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(54) **Implanted sensor processing system**

Implantiertes Sensorverarbeitungssystem

Système de traitement de capteur implanté

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Description

Background of the Invention

Field of the Invention

[0001] This invention relates to a circuit and method for processing the output of an implanted sensing device for detecting the presence or concentration of an analyte in a liquid or gaseous medium, such as, for example, the human body. More particularly, the invention relates to a circuit and method for processing the output of an implanted fluorescence sensor which indicates analyte concentration as a function of the fluorescent intensity of a fluorescent indicator. The implanted fluorescence sensor is a passive device, and contains no power source. The processing circuit powers the sensor through inductively coupled RF energy emitted by the processing circuit. The processing circuit receives information from the implanted sensor as variations in the load on the processing circuit.

Background Art

[0002] U.S. Patent 5,517,313
WO 00/13003 disclose an implantable optical-based sensing device according to the prior art, describes a fluorescence sensing device comprising a layered array of a fluorescent indicator molecule-containing matrix (hereafter "fluorescent matrix"), a high-pass filter and a photodetector. In this device, a light source, preferably a light-emitting diode ("LED"), is located at least partially within the indicator material, such that incident light from the light source causes the indicator molecules to fluoresce. The high-pass filter allows emitted light to reach the photodetector, while filtering out scattered incident light from the light source. An analyte is allowed to permeate the fluorescent matrix, changing the fluorescent properties of the indicator material in proportion to the amount of analyte present. The fluorescent emission is then detected and measured by the photodetector, thus providing a measure of the amount or concentration of analyte present within the environment of interest.

[0003] One advantageous application of a sensor device of the type disclosed in the '313 patent is to implant the device in the body, either subcutaneously or intravenously or otherwise, to allow instantaneous measurements of analytes to be taken at any desired time. For example, it is desirable to measure the concentration of oxygen in the blood of patients under anesthesia, or of glucose in the blood of diabetic patients.

[0004] In order for the measurement information obtained to be used, it has to be retrieved from the sensing device. Because of the size and accessibility constraints on a sensor device implanted in the body, there are shortcomings associated with providing the sensing device with data transmission circuitry and/or a power supply. Therefore, there is a need in the art for an improved sensor device implanted in the body and system for retrieving data from the implanted sensor device.

Summary of the Invention

[0005] In accordance with the present invention, an internal sensor unit comprises: a coil configured to absorb energy provided by an external unit, and an optoelectronic circuit coupled to the coil and characterized in that: the optoelectronic circuit comprises: a radiation source for emitting excitation light for the sensor unit; a voltage regulator for powering the radiation source; a first photodetector which is a signal channel detector and a second photodetector which is a reference channel detector; a comparator having an input terminal being connected to a terminal of one of said photodetectors and also connected to a capacitor which functions as a timing element; and a resistor electrically connected between an output terminal of the comparator and a terminal of the coil for loading the coil, wherein: the optoelectronic circuit is configured to communicate information to the external unit by creating a signal having a duty cycle that is indicative of changes between incident light on the signal channel photodetector and incident light on the reference channel photodetector; and the optoelectronic circuit is configured such that a load on the coil is modified as a function of the information to be communicated, thereby varying the current through the coil.

Brief Description of the Drawings

[0006] The invention will be more fully understood with reference to the following detailed description of a preferred embodiment in conjunction with the accompanying drawings, which are given by way of illustration only and thus are not limitative of the present invention, and wherein:

FIG. 1 is a block diagram of one preferred embodiment according to the present invention;
FIG. 2 is a schematic diagram of an internal sensor device unit according to one preferred embodiment of the

invention;
FIGS. 3 and 4 are waveform diagrams illustrating signal waveforms at various points in the sensor device circuit;
FIGS. 5A-5e are diagrams of signals produced by the external data receiving unit;
FIG. 6 is a schematic, section view of an implantable fluorescence-based sensor according to the invention;
FIG. 7 is a schematic diagram of the fluorescence-based sensor shown in FIG. 6 illustrating the wave guide properties of the sensor;
FIG. 8 is a detailed view of the circled portion of FIG. 6 demonstrating internal reflection within the body of the sensor and a preferred construction of the sensor/tissue interface layer;
FIG. 9 is a schematic diagram of an internal sensor device unit according to a second preferred embodiment of the invention; and
FIG. 10 is a timing diagram illustrating voltage levels of various terminals of the comparator of FIG. 9 as the detector circuit cycles through its operation.

Detailed Description of the Preferred Embodiment

[0007] FIG. 1 shows a block diagram of one preferred embodiment of an implanted fluorescence sensor processing system according to the present invention.

[0008] The system includes an external unit 101 and an internal unit 102. In one example of an application of the system, the internal unit 102 would be implanted either subcutaneously or otherwise within the body of a subject. The internal unit contains optoelectronics circuitry 102b, a component of which may be comprised of a fluorescence sensing device as described more fully hereinafter with reference to FIGS. 6-8. The optoelectronics circuitry 102b obtains quantitative measurement information and modifies a load 102c as a function of the obtained information. The load 102c in turn varies the amount of current through coil 102d, which is coupled to coil 101f of the external unit. An amplitude modulation (AM) demodulator 101b detects the current variations induced in coil 101f by coil 102d coupled thereto, and applies the detected signal to processing circuitry, such as a pulse counter 101c and computer interface 101d, for processing the signal into computer-readable format for inputting to a computer 101e.

[0009] A variable RF oscillator 101a provides an RF signal to coil 101f, which in turn provides electromagnetic energy to coil 102d, when the coils 101f and 102d are within close enough proximity to each other to allow sufficient inductive coupling between the coils. The energy from the RF signal provides operating power for the internal unit 102 to obtain quantitative measurements, which are used to vary the load 102c and in turn provide a load variation to the coil 101f that is detected by the external unit and decoded into information. The load variations are coupled from the internal unit to the external unit through the mutual coupling between the coils 101f and 102d. The loading can be improved by tuning both the internal coil and the external coil to approximately the same frequency, and increasing the Q factor of the resonant circuits by appropriate construction techniques. Because of their mutual coupling, a current change in one coil induces a current in the other coil. The induced current is detected and decoded into corresponding information.

[0010] RF oscillator 101a drives coil 101f, which induces a current in coil 102d. The induced current is rectified by a rectifier circuit 102a and used to power the optoelectronics 102b. Data is generated by the optoelectronics in the form of a pulse train having a frequency varying as a function of the intensity of light emitted by a fluorescence sensor, such as described in the aforementioned '313 patent. The pulse train modulates the load 102c in a manner so as to temporarily short the rectifier output terminal to ground. This change in load causes a corresponding change in the current through the internal coil 102d, thereby causing a change in the magnetic field surrounding external coil 101f. This change in magnetic field causes a proportional change in the voltage across coil 101f, which is observable as an amplitude modulation. The following equation describes the voltage seen on the external coil:

$$V = I[Z + ((\omega M)^2)/Zs] \qquad (1)$$

where V = voltage across the external coil

I = current in the external coil
Z = impedance of the primary coil
ω = frequency (rad/sec)
M = mutual inductance between the coils
Zs = impendance of the sensor equivalent circuit

As shown by equation (1), there is a direct relationship between the voltage across the external coil and the impedance presented by the internal sensor circuit. While the impedance Zs is a complex number having both a real and imaginary part, which corresponds respectively to changes in amplitude and frequency of the oscillation signal, the system according to the present embodiment deals only with the real part of the interaction. It will be recognized by those skilled in the art that both types of interaction may be detected by appropriately modifying the external circuit, to improve the signal-to-noise ratio.

[0011] FIG. 2 shows a schematic diagram of one embodiment of an internal sensor device unit according to the invention. The coil 102d (L1) in conjunction with capacitor C1, diode D1 (rectifier 102a) zener diode D2 and capacitor C2 constitute a power supply for the internal unit 102. Current induced in coil L1 by the RF voltage applied to external coil 101f by oscillator 101a (see FIG. 1) is resonated in the L-C tank formed by L1 and capacitor C1, rectified by diode D1, and filtered by capacitor C2. Zener diode D2 is provided to prevent the voltage being applied to the circuit from exceeding a maximum value, such as 5 volts. As is known by those skilled in the art, if the voltage across capacitor C2 starts to exceed the reverse breakdown voltage of the zener diode D2, diode D2 will start to conduct in its reverse breakdown region, preventing the capacitor C2 from becoming overcharged with respect to the maximum allowable voltage for the circuit.

[0012] Voltage regulator 205 receives the voltage from capacitor C2 and produces a fixed output voltage V_{ref} to the noninverting input of operational amplifier 201. The output terminal of the operational amplifier 201 is connected to a light-emitting diode (LED) 202 connected in series with a feedback resistor R1. The inverting input terminal of operational amplifier 201 is supplied with the voltage across R1, to thereby regulate the current through LED 202 to V_{ref}/R1 (ignoring small bias current). Light emitted from LED 202 is incident on the sensor device (not shown) and causes the sensor device to emit light as a function of the amount of the particular analyte being monitored. The light from the sensor device impinges on the photosensitive resistor 203, whose resistance changes as a function of the amount of light incident thereon. Photoresistor 203 is connected in series with a capacitor C3, and the junction of the photoresistor and the capacitor C3 is connected to the inverting input terminal of comparator 204. The other end of photoresistor 203 is connected to the output terminal of the comparator 204 through a conductor V_{comp}. The output of the comparator 204 is also connected to a load capacitor C4 and a resistor network R2, R3 and R4. The comparator forms a variable resistance oscillator, with switching points determined by the values of R2, R3 and R4. C3 is a charge-up capacitor, which determines the base frequency of the oscillator for a given light level. This frequency is given by

$$f = 1/(1.38 * Rphoto * C3) \tag{2}$$

$$Rphoto = R_{2fc}\left[10^{-\gamma \log(a/2fc)}\right] \tag{3}$$

where R_{2fc} (= 24 kΩ) is the resistance of 203 at 2 footcandles

γ (= 0.8) is the sensitivity of the photoresistor
a = the incident light level in footcandles

Equation (3) can be inverted to determine the intensity of light for a given photoresistance; in conjunction with equation (2), the light intensity can be determined from frequency. Of course, the values given above are provided as examples only for purposes of explanation. Such values are determined on the basis of the particular photoresistor geometry and materials used.

