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(54) **CATHETER-FREE IMPLANTABLE NEEDLE BIOSENSOR**

KATHETERFREIER IMPLANTIERBARER NADEL-BIOSENSOR

BIOCAPTEUR A AIGUILLE IMPLANTABLE SANS CATHETER

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(56) References cited:
EP-A- 1 266 608
WO-A-98/46124
WO-A-2004/063718
DE-C1- 3 502 913
US-A- 5 807 375
US-A- 6 091 975
US-A1- 2004 167 458
US-B1- 6 360 888

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Description

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0001] The present invention relates to electrochemical implantable sensor assemblies for monitoring molecules such as Glucose and Oxygen in subcutaneous tissue.

2. Description of the Prior Art

[0002] Apparatus utilizing biosensors as measurement components can directly measure biochemical properties of molecules without complex separation steps or additional reagents. Apparatus with electrochemical sensors obtain such properties by measuring electrical signals generated from electrochemical redox reactions of the molecules. WO 2004/063718 discloses the use of an analyte measuring device that has an analyte sensing element with a sharpened distal end and further has an indicating electrode covered by an absorbent layer. Also, an electric power, data processing and display device is adapted to mate to and activate the analyte sensing element by applying electric power to it and adapted to receive the raw analyte measurement and to compute and display a refined analyte measurement from the raw analyte measurement. The analyte sensing element is introduced into the animal body, thereby placing the absorbent layer into contact with the body fluid. The absorbent layer becomes saturated with body fluid and the analyte sensing element is removed from the body and is activated to form a raw analyte measurement, which is used to form and display a refined analyte measurement.

[0003] DE 35 02 913 discloses a measuring sensor for biomedical signals, that has as its essential part one or more short needle points which penetrate into the uppermost largely cast-off cell layers of the horny skin and which are retained by means of a preferably flexible mounting, although the needle point does not pass through the skin. The measuring sensor is suitable for detecting and measuring electophysiological quantities and for electrical stimulation.

[0004] Implantable sensors have the advantage of directly monitoring molecule properties of medical importance, such as concentration of oxygen, glucose and lactate. Such information can be used to improve the accuracy of diagnosis, or the effectiveness of treatment. A subcutaneous micro-sensor directly placed in the physiological cellular environment where metabolism takes place can provide more accurate and timely information of the physiological state. For example, the change of glucose concentration for a diabetic patient is often unpredictable due to a number of factors such as diet, temperature, emotional states, physical activities, age, and rate of metabolism, etc. While discrete measurements cannot provide enough information of dynamic changes, continuous monitoring can in essence provide information that can dramatically improve diagnoses and treatment of diseases.

[0005] Reactions of the tissue to an implanted device typically include two types: the first is the tissue's reaction to a foreign body at the cellular and molecular level, which is the mechanism of physiological reactions against a foreign object; the second is the wound healing reaction process that involves a series of time related tissue regeneration steps. Both processes cause perturbation at the implant-tissue interface, forming barrier layer (scar tissue, for example). Such phenomenon may not be a serious problem for some implants of mechanical function (such as artificial bones, ligament, valves, etc.). But for a sensor intended to measure molecules at the interface, the barrier layer isolates the sensor from the ambient issue environment, thus prevents or impairs the molecule infiltration between the sensor and the tissue fluid. Therefore, the sensor measurement would not reflect true molecule properties of the tissue.

[0006] The degree of interaction between implanted sensor and the tissue is usually described by "biocompatibility". One aspect of biocompatibility is biochemical. It may involve physiological reactions such as immune, inflammatory, and anaphylactic reactions caused by the chemical ingredients, additives, or degradation products of the implant. Another aspect of the biocompatibility is mechanical: the physical characteristics of the implanted object such as surface roughness, shape, size, etc. that could cause various degrees of irritations and damages to the tissue. Furthermore, most of the known implanted sensors require auxiliary devices such as catheters or cannula for implanting. Some even requires an incision or surgery. The extra damage to the tissue by the assisting devices is often major factors affecting the performance of the sensors.

[0007] Another important factor is the disturbance to the normal physiological environment caused by an excessive flux of molecules consumed by or released from the sensor measuring process. Since the molecules to be detected participate in physiological processes, the more the reaction consumes/releases, the more serious is the interference to the tissue. A lower rate of molecular consumption per unit area (flux) can always be expected to produce a lower degree of disturbance to the tissue. Most sensor designs feature a very small active sensing area while majority of the implanted parts only serves as the supporting body. Such devices require high flux in a very small area to obtain favorable signal. Thus, the localized high molecular flux can result in strong disturbance to the tissue environment and can cause sensor inaccuracy and instability.

[0008] US-A-6 952 604 discloses a catheter-free subcutaneously implantable apparatus for producing a signal reflecting the concentration of molecules, said apparatus comprising :

- at least one needle shaped anode,
- at least one needle shaped cathode,
- a supporting base for mounting the anodes and the cathodes, and
- a contact means for connecting the anodes and the cathodes with a signal reading system.

[0009] Finally, when there are no conventional equipments readily available, problems often exist when attempt is made to mass produce complicated micro biosensors involving biochemical processes. Therefore, a simple design with reliable manufacturability is a key for product quality and reliability.

SUMMARY OF THE INVENTION

[0010] The present invention overcomes the disadvantage of using catheter to implant sensors.

[0011] The present invention provides subcutaneously implanted needle shaped sensors, with minimal diameter and large sensing surface area. The sensor electrodes can be directly inserted into the skin, without the need of a catheter. It is essentially painless for the procedure of implanting and the entire duration of use.

[0012] In a preferred embodiment, the sensor assembly of the present invention comprises a base with a planar bottom side, and elongated thin needle electrodes fixed perpendicularly to the base. Connection circuits are connected to the electrodes on the topside of the base.

[0013] The sensor assembly has at least one cathode and one anode. The number of electrodes may be two, three or four, one of which may be cathode and the rest anodes; or, one of the electrodes may be anode and the rest cathodes.

[0014] In a preferred embodiment, the anode comprises a hard metal needle core, covered by (in turn) a noble metal layer, a platinum layer, and a biosensing layer. The cathode comprises a hard metal needle core, covered by (in turn) a silver layer, a silver chloride layer, and a polymer diffusion layer. Such a configuration is intended for hydrogen peroxide detection based sensors.

[0015] The bio-sensing layer is a complex membrane wherein the inner layer contains enzyme and the outer layer contains biocompatible polymers and possesses molecular diffusion limiting characteristics.

[0016] In another embodiment of the invention, the anode may have a metal needle core, covered by (in turn) a silver layer and a polymer layer. The cathode may have a metal needle core, a covered by (in turn) a platinum layer, and a bio-sensing layer. Such configuration is for oxygen detection based sensors.

[0017] There may be a medical adhesive tape affixed to the bottom of the base for attaching the sensor assembly to the skin.

[0018] On the upper surface of the base, there may be electric receptacles (or circuit connections) for connecting the electrodes to an amperometric instrument.

[0019] The diameter of the needle electrode core in this invention may be in the range of 0.1-0.3mm.

[0020] In the present invention of the miniature sensor assembly, the two needle electrodes are perpendicularly fixed to the bottom of the base, and are connected to a portable amperometric device through a receptacle on the top of the base. The implanted portion can be directly inserted into the skin without the need of a catheter. The damage to the tissue by such a implanting procedure is minimal. Moreover, because the electrode surface is utilized to near 100 percent, the material exchange rate (molecules in and out of the contact interface of sensor membrane and tissue) around the electrode can be adjusted to minimum while still achieving high overall sensitivity. Such a mechanism can effectively reduce the disturbance to the tissue and ensure that the sensor can truly detect normal state of tissue physiology. In the present invention, the needle electrodes have very small diameters (0.1-0.3mm), miniature needles of this size cause essentially no pain. In terms of manufacturability, since the needle electrodes are separately fabricated and assembled, complicated manufacturing processes can be easily separated into simple steps, making it easier for mass production and quality control.

