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(54) **SENSOR AND APPARATUS FOR ANALYSING GASES PRESENT IN BLOOD**

SENSOR UND VORRICHTUNG FÜR DIE ANALYSE VON BLUTGASEN

CAPTEUR ET APPAREIL D'ANALYSE DES GAZ PRÉSENTS DANS LE SANG

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(56) References cited:
EP-A- 0 267 978
EP-A- 0 302 127
US-A- 3 886 058
US-A- 4 329 214

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Description

[0001] The present invention relates to a sensor and an apparatus for analysing gases present in blood and particularly for determining gases that, like ammonia, hydrogen sulfide and nitrogen monoxide, are present in blood in minimum amounts in the order of parts per million or even lower.

[0002] It is well known that several pathological conditions may be identified by analysing the gases present in blood. The techniques commonly used for these analyses require taking blood samples through various methods and the subsequent storing of these samples in environments that are isolated, thermostated, etc., until the time of the actual analysis. This has various drawbacks well known to those skilled in the art, as well as the impossibility of carrying out a continuous monitoring of the tension of the various gases present in blood. In order to overcome such drawbacks it has been already suggested to dispense with the taking of blood samples and to carry out the determination of the gases present in blood through another way, such as for instance through a transcutaneous way or by analysing saliva samples. These techniques, in addition to being non-invasive, also allow a continuous monitoring of blood gases and the technique for sampling the gases through transcutaneous way in particular has been employed since the beginning in the prenatal diagnostics for determining oxygen and CO_2 present in blood.

[0003] Apparatuses for analysing blood gases are known, generally comprised of gas sampling probes connected through pipings to apparatuses provided with sensors for measuring the gases. Numerous sensors for analysing blood gases are known, e.g. based on measuring galvanic cells that allow to measure the concentration of one or more gases.

[0004] Patent US 5007424, e.g., describes a polarographic/amperometric sensor for measuring the oxygen partial pressure in blood by means of a Clark-type electrode arrangement. The sensor may be provided with a pH electrode for the simultaneous determination of CO_2 partial pressure in blood.

[0005] Patent US 4840179 discloses a thermostated device for the simultaneous and continuous measurement of oxygen and CO_2 present in blood, based on the principle of pH measurement in an electrolyte. The gas sampling is carried out transcutaneously. However, in order to ensure satisfactory measurements of oxygen and CO_2, it is necessary to heat the skin at temperatures of about 42°C in order to enhance its permeability and consequently the flow of gas.

[0006] A problem of galvanic sensors known in the art is that they do not allow to detect the presence of traces of blood gases (such as ammonia, hydrogen sulfide and nitrogen monoxide), which may be related to several pathological conditions. In particular, the gaseous ammonia present in blood may reveal liver and kidney dysfunctions, in which the concentrations increase beyond the physiological values of 0,1-0,6 ppm.

[0007] The measurement and the monitoring of gaseous ammonia could allow a rapid and sure diagnosis of diseases like hyperammoniaemia and hypoammoniaemia, diabetes and hypertension, as well as the diagnosis of infection from Helicobacter Pylori. The transcutaneous determination of gaseous ammonia could also be used in haemodialysis treatments and in periodic check-ups.

[0008] In the article "Identification of ammonia in gas emanated from human skin and its correlation with that in blood" by K. Nose et al., published on Analytical Sciences, December 2005, vol. 21, page 1471 and following, there is described an experimental study through which it has been possible to detect the presence of gaseous ammonia emanated from the skin and to measure its amount. The article underlines the need for collecting the gases transcutaneously by using methods that are non-painful for the patient and in real time, thus allowing to continuously monitor the variations of gaseous ammonia in blood, as well as to make measuring apparatuses also for domestic use.

[0009] It is therefore an object of the present invention to provide a sensor and an apparatus for determining blood gases, in particular traces of gases such as ammonia, hydrogen sulfide and nitrogen monoxide, in real time and by means of an analytical technique which is non-invasive, non-manipulative and non-destructive. Said object is achieved with a sensor and an apparatus, whose main features are disclosed in claim 1 and 11, respectively, while other features are disclosed in the remaining claims.

[0010] The sensor according to the present invention is a measuring galvanic cell specifically made for detecting and measuring gases that, like ammonia, hydrogen sulfide and nitrogen monoxide and present in blood gases in minimum amounts in the order of parts per million or even lower.

[0011] An advantage of the sensor according to the present invention is that is has response and recovery times in the order of seconds, thus being able to be advantageously employed for real time and continuous measurements. -

[0012] Moreover, the sensor according to the invention does not require any heating of the patient's skin in order to enhance the permeability thereof to blood gases. In fact, thanks to the miniaturization of the measuring electrode, minimum amounts of gas are enough for carrying out correct and accurate measurements. The risk of skin bums is therefore completely eliminated.

[0013] Another advantage is that the sensor is very compact and thus allows a low cost manufacturing of measuring apparatuses having a reduced size, being portable and also suitable for the domestic use.

[0014] Still another advantage of the sensor according to the present invention is that it may be used together with different types of sampling probes, suitable for both the transcutaneous sampling and the in-vitro analyses of blood or saliva samples, thus allowing the maximum flexibility of use of the measurement apparatuses in which it is inserted.

[0015] Patent US 3886058 discloses an electro-chemical gas-detection device comprising a galvanic cell provided with a galvanic reference element and a galvanic measuring element immersed in an electrolytic solution. The galvanic measuring element comprises a measuring electrode on which a hydrophilic wick is transversally arranged. The free ends of the wick are both immersed in the electrolytic solution. The wick provides a path for ohmic contact of the electrolyte across the sensing surface of the measuring electrode, thus accomplishing an electrode/electrolyte interface for the detection of gases.

[0016] The device described in the above mentioned patent provides the same advantages of the invention in terms of response and recovery times, but does not teach how to configure the sensor in order to solve the technical problem of measuring small amounts of blood gases and in particular traces of gases such as ammonia, hydrogen sulfide and nitrogen monoxide.

