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

MINIMALINVASIVES SYSTEM UND VERFAHREN ZUR ÜBERWACHUNG VON ANALYTENKONZENTRATIONEN

SYSTEME DES MOINS EFFRACTIF PERMETTANT DE CONTROLER DES CONCENTRATIONS D'ANALYSAT ET METHODE AFFERENTE

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(56) References cited:
EP-A- 0 965 301
EP-A- 1 266 619
EP-A- 1 266 625
EP-A2- 0 964 060
WO-A-00/74763
WO-A-01/13989
WO-A-96/14026
US-B1- 6 183 434
US-B1- 6 256 533

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Description

Field of the Invention:

[0001] 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.

Description of the Related Art:

[0002] 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.

[0003] 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.

[0004] 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.

[0005] 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.

[0006] 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. Patent Nos. 4,953,552, 5,680,858 and 5,820,570, and in PCT publication WO 98/46124.

[0007] 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.

[0008] Accordingly, a need exists for an improved minimally invasive system for monitoring analyte levels in patients. WO 96/14026, to which the preambles of each of independent claims 1 and 19 refer, discloses a liquid delivery device comprising a housing having a lower surface for application to the skin of a subject and having a reservoir and a gas generation chamber therein separated by a displaceable membrane. Gas generated by an electrolytic cell under the control of a microprocessor causes the gas generation chamber to expand and the reservoir to contract, thereby discharging a liquid drug, such as insulin, from the reservoir via a hollow delivery needle extending from the lower surface. The delivery needle and a sensor needle both extend from the lower surface a sufficient distance so as to penetrate through the epidermis and into the dermis when the housing is pressed against the skin. The sensor needle has an

enzymatic coating for the detection of an analyte, such as glucose in the subject's plasma. The delivery needle is made of platinum-iridium and a current passes between the needles and a potentiostat circuit according to the amount of glucose detected. A reference electrode which rests against the subject's skin increases the accuracy of the glucose measurement. The current through the potentiostat circuit is measured by a voltmeter and a signal from the voltmeter is amplified and communicated to the microprocessor which determines the correct rate of delivery of the drug on the basis of the level of analyte detected in the subject's plasma.
EP 0 964 060 A2 discloses a measurement device facilitating accurate quantitation of a substrate from a trace amount of sample. The method uses an analysis element comprising a pair of electrodes for electrochemically quantitating reaction between a substrate in a sample and an oxidoreductase. One of the electrodes of the analysis element is a membrane formed on an inner wall of a cylindrical hollow space having an opening and the other is a needle. The needle electrode is projected temporarily external to the hollow space to puncture a subject and the resultant sample is collected from the subject.

SUMMARY OF THE INVENTION

[0009] The device of the invention is defined by the features in independent claim 1 and the method of the invention is defined by the features in independent claim 19.
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 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

[0010] 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:
[0011] Fig. 1 illustrates an example of a analyte detecting device according to an embodiment of the present invention;
[0012] Fig. 2 is a detailed view of the distal end of the analyte detecting device shown in Fig. 1;
[0013] Fig. 3 is a cross-sectional view of the analyte detecting device shown in Fig. 1;
[0014] 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;
[0015] Fig. 5 is detailed view of an example of an active electrode employed in the analyte detecting device shown in Fig. 1;
[0016] Fig. 6 is a detailed cross-sectional view of a portion of the active electrode shown in Fig. 5;
[0017] Fig. 7 illustrates an example of the manner in which the analyte detecting device shown in Fig. 1 is used on a patient;
[0018] 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;
[0019] Fig. 9 illustrates an example of an analyte detecting device, as shown in Fig. 1, having a reference electrode;
[0020] Fig. 10 is an example of an analyte detecting device according to another embodiment of the present invention;
[0021] 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
[0022] 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

[0023] 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.

[0024] 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 semicircular 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 also includes 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.

[0025] 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.

[0026] 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 100-250μm 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.

[0027] 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.

[0028] 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.

[0029] 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.

[0030] 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).

[0031] 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.

[0032] 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 electrode 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 100-2000μm, 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.

[0033] 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:

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

[0034] 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.

[0035] 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.

[0036] 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.

[0037] 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.

[0038] 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 discussed 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.

[0039] 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.

[0040] 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.

[0041] 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.

[0042] 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.

[0043] 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.

[0044] 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.

[0045] 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.

Claims

1. A device (100) for detecting at least one analyte in a patient, comprising:

at least one active electrode (104), said active electrode having a length in the range of 100 - 2000 μm for passing through the stratum corneum to access said analyte to enable the electrochemical detection of said analyte;

an auxiliary electrode (106) configured to at least partially surround said active electrode, and adapted to contact patient's skin when the device is placed against said patient, wherein said device further includes a base portion (102) integral with said auxiliary electrode;

characterized in that

said active electrode is retractable into said base portion and extendable beyond said base portion for accessing said analyte, and

said auxiliary electrode (106) has an abrasive surface which is adapted to contact and abrade the patient's skin.

2. A device (100) as claimed in claim 1, wherein:

said auxiliary electrode (106) is adapted to pass into the stratum corneum when contacting said patient's skin.

3. A device (100) as claimed in claim 1 or 2, further comprising:

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

4. A device (100) as claimed in one of claims 1-3, further comprising:

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

5. A device (100) as claimed in one of claims 1-4, wherein:

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

6. A device (100) as claimed in one of claims 1-5, wherein:

said device is further adapted to detect at least one parameter of said patient, such that said length of said active electrode (104) 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.

7. A device (100) as claimed in one of claims 1-6, further comprising a plurality of said active electrodes.

8. A device (100) as claimed in one of claims 1-7, wherein:

said auxiliary electrode (106) is configured to entirely surround said active electrode (104).

9. A device (100) as claimed in one of claims 1-8, wherein:

said auxiliary electrode (106) is coupled to at least a portion of the surface of said base portion (102) proximate to that from which said active electrode (104) extends.

