **104** must be maintained at a specific electrical potential relative to the surrounding medium, for example, the patient's skin. This potential is typically within the range from at or about −0.6 V to at or about +0.6 V, depending on the electrochemistry of the analyte at the active electrode **104** and the nature of the metal substrate **124**. Because the auxiliary electrode **106** is separated from the active electrode **104** by a certain distance (e.g., up to about 1 centimeter), a voltage drop (an "IR" drop) occurs between the active electrode **104** and the auxiliary electrode **106** due to the resistance of the patient's skin between these electrodes when the device **100** is applied to the patient's skin. Furthermore, because this IR drop varies due to a multitude of skin conditions and characteristics of the electrodes **104** and **106**, the auxiliary electrode **106** may not be suitable as a reference potential for the electrical potential applied to the active electrode **104**.

[**0039**] Accordingly, as shown by way of example in **FIG. 9**, the device **100** can include a reference electrode **132** positioned near to or adjacent the active electrode **104**, so that the reference electrode **132** is in the electric field that is generated between the active electrode **104** and auxiliary electrode **106**. This reference electrode **132** is electrically coupled to the power supply. However, the reference electrode can be integral with and electrically isolated from either the active electrode or the auxiliary electrode. For example, the tip portion of probe **120** of the active electrode **104** (See **FIGS. 5 and 6**) can have the reference electrode adjacent to the active electrode on one side only or side by side on the same side, provided they are electrically isolated (from active electrode). Because the reference electrode **132** is positioned close to the active electrode **104** and thus, only a slight amount of the patient's skin is present between these electrodes when the device **100** is placed on the patient's skin **130**, there is only a negligible IR drop between the active electrode **104** and the reference electrode **132** due to the patient's skin **130**. Furthermore, since the IR drop is negligible, variations in skin conditions have little overall effect on the magnitude of this IR drop, thus ensuring that the correct electrical potential is being applied to the active electrode **104** during the measurement. For example, the probe portion **120** of the active electrode **104** (see **FIGS. 5 and 6**) can have the glucose oxidase coating on one side only, and an electrically isolated conductive coating on the other side to enable that side of the active electrode **104** to act as the reference electrode.

[**0040**] It is further noted that additional variations to the device **100** discussed above can be made. For example, the device **100** can have any suitable shape. As shown in **FIG. 10**, the device can have a cylindrical shape as does device **100-1**, and can include multiple active electrodes **104-1**, as well as one or more reference electrodes **132-1**, surrounded by an auxiliary electrode **106-1**. By employing multiple active electrodes **104-1**, a plurality of parallel measurements can be taken, thus increasing the overall signal strength of the measurements without increasing pain to the patient. Alternatively, the multiple active electrodes **104-1** can be coated with different types or concentrations of enzymes as discussed above (or with none at all) to simultaneously detect different types of components or parameters as dis-

cussed above. In this arrangement, each different active electrode **104-1** is coupled, for example, to a respective input of a processor (not shown), or are otherwise discernable by the processor, so that the processor can interpret the different measurements.

[**0041**] In addition, the device **100** and its variations discussed above can be combined with a drug or medicament or medication delivery device, such as an insulin delivery device (not shown), which would automatically deliver the appropriate amount of insulin to the patient to correct the patient's blood glucose level. In other words, the device **100** and its variations can communicate with another instrument to recommend an action by the instrument or to adjust the action of an instrument. The device **100** and its variations can include a memory for storing information such as readings obtained by the device **100**, or information provided by other instruments. Furthermore, the device **100** and its variations can be wearable like a watch or bracelet so that it can operation as a continuous or substantially continuous monitoring system.