BRIEF DESCRIPTION OF THE DRAWINGS:

[0021]

Figure Ia is a cross section view of a two-electrode sensor assembly in accordance with a preferred embodiment of the invention;

Figure 1b is a cross section view of a three-electrode sensor assembly in accordance with a preferred embodiment of the invention;

Figure 1c is a perspective view of another two-electrode sensor assembly in accordance with a preferred embodiment of the invention (partially exposed);

Figure 2 is a cross section view of a needle anode structure in accordance with the invention;

Figure 2a is a cross section view of a needle cathode structure in accordance with the invention;

Figure 3 is a graph showing the sensor response in phosphate buffer to incremental glucose increase;

Figure 4 is a graph showing the signals of two independent sensor assemblies implanted in the upper arm of a type 2 diabetes patient during a 72 hour period. (Dots are finger capillary reference glucose values measured by the patient with a commercial glucose meter. The sensor signals demonstrate good agreement with each other and close correlation with the reference blood glucose. There is no

signal drift during the entire period of monitoring.)

DETAILED DESCRIPTION OF THE PRESENT INVENTION

[0022] The present invention provides subcutaneously implanted sensor assembly with two or more separate parallel needle shaped electrodes, wherein the electrodes have diameters approximately 0.2 mm and large sensing surface areas. The electrodes can be directly inserted into the skin, without the need of a catheter. The damage to the surrounding tissue due to the insertion of the sensor is minimum. It is normally painless for the procedure of implanting and the entire duration of use. The needle electrodes are affixed perpendicular to the sensor base bottom surface, and easy to operate for implantation. The physiological tissue fluid surrounding the electrodes serves as the conductive electrolytes, within the normal physiological pH value.

[0023] One advantage of the present invention is that about 100% of the implanted sensor surface is working electrode surface, which maximizes the contact surfaces between electrode and tissue fluid. This will reduce molecule exchange flux between the electrode and tissue while obtaining high degree of sensitivity. Therefore, the overall accuracy and signal stability of the measurement is significantly improved.

[0024] Another advantage of the present invention is that the vertical subcutaneous implantation is basically painless, comparing with conventional implanted devices which may cause various degree of pain. The present invention features the smallest diameters of all current known subcutaneously implanted sensors.

[0025] The present invention reduces the effective diameter of the electrode approximately 0.2 mm. This becomes possible by separating complicated structure and production processes based on the principal of separate cathode and anode. The manufacturing process is simple, easy to repeat and easy for quality control.

[0026] The electrochemical sensor assembly of the present invent comprises at least one cathode and one anode. The number of the electrodes may be two, three or four, one of which may be cathode and the rest anodes; or, one of the electrodes may be anode and the rest cathodes.

[0027] The needle electrodes may have rigid metal cores that are of corrosion resistant conductive materials such as stainless steel, barium alloy, and titanium alloy.

[0028] The sensor assembly may have one cathode and one anode. In case of two-electrode system, the sensor assembly is for short-term use. When used for hydrogen peroxide in electrochemical oxidation measurement, the anode is an indicating electrode, with stainless steel, beryllium bronze, titanium alloy as base material, and platinum deposition as surface material; the cathode is a reference/counter electrode, with stainless steel, beryllium bronze, titanium alloy as base material, and silver or silver chloride as surface material. When used for oxygen detection in electrochemical reduction measurement, the anode is made of stainless steel, beryllium bronze, titanium alloy as base material, and silver as surface material; the cathode is made of stainless steel, beryllium bronze, titanium alloy as base material, and platinum as surface material. Counter electrode material (silver / silver chloride) may be consumed during use. The system, therefore, has a limited lifetime.

[0029] Long-term use sensor assembly should be three-electrode system: platinum or other non-active metal is the surface material for the third needle electrode which is the assisting electrode for carrying electric current, wherein the reference electrode only provides reference voltage, does not carry electric current. The system will not consume reference electrode materials, and can be used for long term application.

[0030] The needle shaped electrodes and their outer sensing layer should possess integrated strength, should be able to withstand the friction and contact with skin and tissue during implantation and measurement. This requires that the sensing membrane have firm attachment to the electrode metal and have enough physical strength.

[0031] As seen in Figure 2, the anode comprises an anode needle core 41, a first anode cover layer 42, a second anode cover layer 43, and a third anode cover layer 44, wherein the anode needle core 41 is a needle shaped metal core in the center of the anode, covered by the first anode cover layer 42, which in turn is covered by the second anode cover layer 43, which in turn is covered by the third anode cover layer 44. In a preferred embodiment, the anode needle core 41 is a hard metal needle core; the first anode cover layer 42 is a noble metal layer; the second anode cover layer 43 is a platinum layer; and the third anode cover layer 43 is a biosensing layer.

[0032] As,seen in Figure 2a, the cathode comprises a cathode needle core 41', a first cathode cover layer 42', a second cathode cover layer 43', and a third cathode cover layer 44', wherein the cathode needle core 41' is a needle shaped metal core in the center of the electrode, covered by the first cover layer 42', which in turn is covered by the second cover layer 43', which in turn is covered by the third cover layer 44'. In a preferred embodiment, the needle core 41' is a hard metal needle core; the first cover layer 42' is a silver layer; the second cover layer 43' is a silver chloride layer; and the third cover layer 44' is a polymer diffusion layer. This configuration is for hydrogen peroxide detection.

[0033] The biosensing layer is a complex membrane that comprises enzyme in the inner portion and biocompatible polymers in the outer portion. The surface layer of the membrane possesses molecular diffusion limiting characteristics.

[0034] In another embodiment of the invention, for an anode, the anode needle core 41 is a metal needle core; the first anode cover layer 42 is a silver layer; the second anode cover layer 43 is a polymer layer; and the third

anode cover layer 43 is omitted. For a cathode, the cathode needle core 41' is a metal needle core; the first cathode cover layer 42' is a platinum layer; the second cathode cover layer 43' is a bio-sensing layer; and the third cathode cover layer 44' is omitted. This configuration is for oxygen detection.

[0035] The diameter of the needle electrode core in this invention may be in the range of 0.1-0.3mm.

[0036] As seen in Figure 1a, in a preferred embodiment, a percutaneously implanted biosensor assembly 10 of the present invention comprises a base 1 with a planar bottom surface 11 and a top surface 12 sustaining a first connection plate 21 and a second connection plate 22, an anode 401 and an cathode 402 in elongated thin needle shapes fixed perpendicularly to the bottom surface 11 of the base 1 respectively. The base 1 of the sensor assembly 10 further comprises a first base mounting hole 111 and a second base mounting hole 112, wherein the first connection plate 21 and the second connection plate 22 further comprise a first plate mounting hole 211 and a second plate mounting hole 221 respectively, wherein the first plate mounting hole 211, second plate mounting hole 221 and the first base mounting hole 111, second base mounting hole 112 are in line with each other respectively, wherein the upper ends of the anode 401 and the cathode 402 penetrate the first base mounting hole 111, the second base mounting hole 112 and the first plate mounting hole 211, the second plate mounting hole 221, wherein the top ends of the anode 401 and the cathode 402 are affixed to the first connection plate 21 and second connection plate 22 respectively.

[0037] The base 1 is of non-conductive materials, serving as the physical support to the body of the biosensor assembly 10. The first base mounting holes 111 and the second base mounting hole 112 may be filled with non-conductive Epoxy to fix electrodes 401 and 402 to the base 1. The first plate mounting holes 211 and the second plate mounting hole 221 may be filled with conductive Epoxy, or may be soldered or welded with conductive materials for electric connection.

[0038] There may be a medical adhesive tape affixed to the bottom of the base for attaching the sensor assembly to the skin.

[0039] On the upper side of the base, there may be electric receptacles for connecting the electrodes to a signal reading instrument for processing, recording and reading the signals. The electrodes can also be connected through contact circuits with the signal reading instrument.