10. A device (100) as claimed in one of claims 1-9, wherein:

said analyte is electrochemically active.

11. A device (100) as claimed in one of claims 1-10, wherein:

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

12. A device (100) as claimed in one of claims 1-11, wherein:

said active electrode (104) is selected from antimony, ruthenium, rhodium, platinum, palladium, graphite, gold, and oxides thereof.

13. A device (100) as claimed in one of claims 1-12, further comprising:

at least one reference electrode (132), disposed at a distance from said active electrode (104) equal to or less than a distance between said active electrode and any portion of said auxiliary electrode (106), said reference electrode being adapted to provide a reference potential for said electric potential applied to said active electrode.

14. A device (100) as claimed in one of claims 1-13, further comprising:

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

15. A device (100) as claimed in one of claims 1-14, further comprising:

a substance delivery device integral therewith.

16. A device (100) as claimed in claim 15, wherein:

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

17. A device (100) as claimed in claim 15, wherein:

said active electrode (104) is further adapted to have an electric potential applied thereto to enable reaction between said analyte in said patient and
said substance (126) to produce at least one electrochemically active product.

18. A device (100) as claimed in claim 15, wherein:

said substance (126) is selected from glucose oxidases, glucose dehydrogenases, and electrochemically responsive receptors.

19. A method for detecting at least one analyte in a patient, comprising:

placing a device (100) against the skin of said patient, said device having at least one active electrode (104), said active electrode having a length in the range of 100-2000 μm for passing through the stratum corneum of said patient to access said analyte,
said device having an auxiliary electrode (106) 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 analyte and said active electrode, or measuring current based on said reaction of said analyte in said patient and said substance,
wherein said device (100) further includes a base portion (102) integral with said auxiliary electrode (106);
characterized in that
said method further includes retracting said active electrode into said base portion and extending said active electrode (104) beyond said base portion for accessing said component, and
said auxiliary electrode has an abrasive surface which is adapted to contact and abrade the patient's skin.

20. A method as claimed in claim 19, wherein:

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

21. A method as claimed in claim 19 or 20, wherein:

said applying an electric potential to said active electrode (104) is selected from ramped, stepped, pulsed, programmed pulse and combinations thereof.

22. A method as claimed in one of claims 19-21, wherein said applying step comprises:

adjusting the amount of said electrical potential applied to said active electrode (104) with reference to a reference electrode (132) of said device wherein said reference electrode (132) is disposed at a distance equal to or less than between said active electrode and any portion of said auxiliary electrode (106).

23. A method as claimed in one of claims 19-22, wherein:

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

24. A method as claimed in one of claims 19-23, further comprising:

storing information pertaining to said component.

25. A method as claimed in one of claims 19-24, further comprising:

communicating information between said device and an external device.

26. A method as claimed in one of claims 19-25, further comprising:

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

27. A method as claimed in one of claims 19-26, 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.

28. A method as claimed in one of claims 19-27, 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.

29. A method as claimed in one of claims 19-28, wherein said analyte 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.

Patentansprüche

1. Vorrichtung (100) zum Detektieren mindestens eines Analyten in einem Patienten, mit:

mindestens einer aktiven Elektrode (104), wobei die aktive Elektrode eine Länge im Bereich von 100 - 2000 μm aufweist, um für einen Zugang zu dem Analyten die Hornschicht zu durchdringen, so dass die elektrochemische Detektion des Analyten ermöglicht ist,
einer Hilfselektrode (106), die derart ausgebildet ist, dass sie die aktive Elektrode zumindest teilweise umgibt, und die geeignet ist, an der Haut eines Patienten anzuliegen, wenn die Vorrichtung an dem Patienten angeordnet ist, wobei die Vorrichtung ferner einen einstückig mit der Hilfselektrode ausgebildeten Basisbereich (102) aufweist;
dadurch gekennzeichnet, dass
die aktive Elektrode in den Basisbereich einziehbar und für einen Zugang zu dem Analyten über den Basisbereich hinaus ausfahrbar ist, und
wobei die Hilfselektrode (106) eine abrasive Fläche aufweist, welche geeignet ist, an der Haut eines Patienten anzuliegen und diese aufzurauen.

2. Vorrichtung (100) nach Anspruch 1, bei welcher:

die Hilfselektrode (106) geeignet ist, bei Anlage an der Haut eines Patienten in die Hornschicht einzudringen.

3. Vorrichtung (100) nach Anspruch 1 oder 2, ferner mit:

einem Datenspeicher, der geeignet ist, Informationen bezüglich des mindestens einen Analyten oder des Patenten zu speichern.

4. Vorrichtung (100) nach einem der Ansprüche 1-3, mit:

einer Kommunikationsvorrichtung, die geeignet ist, Informationen zwischen der Vorrichtung und einer externen Vorrichtung zu übertragen.

5. Vorrichtung (100) nach einem der Ansprüche 1-4, bei welcher:

die Vorrichtung geeignet ist, von einem Patienten über einen Zeitraum getragen zu werden.

6. Vorrichtung (100) nach einem der Ansprüche 1-5, bei welcher:

die Vorrichtung ferner geeignet ist, mindestens einen Parameter des Patienten zu detektieren, so dass die Länge der aktiven Elektrode (104) es der aktiven Elektrode ermöglicht, die Hornschicht bis in eine Tiefe zu durchdringen, die für einen Zugang zu einer Komponente ausreicht, um die elektrochemische Detektion des Parameters zu ermöglichen; und
der mindestens eine Analyt und der mindestens eine Parameter mindestens eines der folgenden Elemente umfassen:
Elektrolyten, Sauerstoff, Stickoxid, Laktat, Insulin, Neurotransmitter, mindestens ein Medikament, den pH-Wert des Bluts des Patienten, die Temperatur des Patienten, den Widerstand der Haut des Patienten, Glucoseoxidase, Glucosedehydrogenase und Laktatdehydrogenase.

