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(54) **OPTICAL SENSOR FOR DETERMINING THE CONCENTRATION OF AN ANALYTE**

OPTISCHER SENSOR ZUR BESTIMMUNG DER KONZENTRATION EINES ANALYTEN

CAPTEUR OPTIQUE POUR DÉTERMINER LA CONCENTRATION D'UNE SUBSTANCE À ANALYSER

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Description

[0001] The present invention relates to optical material analysis, and determining the concentration of an analyte using optical material analysis.

[0002] Diabetes mellitus is a serious disease that affects not only a patient's internal organs, circulation system and eyesight, but also a patient's lifestyle. There are reportedly more than 200 million diabetic people in the world at the moment, and this figure is expected to double within the next ten years. The first step in diabetes care is to monitor the patient's blood glucose level 24 hours a day, as knowing the glucose level assists in determining the right diet and medical treatment.

[0003] Current methods of measuring blood glucose concentrations typically require the diabetic patient to puncture a finger to collect a drop of blood, whose chemical composition is then analyzed by a glucose meter. As the procedure is not totally painless and harms the skin, diabetic patients are often unwilling to check their glucose level as frequently as their doctors prescribe, and are thus unable to sufficiently monitor their glucose level.

[0004] At present, the majority of portable devices for measuring glucose levels require puncturing the fingertip to obtain a blood sample. The blood sample is then placed on a test strip that indicates the glucose concentration. An example is the OneTouch® Ultra® glucose meter sold by LifeScan Inc., a Johnson & Johnson company. These devices are very compact and reasonably accurate, but puncturing the fingertip to obtain a blood sample is inconvenient and can be painful. Moreover, improper puncturing and hygiene may pose a risk of fingertip infection.

[0005] As an alternative to the traditional fingertip-puncturing methods, Cygnus Inc. has developed the GlucoWatch® Biographer monitor. The device, which looks like a wristwatch, pulls interstitial body fluid from the skin using small electric currents to extract glucose into a consumable transdermal pad, which acts as an iontophoretic sensor. The collected glucose triggers an electro-chemical reaction in the sensor, generating electrons. The sensor measures the electrons and equates the level of electron emission to a concentration of glucose in the body fluid. This device checks body fluid glucose levels every 20 minutes for up to 12 hours. Following the twelve hour period of operation, the monitor must be calibrated with a finger-prick reading for comparing with blood glucose levels. The device has a relative measuring error that has been determined to be approximately 10-30% in part because the glucose levels of interstitial fluid lags behind blood. However, in order to be able to even purchase one of these devices, a potential buyer must undergo and pass a physical and biochemical examination. Moreover, the device also has been known to severely inflame the skin in some patients with sensitive skin where the electrical currents are introduced.

[0006] Because of the lack of success of alternative devices such as GlucoWatch®, other non-invasive measurements have begun to be developed. Many of these alternative non-invasive methods involve using optical methods. Some of these optical methods have shown promise in providing a non-invasive measurement alternative. For example, some optical methods have used non-ionizing radiation to obtain a reading, providing fast responses without the need for consumable reagents. Moreover, as the availability of more sophisticated lasers and optical detectors increase, and the costs associated with using these optical devices decrease, optical methods may become an even more appealing alternative form of non-invasive measurement.

[0007] Typical non-invasive optical methods utilize a beam of light to irradiate some selected part of the human body, such as a finger, the forearm, tongue, lip, thigh or abdomen, etc. Light that is transmitted through, reflected, or scattered out of the skin comprises information about the composition of the irradiated tissue. This light is then received by optical detectors and analyzed to determine the concentrations of certain analytes, such as oxygen or hemoglobin. The analysis, however, is inherently complex because the received signal is often very faint and easily interfered with not only by a number of analytes in blood, but also by other factors including the variability and inhomogeneity of the human skin and the constantly changing human physiology, and even the external environment around the skin. Conventional optical methods of material analysis such as absorption and luminescent spectroscopy, Raman spectroscopy, and measuring polarization and reflectance changes are not sufficiently suitable for a turbid medium such as human tissue due to significant diffuse scattering of the reference light beam.

[0008] Other non-invasive methods take advantage of the correlation that exists between glucose content in the interstitial fluid and capillary blood, but suffer from the primary disadvantage of being time consuming. Furthermore, they only provide an indirect measure of glucose concentration, which is, unfortunately, also time-delayed.