[0040] As seen in Figure 1b, in another preferred embodiment, a percutaneously implanted biosensor assembly 10' of the present invention comprises a base 1' with a planar bottom surface 11' and a top surface 12' sustaining a first connection plate 21', a second connection plate 22', and a third connection plate 23', an anode 401', and cathode 402', 403' in elongated thin needle shapes fixed perpendicularly to the bottom surface 11' of the base 1' respectively. The base 1' of the sensor assembly 10' further comprises a first base mounting hole 111', a second base mounting hole 112', and a third base mounting hole 113', wherein the first connection plate 21', the second connection plate 22' and the third connection plate 23' further comprise the first plate mounting hole 211', the second plate mounting hole 221', the third plate mounting hole 231' respectively, wherein the first plate mounting hole 211', the second plate mounting hole 221', the third plate mounting hole 231' and the first base mounting hole 111', the second base mounting hole 112', the third base mounting hole 113' are in line with each other respectively, wherein the upper ends of the anode 401', and the cathode 402', 403' penetrate the first base mounting hole 111', the second base mounting hole 112', the third base mounting hole 113' and the first plate mounting hole 211', the second plate mounting hole 221', the third plate mounting hole 231', wherein the top ends of the anode 401', and the cathode 402', 403' are affixed to the first connection plate 21', the second connection plate 22', and the third connection plate 23' respectively by electric conductive material.

[0041] The sensor assembly as shown in Figure 1a and 1b can be used for measuring glucose concentration in tissue fluid by measuring hydrogen peroxide produced from glucose oxidase catalyzed oxidizing reaction. For example, for a two electrode system, the anode has a diameter of approximately 0.2 mm, and is made of stainless steel, beryllium bronze, titanium alloy, or other hard alloy conductive material as core, electro plated by gold or platinum as inert electrode, plated by platinum. A compound sensing membrane is deposited to the electrode surface. The inner layer of the membrane contains glucose oxidase and the outer layer is of highly biocompatible polymer diffusion membrane. The glucose molecules in the tissue fluid diffuse through the outer portion of the membrane to reach the inner enzyme region, catalytically oxidized by oxygen and produce hydrogen peroxide. This process consumes equivalent amount of oxygen. The hydrogen peroxide produced can be oxidized on the anode by a higher than 0.5V (VS Ag/AgCl) voltage to form a current in the electric circuit of the measuring system. When the diffusion process of the glucose through the diffusion control membrane is the controlling process of the entire reaction process, the electric current through the sensing electrode is proportional to the glucose concentration of the surrounding tissue fluid. The electric current thus reflects the corresponding glucose concentration in the tissue fluid.

[0042] The cathode is made of stainless steel, beryllium bronze, titanium alloy, or other hard alloy conductive material as the core, plated by silver layer. It can also be made of hard silver-rich alloy as the core. The silver electrode surface is prepared with sufficient amount of silver chloride by electrochemical oxidation in potassium chloride solution or chemical chlorinating in ferric chloride solution. The outer surface of the cathode is a highly biocompatible polymer diffusion membrane.

[0043] The surfaces of the anode and cathode com-

prise platinum and silver chloride respectively, which form rough surfaces naturally by the preparing process. They will provide relatively higher surface area and sufficient roughness after chemical affixation. These surface characteristics make the attachment and affixation of the biosensing compound membrane readily achievable.

[0044] The biosensing layer is of a compound membrane. The inner portion contains glucose oxidase affixed by chemical cross-linking and the outer portion is a biocompatible polymer layer that could be used for measuring glucose concentration in the subcutaneous tissue fluid. The thickness of the compound membrane is not more than 10 micron.

[0045] In another preferred embodiment, as shown in Figure 1c, a percutaneously implanted biosensor assembly 10" comprises a molded insulating plastic base 1", a needle anode 401 ", a needle cathode 402", a mold plastic cover 2", and a circular medical adhesive tape 3". The needle anode 401 " and needle cathode 402" are parallel to each other, and perpendicular to the bottom of the base 1". Conducting circuits are on the top of the base 1" and covered by mold plastic cover 2" for electric connection between anode 401", cathode 402" and an external portable amperometric device. The circular medical adhesive tape 3" are fixed to the planar bottom of the base 1". A pair of electric receptacles for connecting the electrodes with the amperometric device are located on the molded insulating plastic base 1" and connected to conducting circuits. The anode 401" has a stainless steel needle core (diameter: 0.16mm), covered by a gold layer, a platinum layer, and biosensing membrane layer. The needle cathode 402" has a stainless steel needle core, covered by a silver layer, a silver chloride layer and a polymer protective layer. The biosensing membrane is a complex membrane. Its inner layer contains enzyme oxidase and the outer layer is of polymeric diffusion membrane, with a thickness of approximately 2-8 micrometer. The diffusion membrane is structured with blend of polydimethysiloxane-polyurethane copolymer, hydrophilic polymers and ionic conducting materials.

[0046] The sensor has a typical response time of less than 30 seconds to an instantaneous glucose concentration change. Linear response range of the glucose concentration is not less than 20 mmole/L. Figure 3 illustrates the response current signal of a sensor assembly in phosphate buffer during a step incremental increase of glucose. In the graph, each increase in current represents the response to the addition of 5 mmol/L glucose. Y-axis is the response current in nA.

[0047] The sensor of this invention, when used in clinical test, demonstrates superior performance as illustrated in Figure 4. For a 3-day period of *in vivo* test, two sensor assemblies are implanted in the upper arm of a type 2 diabetes patient. These two sensor assemblies produced nearly identical signals for the entire duration. The continuous lines in Figure 4 represent the raw sensor signals. Circular dots are values from finger tip capillary blood glucose measurements (in mmol/L) using a conventional blood glucose meter. The graph shows that the sensor possess high sensitivity, reproducibility and stability.

[0048] The needle sensor system in the present invention may be also configured with one anode and two or more cathodes connected in series or parallel to form multi-electrochemical systems; or, the system can be configured to have one cathode and two or more anodes to form multi-electrochemical systems.

[0049] The anode in the present invention features layers of noble metal, platinum and biosensing layers over a rigid non-corrosive conducting needle. The cathode, on the other hand, comprises layers of silver, silver chloride and polymer over a rigid non-corrosive conducting needle. The cathode body may also be formed using a silver alloy needle and covering the surface with silver chloride.

[0050] The biosensing layer is of a compound membrane. The inner portion contains enzyme and the outer portion is of biocompatible polymers that features minimal tissue reactions. The enzyme provides biospecificity, to selectively react with the desired chemical species to convert it into electrochemically active molecules. Typical enzymes may be glucose oxidase, alcohol oxidase, lactate oxidase, and cholesterol oxidase, etc., The membrane may be deposited and immobilized onto the electrode surface through chemical bonding by cross-linking reagents that have two reactive groups. The outer diffusion layer may be of medical grade polydimethylsiloxane copolymer or polymer blend.

[0051] The sensor membrane can be formed from a mixed solution of two different polymers.

[0052] One of the polymers is hydrophilic and the other hydrophobic. A process of solvent evaporation from such a solution is used to prepare the membrane. Usually, the resulting membrane tends to form a non-homogeneous structure. The surface layer is typically hydrophobic which is not permeable to most of water soluble molecules except oxygen.

[0053] To achieve the desired molecular permeability for measuring soluble molecules in aqueous environment, next step involves membrane re-structuring. It requires a special solvent mixture containing a cross-linking reagent to partially dissolve the membrane surface and then re-form the outermost layer in such a way that its composition is re-arranged to be permeable to desired molecules. The cross-linking reagent serves to fix the new structure as it forms.

[0054] The hydrophilic polymer can be one or more of a number of commercial hydrophilic polymers such as polyethylene glycol and its derivatives with end reactive groups. The hydrophobic polymer can be one or more of a class of copolymers that contain polydimethylsiloxane (silicone) as one of the components for a favorable oxygen permeability. Examples are medical grade silicone-polyurethane copolymers, silicone-polycarbonate copolymers, and silicone-methacrylate copolymers.