7. Vorrichtung (100) nach einem der Ansprüche 1-6, ferner mit mehreren der aktiven Elektroden.

8. Vorrichtung (100) nach einem der Ansprüche 1-7, bei welcher:

die Hilfselektrode (106) derart ausgebildet ist, dass sie die aktive Elektrode (104) vollständig umgibt.

9. Vorrichtung (100) nach einem der Ansprüche 1-8, bei welcher:

die Hilfselektrode (106) mit mindestens einem Bereich der Oberfläche des Basisbereichs (102) nahe demjenigen Bereich verbunden ist, von welchem aus sich die aktive Elektrode (104) erstreckt.

10. Vorrichtung (100) nach einem der Ansprüche 1-9, bei welcher:

der Analyt elektrochemisch aktiv ist.

11. Vorrichtung (100) nach einem der Ansprüche 1-10, bei welcher:

das Analyt unter Stickoxid, Neurotransmittern, Insulin und Sauerstoff ausgewählt ist.

12. Vorrichtung (100) nach einem der Ansprüche 1-11, bei welcher:

die aktive Elektrode (104) unter Antimon, Ruthenium, Rhodium, Platin, Palladium, Graphit, Gold und Oxiden derselben ausgewählt ist.

13. Vorrichtung (100) nach einem der Ansprüche 1-12, ferner mit:

mindestens einer Referenzelektrode (132), die in einem Abstand von der aktiven Elektrode (104) angeordnet ist, der gleich dem oder geringer als der Abstand zwischen der aktiven Elektrode und einem beliebigen Bereich der Hilfselektrode (106) ist, wobei die Referenzelektrode geeignet ist, ein Referenzpotential für das an die aktive Elektrode angelegte elektrische Potential zu liefern.

14. Vorrichtung (100) nach einem der Ansprüche 1 - 13, ferner mit:

mehreren aktiven Elektroden, welche zur sequentiellen Verwendung positionierbar sind.

15. Vorrichtung (100) nach einem der Ansprüche 1-14, ferner mit:

einer einstückig mit dieser ausgebildeten Substanzausgabevorrichtung.

16. Vorrichtung (100) nach Anspruch 15, bei welcher:

die Vorrichtung und die Ausgabevorrichtung geeignet sind, miteinander zum Steuern der Verabreichung der von der Ausgabevorrichtung an den Patienten ausgegebenen Substanz zu kommunizieren.

17. Vorrichtung (100) nach Anspruch 15, bei welcher:

die aktive Elektrode (104) ferner zum Anlegen eines elektrischen Potentials an diese geeignet ist, um eine Reaktion zwischen dem Analyten in dem Patienten und der Substanz (126) zur Bildung mindestens eines elektrochemisch aktiven Produkts zu ermöglichen.

18. Vorrichtung (100) nach Anspruch 15, bei welcher:

die Substanz (126) unter Glucoseoxidasen, Glucosedehydrogenasen und elektrochemisch reagierenden Rezeptoren ausgewählt ist.

19. Verfahren zum Detektieren mindestens eines Analyten in einem Patienten, mit den folgenden Schritten:

Platzieren einer Vorrichtung (100) auf der Haut des Patienten, wobei die Vorrichtung mindestens eine aktive Elektrode (104) aufweist, wobei die aktive Elektrode eine Länge im Bereich von 100 - 2000 μm aufweist, um für einen Zugang zu dem Analyten die Hornschicht des Patienten zu durchdringen,
wobei die Vorrichtung eine Hilfselektrode (106) aufweist, die derart ausgebildet ist, dass sie die aktive Elektrode zumindest teilweise umgibt, wobei die Hilfselektrode geeignet ist, an der Haut des Patienten anzuliegen, wenn die Vorrichtung an dem Patienten angeordnet ist;
Anlegen eines Potentials an die aktive Elektrode; und
Messen von Strom oder Ladung aus der elektrochemischen Reaktion des Analyts und der aktiven Elektrode, oder Messen von Strom basierend auf der Reaktion des Analyten in dem Patienten und der Substanz,
wobei die Vorrichtung (100) ferner einen einstückig mit der Hilfselektrode (106) ausgebildeten Basisbereich (102) aufweist;
dadurch gekennzeichnet, dass
das Verfahren ferner das Einziehen der aktiven Elektrode in den Basisbereich und das Ausfahren der aktiven Elektrode (104) über den Basisbereich hinaus umfasst, um Zugang zu der Komponente zu erhalten, und
die Hilfselektrode eine abrasive Fläche aufweist, welche zum Anliegen an der Haut des Patienten und zum Aufrauen derselben geeignet ist.

20. Verfahren nach Anspruch 19, bei welchem:

das Messen anhand eines Integrals des Stroms, einer Ableitung des Stroms oder einer Ableitung der Ladung erfolgt.

21. Verfahren nach Anspruch 19 oder 20, bei welchem:

das Anlegen eines elektrischen Potentials an die aktive Elektrode (104) in Rampenform, Stufenform, als Puls, als programmierter Puls oder als Kombinationen derselben erfolgt.

22. Verfahren nach einem der Ansprüche 19-21, bei welchem der Schritt des Anlegens aufweist:

das Einstellen der Größe des an die aktive Elektrode (104) angelegten elektrischen Potentials unter Bezugnahme auf eine Referenzelektrode (132) der Vorrichtung, wobei die Referenzelektrode (132) in einem Abstand angeordnet ist, der gleich dem oder geringer als der Abstand zwischen der aktiven Elektrode und einem beliebigen

Bereich der Hilfselektrode (106) ist.

23. Verfahren nach einem der Ansprüche 19-22, bei welchem:

die Hilfselektrode geeignet ist, bei Anlage an der Haut eines Patienten in die Hornschicht einzudringen.