[**0042**] The probe portion **120** active electrode **104** can also be coated with a sorbent coating so that when the active electrode **104** comes in contact with the fluid in the patient's skin **130**, it immediately captures the fluid and therefore it does not have to reside in the patient's skin for a long period of time to take a reading. The active electrode **104** can be further configured as a hollow lumen, and the substance adjacent to the active electrode, such as for example glucose oxidase, can be placed inside the lumen. In this configuration, multiple openings can be placed in the lumen to allow free and rapid penetration of the component of interest (e.g., glucose) in the patient's skin **130** to enter the lumen. In this lumen configuration, selective layers can be placed over the openings or as a coating over the device **100** to prevent interfering species, such as ascorbate, urate, and acetaminophen, from encountering the active electrode **104**.

[**0043**] As shown in **FIG. 11**, multiple active electrodes **104-2** can be configured along a strip **105-2**, which can be employed in an alternative configuration of the device **100-2** as shown in **FIG. 12**. That is, the device **100-3** can be configured as a dispenser for dispensing a plurality of active electrodes **104-2**. As indicated, the strip **105-2** of active electrodes **104-2** can be loaded into the device **100-2** so that the device **100-2** thus contains a plurality of active electrodes **104-2** that can be fed sequentially as needed to provide a sterile, disposable component capable of storing the microprobes after use to minimize accidental injury. The device **100-2** further includes an auxiliary electrode **106-2** which can be similar to the auxiliary electrodes discussed above. The device **100-2** can further include a power supply **107-2** for providing an electrical potential across the active electrodes **104-2** and the auxiliary electrode **106-2**.

[**0044**] That is, as indicated, the active electrodes **104-2** can be coupled to the strip **105-2** that is capable of conducting current from the anode of the power supply **107-2** to the active electrodes **104-2**. A cartridge changing button (not shown) can be pressed to rotate the strip **105-2** about pulleys **109-2** to place another active electrode **104-2** at the active location **111-2** for taking a reading. The device **100-2** further includes a memory **113-2** for storing readings that have been taken in the manner described above for device **100**, a display **115-2** for displaying the readings, and a controller **117-2** for controlling the operations of the power supply **107-2**, memory **113-2**, display **115-2** and any of the other components discussed above. The device **100-2** also includes an active electrode extender shown schematically as item **119-2** in **FIG. 12**, which can be controlled to extend and retract the active electrode **104-2** out from and into the device **100-2**, respectively, for use. The extender **119-2** can further be configured to eject the active electrode **104-2** after use as can be appreciated by one skilled in the art. The auxiliary electrode **106-2** can be similarly extendable and retractable.

[**0045**] It is also noted that each active electrode **104-2** can be configured to have a portion which acts as the active electrode, and another portion, electrically isolated from the active electrode portion, that acts as a reference electrode like reference electrode **132** discussed above. In this arrangement, the strip **105-2** can be divided into two electrically isolated sections, one of which contacting the active portion of the active electrodes **104-2** and the other contacting the reference electrode portion of the active electrodes **104-2**. The pulleys **109-2** can likewise be segregated to conduct separate paths of current to the separate portions of the strip **105-2** and thus, to the active and control portions of the active electrodes **104-2**. The controller **115-2** can thus distinguish from the currents flowing through the active and control portions of the active electrode **104-2**.

[**0046**] In addition, the device **100-2** can be configured to perform all the functions discussed above with regard to device **100** discussed above, to detect all of the components as discussed above. Also, the device **100-2** can be configured to communicate with another instrument to recommend an action by the instrument or to adjust the action of an instrument. Furthermore, the device **100-2** can be wearable like a watch or bracelet so that it can operation as a continuous or substantially continuous monitoring system.

[**0047**] Although only a few exemplary embodiments of this invention have been described in detail above, those skilled in the art will readily appreciate that many modifications are possible in the exemplary embodiments without materially departing from the novel teachings and advantages of this invention. Accordingly, all such modifications are intended to be included within the scope of this invention as defined in the following claims.