[0055] In a preferred embodiment, said hydrophilic pol-

ymer is amine terminated polyethylene glycol, the hydrophobic polymer is polydimethysiloxane-polyurethane copolymer, and the cross-linking reagent is glutaraldehyde. The dry weight ratio of the hydrophilic polymer vs hydrophobic polymer may be in the range of 1:19 to 1:3, adjustable on the bases of the membrane ionic conductivity as well as glucose molecular permeability. The polymers may be prepared and used in 3%-7% (weight/volume) solutions in a solvent in which all polymers have sufficient solubility. The special mixture solvent for membrane surface modification may contain water, tetrahydrofuran (THF), and ethanol in volume concentrations of 25%±15%, 65%±25%, and 10%±10%, respectively. The percentage of the three constituents may be adjusted in the given ranges based on the need of the overall sensitivity requirement.

[0056] To reproducibly deposit various solutions onto the electrode surface to form a homogeneous membrane, the following three methods may be used. 1) Dip-coating: Submerge the electrode into a solution and remove it in a preferred angle, spin rate and linear speed to coat a uniform film on the electrode; 2) Spray coating: Spin the electrode horizontally in a nebulized stream of the solution under a controlled spray nozzle to form the film; And 3) Loop-coating: Load a wire loop of adequate diameter with the solution such that a liquid film is formed inside the loop (similar to a bubble blower), and then move the electrode perpendicularly to penetrate the middle of the loop to transfer a liquid film onto the electrode.

[0057] The thickness of the biosensing membrane may be in the range of 2-10 micron, in which the enzyme layer may have the thickness of 1 micron and the diffusion layer may have a thickness of less than 9 micron.

[0058] For using the sensor in the present invention, the needles are directly inserted into the skin. The adhesive tape affixes the sensor base to the skin. Analyte molecules (e.g. glucose) in the surrounding tissue fluid diffuse through the outer membrane to reach the enzyme layer, catalytically oxidized by oxygen, producing hydrogen peroxide. The latter in turn is electrochemically oxidized on the platinum electrode (polarized at 0.5-0.6V vs Ag/AgCl) to form a current in the electrode circuit. The magnitude of the current is proportional to the concentration of glucose. The current is converted into concentration information and recorded by an external electronic device for display and analysis.

Claims

1. A catheter-free subcutaneously implantable apparatus for producing a signal reflecting the concentration of molecules, said apparatus comprising :

at least one needle shaped anode (401),
at least one needle shaped cathode (402),
a supporting base (1) for mounting the anodes and the cathodes, and
a contact means for connecting the anodes and the cathodes with a signal reading system, **characterised in that**
the anode comprises a anode core (41), a first anode cover layer (42) , a second anode cover layer (43), a third anode cover layer (44), and **in that** the cathode comprises a cathode core (41'), a first cathode cover layer (42'), a second cathode cover layer (43'), a third cathode cover layer (44'), wherein the anode core is a metal core, the first anode cover layer is a noble metal layer, the second anode cover layer is a platinum layer, the third anode cover layer is a sensing layer, wherein the cathode core is a metal core, the first cathode cover layer is a silver layer, the second cathode cover layer is a silver chloride layer, and the third cathode cover layer is a polymer layer.

2. The apparatus of claim 1, wherein the molecules are glucose.

3. The apparatus of claim 1, wherein the sensing layer is a compound membrane, including enzyme and biocompatible polymer material.

4. The apparatus of claim 3, wherein the polymer material is a medical grade polydimethylsiloxane copolymer.

5. The apparatus of claim 1, wherein the supporting base is a molded insulating plastic base.

6. The apparatus of claim 5, further comprises a mold plastic cover.

7. The apparatus of claim 6, further comprises conducting circuits.

8. The apparatus of claim 6, further comprises a circular medical adhesive tape.

9. The apparatus of claim 6, wherein the contact means is an electric receptacle.

10. The apparatus of claim 1, wherein the anode comprises a anode core, a first anode cover layer, a second anode cover layer and wherein the 3rd anode cover layer (44) is omitted;
wherein the cathode comprises a cathode core, a first cathode cover layer, a second cathode cover layer, and wherein the 3rd cathode cover layer (44') is omitted.

11. The apparatus of claim 10, wherein the anode core is a metal core; the first anode cover layer is a silver layer; the second anode cover layer is a polymer layer; wherein the cathode core is a metal core, the

first cathode cover layer is a platinum layer, the second cathode cover layer is a biosensing layer.

12. The apparatus of claim 11, wherein the biosensing layer is a complex membrane, including enzyme and biocompatible polymer materials.

13. The apparatus of one of claims 10-12, wherein the molecules are Oxygen.

14. A percutaneously implanted miniature sensor assembly (10,10') comprising an apparatus as claimed in any one of claims 1-13, said assembly comprising a base (1,1'), an anode (401,401'), a cathode (402,402'), a first contact plate (21,21'), and a second contact plate (22,22') ;
wherein the base further comprises a first mounting hole surface, a second mounting hole surface, a base top surface (12,12') and a base bottom surface (11,11'), wherein the first mounting hole surface defines a first mounting hole (111,111'), and the second mounting hole surface defines a second mounting hole (112,112') ;
wherein the first contact plate further comprises a first plate mounting surface defining a first plate mounting hole (211,211'), and the second contact plate further comprises a second plate mounting surface defining a second plate mounting hole (221,221') respectively;
wherein the first contact plate and the second contact plate are set on the base on the base top surface, wherein the first plate mounting hole(211,211'), the second plate mounting hole(221,221') are in line with the first mounting hole(111,111') and the second mounting hole (112,112') respectively;
wherein the anode and cathode are in needle shape and implantable in a body, wherein the anode (401,401') body penetrate the first plate mounting hole(211,211') and the first mounting hole(111,111'), and the cathode(402,402',403') body penetrate the second plate mounting hole(221,221') and the second mounting hole(112, 112'), wherein the top of the anode and cathode are connected with the first contact plate (21,21') and the second contact plate (22,22') by electric conductive material, wherein the anode and the cathode are perpendicular to the base bottom surface (11,11').

15. A percutaneously implanted miniature sensor assembly as claimed in claim 14, comprising a base (1') , an anode (401'), a reference cathode (402'), an assisting cathode (403'), a first contact plate (21'), a second contact plate (22') and a third contact plate (23 ') ;
wherein the base further comprises a first mounting hole surface, a second mounting hole surface, a third mounting hole surface, a base top surface (12') and a base bottom surface (11'), wherein the first mounting hole surface defines a first mounting hole (111'), the second mounting hole surface defines a second mounting hole (112'), and the third mounting hole surface defines a third mounting hole (113');
wherein the first contact plate further comprises a first plate mounting surface defining a first plate mounting hole (211'), the second contact plate further comprises a second plate mounting surface defining a second plate mounting hole (221'), and the third contact plate further comprises a third plate mounting surface defining a third plate mounting hole (231') respectively;
wherein the first contact plate (21'), the second contact plate (22') and the third contact plate (23') are set on the base on the base top surface, wherein the first plate mounting hole (211'), the second plate mounting hole (221'), the third plate mounting hole (231') are in line with the first mounting hole (111'), the second mounting hole (112') and the third mounting hole (113') respectively;
wherein the anode (401'), the referencing cathode (402') and the assisting cathode (403') are in needle shape and implantable in a body, wherein the anode body penetrate the first plate mounting hole (211') and the first mounting hole (111') , the referencing cathode body penetrate the second plate mounting hole (221') and the second mounting hole (112'), and the assisting cathode body penetrate the third plate mounting hole (231') and the third mounting hole (113'), wherein the top of the anode, the referencing cathode and the assisting cathode are connected with the first contact plate (21'), the second contact plate (22'), and the third contact plate (23') by electric conductive material, wherein the anode, the referencing cathode and the assisting cathode are perpendicular to the base bottom surface (11') respectively.