[0017] Further advantages and features offered by the sensor and apparatus according to the present invention will become clear to those skilled in the art from the following detailed and non-limiting description of some embodiments thereof with reference to the attached drawings, wherein:

- figure 1 shows a cross-sectional view of the sensor according to the present invention;
- figure 2 shows a schematic view of a measuring apparatus including the sensor of figure 1;
- figure 3 shows a cross-sectional view of a first embodiment of a sampling probe that can be used with the apparatus of figure 2;
- figure 4 shows a cross-sectional view of a second embodiment of a sampling probe that can be used with the apparatus of figure 2;
- figure 5 is a graph shoving the trend over time of gaseous ammonia concentration measured during a transcutaneous sampling with the apparatus of figure 2;
- figure 6 is a graph showing the trend over time of gaseous ammonia concentration measured with the apparatus of figure 2 on blood samples taken at regular intervals during a haemodialysis cycle; and
- figure 7 is a graph showing the trend over time of gaseous ammonia concentration measured with the apparatus of figure 2 on samples of discharged dialytic fluid taken at regular intervals during a haemodialysis cycle.

[0018] Referring to figure 1, there is seen that the galvanic sensor according to the present invention comprises a duct 1 suitable for being crossed by a flow of gas and provided with an inlet opening 2 and an outlet opening 3. Duct 1 may be made of any suitable material. For instance it may be a glass tube, which has a T shape in a preferred embodiment. Outlet 3 is arranged at a transverse arm 1 a of the tube.

[0019] The sensor according to the present invention further includes a reference galvanic element, comprised of a container 4 containing an electrolytic solution 5 and of a reference electrode 6 inserted in container 4. Container 4 is fixed to duct 1, e.g. by friction or by means of a threaded connection. The measuring galvanic element of the sensor comprises a measuring electrode 7 arranged substantially transversally to the axis of duct 1 and a filiform element 8 having a high capillarity, e.g. a braided cotton yam, anchored to container 4 and having a first end 8a contacting the measuring electrode 7 and a second end 8b contacting the electrolytic solution 5. In the embodiment shown in the drawing, the filiform element 8 is mounted in a position substantially coincident with the axis of duct 1.

[0020] The working solution wets the measuring electrode 7 by going up through the filiform element 8 by capillarity, i.e. element 8 acts as a wick. Therefore, between the measuring electrode 7 and the reference electrode 6 a potential difference based on the redox potentials of the two galvanic elements is present and can be measured.

[0021] In a preferred embodiment, the measuring electrode 7 and the reference electrode 6 are small metal bars made of stainless steel, however other materials already known for the use as electrodes may be used.

[0022] In the sensor according to the present invention, the galvanic element containing the measuring electrode is extremely miniaturized, as the volume of electrolytic solution wetting the measuring electrode 7 is determined by the very small size of the contact area between the first end 8a of the filiform element 8 and the measuring electrode 7. For example, if the electrode has a diameter of 1 mm and the filiform element has a diameter of 0,1 mm, and the filiform element forms a complete coil around the electrode, the volume of electrolytic solution wetting electrode 7 is in the order of 1 μl.

[0023] On the basis of a plurality of tests carried out by the inventor with standard solutions containing a known amount of gas, it was possible to verify that such a very small volume of electrolytic solution obtained through the wicking effect of element 8 is suitable to detect amounts of gas in the order of 0,1 ppm or even lower. Similarly, by suitably choosing the diameter of the filiform element, the diameter of the electrode and the size of the contact area between the filiform element and the measuring electrode it is possible to achieve, through an adequate calibration, the desired sensibility for a correct measurement of the amounts of the desired blood gases present in blood.

[0024] This particular feature of the present invention allows to carry out analyses of the gases present in blood with minimum amounts of sampled gas and make it suitable for measuring gases that, like ammonia, hydrogen sulfide and nitrogen monoxide, are present in traces only. Therefore, in the case of a transcutaneous sampling there is no need for heating the patient's skin in order to enhance its permeability and collect a larger amount of blood gases. Moreover, the response times of the sensor are much faster since they only depend on the kinetics of the reactions occurring between the analysed gas and the electrolytic solution used in the sensor.

[0025] In the case of ammonia, for example, the electrolytic solution 5 employed may be e.g. a diluted aqueous solution of ammonium chloride.

[0026] In addition, the electrolytic solution employed must be chosen so as to avoid interferences by the other gases present in blood. In the case of a diluted aqueous solution of ammonium chloride there are no interferences from oxygen, which does not react with it. In order to avoid that CO_2 reacts with water, there may be advantageously exploited the fact that the reaction kinetics of CO_2 is much slower than that of ammonia. Thus, by suitably setting the time during which the flow of gas crosses the sensor, it is possible to completely avoid interferences by CO_2.

[0027] The choice of the electrolytic solution, the material and the geometry of the filiform element and the number of its coils around the measuring electrode, as well as the measuring times, are important parameters in the configuration of the sensor, which simultaneously contribute in defining its sensibility and rapidity of response.

[0028] Figure 2 shows an apparatus for analysing blood gases, which comprises a galvanic sensor 9 according to the present invention as well as a first device 10 connected thereto and suitable for detecting a potential difference between the electrodes, e.g. a potentiometer. A second device 11, e.g. a personal computer, is connected to the first device 10 and is suitable for processing and storing potential difference data detected by the first device 10. As described above, a potential difference is present between the measuring electrode 7 and the reference electrode 6, which is based on the redox potentials of the two galvanic elements. Therefore, by measuring this potential difference over time with a potentiometer and by acquiring, storing and processing the measurements continuously, it is possible to carry out a real time monitoring of the ammonia contained in blood gases.

[0029] As shown in the drawing, the apparatus according to the present invention further comprises a probe 12 for sampling the gases. A downstream end of probe 12 is connected to the galvanic sensor 9 and an upstream end to a source 13 of a carrier gas, e.g. ambient air, which is suitable for transporting the gases present in blood towards the galvanic sensor 9. The carrier gas is pumped from source 13 by means of a pump 14 and filtered and purified through a series of filters 15 arranged downstream of pump 14. Between filters 15 and probe 12 a flow bypass 16 is arranged, allowing to direct the carrier gas alternately towards probe 12, and consequently towards the galvanic sensor 9, or directly towards the galvanic sensor 9 without crossing probe 12.