[0013] The comparator 204 switches to a high output when Vtime = V/3, Vcomp = V, and Vtrip = 2V/3. Capacitor C3 begins to charge with time constant Rphoto*Ctime. When Vtime reaches 2V/3 the comparator switches states to a low output, changing Vcomp to Vcomp = 0, and Vtrip to Vtrip = V/3. At this point C3 will discharge through Rphoto. Therefore a 50% duty cycle is established, with the frequency being determined by equation (2). Rphoto varies as a function of incident light, given by equation (3).

[0014] C4 is a load capacitor, which causes a voltage across C2 to decrease when the comparator switches states. C4 must be charged from 0V to V de when comparator 204 switches to a high output level state. The current through C4 is supplied by C2, causing the voltage across C2 to decrease. This in turn causes current to flow through rectifier 102a to begin charging capacitor C2, changing the instantaneous load on the tank circuit including internal coil 102d. This load is reflected into the impedance of the external coil 101f as given by equation (1).

[0015] The sensor operation for a single pulse is illustrated in FIG. 3. Channel 4 is the DC voltage on C2, channel 3 shows the same pulse on the external coil 101f, and the output of the AM demodulator is shown at channel 2. Channel 1 shows the output of a comparator which converts the AM demodulator output to a square wave capable of being processed by a digital counter. FIG. 4 shows two complete operation cycles, with the same channel designations indicating the same points in the circuit.

[0016] The external unit 101 uses a microprocessor to implement the pulse counter 101c. When sufficient data has been received to obtain a valid reading, the processor shuts down the RF oscillator. FIGS. 5A-5E illustrate timing diagrams for a measurement reading. FIG. 5A shows the envelope of the RF voltage signal applied to the external coil; FIG. 5B shows the waveform of the internal power supply voltage; FIG. 5C shows a waveform of the intensity of LED 202; FIG. 5D shows the output of the AM demodulator 101b; and FIG. 5E shows the timing of the state of circuit operations in accordance with the power supplied to the sensor unit. The internal unit power supply ramps up as the field strength increase. When the power supply output crosses the threshold voltage of the LED plus the feedback voltage, the LED turns on. The AM demodulator output contains the measurement data and digital data in the form of ID codes and other parameters specific to the subject in which the internal unit is implanted. This data is encoded on the RF voltage signal through time division multiplexing of the optoelectronic output with digital identification and parameter storage circuits (not shown). The digital circuits use the RF voltage to generate appropriate clock signals.

[0017] The internal storage circuits can store ID codes and parametric values such as calibration constants. This information is returned along with each reading or quantitative measurement. The signals are clocked out by switching from analog pulse train loading to digitally controlled loading at a predefined point in the measurement sequence. This point is detected in the external unit by detecting a predefined bit synchronization pattern in the output data stream. The ID number is used to identify a particular subject and to prevent data corruption when two or more subjects are in the vicinity of the external unit. The calibration factors are applied to the measurement information to obtain analyte levels in clinical units.

[0018] A sensor 10 according to one aspect of the invention, which operates based on the fluorescence of fluorescent indicator molecules, is shown in FIG. 6. The sensor 10 is composed of a sensor body 12; a matrix layer 14 coated over the exterior surface of the sensor body 12, with fluorescent indicator molecules 16 distributed throughout the layer; a radiation source 18, e.g. an LED, that emits radiation, including radiation over a wavelength or range of wavelengths which interact with the indicator molecules, i.e., in the case of a fluorescence-based sensor, a wavelength or range of wavelengths which cause the indicator molecules 16 to fluoresce; and a photosensitive element 20, e.g. a photodetector, which, in the case of a fluorescence-based sensor, is sensitive to fluorescent light emitted by the indicator molecules 16 such that a signal is generated in response thereto that is indicative of the level of fluorescence of the indicator molecules. The sensor 10 further includes a module or housing 66 containing electronic circuitry, and a temperature sensor 64 for providing a temperature reading. In the simplest embodiments, indicator molecules 16 could simply be coated on the surface of the sensor body. In preferred embodiments, however, the indicator molecules are contained within the matrix layer 14, which comprises a biocompatible polymer matrix that is prepared according to methods known in the art and coated on the surface of the sensor body, Suitable biocompatible matrix materials, which must be permeable to the analyte, include methacrylates and hydrogels which advantageously can be made selectively permeable to the analyte.

[0019] The sensor body 12 advantageously is formed from a suitable, optically transmissive polymer material which has a refractive index sufficiently different from that of the medium in which the sensor will be used such that the polymer will act as an optical wave guide. Preferred materials are acrylic polymers such as polymethylmethacrylate, polyhydroxypropylmethacrylate and the like, and polycarbonates such as those sold under the trademark Lexan®. The material allows radiation generated by the radiation source 18 (e.g., light at an appropriate wavelength in embodiments in which the radiation source is an LED) and, in the case of a fluorescence-based embodiment, fluorescent light emitted by the indicator molecules, to travel through it. Radiation source or LED 18 corresponds to LED 202 shown in FIG. 2.

[0020] As shown in Figure 7, radiation (e.g., light) is emitted by the radiation source 18 and at least some of this radiation is reflected internally at the surface of the sensor body 12, e.g., as at location 22, thereby "bouncing" back-and-forth throughout the interior of the sensor body 12.

[0021] It has been found that light reflected from the interface of the sensor body and the surrounding medium is capable of interacting with indicator molecules coated on the surface (whether coated directly thereon or contained within a matrix), e.g., exciting fluorescence in fluorescent indicator molecule coated on the surface. In addition, light which strikes the interface at angles (measured relative to a direction normal to the interface) too small to be reflected passes through the interface and also excites fluorescence in fluorescent indicator molecules. Other modes of interaction between the light (or other radiation) and the interface and the indicator molecules have also been found to be useful depending on the construction of and application for the sensor. Such other modes include evanescent excitation and surface plasma resonance type excitation.

[0022] As demonstrated by FIG. 8, at least some of the light emitted by the fluorescent indicator molecules 16 enters the sensor body 12, either directly or after being reflected by the outermost surface (with respect to the sensor body 12) of the matrix layer 14, as illustrated in region 30. Such fluorescent light 28 is then reflected internally throughout the sensor body 12, much like the radiation emitted by the radiation source 18 is, and, like the radiation emitted by the radiation source, some will strike the interface between the sensor body and the surrounding medium at angles too small to be reflected and will pass back out of the sensor body.

[0023] As further illustrated in FIG. 6, the sensor 10 may also include reflective coatings 32 formed on the ends of the sensor body 12, between the exterior surface of the sensor body and the matrix layer 14, to maximize or enhance the internal reflection of the radiation and/or light emitted by fluorescent indicator molecules. The reflective coatings may be formed, for example, from paint or from a metallized material.

[0024] An optical filter 34 preferably is provided on the light-sensitive surface of the photodetector 20, which is manufactured of a photosensitive material. Photodetector 20 corresponds to photodetector 203 shown in FIG. 2. Filter 34, as is known from the prior art, prevents or substantially reduces the amount of radiation generated by the source 18 from impinging on the photosensitive surface of the photosensitive element 20. At the same time, the filter allows fluorescent light emitted by fluorescent indicator molecules to pass through it to strike the photosensitive region of the detector. This significantly reduces "noise" in the photodetector signal that is attributable to incident radiation from the source 18.

[0025] The application for which the sensor 10 according to one aspect of the invention was developed in particular -- although by no means the only application for which it is suitable -- is measuring various biological analytes in the human body, e.g., glucose, oxygen, toxins, pharmaceutical or other drugs, hormones, and other metabolic analytes. The specific composition of the matrix layer 14 and the indicator molecules 16 may vary depending on the particular analyte the sensor is to be used to detect and/or where the sensor is to be used to detect the analyte (i.e., in the blood or in subcutaneous tissues). Two constant requirements, however, are that the matrix layer 14 facilitate exposure of the indicator molecules to the analyte and that the optical characteristics of the indicator molecules (e.g., the level of fluorescence of fluorescent indicator molecules) are a function of the concentration of the specific analyte to which the indicator molecules are exposed.

[0026] To facilitate use in-situ in the human body, the sensor 10 is formed, preferably, in a smooth, oblong or rounded shape. Advantageously, it has the approximate size and shape of a bean or a pharmaceutical gelatin capsule, i.e., it is on the order of approximately 300-500 microns to approximately 0.5 inch in length L and on the order of approximately 300 microns to approximately 0.3 inch in depth D, with generally smooth, rounded surfaces throughout. The device of course could be larger or smaller depending on the materials used and upon the intended uses of the device. This configuration permits the sensor 10 to be implanted into the human body, i.e., dermally or into underlying tissues (including into organs or blood vessels) without the sensor interfering with essential bodily functions or causing excessive pain or discomfort.

[0027] Moreover, it will be appreciated that any implant placed within the human (or any other animal's) body -- even an implant that is comprised of "biocompatible" materials -- will cause, to some extent, a "foreign body response" within the organism into which the implant is inserted, simply by virtue of the fact that the implant presents a stimulus. In the case of a sensor 10 that is implanted within the human body, the "foreign body response" is most often fibrotic encapsulation, i.e., the formation of scar tissue. Glucose -- a primary analyte which sensors according to the invention are expected to be used to detect -- may have its rate of diffusion or transport hindered by such fibrotic encapsulation. Even molecular oxygen (O2), which is very small, may have its rate of diffusion or transport hindered by such fibrotic encapsulation as well. This is simply because the cells forming the fibrotic encapsulation (scar tissue) can be quite dense in nature or have metabolic characteristics different from that of normal tissue.