24. Verfahren nach einem der Ansprüche 19-23, bei welchem:

Informationen bezüglich der Komponente gespeichert werden.

25. Verfahren nach einem der Ansprüche 19-24, ferner mit dem folgenden Schritt:

Übertragen von Informationen zwischen der Vorrichtung und einer externen Vorrichtung.

26. Verfahren nach einem der Ansprüche 19-25, ferner mit dem folgenden Schritt:

Tragen der Vorrichtung an einem Patienten über einen Zeitraum.

27. Verfahren nach einem der Ansprüche 19-26, bei welchem:

die Vorrichtung mehrere der aktiven Elektroden aufweist; und
das Verfahren das Durchführen der Schritte des Platzierens, des Anlegens und des Messens unter Verwendung der mehreren aktiven Elektroden umfasst.

28. Verfahren nach einem der Schritte 19-27, ferner mit dem folgenden Schritt:

Ermöglichen der Kommunikation zwischen der Vorrichtung und einer Ausgabevorrichtung, um die Verabreichung einer durch die Ausgabevorrichtung an den Patienten ausgegebenen Substanz zu steuern.

29. Verfahren nach einem der Ansprüche 19-28, bei welchem der Analyt eines der folgenden Elemente aufweist:

einen Elektrolyt, Sauerstoff, Stickoxid, Laktat, Insulin, Neurotransmitter, ein Medikament, den pH-Wert des Bluts des Patienten, eine die Temperatur des Patienten angebende Komponente, eine den Widerstand der Haut des Patienten angebende Komponente, Glucoseoxidase, Glucosedehydrogenase und Laktatdehydrogenase.

Revendications

1. Dispositif (100) de détection d'au moins un analyte dans un patient, comprenant:

au moins une électrode active (104), ladite électrode active ayant une longueur se situant dans la plage de 100 - 2000 μm pour traverser la couche cornée pour accéder audit analyte afin de permettre la détection électrochimique dudit analyte;
une électrode auxiliaire (106) configurée pour entourer ladite électrode active au moins partiellement, et apte à contacter la peau d'un patient quand le dispositif est placé sur le patient, le dispositif comprenant en outre une partie de base (102) formée d'un seul tenant avec ladite électrode auxiliaire;
caractérisé en ce que
ladite électrode active est apte à être rentrée dans ladite partie de base et à être sortie au-delà de ladite partie de base pour accéder audit analyte, et
ladite électrode auxiliaire (106) comprend une face abrasive apte à contacter et abraser la peau du patient.

2. Dispositif (100) selon la revendication 1, dans lequel
ladite électrode auxiliaire (106) est apte à passer dans ladite couche cornée lors du contact avec la peau dudit patient.

3. Dispositif (100) selon les revendications 1 ou 2, comprenant en outre une mémoire de données apte à stocker des informations concernant ledit au moins un analyte ou ledit patient.

4. Dispositif (100) selon l'une quelconque des revendications 1 - 3, comprenant en outre:

un dispositif de communication apte à la communication d'informations entre ledit dispositif et un dispositif externe.

5. Dispositif (100) selon l'une quelconque des revendications 1 - 4, dans lequel
ledit dispositif est apte à être porté sur ledit patient pendant une durée de temps.

6. Dispositif (100) selon l'une quelconque des revendications 1 - 5, dans lequel
ledit dispositif est apte en outre à détecter au moins un paramètre dudit patient, de sorte que la longueur de ladite électrode active (104) permet à ladite électrode active de traverser la couche cornée jusqu'à une profondeur suffisant à accéder à un composant afin de permettre la détection électrochimique dudit paramètre; et
ledit au moins un analyte et ledit au moins un paramètre comprenant au moins un des éléments suivants:

électrolytes, oxygène, oxyde d'azote, lactate, insuline, neurotransmetteurs, au moins un médicament, le pH dans le sang du patient, la température du patient, la résistance de la peau du patient, glucose oxydase, glucose déshydrogénase, et lactate déshydrogénase.

7. Dispositif (100) selon l'une quelconque des revendications 1 - 6, comprenant en outre plusieurs électrodes actives.

8. Dispositif (100) selon l'une quelconque des revendications 1 - 7, dans lequel
ladite électrode auxiliaire (106) est configurée pour entourer complètement ladite électrode active (104).

9. Dispositif (100) selon l'une quelconque des revendications 1 - 8, dans lequel
ladite électrode auxiliaire (106) est couplée à au moins une partie de la face de la partie de base (102) à proximité de la face d'où s'étend ladite électrode active (104).

10. Dispositif (100) selon l'une quelconque des revendications 1 - 9, dans lequel
ledit analyte est électrochimiquement actif.

11. Dispositif (100) selon l'une quelconque des revendications 1 - 10, dans lequel
ledit analyte est choisi parmi l'oxyde d'azote, les neurotransmetteurs, l'insuline et l'oxygène.

12. Dispositif (100) selon l'une quelconque des revendications 1 - 11, dans lequel
ladite électrode active (104) est choisie parmi l'antimoine, le ruthénium, le rhodium, le platine, le palladium, le graphite, l'or et leurs oxydes.

13. Dispositif (100) selon l'une quelconque des revendications 1 - 12, comprenant en outre
au moins une électrode de référence (132) disposée à une distance de ladite électrode active (104) égale ou inférieure à la distance entre ladite électrode active et n'importe quelle partie de ladite électrode auxiliaire (106), ladite électrode de référence étant apte à fournir un potentiel de référence par rapport au potentiel appliqué à ladite électrode active.

14. Dispositif (100) selon l'une quelconque des revendications 1 - 13, comprenant en outre
plusieurs électrodes actives aptes à être positionnées pour l'utilisation en série.

15. Dispositif (100) selon l'une quelconque des revendications 1 - 14, comprenant en outre
un dispositif de distribution d'une substance solidaire avec ledit dispositif.