[0030] The connections among the various above-described components of the apparatus, i.e. the galvanic sensor 9, probe 12, source 13, pump 14, filters 15 and flow bypass 16, are made through tubes 17 that are impermeable to gases. These tubes 17 may be made of PTFE or stainless steel and preferably have an inner diameter of about 1 mm, suitable for ensuring a flow rate of carrier gas preferably comprised between 1 and 5 ml/s.

[0031] Figure 3 shows a first embodiment of probe 12, particularly suitable for the transcutaneous sampling of the gases. The probe is comprised of a bell-shaped member having a base with an opening 18 in order to allow a transcutaneous retrieval of the gases. The bell-shaped member is also provided with an inlet 19 and an outlet 20 suitable for allowing a flow of the carrier gas through the bell. In particular, inlet 19 is connected to a tube 17a coming from the bypass 16 and outlet 20 is connected to a tube 17b leading to the galvanic sensor 9. The base opening 18 of the bell-shaped member defines an area not larger than 1 cm^2, which is necessary for ensuring an adequate flow of blood gases into the bell.

[0032] Figure 4 shows a second embodiment of probe 12, which may be employed either for sampling gases through transcutaneous way or for sampling gases from blood or saliva samples collected in an analysis cell.

[0033] Probe 12 is comprised of a small tube of porous material, e.g. PTFE, having a pore diameter in the order of microns. Similarly to the bell-shaped probe, the small tube of porous PTFE is inserted between tubes 17a and 17b and is crossed by the carrier gas. In order to allow the retrieval of a sufficient amount of gas, the portion of the small tube comprised between the ends of tubes 17a and 17b has a length preferably comprised between 1 and 2 cm.

[0034] In the case of a transcutaneous sampling, the small tube is bent like a "U" and arranged astride the finger of a patient, who closes the hand thus retaining probe 12.

[0035] When sampling gases from samples of blood or saliva contained in an analysis cell, tubes 17a and 17b are airtightly inserted in a cap closing the cell, so that the small tube is suspended above the sample to be analysed.

[0036] During the operation of the apparatus, a flow of carrier gas is pumped through probe 12 for a preset measuring time t_M, e.g. 10 s, during which blood gases collected by probe 12 are taken and transported to the galvanic sensor 9 thus hitting the measuring electrode 7. When measuring ammonia, a portion of the molecules of ammonia enters in solution in the ammonium chloride contained inside the end of the filiform element 8 contacting the measuring electrode 7, thus forming NH_4^+ and OH^- ions. Negative OH^- ions bond to iron ions already in solution, thus altering the redox potential of the measuring element according to Nernst law. Therefore potentiometer 10, which is connected to electrodes 6 and 7, detects a potential difference that is different from the initial potential difference and may be related to the concentration of ammonia present in blood gases through a suitable calibration of the galvanic sensor 9. Subsequently, by acting on the flow bypass 16, the carrier gas is made to flow directly towards the sensor for a recovering time t_R, e.g. 50 s, during which the initial conditions of the galvanic sensor are restored.

[0037] A standard reference cell 21 may be optionally arranged between filters 15 and bypass 16, said cell containing a solution of the gas to be analysed at a known concentration, e.g. an aqueous solution of ammonia. In this way it is possible to set different starting conditions of the galvanic sensor 9, thus obtaining more or less rapid recovering times according to the established operation mode of the apparatus.

[0038] By repeating measuring and recovering cycles of the sensor over time, it is possible to carry out continuously the analysis of the gases present in blood, thus allowing the diagnosis of the different pathologies that may be related to blood gases as well as the monitoring of the patient.

[0039] The following examples show some cases of use of the apparatus and sensor according to the present invention.

Example 1

[0040] An apparatus for the analysis of gases was prepared, comprising a galvanic sensor according to the present invention, a potentiometer and a computer suitable to acquire, store and process the measurements of potential difference taken by the potentiometer. The apparatus was also provided with a probe for the transcutaneous sampling of blood gases of the type shown in figure 4, and with a source of carrier gas, ambient air in particular, connected to a pump and a series of filters, as well as to a flow bypass, by means of a piping made of PTFE and having a diameter of 1,2 mm.

[0041] The galvanic sensor was provided with a reference element containing a diluted aqueous solution of ammonium chloride. The filiform element used was a cotton yarn having a diameter of 0,1 mm and wound so as to form one coil around a measuring electrode made of stainless steel and having a diameter of 1 mm.

[0042] The sampling probe was applied astride the middle finger of a healthy patient at the metacarpal joint, so as to be easily retained in position by closing the hand.

[0043] Three capsules containing a dose of 0,5 g of ammonium chloride each were initially administered to the patient. Subsequently the apparatus was turned on activating a flow of carrier gas at a flow rate of 3 ml/s. By acting on the bypass, the flow of carrier gas was alternately pumped through the probe for a measuring time of 10 s, thus transporting blood gases retrieved by the probe towards the sensor, and directly towards the sensor for a recovering time of 20 s.

[0044] The apparatus was continuously operated for 30 minutes, detecting for each interval of measuring time and recovering time values of potential difference proportional to the concentration of ammonia in blood gases. These values are set forth in Table 1 below and illustrated in the graph of figure 5.

[0045] As it may be seen, after about 5 minutes from the administration of ammonium chloride, the values of the concentration of gaseous ammonia progressively increase up to a maximum value and then decrease to values that are equal to the initial ones.

TABLE 1

Time [min]	ΔE [mV]	C NH_3 [ppm atm]
0	2.7	56
5	2.7	56
8	3.2	67
9	3.4	71
10	3.8	79
11	4.8	100
13	4.3	90
15	3.8	79
16	3.5	73
17	3.2	67
18	3.1	65
19	2.7	56
20	2.7	56
23	2.7	56
30	2.7	56

Example 2

[0046] A gas analysing apparatus similar to the apparatus described in Example 1 was prepared by airtightly inserting the probe into the cap of an analysis cell suitable for containing blood samples.