What is claimed is:

1. A device for detecting at least one analyte in a patient, comprising:

at least one active electrode, said active electrode having a length such that said active electrode is adapted to pass through the stratum corneum to a depth sufficient to access said analyte to enable the electrochemical detection of said analyte; and

at least one auxiliary electrode configured to at least partially surround said active electrode, and adapted to contact patient's skin when the device is placed against said patient.

2. A device as claimed in claim 1, wherein:

said device further includes a base portion integral with said auxiliary electrode; and

said active electrode is extendable beyond said base portion to a length sufficient to access said analyte.

3. A device as claimed in claim 2, wherein:

said active electrode is retractable into said base portion.

4. A device as claimed in claim 3, wherein:

said active electrode is automatically extendable beyond said base portion and automatically retractable into said base portion.

5. A device as claimed in claim 3, wherein:

said active electrode is manually extendable beyond said base portion and automatically retractable into said base portion.

6. A device as claimed in claim 1, wherein:

said auxiliary electrode has an abraded surface which is adapted to contact said patient's skin.

7. A device as claimed in claim 1, wherein:

said auxiliary electrode is adapted to pass into the stratum corneum when contacting said patient's skin.

8. A device as claimed in claim 1, further comprising:

a data storage, adapted to store information pertaining to said at least one analye or said patient.

9. A device as claimed in claim 1, further comprising:

a communication device, adapted to communicate information between said device and an external device.

10. A device as claimed in claim 1, wherein:

said device is adapted for wearing by said patient for a duration of time.

11. A device as claimed in claim 1, wherein:

said device is further adapted to detect at least one parameter of said patient, such that said length of said active electrode enables said active electrode to pass through the stratum corneum to said depth sufficient to access a component to enable the electrochemical detection of said parameter; and

said at least one analyte and said at least one parameter includes at least one of the following:

electrolytes, oxygen, nitric oxide, lactate, insulin, neurotransmitters, at least one drug, pH level in the patient's blood, the patient's temperature, resistance of the patient's skin, glucose oxidase, glucose dehydrogenase and lactate dehydrogenase.

12. A device as claimed in claim 1, further comprising:

a plurality of said active electrodes.

13. A device as claimed in claim 1, wherein:

said auxiliary electrode is configured to substantially entirely surround said active electrode.

14. A device as claimed in claim 1, wherein:

said auxiliary electrode is coupled to at least a portion of the surface of said base portion proximate to that from which said active electrode extends.

15. A device as claimed in claim 1, wherein:

said active electrode is further adapted to have an electrical potential applied thereto to enable the electrochemical detection of said analyte.

16. A device as claimed in claim 1, wherein:

said analyte is electrochemically active.

17. A device as claimed in claim 1, wherein:

said analyte is selected from nitric oxide, neurotransmitters, insulin, and oxygen.

18. A device as claimed in claim 1, wherein:

said active electrode is selected from antimony, ruthenium, rhodium, platinum, palladium, graphite, gold, and oxides thereof.

19. A device as claimed in claim 1, further comprising:

at least one reference electrode, disposed at a distance from said active electrode equal to or less than a distance between said active electrode and any portion of said auxiliary electrode, said reference electrode being adapted to provide a reference potential for said electric potential applied to said active electrode.

20. A device as claimed in claim 1, further comprising:

a plurality of active electrodes adapted to be positioned for use in a sequential manner.

21. A device as claimed in claim 20, wherein:

said plurality of active electrodes are contained after use.

22. A device as claimed in claim 1, further comprising:

a delivery device integral therewith.

23. A device as claimed in claim 22, wherein:

said device and said delivery device are adapted to communicate with each other to control administration of a substance that said delivery device delivers to said patient.

24. A device for detecting at least one analyte in a patient, comprising:

at least one active electrode having a length such that said active electrode is adapted to pass through the stratum corneum of said patient to a depth sufficient to access said analyte; and

at least one substance adjacent to at least a portion of said active electrode capable of reacting with at least one analyte to produce at least one electrochemically active product; and

an auxiliary electrode configured to at least partially surround said active electrode, and adapted to contact said patient's skin when the device is placed against said patient.