[0028] To overcome this potential hindrance to or delay in exposing the indicator molecules to biological analytes, two primary approaches are contemplated. According to one approach, which is perhaps the simplest approach, a sensor/tissue interface layer -- overlying the surface of the sensor body 12 and/or the indicator molecules themselves when the indicator molecules are immobilized directly on the surface of the sensor body, or overlying the surface of the matrix layer 14 when the indicator molecules are contained therein -- is prepared from a material which causes little or acceptable levels of fibrotic encapsulation to form. Two examples of such materials described in the literature as having this characteristic are PrecludeTM Periocardial Membrane, available from W.L. Gore, and polyisobutylene covalently combined with hydrophile as described in Kennedy, "Tailoring Polymers for Biological Uses," Chemtech, February 1994, pp. 24-31.

[0029] Alternatively, a sensor/tissue interface layer that is composed of several layers of specialized biocompatible materials can be provided over the sensor. As shown in FIG. 8, for example, the sensor/tissue interface layer 36 may include three sublayers 36a, 36b, and 36c. The sublayer 36a, a layer which promotes tissue ingrowth, preferably is made from a biocompatible material that permits the penetration of capillaries 37 into it, even as fibrotic cells 39 (scar tissue) accumulate on it. Gore-Tex® Vascular Graft material (ePTFE), Dacron® (PET) Vascular Graft materials which have been in use for many years, and MEDPOR Biomaterial produced from high-density polyethylene (available from POREX Surgical Inc.) are examples of materials whose basic composition, pore size, and pore architecture promote tissue and vascular ingrowth into the tissue ingrowth layer.

[0030] The sublayer 36b, on the other hand, preferably is a biocompatible layer with a pore size (less than 5 micrometers) that is significantly smaller than the pore size of the tissue ingrowth sublayer 36a so as to prevent tissue ingrowth. A presently preferred material from which the sublayer 36b is to be made is the Preclude Periocardial Membrane (formerly called GORE-TEX Surgical Membrane), available from W.L. Gore, Inc., which consists of expanded polytetrafluoroethylene (ePTFE).

[0031] The third sublayer 36c acts as a molecular sieve, i.e., it provides a molecular weight cut-off function, excluding molecules such as immunoglobulins, proteins, and glycoproteins while allowing the analyte or analytes of interest to pass through it to the indicator molecules (either coated directly on the sensor body 12 or immobilized within a matrix layer 14). Many well known cellulose-type membranes, e.g., of the sort used in kidney dialysis filtration cartridges, may be used for the molecular weight cut-off layer 36c.

[0032] As will be recognized, the sensor as shown in FIG. 6 is wholly self-contained such that no electrical leads extend into or out of the sensor body, either to supply power to the sensor (e.g., for driving the source 18) or to transmit signals from the sensor. All of the electronics illustrated in FIG. 2 may be housed in a module 66 as shown in FIG. 6.

[0033] A second preferred embodiment of the invention is shown in FIG. 9, in which two detectors are employed, a signal channel detector 901 and a reference channel detector 902. In the first embodiment as shown in FIG. 2, a single detector 203 is used to detect radiation from the fluorescent indicator sensor device. While this system works well, it is possible that various disturbances to the system will occur that may affect the accuracy of the sensor output as originally calibrated.

[0034] Examples of such disturbances include: changes or drift in the component operation intrinsic to the sensor make-up; environmental conditions external to the sensor; or combinations thereof. Internal variables may be introduced by, among other things: aging of the sensor's radiation source; changes affecting the performance or sensitivity of the photosensitive element; deterioration of the indicator molecules; changes in the radiation transmissivity of the sensor body, of the indicator matrix layer, etc.; and changes in other sensor components; etc. In other examples, the optical reference channel could also be used to compensate or correct for environmental factors (e.g., factors external to the sensor) which could affect the optical characteristics or apparent optical characteristies of the indicator molecule irrespective of the presence or concentration of the analyte. In this regard, exemplary external factors could include, among other things: the temperature level; the pH level; the ambient light present; the reflectivity or the turbidity of the medium that the sensor is applied in; etc. The optical reference channel can be used to compensate for such variations in the operating conditions of the sensor. The reference channel is identical to the signal channel in all respects except that the reference channel is not responsive to the analyte being measured.

[0035] Use of reference channels in optical measurement is generally known in the art. For example, U.S. Patent No. 3,612,866, the entire disclosure of which is incorporated herein by reference, describes a fluorescent oxygen sensor having a reference channel containing the same indicator chemistry as the measuring channel, except that the reference channel is coated with varnish to render it impermeable to oxygen.

[0036] U.S. Patent Nos. 4,861,727 and 5,190,729 describe oxygen sensors employing two different lanthanide-based indicator chemistries that emit at two different wavelengths, a terbium-based indicator being quenched by oxygen and a europium-based indicator being largely unaffected by oxygen. U.S. Patent No. 5,094,959 describes an oxygen sensor in which a single indicator molecule is irradiated at a certain wavelength and the fluorescence emitted by the molecule is measured over two different emission spectra having two different sensitivities to oxygen. Specifically, the emission spectra which is less sensitive to oxygen is used as a reference to ratio the two emission intensities. U.S. Patent Nos. 5,462,880 and 5,728,422 describe a rotiometric fluorescence oxygen sensing method employing a reference molecule that is substantially unaffected by oxygen and has a photodecomposition rate similar to the indicator molecule. Additionally, Muller, B., et al., ANALYST, Viol 121, pp. 339-343 (March 1996) describes a fluorescence sensor for dissolved CO_2, in which a blue LED light source is directed through a fiber optic coupler to all indicator channel and to a separate reference photodetector which detects changes in the LED light intensity.

[0037] In addition, U.S. Patent No. 4,580,059 describes a fluorescent-based sensor containing a reference light measuring cell for measuring changes in the intensity of the excitation light source -- see, e.g., column 10, lines 1, *et seq.*

[0038] As shown in FIG. 9, the signal and reference channel detectors are back-to-back photodiodes 901 and 902. While photodiodes are shown, many other types of photodetectors also could be used, such as photoresistors, phototransistors, and the like. LED 903 corresponds to light source 202 in FIG. 2. In operation, comparator 904 is set to trigger at 1/3 and 2/3 of the supply voltage Vss, as biased by resistors 905, 906, and 907. The trigger voltages for comparator 904 could be modified, if desired, by changing the values of the resistors. Capacitor C2 is a timing element, the value of which is adjusted for the magnitude of the signal and reference channel. The current through each photodiode is a function of the intensity or power of incident light entering it, as represented by the equation I=RP, where

I = current
R = responsivity (Amp/Watt) and
P = light power in watts.

In the fluorescence embodiment, the incident light power impinging upon the photodiode detectors changes with analyte concentration.

[0039] FIG. 10 is a timing diagram showing the voltage levels of the terminals 904a, 904b, and 904c of the comparator 904. At the cycle start, the voltage level of output terminal 904c is at ground (low output state), the voltage level of capacitor C2 (which corresponds to the voltage level at input terminal 904b) is at 2/3 Vss, and the voltage level of input terminal 904a is at 1/3 Vss. In this instance, photodiode 901 is forward-biased and photodiode 902 is reverse-biased. The voltage drop across the forward-biased photodiode 901 is simply its threshold voltage, while the reverse-biased photodiode 902 exhibits a current flow proportional to the incident light impinging upon it. This current discharges the capacitor C2 at a rate of $dV/dt = I902/C2$, until it reaches a voltage level of 1/3 Vss as shown in FIG. 10. Inserting the above equation for photodiode current results in the equation $dV/dt=RP/C2$. Solving for P, $P=(dV*C2)/(dt*R)$, where

dV = difference between comparator trigger points (in the example 1/3 Vss)
C2 = value of capacitor C2 in farads
dt = time to charge or discharge (as measured by the external unit) and
R = responsivity (in amps/watts) of the photodetector

At this time, the comparator 904 switches to a high output state V ss on output terminal 904c. The trigger point (input terminal 904a) is now at 2/3 Vss, and the polarity of the photodiodes 901 and 902 is now reversed. That is, photodiode 901 is now reverse-biased and photodiode 902 is now forward-biased.

[0040] Photodiode 901 now controls the charging of capacitor C2 at a rate of $dV/dt = I901/C2$ until the voltage of capacitor C2 reaches 2/3 Vss. When the voltage across capacitor C2 reaches 2/3 Vss, the output of the comparator 904 again switches to the low output state. So long as the system is powered and incident light is present on the photodiodes, the cycle will continue to repeat as shown in FIG. 10.

[0041] If the incident light intensity on each photodiode detector 901 and 902 is equal, then the comparator output will be a 50% duty cycle. If the incident light on each photodiode detector is not equal, then the capacitor charge current will be different than the capacitor discharge current. This is the case shown in FIG. 10, wherein the capacitor charge current is higher than the capacitor discharge current. Because the same capacitor is charged and discharged, the different charge and discharge times are a function only of the difference between the incident light levels on the two photodiode detectors. Consequently, the duty cycle of the squarewave produced by the comparator 904 is indicative of changes between incident light on the signal channel photodiode and incident light on the reference channel photodiode. Suitable algorithms for taking into account changes in duty cycle of the squarewave from the comparator in determining analyte concentration are generally known in the art (see prior art references discussed *supra*) and will not be further discussed herein.