[0047] The apparatus was used during a haemodialysis cycle in the same fashion described in Example 1. During the haemodialysis cycle a patient had, as usual, a snack after about 30 minutes from the beginning of the treatment and had lunch and drank a coffee after about 60 minutes from the snack.

[0048] Samples of blood in the order of 1 g were taken at regular 30-minute intervals for a period of 4 hours by inserting a syringe in a tube transporting the patient's blood towards the inlet of the haemodialysis machine. These blood samples were treated with buffer solutions suitable for bringing the pH at a known level, e.g. 9,1.

[0049] The data detected by the sensor are set forth in Table 2 below and in the graph of figure 6 and show how the variations in the concentration of the ammonia contained in blood gases may be related to the assumption of food by the patient and to the subsequent digestion step. In particular, the content of ammonia initially decreases as an effect of the filtering operated by the haemodialysis machine and increases after the assumption of food during the digestion step.

TABLE 2

Time [min]	ΔE [mV]	C NH_3 [ppm atm]
0	-26.5	60.8
30	-26.0	59.6
60	-23.0	52.8
90	-22.7	52.4
120	-23.1	53.0
150	-24.6	56.4
180	-23.9	54.8
210	-21.5	49.3
240	-21.8	50.0

[0050] For a comparative purpose, Example 2 was repeated on samples of discharged dialytic fluid taken during the same haemodialysis treatment, thus proving the correlation between the variations in the concentration of gaseous ammonia in blood and the variations in the concentration of ammonia in the discharged dialytic fluid. The data detected by the sensor are set forth in Table 3 below and in the graph of figure 7.

TABLE 3

Time [min]	ΔE [mV]	C NH_3 (ppm atm)
5	-37.8	20.7
30	-6.5	3.6
60	-6.8	3.7
90	-9.8	5.4
120	-13.0	7.1
150	-21.0	11.5
180	-20.9	11.4
210	-20.8	11.3
240	-21.0	11.5

[0051] The above described and illustrated embodiments of the sensor and apparatus according to the invention are only examples susceptible of numerous variants. In particular, it is possible to make other sampling probes according to the parts of the body chosen for analysing the gases present in blood, such as, for example, compact tubular probes made of silicon rubber that may be inserted in the oral cavity of the patient between the palate and the tongue.

Claims

1. A sensor for analysing gases comprising a duct (1) suitable for being crossed by a flow of gas and provided with an inlet opening (2) and an outlet opening (3), a galvanic reference element comprised of a container (4) containing an electrolytic solution (5) in which a reference electrode (6) is inserted, and a galvanic measuring element comprising a measuring electrode (7) and a wick (8) associated to said measuring electrode (7) and suitable for defining an electrode/electrolyte interface thereon, **characterized in that** said container (4) is fixed to said duct (1) and the measuring electrode (7) is arranged transversally to the axis of the duct (1), the wick (8) being in the form of a filiform element anchored to the container (4) and having a first end (8a) contacting the measuring electrode (7) and a second end (8b) contacting said electrolytic solution (5), the wick (8) forming at least one coil around the measuring electrode (7).

2. A sensor according to the previous claim, **characterized in that** the volume of electrolytic solution (5) wetting the measuring electrode (7) is in the order of 1 μl.

3. A sensor according to one of the previous claims, **characterized in that** the duct (1) is a T-shaped glass tube, the gas inlet (2) being arranged at one end of the tube and the gas outlet (3) being arranged on a transverse arm (1a) of the tube.

4. A sensor according to one of the previous claims, **characterized in that** the electrolytic solution (5) is a diluted aqueous solution of ammonium chloride.

5. A sensor according to one of the previous claims, **characterized in that** the measuring electrode (7) is a small metal bar.

6. A sensor according to the previous claim, **characterized in that** the measuring electrode (7) is made of stainless steel.

7. A sensor according to one of the previous claims, **characterized in that** the reference electrode (6) is a small metal bar.

8. A sensor according to the previous claim, **characterized in that** the reference electrode (6) is made of stainless steel.

9. A sensor according to one of the previous claims, **characterized in that** the wick (8) is made of cotton.

10. A sensor according to the previous claim, **characterized in that** the wick (8) is a braided cotton yarn.

11. An apparatus for analysing blood gases, **characterized by** comprising a galvanic sensor (9) according to any of claims 1-10, a first device (10) connected thereto and suitable for measuring a potential difference between the measuring electrode (7) and the reference electrode (6) of the sensor (9), and a second device (11) connected to said first device (10) and suitable for acquiring, storing and processing the potential difference measurements taken by the first device (10).

12. An apparatus according to claim 11, **characterized by** further comprising a probe (12) for sampling blood gases, the galvanic sensor (9) being connected downstream of the probe (12) and a carrier gas source (13) being connected upstream of the probe (12), the carrier gas being pumped from said source (13) by means of a pump (14) and filtered and purified by means of a series of filters (15) arranged downstream of said pump (14), a flow bypass (16) being arranged between said filters (15) and said probe (12) and the components (9, 12, 13, 14, 15, 16) of the apparatus being connected through a piping of gas impermeable tubes (17).

13. An apparatus according to the previous claim, **characterized in that** said probe (12) for sampling gases is comprised of a bell-shaped member having an opening (18) in the base suitable for allowing a transcutaneous retrieval of the gases.

14. An apparatus according to the previous claim, **characterized in that** the probe (12) is also provided with an inlet (19) and an outlet (20), said inlet (19) being connected to a tube (17a) coming from the bypass (16) and said outlet being connected to a tube (17b) leading towards the galvanic sensor (9).

15. An apparatus according to the previous claim, **characterized in that** the opening (18) in the base of the probe (12) defines an area not larger than 1 cm^2.

16. An apparatus according to claim 12, **characterized in that** said gas sampling probe (12) is comprised of a small tube made of porous material, said tube having its ends respectively inserted between a tube (17a) coming from the bypass (16) and a tube (17b) leading towards the galvanic sensor (9), and having a free portion suitable for allowing the retrieval of the gases.