16. Dispositif (100) selon la revendication 15, dans lequel
ledit dispositif et ledit dispositif de distribution sont aptes à communiquer entre eux afin de contrôler la distribution de ladite substance distribuée au patient par ledit dispositif de distribution.

17. Dispositif (100) selon la revendication 15, dans lequel
ladite électrode active (104) est apte en outre à être alimentée en un potentiel électrique pour permettre une réaction entre ledit analyte dans le patient et ladite substance (126) afin de produire au moins un produit électrochimiquement actif.

18. Dispositif (100) selon la revendication 15, dans lequel
ladite substance (126) est choisie parmi les glucose oxidases, les glucose déshydrogénases et les récepteurs

électrochimiquement responsifs.

19. Procédé de détection d'au moins un analyte dans un patient, comprenant les étapes suivantes:

placer un dispositif (100) sur la peau du patient, ledit dispositif comprenant au moins une électrode active (104), ladite électrode active ayant une longueur se situant dans la plage de 100 - 2000 μm pour traverser la couche cornée du patient pour accéder audit analyte;
ledit dispositif comprenant une électrode auxiliaire (106) configurée pour entourer ladite électrode active au moins partiellement, ladite électrode auxiliaire étant apte à contacter la peau du patient quand le dispositif est placé sur le patient;
appliquer un potentiel à ladite électrode active; et
mesurer du courant ou de la charge résultant de la réaction électrochimique entre ledit analyte et ladite électrode active, ou mesurer du courant en se basant sur ladite réaction entre ledit analyte dans le patient et ladite substance;
le dispositif (100) comprenant en outre une partie de base (102) solidaire de ladite électrode auxiliaire (106);
caractérisé en ce que
le procédé comprend en outre la rentrée de ladite électrode active dans la partie de base et la sortie de ladite électrode active (104) au-delà de ladite partie de base pour accéder au composant, et
ladite électrode auxiliaire comprend une face abrasive apte à contacter et abraser la peau du patient.

20. Procédé selon la revendication 19, dans lequel
le mesurage est fait sur le courant intégré, une dérivée du courant ou une dérivée de la charge.

21. Procédé selon les revendications 19 ou 20, dans lequel
l'application d'un potentiel électrique à ladite électrode active (104) est faite par une impulsion à rampe, pas à pas, pulsée, programmée ou combinaisons de celles-ci.

22. Procédé selon l'une quelconque des revendications 19-21, dans lequel l'étape d'application comprend
l'ajustage de la magnitude du potentiel électrique appliqué à ladite électrode active (104) en se référant à une électrode de référence (132) dudit dispositif, ladite électrode de référence (132) étant disposée à une distance égale ou inférieure à la distance entre ladite électrode active et n'importe quelle partie de ladite électrode auxiliaire (106).

23. Procédé selon l'une quelconque des revendications 19-22, dans lequel
ladite électrode auxiliaire est apte à passer dans ladite couche cornée lors du contact avec la peau du patient.

24. Procédé selon l'une quelconque des revendications 19-23, comprenant en outre
l'enregistrement d'informations concernant ledit composant.

25. Procédé selon l'une quelconque des revendications 19-24, comprenant en outre
la communication d'informations entre le dispositif et un dispositif externe.

26. Procédé selon l'une quelconque des revendications 19-25, comprenant en outre
le port du dispositif sur le patient pendant une durée de temps.

27. Procédé selon l'une quelconque des revendications 19-26, dans lequel
ledit dispositif comprend plusieurs électrodes actives, et
le procédé comprend la mise en oeuvre des étapes de positionnement, application et mesurage en utilisant les plusieurs électrodes actives.

28. Procédé selon l'une quelconque des revendications 19-27, comprenant en outre
de permettre au dispositif et à un dispositif de distribution de communiquer entre eux pour contrôler la distribution d'une substance que ledit dispositif de distribution distribue au patient.

29. Procédé selon l'une quelconque des revendications 19-28, dans lequel ledit analyte comprend un des éléments suivants:

électrolytes, oxygène, oxyde d'azote, lactate, insuline, neurotransmetteurs, un médicament, un composant indiquant le pH dans le sang du patient, un composant indiquant la température du patient, un composant indiquant la résistance de la peau du patient, glucose oxydase, glucose déshydrogénase, et lactate déshydrogénase.