25. A device as claimed it in claim 24, wherein:

said auxiliary electrode is configured to substantially entirely surround said active electrode.

26. A device as claimed in claim 24, wherein:

said device further includes a base portion integral with said auxiliary electrode; and

said active electrode is extendable beyond said base portion for a length sufficient to access said analyte.

27. A device as claimed in claim 26, wherein:

said active electrode is retractable into said base portion.

28. A device as claimed in claim 27, wherein:

said active electrode is automatically extendable beyond said base portion and automatically retractable into said base portion.

29. A device as claimed in claim 27, wherein:

said active electrode is manually extendable beyond said base portion and automatically retractable into said base portion.

30. A device as claimed in claim 24, wherein:

said auxiliary electrode has an abraded surface which is adapted to contact said patient's skin.

31. A device as claimed in claim 24, wherein:

said auxiliary electrode is adapted to pass into the stratum corneum when contacting said patient's skin.

32. A device as claimed in claim 24, further comprising:

a data storage, adapted to store information pertaining to said at least one analye or said patient.

33. A device as claimed in claim 24, further comprising:

a communication device, adapted to communicate information between said device and an external device.

34. A device as claimed in claim 24, wherein:

said device is adapted for wearing by said patient for a duration of time.

35. A device as claimed in claim 24, wherein:

said device is further adapted to detect at least one parameter of said patient, such that said length of said active electrode enables said active electrode to pass through the stratum corneum to said depth sufficient to access a component to enable the electro chemical detection of said parameter; and

said at least one analyte and said at least one parameter includes at least one of the following:

electrolytes, oxygen, nitric oxide, lactate, insulin, neurotransmitters, at least one drug, pH level in the patient's blood, the patient's temperature, resistance of the patient's skin, glucose oxidase, glucose dehydrogenase and lactate dehydrogenase.

36. A device as claimed in claim 24, further comprising:

a plurality of said active electrodes.

37. A device as claimed in claim 24, wherein:

said auxiliary electrode is coupled to at least a portion of the surface of said base portion proximate to that from which said active electrode extends.

38. A device as claimed in claim 24, wherein:

said active electrode is further adapted to have an electric potential applied thereto to enable reaction between said analyte in said patient and said substance to produce at least one electrochemically active product.

39. A device has claimed in claim 24, further comprising:

at least one reference electrode, disposed at a distance from said active electrode equal to or less than a distance between said active electrode and any portion of said auxiliary electrode, said reference electrode being adapted to act as a reference potential for said electric potential applied to said active electrode.

40. A device as claimed in claim 24, wherein:

said substance is selected from glucose oxidases, glucose dehydrogenases, and electrochemically responsive receptors.

41. A device as claimed in claim 24, further comprising:

a plurality of active electrodes adapted to be positioned for use in a sequential manner.

42. A device as claimed in claim 41, wherein:

said plurality of active electrodes are contained after use.

43. A device as claimed in claim 24, further comprising:

a delivery device integral therewith.

44. A device as claimed in claim 22, wherein:

said device and said delivery device are adapted to communicate with each other to control administration of a substance that said delivery device delivers to said patient.

45. A method for detecting an electrochemically active component in a patient, comprising:

placing a device against the skin of said patient, said device having at least one active electrode, said active electrode having a length adapted to pass through the stratum corneum of said patient to a depth sufficient to access said analyte, said device having at least one auxiliary electrode configured to at least partially surround said active electrode, said auxiliary electrode being adapted to contact said patient's skin when said device is placed against said patient;

applying a potential to said active electrode; and,

measuring current or charge from the electrochemical reaction of said electrochemically active component and said active electrode.

46. A method as claimed in claim 45, wherein

said measuring is selected from integrated current, derivative of current, and derivative of charge.

47. A method as claimed in claim 45, wherein:

said applying an electric potential to said active electrode is selected from ramped, stepped, pulsed, programmed pulse and combinations thereof.