[0042] Once the squarewave is established, it must be transferred to the external unit. This is done by loading the internal coil 908, and then detecting the change in load on the external coil inductively coupled to the internal coil. The loading is provided by resistor 910, which is connected to the output terminal 904c of the comparator 904. When the comparator is in a high output state, an additional current Vss/R910 is drawn from the voltage regulator 909. When the comparator is in a low output state, this additional current is not present. Consequently, resistor 910 acts as a load that is switched into and out of the circuit at a rate determined by the concentration of analyte and the output of the reference channel. Because the current through resistor 910 is provided by the internal tuned tank circuit including coil 908, the switching of the resistor load also switches the load on the tank including internal coil 908. The change in impedance of the tank caused by the changing load is detected by a corresponding change in load on the inductively coupled external coil, as described above. The voltage regulator 909 removes any effects caused by coil placement in the field. The LED 903 emits the excitation light for the indicator molecule sensor. Power for the LED 903 is provided by the voltage regulator. It is important to keep the intensity of the LED constant during an analyte measurement reading. Once the output of the voltage regulator is in regulation, the LED intensity will be constant. The step recovery time of the regulator is very fast, with the transition between loading states being rapid enough to permit differentiation and AC coupling in the external unit.

[0043] As also will be recognized, the fluorescence-based sensor embodiments described in FIGS. 6-8 are just examples to which the disclosed invention may be applied. The present invention may also be applied in a number of other applications such as, for example, an absorbance-based sensor or a refractive-index-based sensor as described in U.S. Patent Application No. 09/383,148, filed August 28, 1999.

[0044] The invention having been thus described, it will be apparent to those skilled in the art that the same may be varied in many ways without departing from the scope of the invention, which is defined by the claims, For example, while the invention has been described with reference to an analog circuit, the principles of the invention may be carried out equivalently through the use of an appropriately programmed digital signal processor. Any and all such modifications are intended to be encompassed by the following claims.

Claims

1. An internal sensor unit (102), comprising:

a coil (908) forming part of a power supply for said internal sensor unit and configured to absorb energy provided by an external unit, and an optoelectronic circuit (102b) coupled to the coil (908) and **characterized in that**:

the optoelectronic circuit (102b) comprises:

a radiation source (903) for emitting excitation light for the sensor unit;
a first photodetector (901) which is a signal channel detector and a second photodetector (902) which is a reference channel detector, the second photodetector back-to-back in series with the first photodetector;
a comparator (904) having an input terminal (904b) being connected to a terminal of one of said photodetectors (901, 902) and the input terminal also connected to a capacitor (C2) which functions as a timing element for determining the duty cycle;
a voltage regulator (909) for powering the radiation source (18) and the comparator; and
a resistor (910) electrically connected between an output terminal (904c) of the comparator (904) and a terminal of the coil (908) for loading the coil,
wherein:

the optoelectronic circuit (102b) is configured to communicate information to the external unit by creating a square wave signal switched by the output of the comparator having a duty cycle that is controlled by the difference current between current in the first photodetector generated by incident light on the signal channel photodetector (901) and current in the second photodetector generated by incident light on the reference channel photodetector (902); and
the optoelectronic circuit (102b) is configured such that a load (910) on the coil (908) formed by the impedance of the optoelectronic circuit is switched with said duty cycle, thereby varying the current through the coil (908).

2. The internal sensor unit of claim 1, wherein the resistor functions as a load that is switched into and out of a circuit comprising the coil based on the signal.

3. The internal sensor unit of claims 1 or 2, wherein the optoelectronic circuit further includes:

a first bias resistor (907) having a first terminal and a second terminal, the first terminal being connected to an output terminal (904c) of the comparator (904);
a second bias resistor (905) having a first terminal and a second terminal, the first terminal being connected to the second terminal of the first bias resistor (907); and
a third bias resistor (906) having a first terminal and a second terminal, the first terminal being connected to the second terminal of the first bias resistor (907); wherein
the capacitor (C2) has a first terminal and a second terminal, the first terminal being connected to the input terminal (904b) of the comparator (904) and the second terminal being connected to the second terminal of the second bias resistor (905).

4. The internal sensor unit of claims 1, 2 or 3, further comprising an indicator element (16) which emits radiation in proportion to levels of an analyte.

5. The internal sensor unit of claim 4, wherein the radiation source (18) is for illuminating the indicator element.

6. A sensor system comprising the internal sensor unit of any of claims 1 to 5 and further comprising an external unit (101) for providing energy to the internal sensor unit.

7. The sensor system of claim 6, wherein the external unit includes:

a second coil (101f) which is mutually inductively coupled to said first coil (102d) upon said second coil (101f) being placed within a predetermined proximal distance from said first coil (102d), an oscillator (101a) for driving said second coil (101f) to induce a charging current in said first coil (102d), and a detector (101c,101e) for detecting variations in the energy absorbed by the internal sensor unit and for providing information signals corresponding to said energy absorption variations.

Patentansprüche

1. Interne Sensoreinheit (102), umfassend:

   eine Spule (908), die einen Teil einer Stromversorgung für die interne Sensoreinheit bildet und so konfiguriert ist, dass sie von einer externen Einheit bereitgestellte Energie absorbiert, und eine optoelektronische Schaltung (102b), die mit der Spule (908) gekoppelt ist, und **dadurch gekennzeichnet, dass**:

   die optoelektronische Schaltung (102b) folgendes umfasst:

   eine Strahlungsquelle (903) zum Emittieren von Erregungslicht für die Sensoreinheit;
   einen ersten Photodetektor (901), der ein Signalkanaldetektor ist, und einen zweiten Photodetektor (902), der ein Referenzkanaldetektor ist, wobei der zweite Photodetektor in Reihe hinter dem ersten Photodetektor angeordnet ist;
   einen Komparator (904) mit einem Eingangsanschluss (904b), der mit einem Anschluss eines der Photodetektoren (901, 902) verbunden ist, und wobei der Eingangsanschluss ferner mit einem Kondensator (C2) verbunden ist, der als ein Zeitsteuerungselement zur Bestimmung des Arbeitszyklus funktioniert;
   einen Spannungsregler (909) für den Betrieb der Strahlungsquelle (18) und des Komparators; und
   einen Widerstand (910), der elektrisch zwischen einen Ausgangsanschluss (904c) des Komparators (904) und einen Anschluss der Spule (908) zum Laden der Spule geschaltet ist, wobei:

   die optoelektronische Schaltung (102b) so konfiguriert ist, dass sie Informationen zu der externen Schaltung kommuniziert, indem ein Rechtecksignal erzeugt wird, das durch die Ausgabe des Komparators mit einem Arbeitszyklus geschaltet wird, der gesteuert wird durch den Differenzstrom zwischen dem Strom in dem ersten Photodetektor, der erzeugt wird durch einfallendes Licht an dem Signalkanaldetektor (901), und dem Strom in dem zweiten Photodetektor, der erzeugt wird durch einfallendes Licht an dem Referenzkanalphotodetektor (902); und wobei
   die optoelektronische Schaltung (102b) so konfiguriert ist, dass ein Verbraucher (910) an der Spule (908), gebildet durch die Impedanz der optoelektronischen Schaltung, mit dem Arbeitszyklus geschaltet wird, wodurch der Strom durch die Spule (908) variiert wird.

2. Interne Sensoreinheit nach Anspruch 1, wobei der Widerstand als ein Verbraucher funktioniert, der auf der Basis des Signals in eine und aus einer die Spule umfassenden Schaltung geschaltet wird.

3. Interne Sensoreinheit nach Anspruch 1 oder 2, wobei die optoelektronische Schaltung ferner folgendes aufweist:

   einen ersten Vorspannungswiderstand (907) mit einem ersten Anschluss und mit einem zweiten Anschluss, wobei der erste Anschluss mit einem Ausgangsanschluss (904c) des Komparators (904) verbunden ist;
   einen zweiten Vorspannungswiderstand (905) mit einem ersten Anschluss und mit einem zweiten Anschluss, wobei der erste Anschluss mit dem zweiten Anschluss des ersten Vorspannungswiderstands (907) verbunden ist; und
   einen dritten Vorspannungswiderstand (906) mit einem ersten Anschluss und mit einem zweiten Anschluss, wobei der erste Anschluss mit dem zweiten Anschluss des ersten Vorspannungswiderstands (907) verbunden ist; wobei
   der Kondensator (C2) einen ersten Anschluss und einen zweiten Anschluss aufweist, wobei der erste Anschluss mit dem Eingangsanschluss (904b) des Komparators (904) verbunden ist, und wobei der zweite Anschluss mit dem zweiten Anschluss des zweiten Vorspannungswiderstands (905) verbunden ist.

4. Interne Sensoreinheit nach Anspruch 1, 2 oder 3, ferner umfassend ein Indikatorelement (16), das Strahlung im Verhältnis zu den Werten eines Analyts emittiert.

5. Interne Sensoreinheit nach Anspruch 4, wobei die Strahlungsquelle (18) zur Illumination des Indikatorelements vorgesehen ist.

6. Sensorsystem, umfassend die interne Sensoreinheit nach einem der Ansprüche 1 bis 5 und ferner umfassend eine externe Einheit (101) zum Bereitstellen von Energie an die interne Sensoreinheit.

7. Sensorsystem nach Anspruch 6, wobei die externe Einheit folgendes aufweist:

eine zweite Spule (101f), die mit Gegeninduktion mit der ersten Soule (102d) gekoppelt ist, nachdem die zweite Spule (101f) innerhalb eines vorbestimmten proximalen Abstands von der ersten Spule (102d) angeordnet worden ist; einen Oszillator (101 a) zur Steuerung der zweiten Spule (101f), um einen Ladestrom in der ersten Spule (102d) zu induzieren; und einen Detektor (101c, 101e) zum Erkennen von Schwankungen in Bezug auf die durch die interne Sensoreinheit absorbierte Energie und zum Bereitstellen von Informationssignalen, die den Energieabsorptionsschwankungen entsprechen.