Patentansprüche

1. Katheterfreie subcutan implantierbare Vorrichtung zur Erzeugung eines Signals, das die Konzentration von Molekülen wiedergibt, wobei die Vorrichtung enthält:

mindestens eine nadelförmige Anode (401),
mindestens eine nadelförmige Kathode (402),
einen Träger (1) zum Anbringen der Anoden und der Kathoden,
und
ein Kontaktmittel zur Verbindung der Anoden und der Kathoden mit einem System zum Auslesen der Signale, **dadurch gekennzeichnet, dass** die Anode einen Anodenkern (41), eine erste Anoden-Deckschicht (42), eine zweite Anoden-Deckschicht (43) sowie eine dritte Anoden-Deckschicht (44) aufweist, und dass die

Kathode einen Kathodenkern (41'), eine erste Kathoden-Deckschicht (42'), eine zweite Kathoden-Deckschicht (43') sowie eine dritte Kathoden-Deckschicht (44') enthält, und bei welcher der Anodenkern ein Metallkern ist, die erste Anoden-Deckschicht eine Edelmetallschicht ist, die zweite Anoden-Deckschicht eine Platinschicht ist, die dritte Anoden-Deckschicht eine Sensorschicht ist, der Kathodenkern ein Metallkern ist, die erste Kathoden-Deckschicht eine Silberschicht ist, die zweite Kathoden-Deckschicht eine Schicht aus Silberchlorid ist und die dritte Kathoden-Deckschicht eine Polymerschicht ist.

2. Vorrichtung nach Anspruch 1, bei der die Moleküle aus Glucose bestehen.

3. Vorrichtung nach Anspruch 1, bei der die Sensorschicht eine Verbundmembran ist, einschliesslich Enzymen und bioverträglichem Polymermaterial.

4. Vorrichtung nach Anspruch 3, bei der das Polymermaterial ein medizinisch klassifiziertes Polydimethylsiloxan-Copolymer ist.

5. Vorrichtung nach Anspruch 1, bei der der Träger aus einem spritzgegossenen isolierenden Kunststoff besteht.

6. Vorrichtung nach Anspruch 5, welche weiterhin einen geformten Kunststoffdeckel aufweist.

7. Vorrichtung nach Anspruch 6, welche zusätzlich Leiterschaltkreise enthält.

8. Vorrichtung nach Anspruch 6, welche zusätzlich ein medizinisches Umschlingungs-Klebeband aufweist.

9. Vorrichtung nach Anspruch 6, bei der die Kontaktmittel aus einem elektrischen Steckanschluss bestehen.

10. Vorrichtung nach Anspruch 1, bei welcher die Anode einen Anodenkern, eine erste Anoden-Deckschicht und eine zweite Anoden-Deckschicht aufweist, und bei welcher die dritte Anoden-Deckschicht (44) nicht vorhanden ist;
und worin die Kathode einen Kathodenkern, eine erste Kathoden-Deckschicht und eine zweite Kathoden-Deckschicht aufweist, und bei welcher die dritte Kathoden-Deckschicht (44') nicht vorhanden ist.

11. Vorrichtung nach Anspruch 10, bei welcher der Anodenkern ein Metallkern ist, die erste Anoden-Deckschicht eine Silberschicht ist, die zweite Anoden-Deckschicht eine Polymerschicht ist, der Kathodenkern ein Metallkern ist, die erste Kathoden-Deckschicht eine Platinschicht ist und die zweite Kathoden-Deckschicht eine Biosensorschicht ist.

12. Vorrichtung nach Anspruch 11, bei der die Biosensorschicht eine Komplexmembran ist, einschliesslich Enzymen und bioverträglichem Polymermaterial.

13. Vorrichtung nach einem der Ansprüche 10 bis 12, bei der die Moleküle Sauerstoffmoleküle sind.

14. Percutan implantierte Miniatur-Sensor-Anordnung (10, 10'), welche eine Vorrichtung nach einem der Ansprüche 1 bis 13 umfasst, wobei die Anordnung eine Basis (1, 1'), eine Anode (401, 401'), eine Kathode (402, 402'), eine erste Kontaktplatte (21, 21') und eine zweite Kontaktplatte (22, 22') aufweist;
bei welcher die Basis weiterhin eine erste Montagelochfläche, eine zweite Montagelochfläche, eine obere Basisfläche (12, 12') und eine untere Basisfläche (11, 11') enthält, wobei die erste Montagelochfläche ein erstes Montageloch (111, 111') und die zweite Montagelochfläche ein zweites Montageloch (112, 112') definiert;
bei welcher die erste Kontaktplatte weiterhin eine erste Plattenmontagefläche, die ein erstes Platten-Montageloch (211, 211') definiert, und die zweite Kontaktplatte weiterhin eine zweite Plattenmontagefläche, die ein zweites Platten-Montageloch (221, 221') definiert, aufweist;
bei welcher die erste Kontaktplatte und die zweite Kontaktplatte auf der Basis-Oberfläche der Basis angeordnet sind und das erste Platten-Montageloch (211, 211') sowie das zweite Platten-Montageloch (221, 221') jeweils mit dem ersten Montageloch (111, 111') bzw. dem zweiten Montageloch (112, 112') fluchten;
bei welcher die Anode und die Kathode beide die Form von Nadeln haben und in einen Körper implantierbar sind und der Anodenkörper (401, 401') durch das erste Platten-Montageloch (211, 211') und das erste Montageloch (111, 111') hindurchgeht sowie der Kathodenkörper (402, 402', 403') durch das zweite Platten-Montageloch (221, 221') und das zweite Montageloch (112, 112') hindurchgeht, wobei der Kopf der Anode und der Kopf der Kathode mittels elektrisch leitendem Verbindungsmaterial mit der ersten Kontaktplatte (21, 21') bzw. der zweiten Kontaktplatte (22, 22') verbunden sind, und wobei die Anode und die Kathode senkrecht zur Unterfläche (11, 11') der Basis verlaufen.

15. Percutan implantierte Miniatur-Sensor-Anordnung nach Anspruch 14, mit einer Basis (1'), einer Anode (401'), einer Bezugskathode (402'), einer Hilfskathode (403'), einer ersten Kontaktplatte (21'), einer zweiten Kontaktplatte (22') und einer dritten Kontaktplatte (23');

bei welcher die Basis weiterhin eine erste Montagelochfläche, eine zweite Montagelochfläche, eine dritte Montagelochfläche, eine obere Basisfläche (12') und eine untere Basisfläche (11') aufweist, worin die erste Montagelochfläche ein erstes Montageloch (111'), die zweite Montagelochfläche ein zweites Montageloch (112') und die dritte Montagelochfläche ein drittes Montageloch (113') definiert;
bei welcher die erste Kontaktplatte weiterhin eine erste Plattenmontagefläche besitzt, die ein erstes Plattenmontageloch (211') definiert, die zweite Kontaktplatte eine zweite Plattenmontagefläche besitzt, die ein zweites Plattenmontageloch (221') definiert, und die dritte Kontaktplatte eine dritte Plattenmontagefläche aufweist, die ein drittes Plattenmontageloch (231') definiert;
bei welcher die erste Kontaktplatte (21'), die zweite Kontaktplatte (22') und die dritte Kontaktplatte (23') auf der oberen Fläche der Basis angebracht sind, und das erste Platten-Montageloch (211') sowie das zweite Platten-Montageloch (221') und das dritte Platten-Montageloch (231') jeweils mit dem ersten Montageloch (111'), dem zweiten Montageloch (112') bzw. dem dritten Montageloch (113') fluchten;
bei welcher die Anode (401'), die Bezugskathode (402') und die Hilfskathode (403') die Form von Nadeln haben und in einen Körper implantierbar sind, wobei der Anodenkörper durch das erste Platten-Montageloch (211') und das erste Montageloch (111'), der Körper der Bezugskathode durch das zweite Platten-Montageloch (221') und das zweite Montageloch (112') und der Körper der Hilfskathode durch das dritte Platten-Montageloch (231') und das dritte Montageloch (113') hindurchgeht, und wobei die Köpfe der Anode, der Bezugskathode und der Hilfskathode mit der ersten Kontaktplatte (21'), der zweiten Kontaktplatte (22') bzw. der dritten Kontaktplatte (23') über elektrisch leitendes Material verbunden sind und die Anode, die Bezugskathode und die Hilfskathode jeweils senkrecht auf der unteren Basisfläche (11') stehen.