[0009] The technique of laser photoacoustic spectroscopy has been used in trace detection due to the high sensitivity it offers. In the method of laser photoacoustic spectroscopy, a high-energy laser beam is used to irradiate the matter under study. The beam produces a thermal expansion in the matter, thereby generating an acoustic wave. The characteristics of the wave are determined not only by the optical absorption coefficient of the matter, but also by such thermal physical parameters as thermal expansion, specific heat, and sound velocity. In addition, the acoustic wave may also be affected by optical scattering, which influences the distribution of light in the matter that can be measured by high-sensitivity ultrasonic detectors such as piezo-electric crystals, microphones, optical fiber sensors, laser interferometers or diffraction sensors.

[0010] For example, U.S. Patents No. 5,941,821 and 6,049,728 to Chou describe a method and apparatus for noninvasive measurement of blood glucose by photoa-

coustics. Upon irradiation, acoustic energy is generated in a relatively thin layer of the sample to be measured, characterized by a heat-diffusing length. The acoustic emission is detected with a differential microphone, one end of which is positioned in a measuring cell and the other end of which is positioned in a reference cell. A processor determines the concentration of the substance being measured based upon the detected acoustic signal. In order to determine the concentration of glucose in the bloodstream, the excitation source is preferably tuned to the absorption bands of glucose in spectral ranges from about 1520-1850 nm and about 2050-2340 nm to induce a strong photoacoustic emission. In these wavelength ranges, water absorption is relatively weak and glucose absorption is relatively strong.

[0011] As another example, U.S. Patent No. 6,833,540 to MacKenzie, et al describes a system for measuring a biological parameter, such as blood glucose, the system directing laser pulses from a light guide into a body part consisting of soft tissue, such as the tip of a finger to produce a photoacoustic interaction. The resulting acoustic signal is detected by a transducer and analyzed to provide the desired parameter.

[0012] All of the above optical techniques are disadvantageous for at least the reason that they teach the application of energy to a medium without giving consideration to its acoustic oscillation properties, thus requiring relatively high laser power. Consequently, such techniques are energy inefficient, and provide an inadequate level of sensitivity.

[0013] Another prior art photoacoustic material analysis system is described in U.S. Patent No. 6,466,806 to Geva, et al, in which the concentration of a component of interest in a medium is determined by resonant photoacoustic spectroscopy with a light pulse-train comprising equidistant short pulses having variable duration, frequency, number, and power. The light wavelength is selected so as to be absorbed by the component of interest. Upon irradiation, acoustic oscillations are generated by the absorbed light in a relatively thin layer of the medium, characterized by a heat-diffusing length. The frequency repetition of the short light pulses in the pulse-train is chosen to be equal to the natural acoustic oscillation frequency of the thin layer of the medium that can be considered as a thin membrane, such that the acoustic oscillation becomes resonant. Measuring of the amplitude and the frequency of the resonant oscillations determine the concentration of the component of interest, making the system suitable for monitoring of blood components, especially glucose.

[0014] Unfortunately, the above system, as well as the majority of prior art photoacoustic material analysis techniques, are disadvantageous. Contrary to the present invention, they teach the application of energy to a medium without giving consideration to the overlapping of absorption bands of different components, and the irregularity of elastic properties of a medium, such as human skin. Consequently, such prior art techniques provide an inadequate level of sensitivity and large errors of measuring.

[0015] WO 97/02781 discloses an apparatus which can be used for monitoring glucose levels in a patient. The apparatus includes means for periodically heating the sample to create thermal waves, and means for monitoring the thermal waves using an optical probe beam.

[0016] According to one aspect of the present invention there is provided an apparatus for determining a concentration of an analyte in tissue as recited in claim 1.

[0017] According to another aspect of the invention there is provided a method for determining a concentration of an analyte as recited in claim 15.

[0018] Preferred features of the invention are recited in the dependent claims.

[0019] Additional features and advantages consistent with the invention will be set forth in part in the description which follows, and in part will be obvious from the description, or may be learned by practice of the invention. The features and advantages consistent with the invention will be realized and attained by means of the elements and combinations particularly pointed out in the appended claims.

[0020] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

[0021] The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate several embodiments of the invention and together with the description, serve to explain the principles of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0022] The present invention will be understood and appreciated more fully from the following detailed description taken in conjunction with the appended drawings in which:

FIG. 1 is a simplified block diagram illustrating an optical apparatus for determining a concentration of an analyte, consistent with the present invention.

FIG. 2 is a flowchart illustrating a method for determining a concentration of an analyte, consistent with the present invention.

FIG. 3 illustrates an embodiment of the optical components enclosure of FIG. 1.

FIG. 4 is a graph illustrating the intensity and duration of the different types of radiation emitted by an optical apparatus consistent with the present invention as used in Example 1.

FIG. 5 is a graph illustrating the intensity and duration of the different types of radiation emitted by an optical apparatus consistent with the present invention as used in Example 2.