Revendications

1. Un détecteur interne (102), comprenant :

une bobine (908) **faisant partie d'une alimentation électrique dudit détecteur interne, et** étant configurée pour absorber de l'énergie fournie par un dispositif externe, et un circuit optoélectronique (102b) accouplé à la bobine (908), et **caractérisé par le fait que** :

le circuit optoélectronique (102b) comprend :

une source de rayonnement (903) pour l'émission d'une lumière d'excitation pour le détecteur ;
un premier photo-détecteur (901), qui est un détecteur de canal de signaux, et un deuxième photo-détecteur (902), qui est un détecteur de canal de référence, **le deuxième photo-détecteur étant installé « back-to-back » en série avec le premier photo-détecteur ;**
un comparateur (904) dont une borne d'entrée (904b) est connectée à une borne d'un desdits photo-détecteurs (901, 902), et **la borne d'entrée** étant également connectée à un condensateur (C2) fonctionnant comme une minuterie **pour la détermination du cycle de service ;**
un régulateur de tension (909) pour l'alimentation de la source de rayonnement (18) **et du comparateur ;** et
une résistance (910) reliée électriquement entre la borne de sortie (904c) du comparateur (904) et une borne de la bobine (908) pour le chargement de la bobine, dans lequel :

le circuit optoélectronique (102b) est configuré pour communiquer des informations au dispositif externe, en créant un signal **à onde rectangulaire commuté par la sortie du comparateur** ayant un cycle de service **commandé par la différence de courant entre le courant dans le premier photo-détecteur, produit par** la lumière incidente sur le photo-détecteur du canal de signal (901) et le **courant dans le deuxième photo-détecteur produit par** la lumière incidente sur le photo-détecteur du canal de référence (902) ; et le circuit optoélectronique (102b) est configuré de sorte qu'une charge (910) sur la bobine (908), **formée par l'impédance sur le circuit optoélectronique, est commutée avec ledit cycle de service,** en variant ainsi le courant passant par la bobine (908).

2. Le détecteur interne selon la revendication 1, dans lequel la résistance fonctionne comme une charge qui est connectée dans un circuit, et déconnectée de ce circuit, comprenant la bobine, en fonction du signal.

3. Le détecteur interne selon les revendications 1 ou 2, dans lequel le circuit optoélectronique comprend également :

une première résistance de polarisation (907) possédant une première borne et une deuxième borne, la première borne étant reliée à une borne de sortie (904c) du comparateur (904) ;
une deuxième résistance de polarisation (905) possédant une première borne et une deuxième borne, la première borne étant reliée à la deuxième borne de la première résistance de polarisation (907) ;
et
une troisième résistance de polarisation (906) possédant une première borne et une deuxième borne, la première borne étant reliée à la deuxième borne de la première résistance de polarisation (907) ;
le condensateur (C2) est doté d'une première borne et d'une deuxième borne, la première borne étant reliée à la borne d'entrée (904b) du comparateur (904) et la deuxième borne étant reliée à la deuxième borne de la deuxième résistance de polarisation (905).

4. Le détecteur interne selon les revendications 1, 2 ou 3, comprenant également un indicateur (16) émettant un rayonnement proportionnel aux niveaux d'un analyte.

5. Le détecteur interne selon la revendication 4, dans lequel la source de rayonnement (18) assure l'illumination de l'indicateur.

6. Un système de détecteur comprenant le détecteur interne d'une quelconque des revendications 1 à 5, et comprenant en outre un dispositif externe (101) pour la fourniture d'énergie au détecteur interne.

7. Le système de détecteur selon la revendication 6, dans lequel le dispositif externe comprend :

   une deuxième bobine (101f) à couplage mutuellement inductif avec ladite première bobine (102d) lorsque ladite deuxième bobine (101f) est placée à une distance proximale prédéterminée de ladite première bobine (102d), un oscillateur (101a) pour commander ladite deuxième bobine (101f) afin d'induire un courant de charge dans ladite première bobine (102d), et un détecteur (101c, 101e) pour détecter des variations de l'énergie absorbée par le détecteur interne et fournir des signaux d'information correspondant auxdites variations d'absorption de l'énergie.

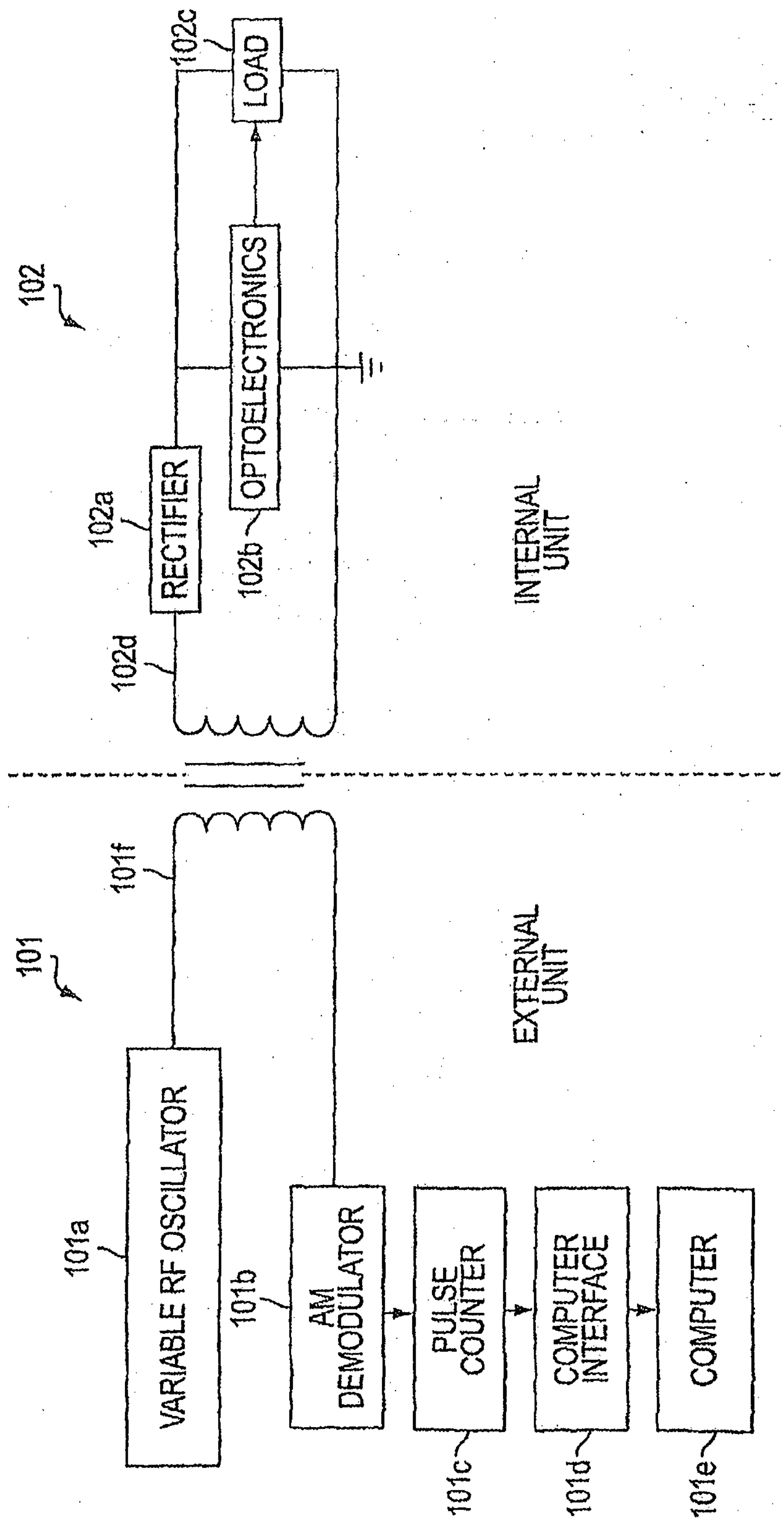
102
102c
LOAD
OPTOELECTRONICS
102a
RECTIFIER
102b
102d
INTERNAL UNIT
101
101f
EXTERNAL UNIT
101a
VARIABLE RF OSCILLATOR
101b
AM DEMODULATOR
PULSE COUNTER
COMPUTER INTERFACE
COMPUTER
101c
101d
101e

FIG. 1

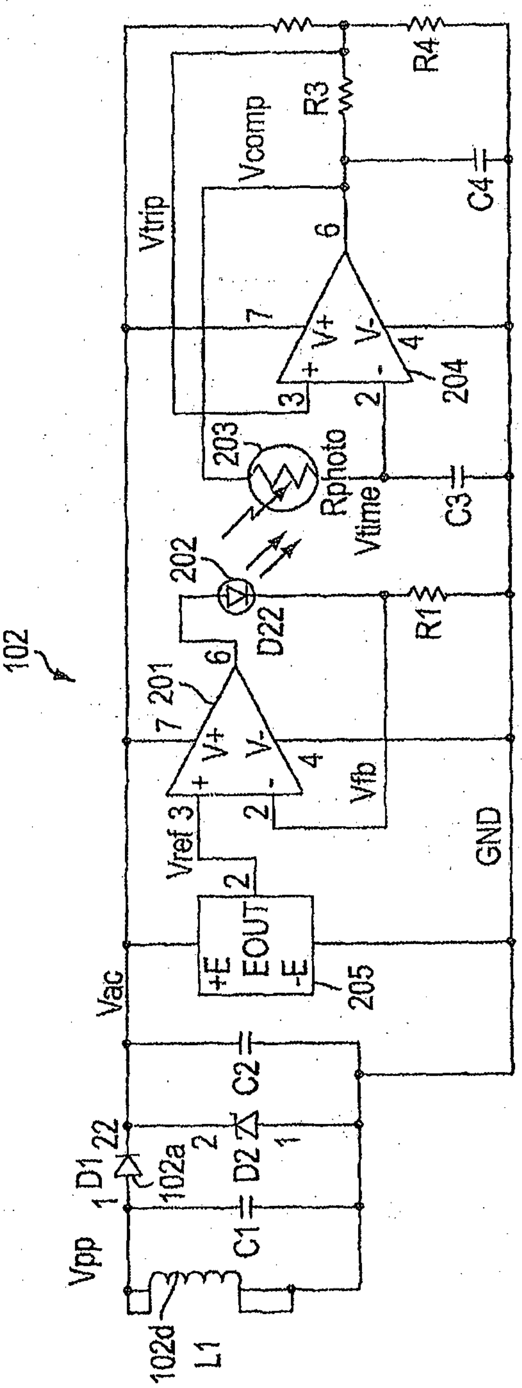
102
Vtrip
Vcomp
R3
R4
C4
6
7
V+
V-
+
-
3
2
4
204
203
Rphoto
Vtime
C3
202
D22
R1
201
6
7
V+
V-
+
-
Vref 3
2
4
Vfb
GND
2
EOUT
+E
-E
205
Vac
C2
D1
22
1
102a
2
D2
1
C1
Vpp
102d
L1