17. An apparatus according to the previous claim, **characterized in that** said porous material is PTFE and the pore diameter is in the order of microns.

18. An apparatus according to claim 16 or 17, **characterized in that** the free portion of the small tube of porous material comprised between the ends of the tubes (17a, 17b) has a length comprised between 1 and 2 cm..

19. An apparatus according to any of claims 12-18, **characterized in that** said carrier gas source (13) is suitable for providing ambient air.

20. An apparatus according to any of claims 12-19, **characterized in that** the tubes (17) connecting its various components are made of a material chosen between PTFE and stainless steel.

Patentansprüche

1. Sensor zum Analysieren von Gasen, umfassend einen Kanal (1), der geeignet ist, um von einem Gasstrom durchquert zu werden und der mit einer Einlassöffnung (2) und einer Auslassöffnung (3) versehen ist, ein galvanisches Referenzelement, umfassend einen Behälter (4), der eine Elektrolytlösung (5) enthält, in die eine Referenzelektrode (6) eingebracht ist, und ein galvanisches Messelement, umfassend eine Messelektrode (7) und einen dieser Messelektrode (7) zugeordneten Docht (8), der geeignet ist, um eine Elektrode/Elektrolyt-Schnittstelle darauf zu definieren,
dadurch gekennzeichnet, dass
der Behälter (4) an dem Kanal (1) befestigt ist und die Messelektrode (7) querlaufend zu der Achse des Kanals (1) angeordnet ist, der Docht (8) in der Form eines fadenförmigen Elements ausgebildet ist, das an dem Behälter (4) verankert ist und ein die Messelektrode (7) kontaktierendes erstes Ende (8a) und ein die Elektrolytlösung (5) kontaktierendes zweites Ende (8b) hat, der Docht (8) zumindest eine Windung um die Messelektrode (7) herum bildet.

2. Sensor nach dem vorstehenden Anspruch, **dadurch gekennzeichnet, dass** das Volumen der Elektrolytlösung (5), die die Messelektrode (7) benässt, im Bereich von 1 μl ist.

3. Sensor nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** der Kanal (1) eine T-förmige Glasröhre ist, wobei der Gaseinlass (2) an einem Ende der Röhre angeordnet ist und der Gasauslass (3) an einem Querarm (1a) der Röhre angeordnet ist.

4. Sensor nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** die Elektrolytlösung (5) eine verdünnte wässrige Lösung von Ammoniumchlorid ist.

5. Sensor nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** die Messelektrode (7) eine kleine Metallstange ist.

6. Sensor nach dem vorhergehenden Anspruch, **dadurch gekennzeichnet, dass** die Messelektrode (7) aus Edelstahl hergestellt ist.

7. Sensor nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** die Referenzelektrode (6) eine kleine Metallstange ist.

8. Sensor nach dem vorhergehenden Anspruch, **dadurch gekennzeichnet, dass** die Referenzelektrode (6) aus Edelstahl hergestellt ist.

9. Sensor nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** der Docht (8) aus Baumwolle hergestellt ist.

10. Sensor nach dem vorhergehenden Anspruch, **dadurch gekennzeichnet, dass** der Docht (8) ein geflochtenes Baumwollgarn ist.

11. Vorrichtung zur Analyse von Blutgasen, **dadurch gekennzeichnet, dass** diese umfasst: einen galvanischen Sensor (9) nach einem der Ansprüche 1 bis 10, ein erstes Gerät (10), das daran angeschlossen ist und geeignet ist, eine Potentialdifferenz zwischen der Messelektrode (7) und der Referenzelektrode (6) des Sensors (9) zu messen, und ein zweites Gerät (11), das mit dem ersten Gerät (10) verbunden ist und geeignet ist, die Potentialdifferenzmessungen, die von dem ersten Gerät (10) vorgenommen werden, zu erfassen, zu speichern und zu verarbeiten.

12. Eine Vorrichtung nach Anspruch 11, **dadurch gekennzeichnet, dass** diese ferner umfasst: einen Tester (12) zum Sampeln von Blutgasen, den galvanischen Sensor (9), der stromab des Testers (12) angeschlossen ist und eine Trägergasquelle (13), die stromauf des Testers (12) angeschlossen ist, wobei das Trägergas von dieser Quelle (13) mittels einer Pumpe (14) gepumpt wird und mittels einer Reihe von Filtern (15), die stromab der Pumpe (14) angeordnet sind, gefiltert und gereinigt wird, eine Umgehungsleitung (16), die zwischen den Filtern (15) und dem Tester (12) angeordnet ist, und wobei die Komponenten (9, 12, 13, 14, 15, 16) der Vorrichtung durch ein Rohrleitungssystem aus gasundurchlässigen Röhren (17) verbunden sind.

13. Eine Vorrichtung nach dem vorhergehenden Anspruch, **dadurch gekennzeichnet, dass** der Tester (12) zum Sampeln von Gasen ein glockenförmiges Element umfasst, das eine Öffnung (18) in der Basis aufweist zur Ermöglichung einer transkutanen Gewinnung von Gasen.

14. Eine Vorrichtung nach dem vorherigen Anspruch, **dadurch gekennzeichnet, dass** der Tester (12) ferner einen Einlass (19) und einen Auslass (20) aufweist, wobei der Einlass (19) mit einer von der Umgehungsleitung (16) kommenden Röhre (17a) verbunden ist und wobei der Auslass mit einer zu dem galvanischen Sensor (9) führenden Röhre (17b) verbunden ist.

15. Eine Vorrichtung nach dem vorherigen Anspruch, **dadurch gekennzeichnet, dass** die Öffnung (18) in der Basis des Testers (12) einen Bereich definiert, der nicht größer als 1 cm^2 ist.

16. Eine Vorrichtung nach Anspruch 12, **dadurch gekennzeichnet, dass** der Gassampling-Tester (12) eine kleine Röhre aus porösem Material umfasst, wobei die Enden der Röhre jeweils zwischen einer von der Umgehungsleitung (16) kommenden Röhre (17a) und einer zu dem galvanischen Sensor (9) führenden Röhre (17b) eingefügt sind und die einen freien Bereich aufweist, der geeignet ist, um die Gewinnung von Gasen zu ermöglichen.