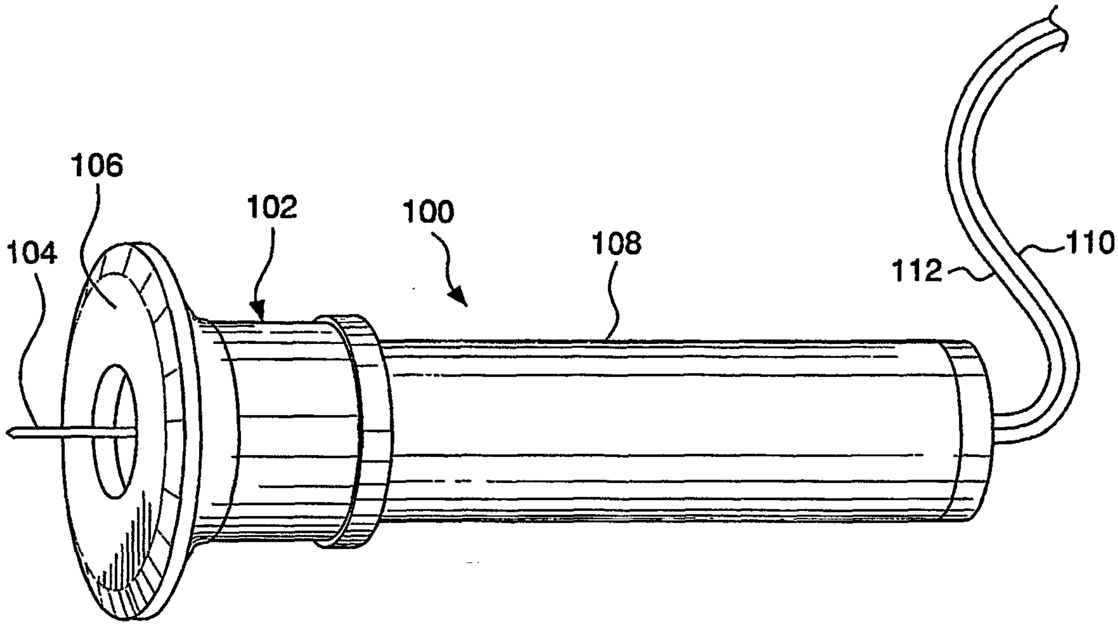

FIG. 1

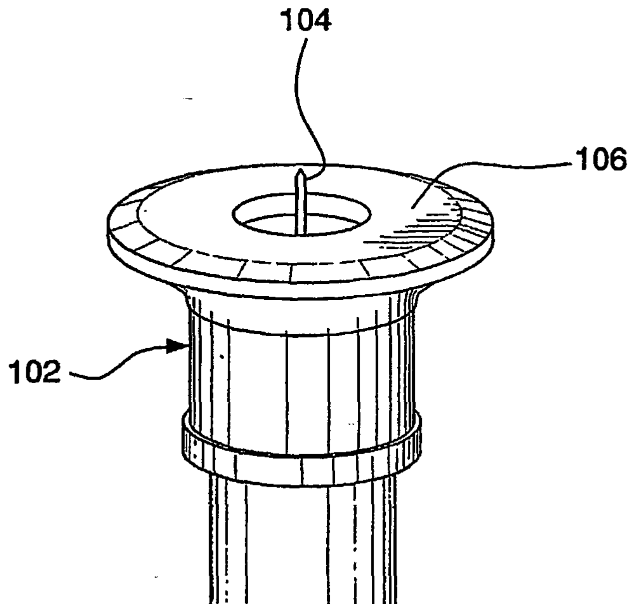

FIG. 2

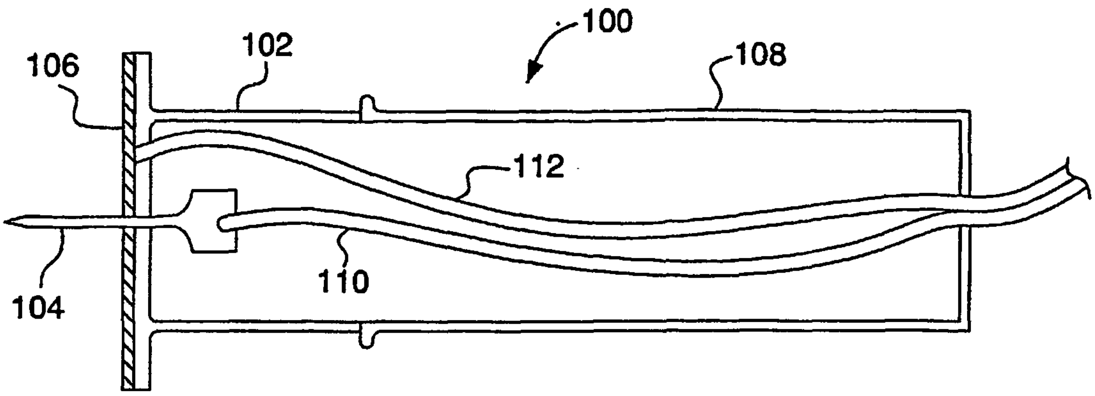
100
106
102
108
112
104
110

FIG. 3

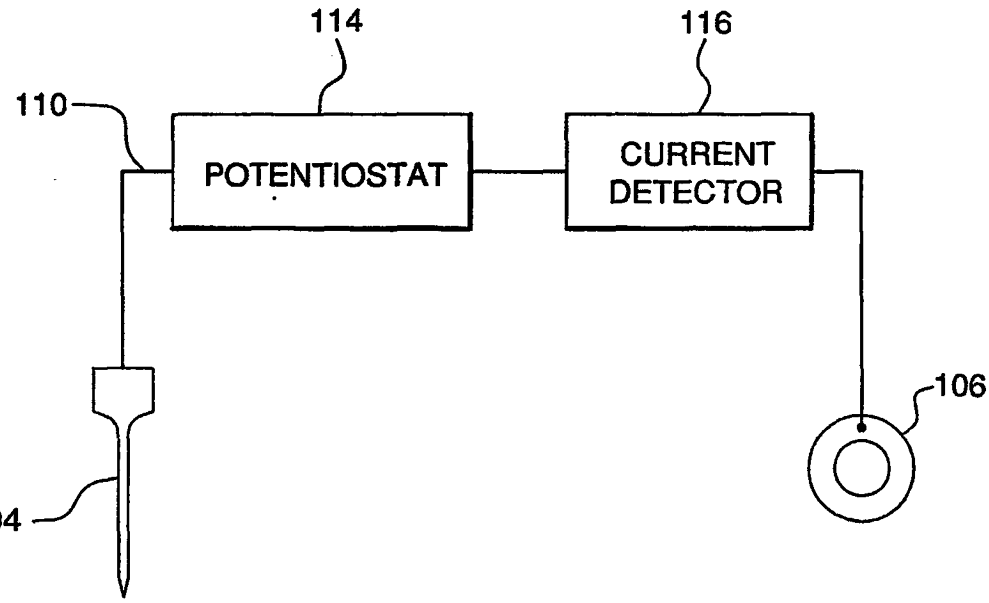
114
116
110
POTENTIOSTAT
CURRENT DETECTOR
106
104