FIG. 2

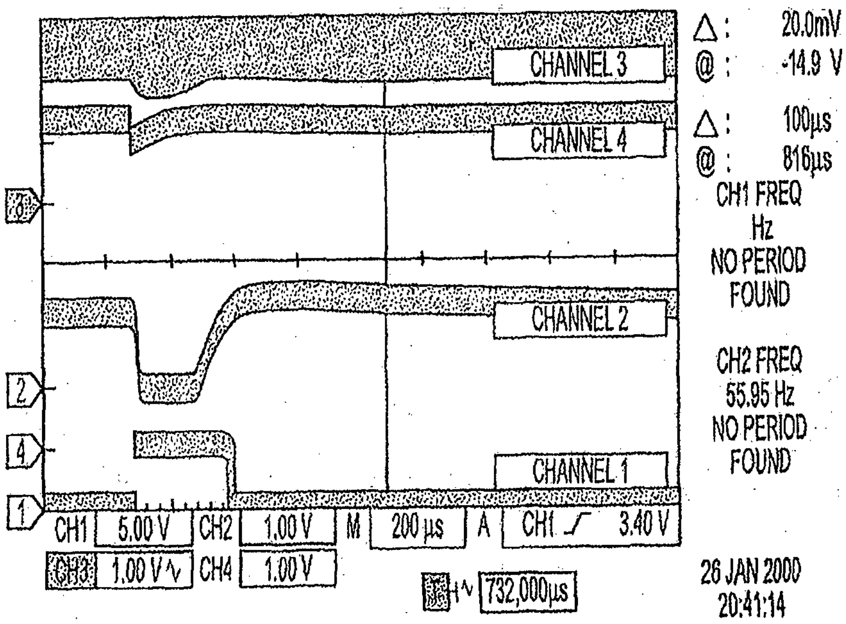
Δ: 20.0mV
@: -14.9 V
Δ: 100μs
@: 816μs
CH1 FREQ
Hz
NO PERIOD
FOUND
CH2 FREQ
55.95 Hz
NO PERIOD
FOUND
CHANNEL 3
CHANNEL 4
CHANNEL 2
CHANNEL 1
3
2
4
1
CH1 5.00 V CH2 1.00 V M 200 μs A CH1 ⁄ 3.40 V
CH3 1.00 V∿ CH4 1.00 V
T H∿ 732,000μs
26 JAN 2000
20:41:14

FIG. 3

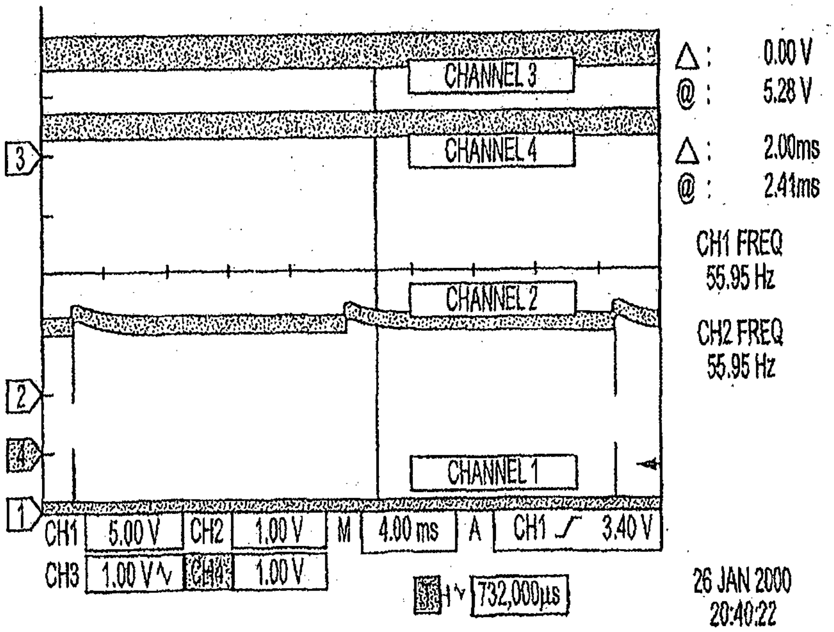
Δ: 0.00 V
@: 5.28 V
Δ: 2.00ms
@: 2.41ms
CH1 FREQ
55.95 Hz
CH2 FREQ
55.95 Hz
CHANNEL 3
CHANNEL 4
CHANNEL 2
CHANNEL 1
3
2
4
1
CH1 5.00 V CH2 1.00 V M 4.00 ms A CH1 ⁄ 3.40 V
CH3 1.00 V∿ CH4 1.00 V
T H∿ 732,000μs
26 JAN 2000
20:40:22

FIG. 4

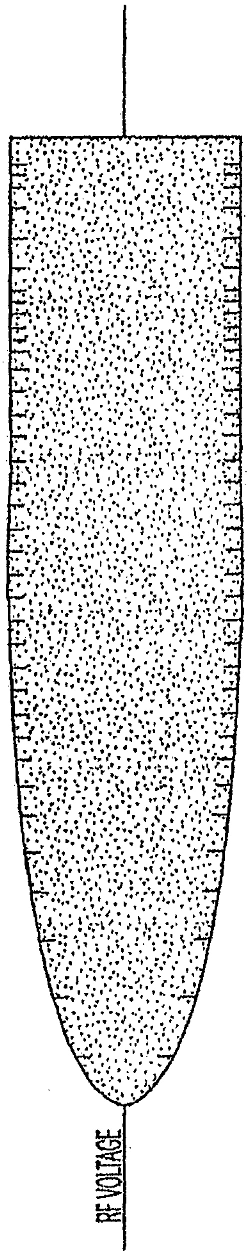

FIG. 5A

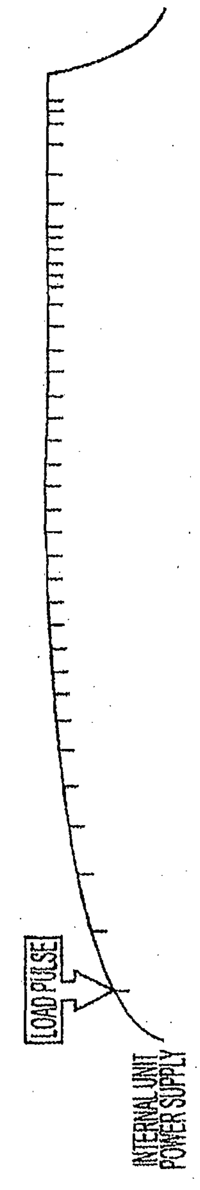

FIG. 5B

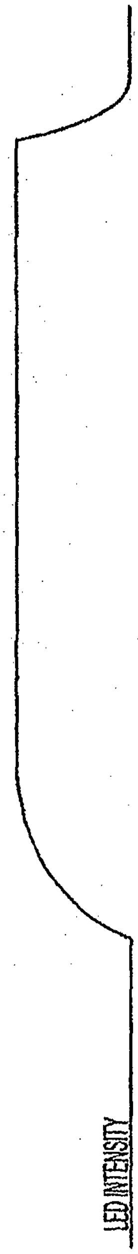

FIG. 5C

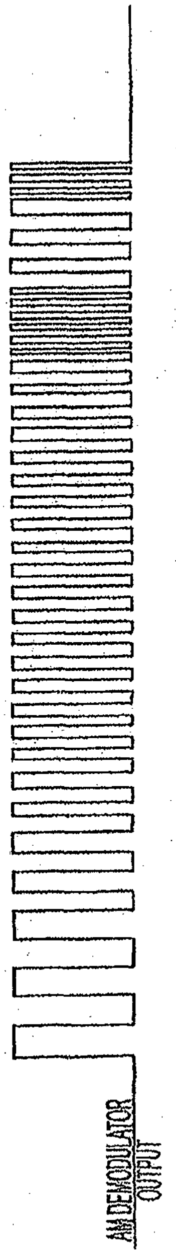
AM DEMODULATOR OUTPUT

FIG. 5D

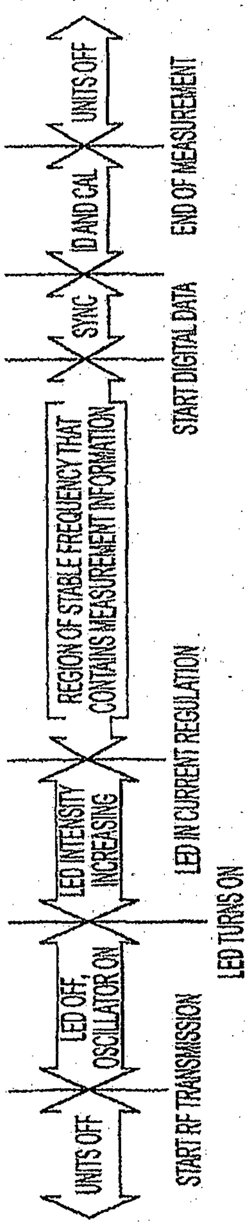
UNITS OFF
LED OFF, OSCILLATOR ON
LED INTENSITY INCREASING
REGION OF STABLE FREQUENCY THAT CONTAINS MEASUREMENT INFORMATION
SYNC
ID AND CAL
UNITS OFF
START RF TRANSMISSION
LED TURNS ON
LED IN CURRENT REGULATION
START DIGITAL DATA
END OF MEASUREMENT