17. Eine Vorrichtung nach dem vorherigen Anspruch, **dadurch gekennzeichnet, dass** dieses poröse Material PTFE ist und dass der Porendurchmesser in der Größenordnung von Mikrometern ist.

18. Vorrichtung nach Anspruch 16 oder 17, **dadurch gekennzeichnet, dass** der freie Bereich der kleinen Röhre aus porösem Material, der sich zwischen den Enden der Röhren (17a, 17b) befindet, eine Länge zwischen 1 und 2 cm aufweist.

19. Vorrichtung nach einem der Ansprüche 12 bis 18, **dadurch gekennzeichnet, dass** die Trägergasquelle (13) geeignet ist, um Umgebungsluft bereitzustellen.

20. Vorrichtung nach einem der Ansprüche 12 bis 19, **dadurch gekennzeichnet, dass** die Röhren (17), die die verschiedenen Komponenten der Vorrichtung verbinden, aus einem Material hergestellt sind, das aus PTFE oder Edelstahl ausgewählt ist.

Revendications

1. Capteur pour analyser des gaz, comprenant un conduit (1) approprié pour être traversé par un écoulement de gaz et muni d'une ouverture d'entrée (2) et d'une ouverture de sortie (3), un élément de référence galvanique constitué par un récipient (4) contenant une solution électrolytique (5) dans laquelle est insérée une électrode de référence (6), et un élément de mesure galvanique comprenant une électrode de mesure (7) et une mèche (8) associée à ladite électrode de mesure (7), et approprié pour définir une interface électrode/électrolyte sur celui-ci, **caractérisé en ce que** ledit récipient (4) est fixé audit conduit

(1) et **en ce que** l'électrode de mesure (7) est disposée transversalement par rapport à l'axe du conduit (1), la mèche (8) se présentant sous la forme d'un élément filiforme ancré au récipient (4) et comportant une première extrémité (8a) venant en contact avec l'électrode de mesure (7) et une deuxième extrémité (8b) venant en contact avec ladite solution électrolytique (5), la mèche (8) formant au moins un enroulement autour de l'électrode de mesure (7).

2. Capteur selon la revendication précédente, **caractérisé en ce que** le volume de solution électrolytique (5) mouillant l'électrode de mesure (7) est de l'ordre de 1 μl.

3. Capteur selon l'une des revendications précédentes, **caractérisé en ce que** le conduit (1) est un tube de verre en forme de T, l'orifice d'entrée de gaz (2) étant disposé à une extrémité du tube et l'orifice de sortie de gaz (3) étant disposé sur un bras transversal (1 a) du tube.

4. Capteur selon l'une des revendications précédentes, **caractérisé en ce que** la solution électrolytique (5) est une solution aqueuse diluée de chlorure d'ammonium.

5. Capteur selon l'une des revendications précédentes, **caractérisé en ce que** l'électrode de mesure (7) est une petite barre métallique.

6. Capteur selon la revendication précédente, **caractérisé en ce que** l'électrode de mesure (7) est réalisée en acier inoxydable.

7. Capteur selon l'une des revendications précédentes, **caractérisé en ce que** l'électrode de référence (6) est une petite barre métallique.

8. Capteur selon la revendication précédente, **caractérisé en ce que** l'électrode de référence (6) est réalisée en acier inoxydable.

9. Capteur selon l'une des revendications précédentes, **caractérisé en ce que** la mèche (8) est réalisée en coton.

10. Capteur selon la revendication précédente, **caractérisé en ce que** la mèche (8) est un fil de coton tressé.

11. Appareil pour analyser des gaz sanguins, **caractérisé en ce qu'**il comprend un capteur galvanique (9) selon l'une quelconque des revendications 1 à 10, un premier dispositif (10) connecté à celui-ci et approprié pour mesurer une différence de potentiel entre l'électrode de mesure (7) et l'électrode de référence (6) du capteur (9), et un deuxième dispositif (11) connecté audit premier dispositif (10) et approprié pour acquérir, mémoriser et traiter les mesures de différence de potentiel effectuées par le premier dispositif (10).

12. Appareil selon la revendication 11, **caractérisé en ce qu'**il comprend de plus une sonde (12) pour échantillonner des gaz sanguins, le capteur galvanique (9) étant relié en aval de la sonde (12), et une source de gaz porteur (13) étant reliée en amont de la sonde (12), le gaz porteur étant pompé à partir de ladite source (13) à l'aide d'une pompe (14), et filtré et purifié à l'aide d'une série de filtres (15) disposés en aval de ladite pompe (14), une dérivation d'écoulement (16) étant disposée entre lesdits filtres (15) et ladite sonde (12) et les composants (9, 12, 13, 14, 15, 16) de l'appareil étant reliés par l'intermédiaire de tubulures de tubes imperméables aux gaz (17).

13. Appareil selon la revendication précédente, **caractérisé en ce que** ladite sonde (12) pour échantillonner des gaz est constitué par un élément en forme de cloche comportant une ouverture (18) dans la base, appropriée pour permettre une récupération transcutanée des gaz.

14. Appareil selon la revendication précédente, **caractérisé en ce que** la sonde (12) est également munie d'un orifice d'entrée (19) et d'un orifice de sortie (20), ledit orifice d'entrée (19) étant relié à un tube (17a) venant de la dérivation (16) et ledit orifice de sortie étant relié à un tube (17b) menant vers le capteur galvanique (9).

15. Appareil selon la revendication précédente, **caractérisé en ce que** l'ouverture (18) dans la base de la sonde (12) définit une surface qui n'est pas supérieure à 1 cm^2.

16. Appareil selon la revendication 12, **caractérisé en ce que** ladite sonde d'échantillonnage de gaz (12) est constituée par un petit tube constitué par un matériau poreux, ledit tube ayant ses extrémités respectivement insérées entre un tube (17a) venant de la dérivation (16) et un tube (17b) menant vers le capteur galvanique (9), et comportant une partie libre appropriée pour permettre la récupération des gaz.