FIG. 4

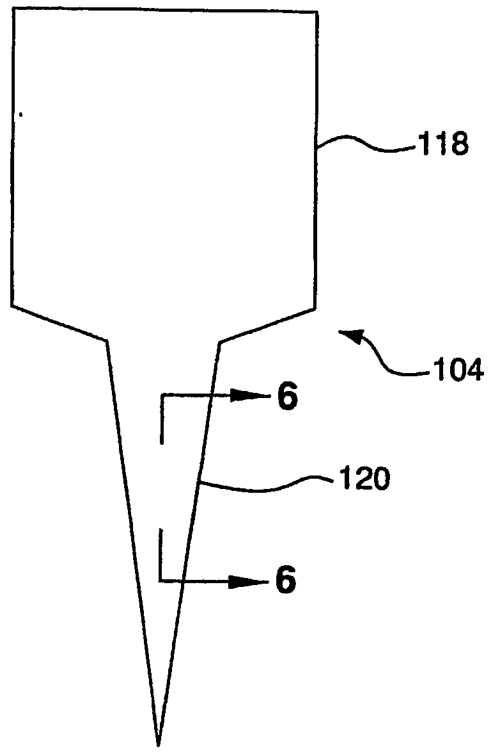

FIG. 5

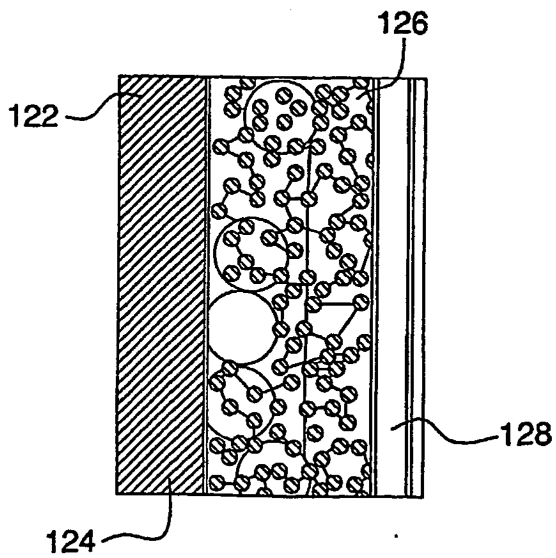

FIG. 6

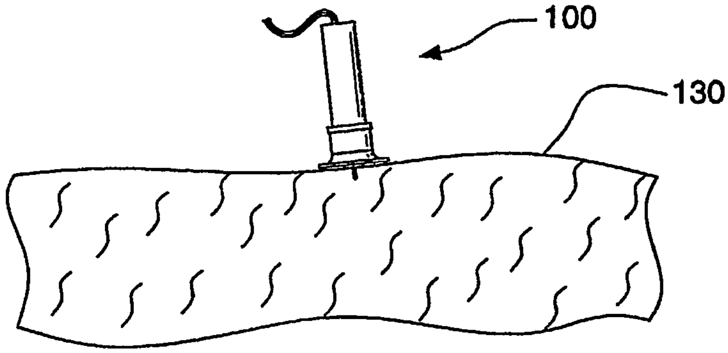
100
130

FIG. 7

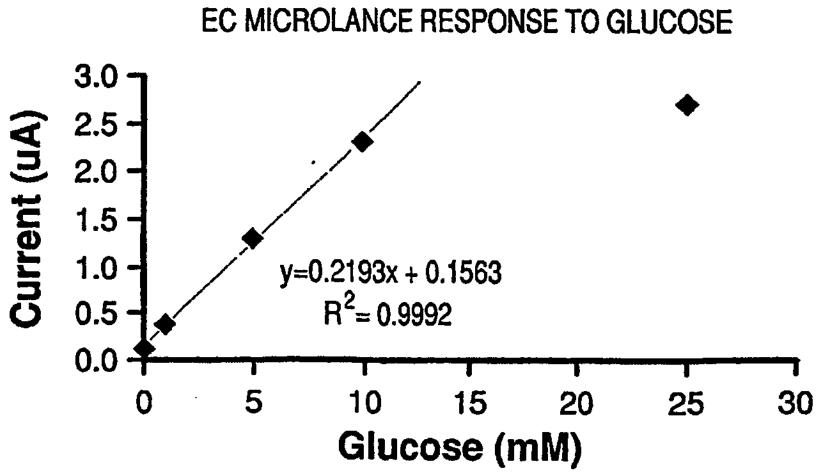
EC MICROLANCE RESPONSE TO GLUCOSE
Current (uA)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
y=0.2193x + 0.1563
R2= 0.9992
0
5
10
15
20
25
30
Glucose (mM)