Revendications

1. Dispositif souscutanément implantable sans cathéter pour générer un signal représentant la concentration de molécules, ce dispositif comprenant :

au moins une anode aciculaire (401),
au moins une cathode aciculaire (402),
une base de support (1) pour le montage des anodes et des cathodes, et
un moyen de contact pour relier les anodes et les cathodes à un système de lecture de signaux,
caractérisé en ce que l'anode comprend un noyau anodique (41), une première couche de recouvrement anodique (42), une deuxième couche de recouvrement anodique (43), une troisième couche de recouvrement anodique (44), et **en ce que** la cathode comprend un noyau cathodique (41'), une première couche de recouvrement cathodique (42'), une deuxième couche de recouvrement cathodique (43') et une troisième couche de recouvrement cathodique (44'), et dans lequel le noyau anodique est un noyau métallique, la première couche de recouvrement anodique est une couche en métal noble, la deuxième couche de recouvrement anodique est une couche en platine, la troisième couche de recouvrement anodique est une couche captrice, le noyau cathodique est un noyau métallique, la première couche de recouvrement cathodique est une couche en argent, la deuxième couche de recouvrement cathodique est une couche en chlorure d'argent, et la troisième couche de recouvrement cathodique est une couche en polymère.

2. Dispositif selon la revendication 1, dans lequel les molécules sont du glucose.

3. Dispositif selon la revendication 1, dans lequel la couche captrice est une membrane composée y compris des enzymes et de la matière polymère biocompatible.

4. Dispositif selon la revendication 3, dans lequel la matière polymère est un copolymère de polydiméthyl siloxane de qualité médicale.

5. Dispositif selon la revendication 1, dans lequel la base de support est une base en matière plastique isolante injectée.

6. Dispositif selon la revendication 5, comprenant en plus un couvercle en matière plastique injectée.

7. Dispositif selon la revendication 6, comprenant en plus des circuits conducteurs.

8. Dispositif selon la revendication 6, comprenant en plus une bande adhésive médicale circulaire.

9. Dispositif selon la revendication 6, dans lequel le moyen de contact est une prise électrique.

10. Dispositif selon la revendication 1, dans lequel l'anode comprend un noyau anodique, une première couche de recouvrement anodique et une deuxième couche de recouvrement anodique, et dans lequel la troisième couche de recouvrement anodique (44) est omise, et dans lequel la cathode comprend un noyau cathodique, une première couche de recouvrement cathodique et une deuxième couche de re-

couvrement cathodique, et dans lequel la troisième couche de recouvrement cathodique (44') est omise.

11. Dispositif selon la revendication 10, dans lequel le noyau anodique est un noyau métallique, la première couche de recouvrement anodique est une couche en argent, la deuxième couche de recouvrement anodique est une couche en matière polymère, le noyau cathodique est un noyau métallique, la première couche de recouvrement cathodique est une couche en platine, et la deuxième couche de recouvrement cathodique est une couche biosensible.

12. Dispositif selon la revendication 11, dans lequel la couche biosensible est une membrane complexe y compris des enzymes et des matières polymères biocompatibles.

13. Dispositif selon l'une des revendications 10 à 12, dans lequel les molécules sont de l'oxygène.

14. Agencement de capteurs miniatures percutanément implanté (10, 10'), comprenant un dispositif selon l'une quelconque des revendications 1 à 13, ledit agencement comportant une base (1, 1'), une anode (401, 401'), une cathode (402, 402'), une première plaque de contact (21, 21') et une deuxième plaque de contact (22, 22') ;
dans lequel la base comprend encore une première surface de trou de montage, une deuxième surface de trou de montage, une surface de base supérieure (12, 12') et une surface de base inférieure (11, 11'), la première surface de trou de montage définissant un premier trou de montage (111, 111') et la deuxième surface de trou de montage définissant un deuxième trou de montage (112, 112') ;
dans lequel la première plaque de contact comprend de plus une surface de montage de la première plaque définissant un trou de montage de la première plaque (211, 211') et la deuxième plaque de contact comprend de plus une surface de montage de la deuxième plaque définissant un trou de montage de la deuxième plaque (221, 221'), respectivement ;
dans lequel la première plaque de contact et la deuxième plaque de contact sont posées sur la surface supérieure de la base, le trou de montage de la première plaque (211, 211') et le trou de montage de la deuxième plaque (221, 221') étant alignés au premier trou de montage (111, 111') et au deuxième trou de montage (112, 112'), respectivement ; et
dans lequel l'anode et la cathode sont de forme aciculaire et implantables dans un corps, le corps de l'anode (401, 401') passant par le trou de montage de la première plaque (211, 211') et le premier trou de montage (111, 111'), le corps de la cathode (402, 402', 403) passant par le trou de montage de la deuxième plaque (221, 221') et le deuxième trou de montage (112, 112'), les têtes de l'anode et de la cathode étant reliées à la première plaque de contact (21, 21') et à la deuxième plaque de contact (22, 22') par une matière électriquement conductrice, l'anode et la cathode s'étendant perpendiculairement à la surface inférieure de la base (11, 11').

15. Agencement de capteurs miniatures percutanément implanté selon la revendication 14, comprenant une base (1'), une anode (401'), une cathode de référence (402'), une cathode d'assistance (403'), une première plaque de contact (21'), une deuxième plaque de contact (22') et une troisième plaque de contact (23') ;
dans lequel la base comprend de plus une première surface de trou de montage, une deuxième surface de trou de montage, une troisième surface de trou de montage, une surface de base supérieure (12') et une surface de base inférieure (11'), la première surface de trou de montage définissant un premier trou de montage (111'), la deuxième surface de trou de montage définissant un deuxième trou de montage (112') et la troisième surface de trou de montage définissant un troisième trou de montage (113') ;
dans lequel la première plaque de contact comprend de plus une surface de montage de la première plaque définissant un trou de montage de la première plaque (211'), la deuxième plaque de contact comprend de plus une surface de montage de la deuxième plaque définissant un trou de montage de la deuxième plaque (221'), et la troisième plaque de contact comprend de plus une surface de montage de la troisième plaque définissant un trou de montage de la troisième plaque (231'), respectivement ;
dans lequel la première plaque de contact (21'), la deuxième plaque de contact (22') et la troisième plaque de contact (23') sont posées sur la surface supérieure de la base, le trou de montage de la première plaque (211'), le trou de montage de la deuxième plaque (221') et le trou de montage de la troisième plaque (231') étant alignés au premier trou de montage (111'), au deuxième trou de montage (112') et au troisième trou de montage (113'), respectivement ; et
dans lequel l'anode (401'), la cathode de référence (402') et la cathode d' assistance (403') sont de forme aciculaire et implantables dans un corps, le corps de l'anode passant par le trou de montage de la première plaque (211') et le premier trou de montage (111'), le corps de la cathode de référence passant par le trou de montage de la deuxième plaque (221') et le deuxième trou de montage (112'), et le corps de la cathode d'assistance passant par le trou de montage de la troisième plaque (231') et le troisième trou de montage (113'), les têtes de l'anode, de la cathode de référence et de la cathode d'assistance étant reliées à la première plaque de contact (21'), à la deuxième plaque de contact (22') et à la troisième plaque de contact (23') par une matière électri-

quement conductrice, l'anode, la cathode de référence et la cathode d'assistance s'étendant perpendiculairement à la surface inférieure de la base (11'), respectivement.