17. Appareil selon la revendication précédente, **caractérisé en ce que** ledit matériau poreux est du polytétrafluoroéthylène, et **en ce que** le diamètre de pore est de l'ordre des micromètres.

18. Appareil selon la revendication 16 ou 17, **caractérisé en ce que** la partie libre du petit tube de matériau poreux incluse entre les extrémités des tubes (17a, 17b) a une longueur comprise entre 1 et 2 cm.

19. Appareil selon l'une quelconque des revendications 12 à 18, **caractérisé en ce que** ladite source de gaz porteur (13) est appropriée pour délivrer de l'air ambiant.

20. Appareil selon l'une quelconque des revendications 12 à 18, **caractérisé en ce que** les tubes (17) reliant ses différents composants sont réalisés en un matériau choisi entre le polytétrafluoroéthylène et l'acier inoxydable.

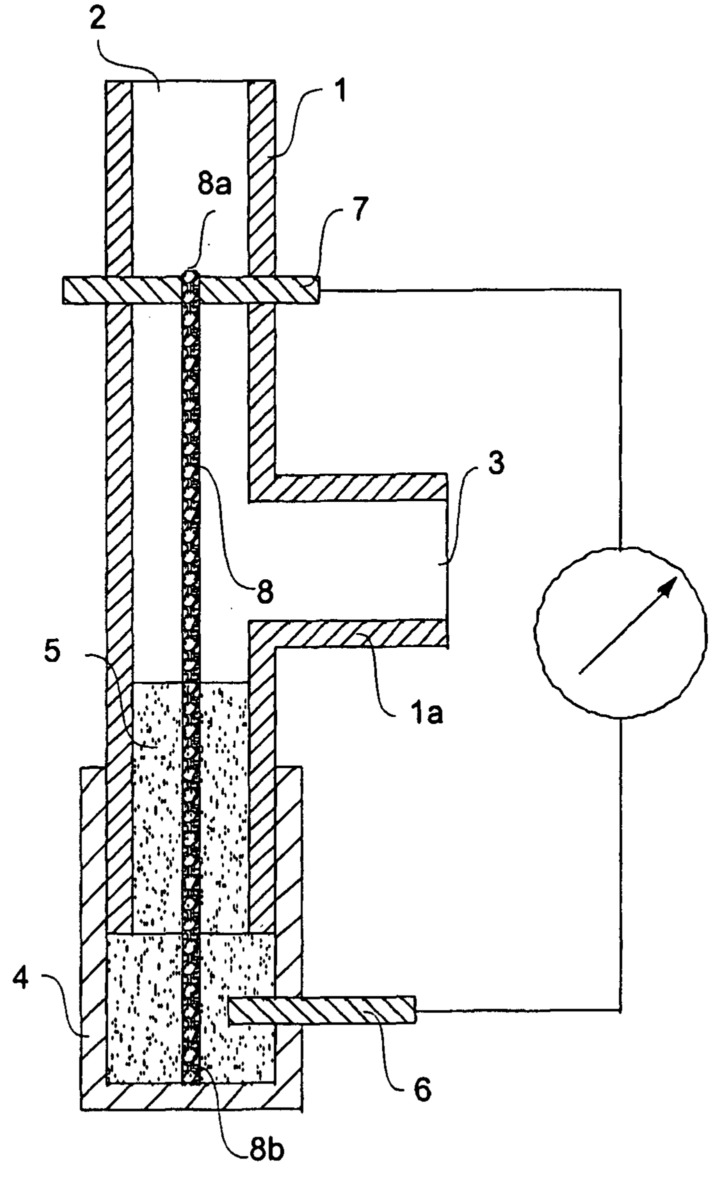

Fig.1

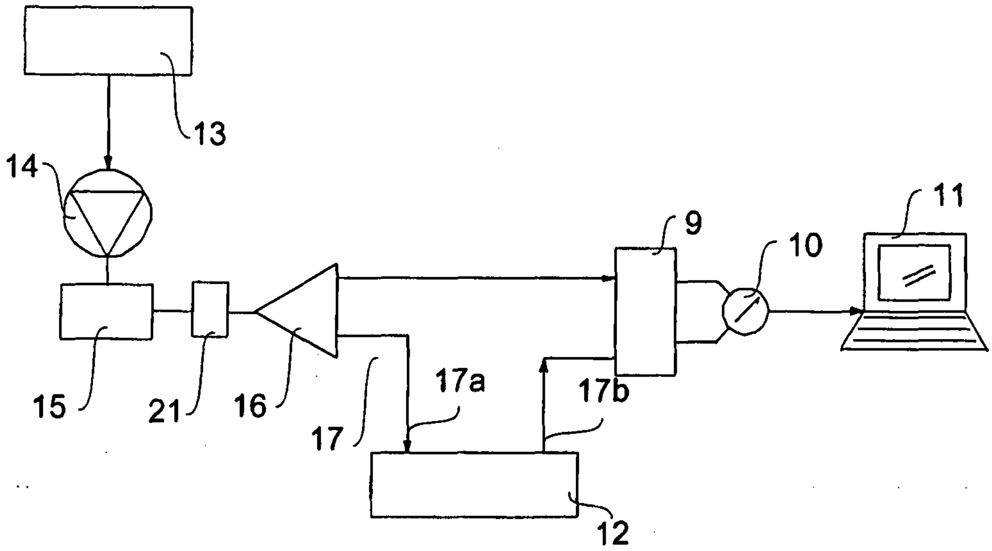

Fig.2

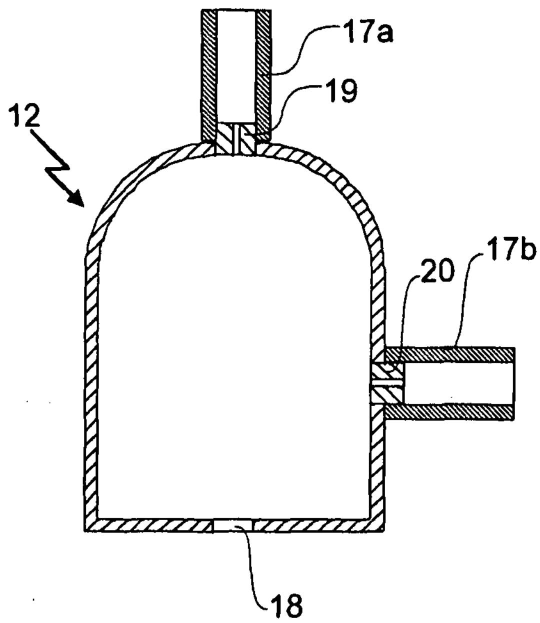

Fig.3

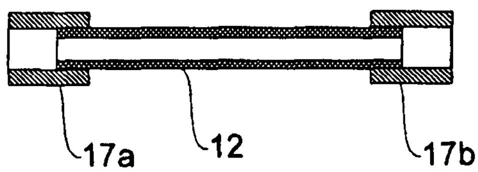

Fig.4

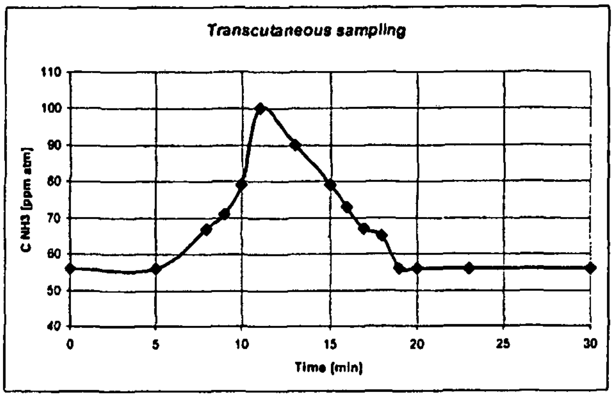

Fig.5

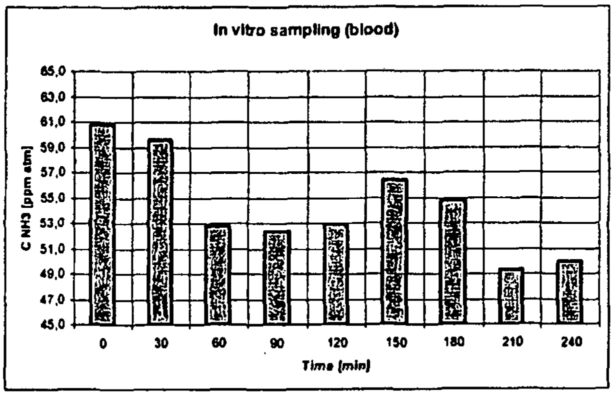