48. A method as claimed in claim 45, wherein said applying step comprises:

adjusting the amount of said electrical potential applied to said active electrode with reference to a reference electrode of said device wherein said reference electrode is disposed at a distance equal to or less than between said active electrode and any portion of said auxiliary electrode.

49. A method as claimed in claim 45, wherein:

said device further includes a base portion integral with said auxiliary electrode; and

said method further includes extending said active electrode beyond said base portion to a length sufficient to access said component.

50. A method as claimed in claim 49, further comprising:

retracting said active electrode into said base portion.

51. A method as claimed in claim 50, wherein:

said extending and retracting of active electrode are performed automatically.

52. A method as claimed in claim 50, wherein:

said extending and retracting of active electrode are performed manually.

53. A method as claimed in claim 45, wherein:

said auxiliary electrode has an abraded surface which is adapted to contact said patient's skin.

54. A method as claimed in claim 45, wherein:

said auxiliary electrode is adapted to pass into the stratum corneum when contacting said patient's skin.

55. A method as claimed in claim 45, further comprising:

storing information pertaining to said component.

56. A method as claimed in claim 45, further comprising:

communicating information between said device and an external device.

57. A method as claimed in claim 45, further comprising:

wearing said device on said patient for a duration of time.

58. A method as claimed in claim 45, wherein:

said device includes a plurality of said active electrodes; and

said method includes performing said placing, applying and measuring steps using said plurality of active electrodes.

59. A method as claimed in claim 45, further comprising:

enabling said device and a delivery device to communicate with each other to control administration of a substance that said delivery device delivers to said patient.

60. A method as claimed in claim 45, wherein said component includes one of the following:

an electrolyte, oxygen, nitric oxide, lactate, insulin, neurotransmitters, a drug, pH level in the patient's blood, a component indicative of the patient's temperature, a component indicative of resistance of the patient's skin, glucose oxidase, glucose dehydrogenase and lactate dehydrogenase.

61. A method for detecting a component in a patient, comprising:

placing a device against the skin of said patient, said device having at least one active electrode, said active electrode having a length adapted to pass through the stratum corneum of said patient to a depth sufficient to access said analyte, said active electrode having at least one substance adjacent to at least a portion of said active electrode to enable said component to react with said substance to produce at least one electrochemically active product, said device having at least one auxiliary electrode configured to at least partially surround said active electrode, said auxiliary electrode being adapted to contact said patient's skin when said device is placed against said patient;

applying a potential to said active electrode; and

measuring current based on said reaction of said electrochemically active component in said patient and said substance.

62. A method as claimed in claim 61, wherein

said measuring is selected from integrated current, derivative of current, and derivative of charge.

63. A method as claimed in claim 61, wherein:

said applying an electric potential to said active electrode is selected from ramped, stepped, pulsed, programmed pulse and combinations thereof.

64. A method as claimed in claim 61, wherein said applying step comprises:

adjusting the amount of said electrical potential applied to said active electrode with reference to a reference electrode of said device wherein said reference electrode is disposed at a distance equal to or less than between said active electrode and any portion of said auxiliary electrode.

65. A method as claimed in claim 61, wherein:

said substance is selected from glucose oxidases, glucose dehydrogenases, and electrochemically responsive receptors.

* * * * *

专利名称(译)	用于监测分析物水平的微创系统和方法		
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摘要(译)

一种微创分析物检测装置及其使用方法。该系统和方法采用具有任选地涂覆有物质的有源电极的装置，以及配置为至少部分地围绕有源电极的对电极。辅助电极和有源电极的配置改善了通过器件的电流并增加了器件的灵敏度。当将装置放置在患者皮肤上时，活性电极适于通过患者的角质层进入深度小于真皮末端所在的真皮深度。将电势施加到有源电极，并且基于流过器件的电流或电荷量确定分析物水平。