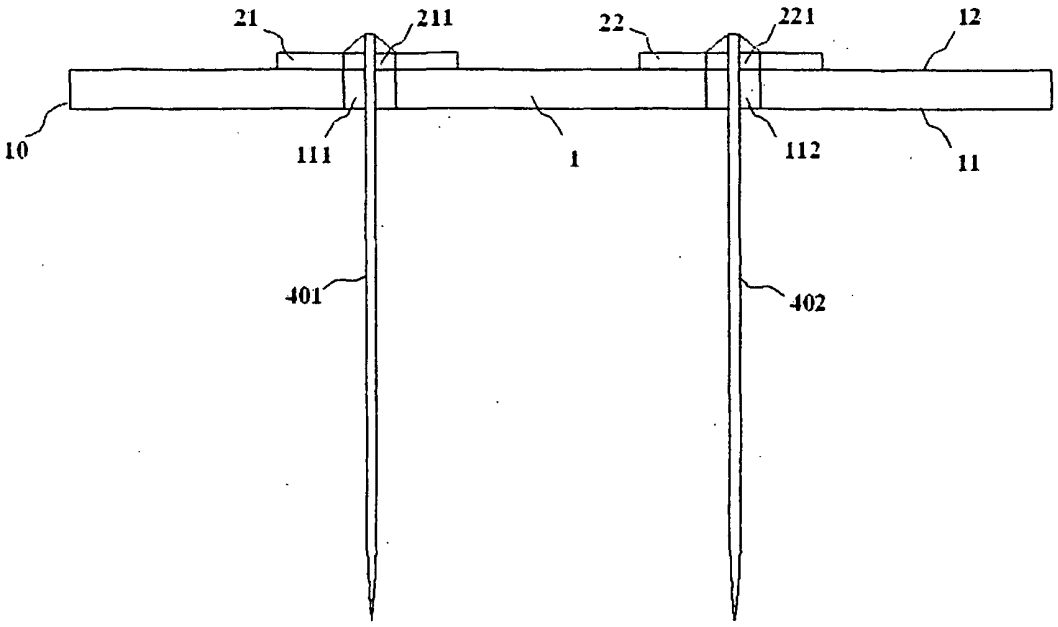

Figure 1a

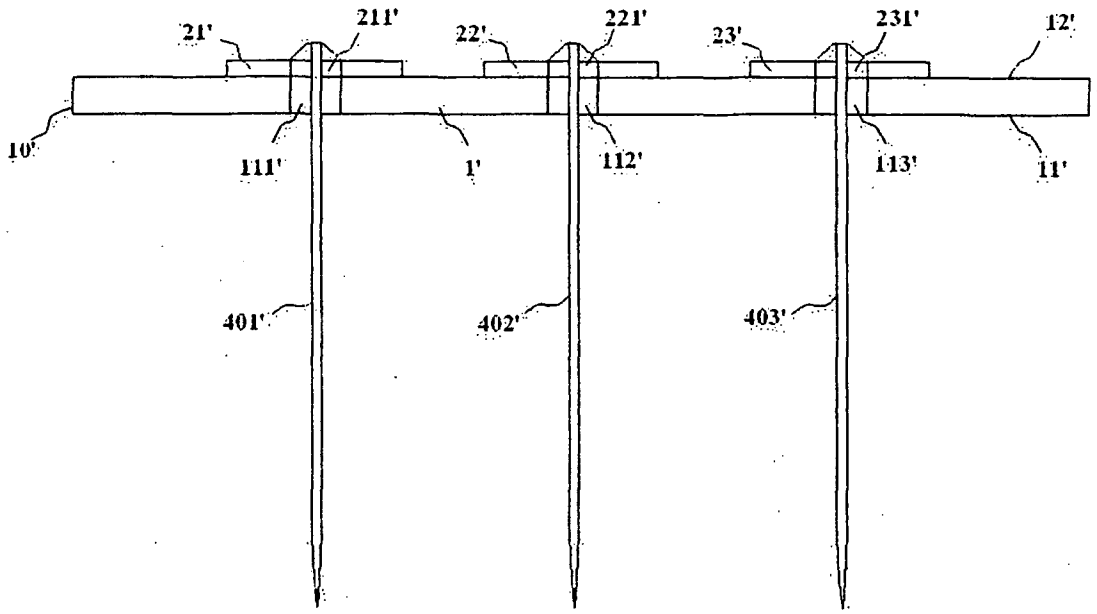

Figure 1b

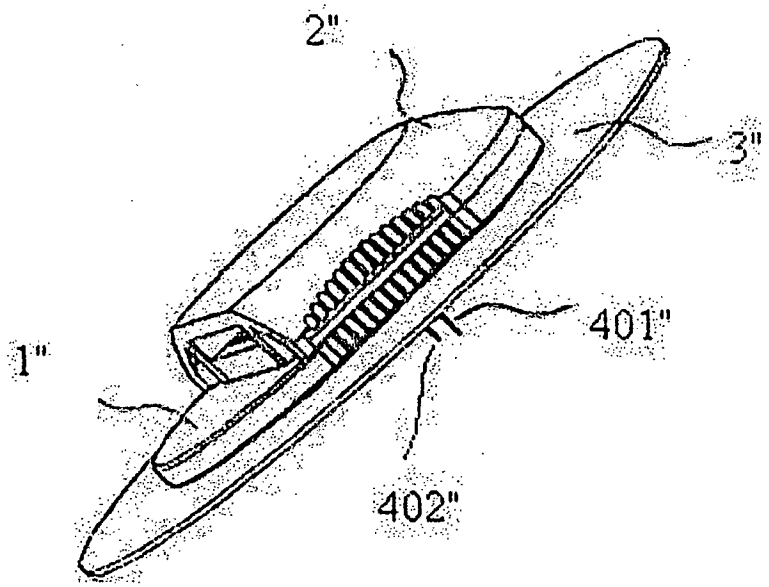

Figure 1c

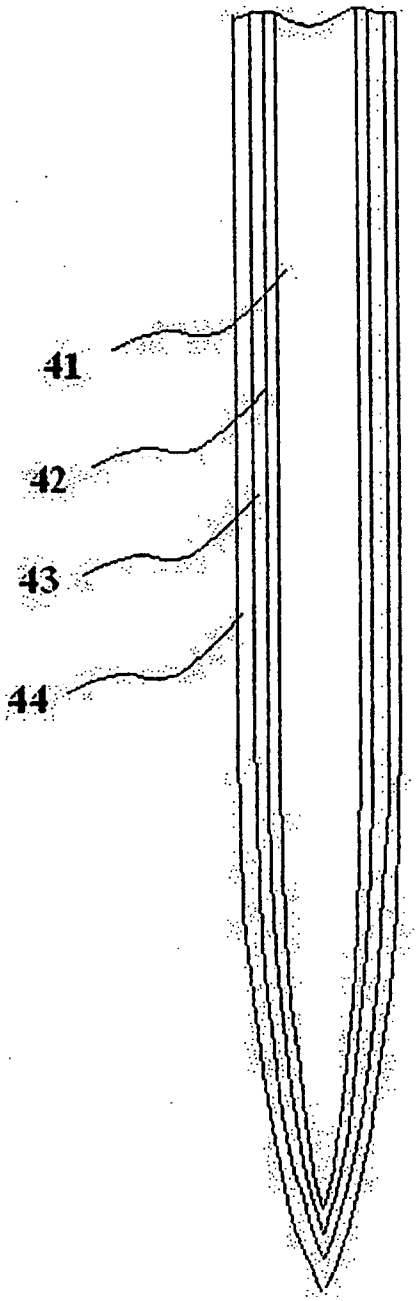

Figure 2

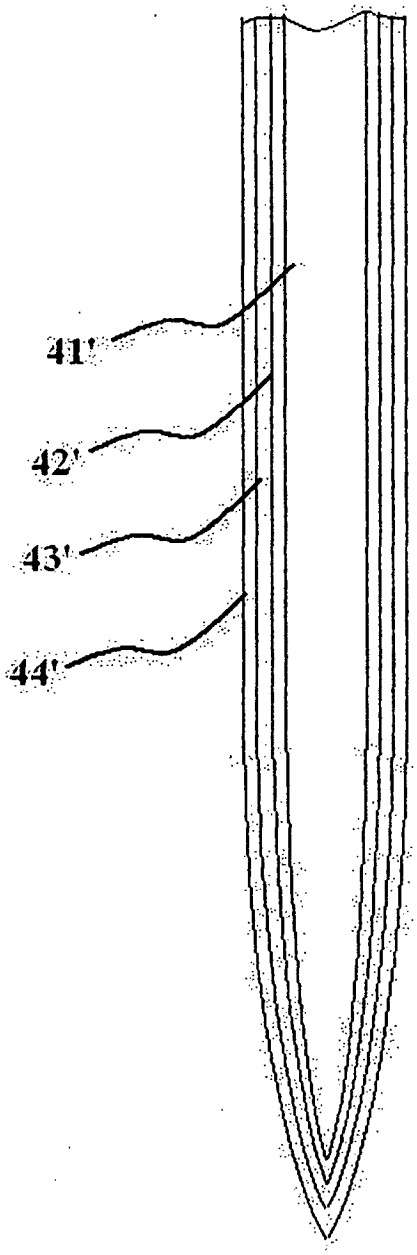

Figure 2a

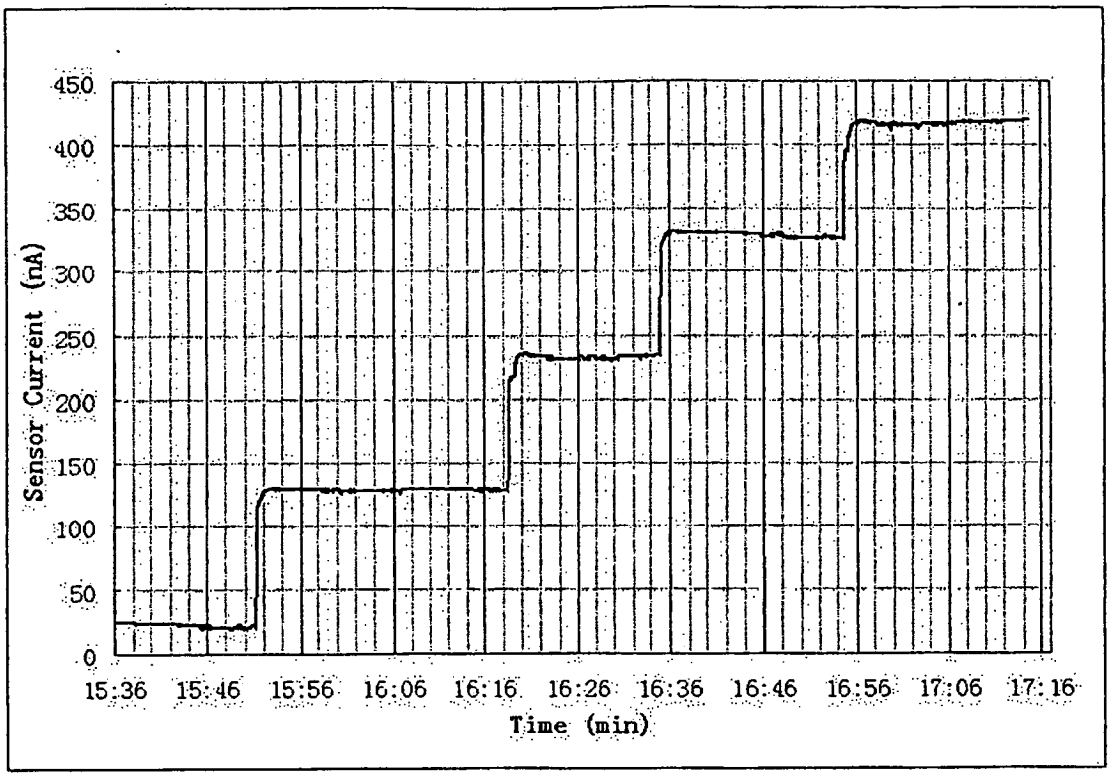
Sensor Current (nA)
450
400
350
300
250
200
150
100
50
0
15:36
15:46
15:56
16:06
16:16
16:26
16:36
16:46
16:56
17:06
17:16
Time (min)

Figure 3

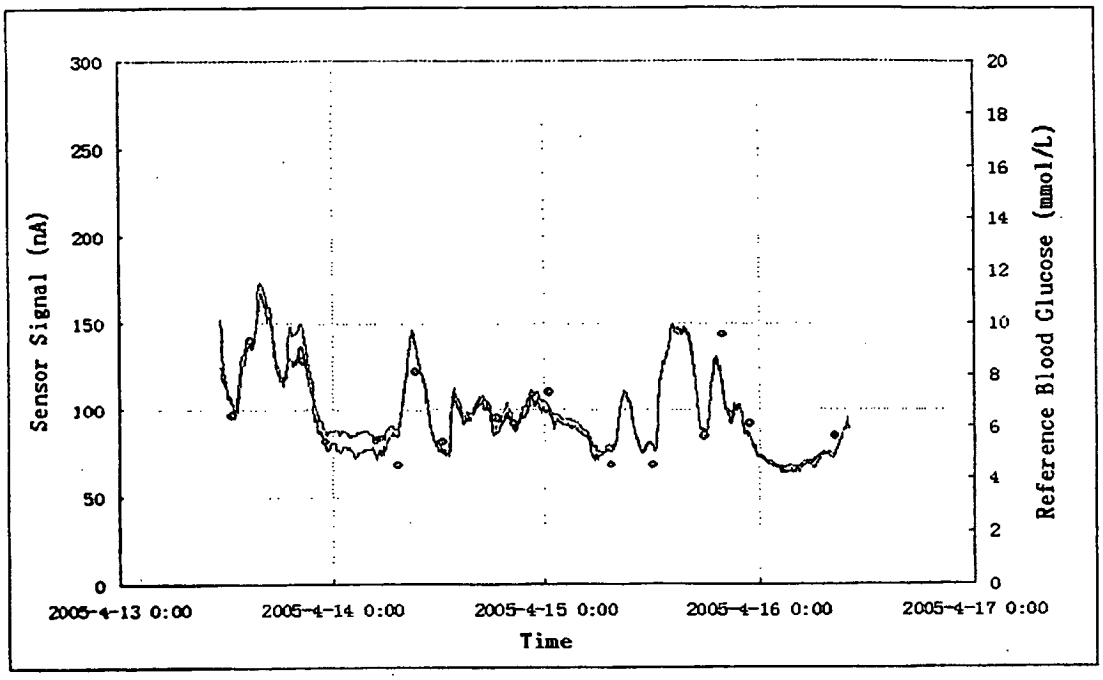
Sensor Signal (nA)
300
250
200
150
100
50
0
Reference Blood Glucose (mmol/L)
20
18
16
14
12
10
8
6
4
2
0
2005-4-13 0:00
2005-4-14 0:00
2005-4-15 0:00
2005-4-16 0:00
2005-4-17 0:00
Time

Figure 4

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- WO 2004063718 A **[0002]**