Fig.6

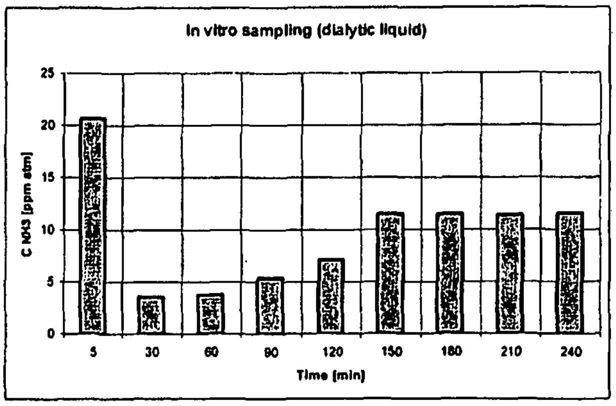

Fig.7

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- US 5007424 A **[0004]**
- US 4840179 A **[0005]**
- US 3886058 A **[0015]**

Non-patent literature cited in the description

- **K. NOSE et al.** Identification of ammonia in gas emanated from human skin and its correlation with that in blood. *Analytical Sciences,* December 2005, vol. 21, 1471 **[0008]**

专利名称(译)	用于分析血液中存在的气体的传感器和设备		
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申请(专利权)人(译)	生物技术研究和金融公司		
当前申请(专利权)人(译)	生物技术研究和金融公司		
[标]发明人	SCARANO ELIO		
发明人	SCARANO, ELIO		
IPC分类号	G01N27/413 G01N27/403 A61B5/00		
CPC分类号	G01N33/4925 A61B5/14542 A61B5/14546 A61B5/1477		
优先权	102007901487315 2007-01-25 IT		
其他公开文献	EP2135066A1		
外部链接	Espacenet		

摘要(译)

用于分析血液中存在的气体的电流传感器包括适于被气流穿过的管道（1），并设置有入口开口（2）和出口开口（3），由容器组成的参考原电池元件（ 4）含有插入参比电极（6）的电解液（5）和测量原电池。容器（4）固定到管道（1）上，并且测量原电池包括横向于管道（1）的轴线布置的测量电极（7）和具有高毛细管的丝状元件（8），以便充当灯芯。丝状元件（8）固定在容器（4）上，并具有与测量电极（7）接触的第一端（8a）和与电解液（5）接触的第二端（8b）。根据本发明的电流传感器的测量元件非常小型化并且允许实时和连续地检测痕量气体，例如，按百万分率甚至更低的顺序排列。

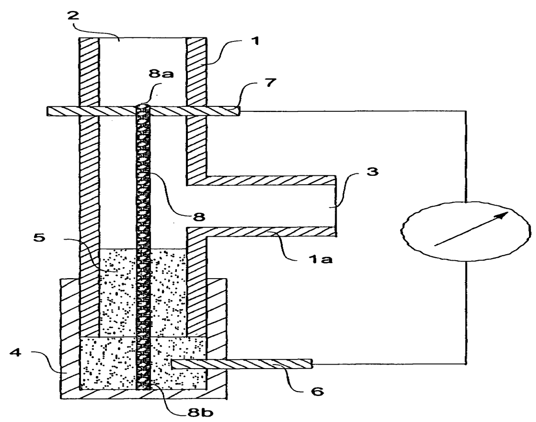

Fig.1