FIG. 5E

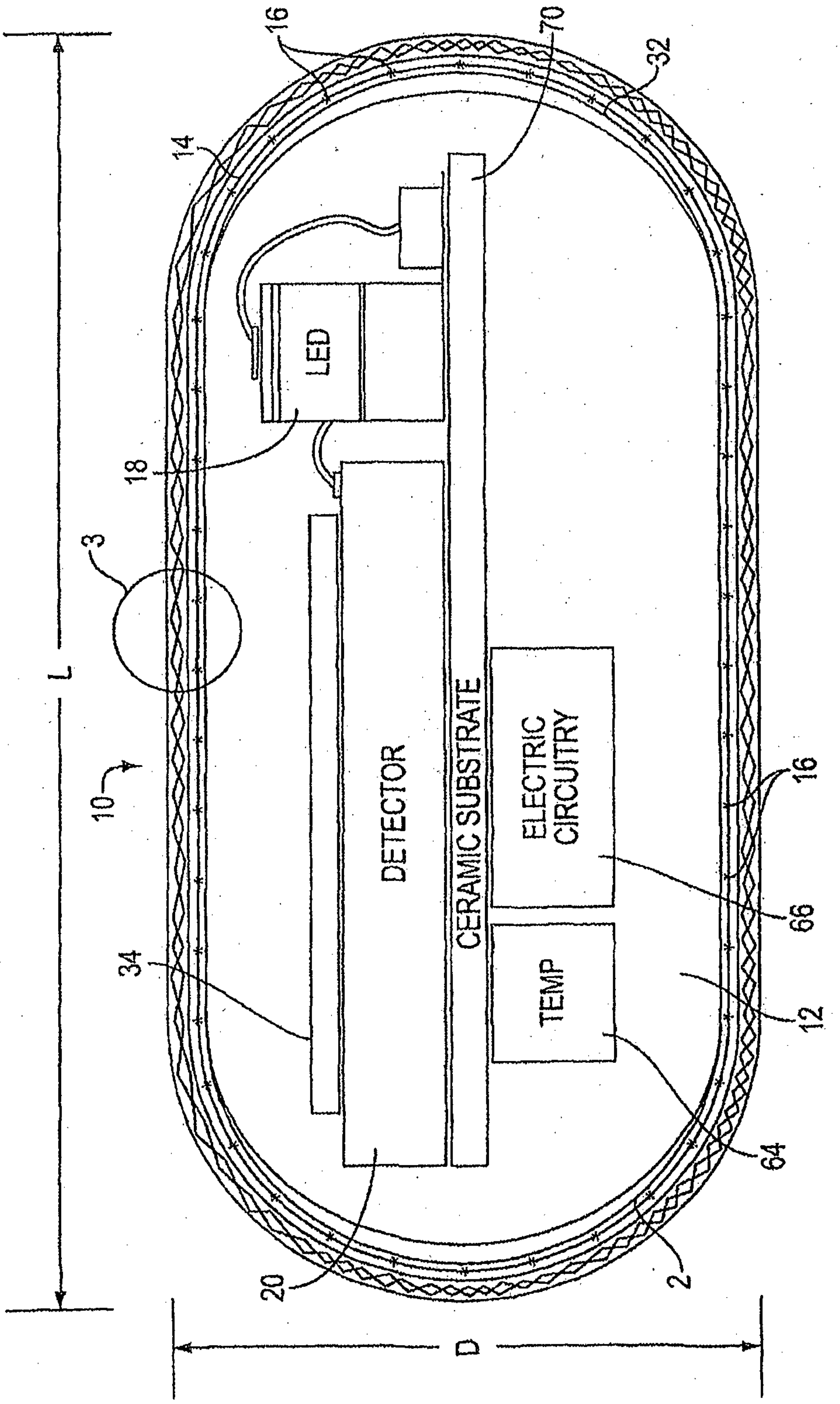
16
70
32
14
LED
18
3
L
10
DETECTOR
CERAMIC SUBSTRATE
ELECTRIC CIRCUITRY
16
66
34
TEMP
12
64
20
2
D

FIG. 6

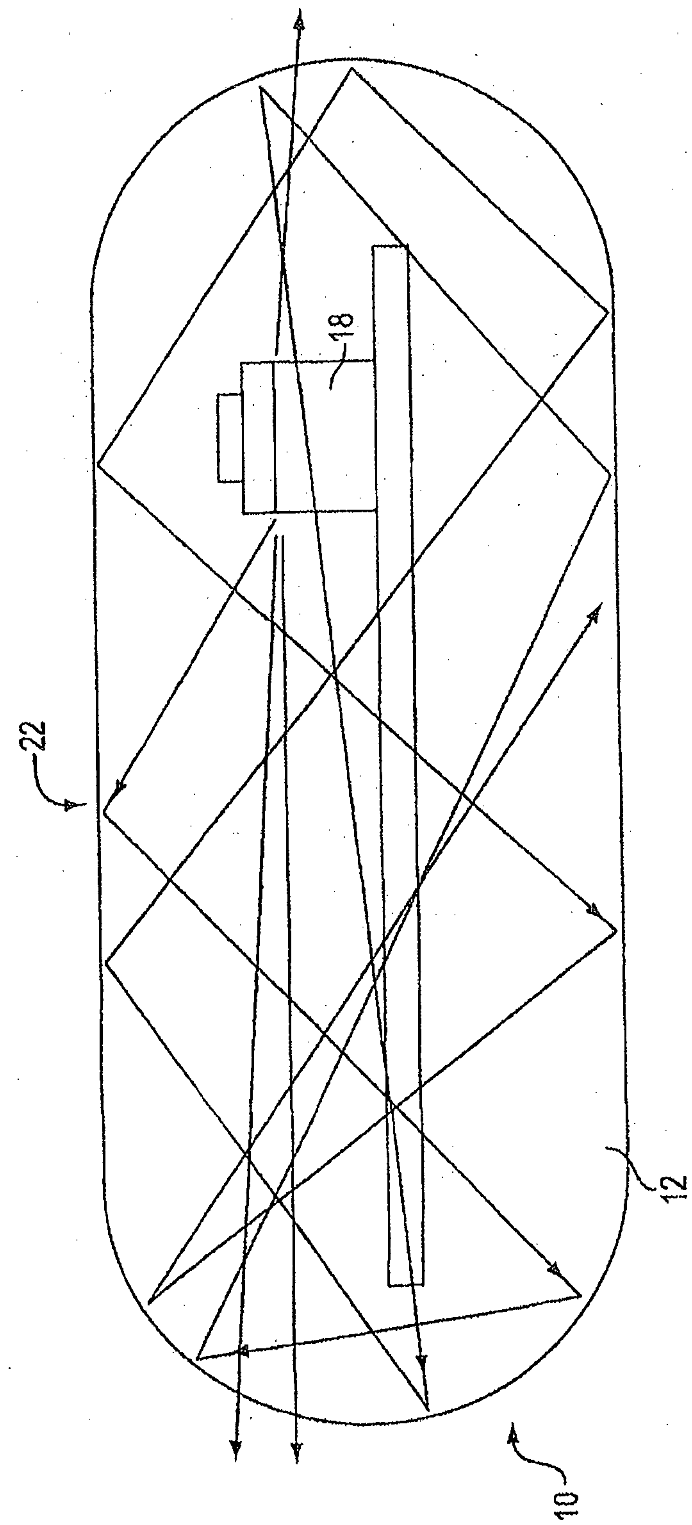

FIG. 7

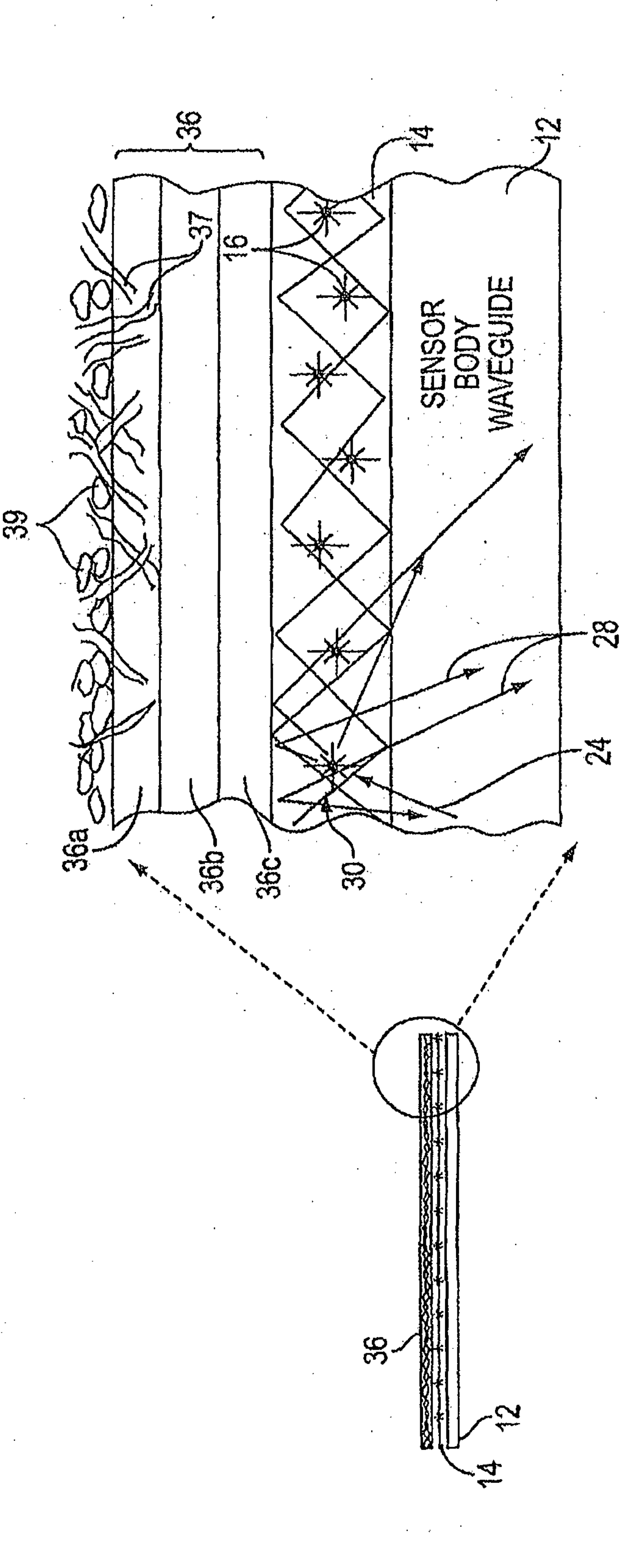
36
14
12
37
16
SENSOR
BODY
WAVEGUIDE
39
28
24
36a
36b
36c
30
36
12
14