- DE 3502913 **[0003]**
- US 6952604 A **[0008]**

专利名称(译)	无导管植入式针头生物传感器		
公开(公告)号	EP1841363B1	公开(公告)日	2011-10-05
申请号	EP2005819013	申请日	2005-11-09
[标]申请(专利权)人(译)	张燕		
申请(专利权)人(译)	SAN MEDITECH（湖州）有限公司 延安，张		
当前申请(专利权)人(译)	SAN MEDITECH（湖州）有限公司		
[标]发明人	YANAN ZHANG		
发明人	YANAN, ZHANG		
IPC分类号	A61B5/00 A61B8/00 A61B8/14 A61B8/12 G01N33/487 A61B5/145 A61B10/00		
CPC分类号	A61B5/14532 A61B5/14542 A61B5/14865 A61B5/6849		
优先权	200410101080.6 2004-12-08 CN		
其他公开文献	EP1841363A4 EP1841363A2		
外部链接	Espacenet		

摘要(译)

提供了由两个或更多个针状电极组成的电化学生物传感器，用于监测皮下组织中的分子，例如葡萄糖。两个电极彼此平行，并且垂直于传感器基座的平面侧固定，该传感器基座提供皮肤固定和电连接。针电极由刚性导电材料制成，能够在不需要导管的情况下插入皮肤。一个电极是传感电极，另一个是参考电极。将复合传感膜附着在传感电极表面上以检测分析的分子。

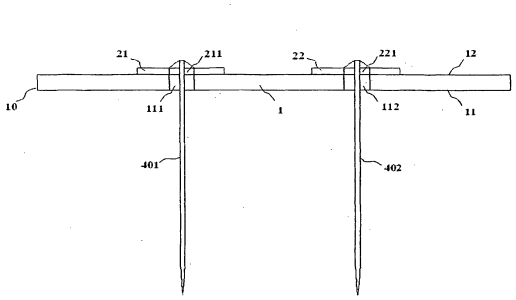

Figure 1a