FIG. 8

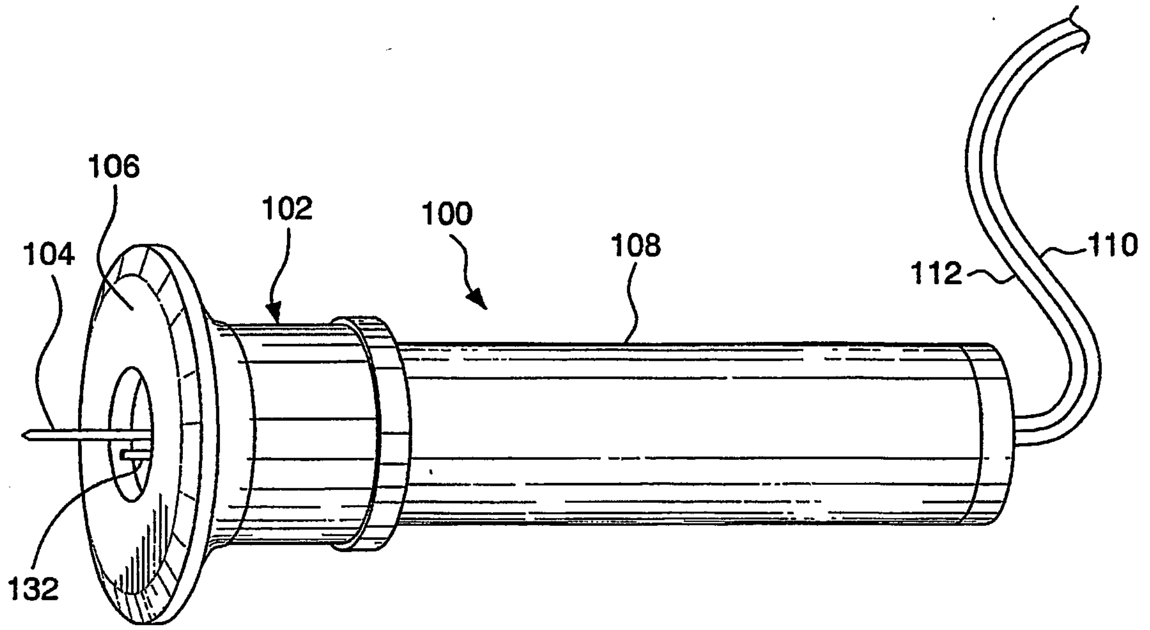

FIG. 9

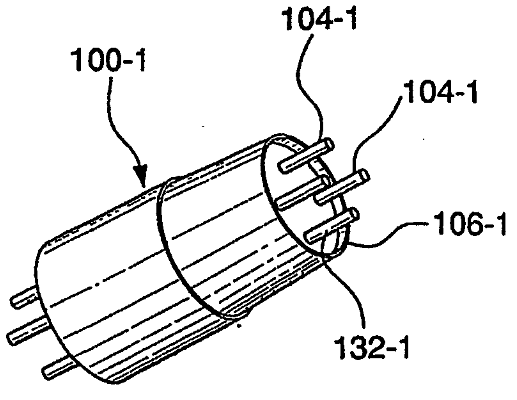

FIG. 10

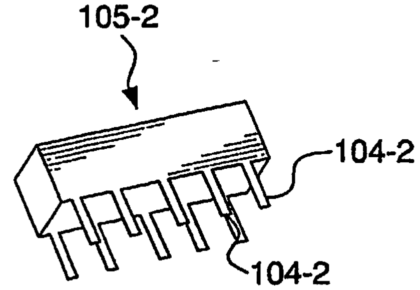

FIG. 11

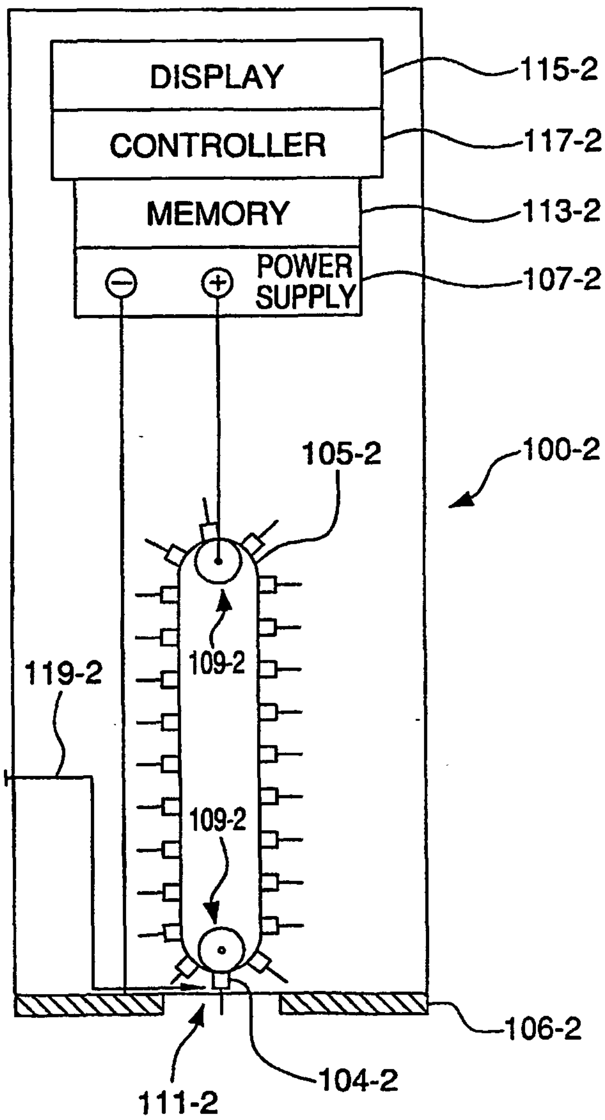
DISPLAY
CONTROLLER
MEMORY
POWER SUPPLY
115-2
117-2
113-2
107-2
105-2
100-2
109-2
119-2
109-2
106-2
104-2
111-2

FIG. 12

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- US 4953552 A **[0006]**
- US 5680858 A **[0006]**
- US 5820570 A **[0006]**
- WO 9846124 A **[0006]**
- WO 9614026 A **[0008]**
- EP 0964060 A2 **[0008]**

Non-patent literature cited in the description

- **Jung, S. K. et al.** *Analytical Chemistry,* 1999, vol. 71, 3642-3649 **[0030]**
- **Gorski et al.** *J. Electroanalytical Chem.,* 1997, vol. 425 (1-2), 191-199 **[0030]**
- **Zen et al.** *Analyst,* 2000, vol. 125 (12), 2169-2172 **[0030]**

专利名称(译)	一种用于监测分析物水平的微创系统和方法		
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摘要(译)

微创分析物检测装置（100）及其使用方法。该系统和方法采用具有可选地涂覆有物质（126）的有源电极（104）和对电极（106）的装置，该对电极（106）被配置为至少部分地围绕有源电极（104）。辅助电极（106）和有源电极（104）的配置改善了流过器件（100）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（104）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（104），并且基于流过器件（100）的电流或电荷量确定分析物水平。