FIG. 8

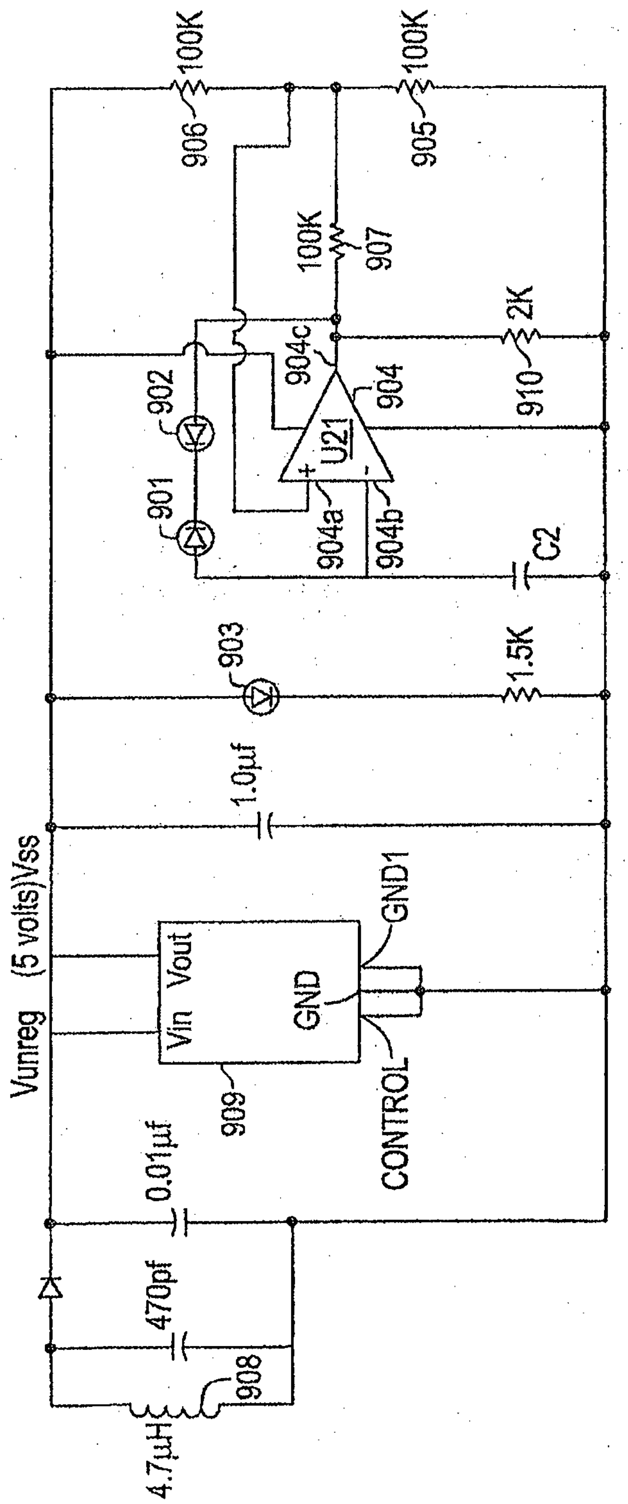
906
100K
905
100K
100K
907
2K
910
904c
904
902
901
U21
904a
904b
C2
903
1.5K
1.0µf
Vunreg
(5 volts)Vss
Vin
Vout
GND
GND1
CONTROL
909
0.01µf
470pf
908
4.7µH

FIG. 9

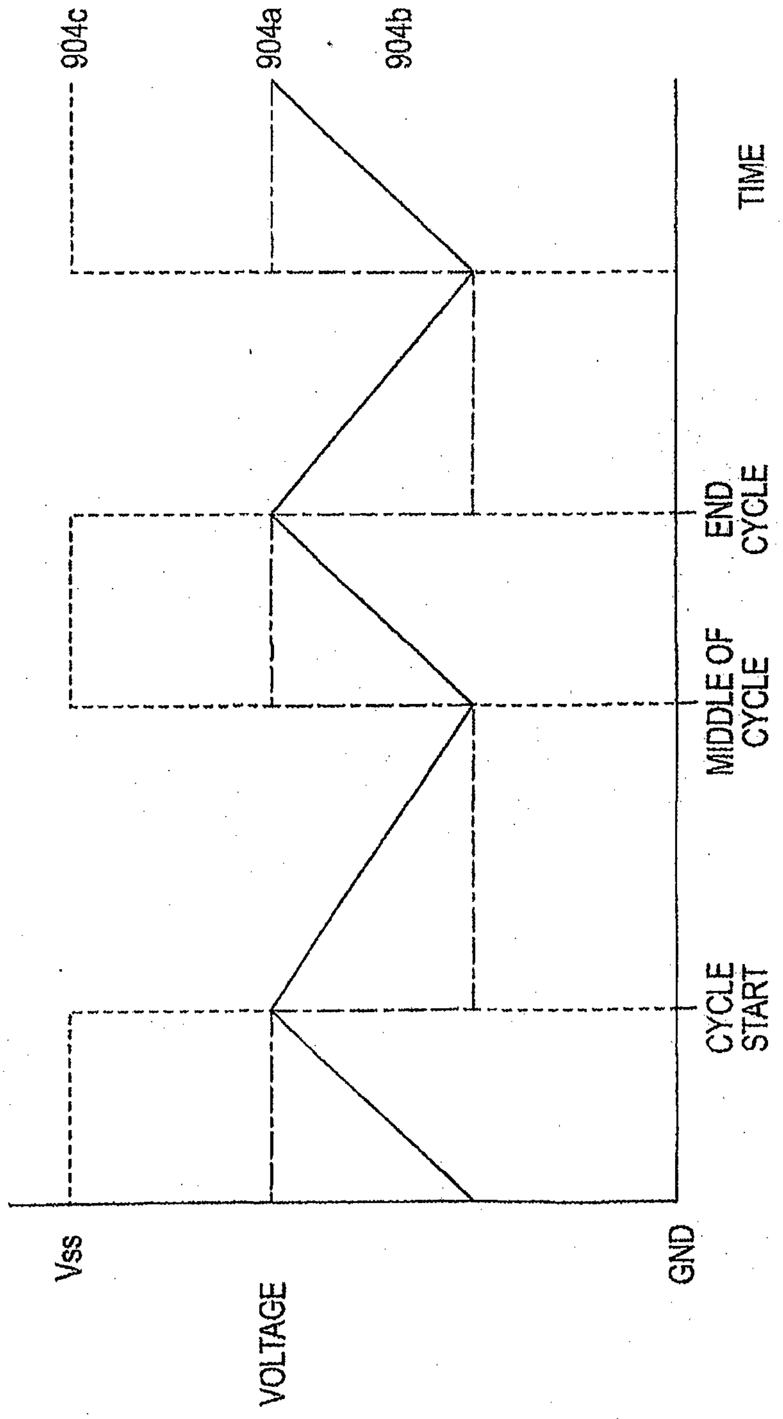
904c
904a
904b
Vss
VOLTAGE
GND
CYCLE START
MIDDLE OF CYCLE
END CYCLE
TIME

FIG. 10

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

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- US 5190729 A **[0036]**
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- US 5728422 A **[0036]**
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- **MULLER, B. et al.** *ANALYST,* March 1996, vol. 121, 339-343 **[0036]**

专利名称(译)	植入式传感器处理系统		
公开(公告)号	[EP2103250B1](EP2103250B1)	公开(公告)日	2015-08-05
申请号	EP2009160589	申请日	2001-06-27
[标]申请(专利权)人(译)	医药及科学传感器公司		
申请(专利权)人(译)	医学和科学传感器公司		
当前申请(专利权)人(译)	医学和科学传感器公司		
[标]发明人	LESHO JEFFERY C		
发明人	LESHO, JEFFERY, C.		
IPC分类号	A61B5/00 G08C19/00 A61B5/07 G01N21/64 G08C17/00 G08C23/04		
CPC分类号	A61B5/0031 A61B2560/0219 G01N21/645		
优先权	09/605706 2000-06-29 US		
其他公开文献	EP2103250A1		
外部链接	Espacenet		

摘要(译)

定量测量系统包括外部单元（101a）和内部单元（102a），用于获得定量分析物测量，例如在体内。在该系统的应用的一个示例中，内部单元（102a）可以皮下植入或以其他方式植入受试者体内。内部单元（102a）包含光电子电路（102b），其组件可以包括荧光传感装置。光电子电路（102b）获得定量测量信息并根据获得的信息修改负载（102c）。负载（102c）又改变通过线圈（102d）的电流量，线圈（102d）耦合到外部单元（101a）的线圈（101f）。解调器（101b）检测由耦合到其的内部线圈（102d）在外部线圈（101f）中感应的电流变化，并将检测到的信号施加到处理电路，例如脉冲计数器（101c）和计算机接口（101d）。用于将信号处理成计算机可读格式以输入计算机（101e）。