FIG. 6 is a flowchart illustrating a method for calibrating an optical apparatus consistent with the present

invention.

FIG. 7 illustrates examples of optical fiber arrangements consistent with the present invention

DETAILED DESCRIPTION

[0023] Reference will now be made in detail to the exemplary embodiments of the invention, examples of which are illustrated in the accompanying drawings. Wherever possible, the same reference numbers will be used throughout the drawings to refer to the same or like parts.

[0024] FIG. 1 is a simplified block diagram illustrating an optical apparatus for determining a concentration of an analyte, consistent with the present invention. As shown in FIG. 1, the optical apparatus includes an electronics enclosure 102 connected to an optical components enclosure 104. Electronics enclosure 102 may be connected to optical components enclosure 104 through conductors, wires, wirelessly, or electronics enclosure 102 and optical components enclosure 104 may be contained in a single enclosure, with electrical connection therebetween. Consistent with embodiments of the present invention, optical components enclosure 104 may comprise a probe, as further illustrated in FIG. 3.

[0025] Optical components in optical components enclosure 104 may be operable to irradiate surface 106 with radiation beams B_1 and B_2, and detect first and second scatterings of radiation D_1 and D_2. Consistent with the present invention, the optical apparatus may be connected to power source 108 for providing power to both electronics enclosure 102 and optical components enclosure 104, and components located therein. Although illustrated as an external AC power source, power source 108 may be included in either of electronics enclosure 102 or optical components enclosure 104, and may be AC or DC. Moreover, if electronics enclosure 102 and optical components enclosure 104 are connected wirelessly, a separate additional power source may be connected to optical components enclosure 104. The optical apparatus may further be connected to an external processing device 110 for displaying, monitoring, tracking results, and calibrating the optical apparatus. External processing device may comprise a personal computer (PC), a personal digital assistant (PDA), a smartphone, or other such device.

[0026] Consistent with the present invention, electronics enclosure 102 may house an array of electronic components suitable for facilitating the determination of a concentration of an analyte. For example, electronics enclosure 102 may include a processor or CPU 112, a first radiation driver 114, a second radiation driver 116, a first peak detector 118, a second peak detector 120, a multiplexer (MUX) 122, and an analog to digital converter (ADC) 124. The operation of these components will be discussed further in conjunction with the discussion of FIG. 2.

[0027] Similarly, optical components enclosure 104 may house an array of optical components for use in determining the concentration of an analyte. As shown in FIG. 1, optical electronics enclosure 104 may include first radiation source 126 and second radiation source 128 for irradiating a testing area 130 on surface 106 with first and second radiation beams B_1 and B_2. Consistent with the present invention, first and second radiation beams B_1 and B_2 may be emitted from a single radiation source 127 capable of generating first and second radiation beams B_1 and B_2. Optical electronics enclosure 104 may further include a detector for receiving first and second scatterings of radiation D_1 and D_2. Consistent with the present invention a single detector 132 may be configured to receive first, second, and any other scatterings of radiation. Further consistent with the present invention, detector 132 may include separate scattered radiation detectors, as shown in FIG. 3, to separately receive first and second scatterings of radiation D_1 and D_2. Consistent with embodiments of the present invention, and may include optical receiving sensors, such as a photodiode, including a P-Intrinsic-N (PIN) photodiode, an avalanche photodiode, a photoelectrical multiplier, or a photoresistor. An optical amplifier (not shown) may further be included in optical electronics enclosure 104, for amplifying the power of the first or second radiation beams. Consistent with the present invention, optical amplifier may be an optical fiber amplifier. Optical electronics enclosure 104 may also further house an optical converter (not shown) for converting wavelengths of first and second radiation beams B_1 and B_2.

[0028] First and second radiation sources used in embodiments consistent with the present invention may be selected depending on such factors as the power or wavelength of radiation needed for accurately determining the concentration of an analyte, the periodicity of the radiation needed, size constraints or cost. For example, first radiation source 126 and second radiation source 128 may be pulsed laser diodes, fiber-coupled diode laser arrays, flash lamps or pulsed fiber optical lasers. First radiation source 126 and second radiation source, or single radiation source 127, may further include combinations of these types of radiation sources. For example, in one embodiment, first radiation source 126 or second radiation source 128 may include an erbium (Er)-glass rod or slab laser pumped by additional diode lasers. In another embodiment, first radiation source 126 or second radiation source 128 may include a tunable Co:MgF_2 laser. In yet another embodiment, first radiation source 126 or second radiation source 128 may include a Q-switched neodymium containing optical medium laser.

[0029] Consistent with the present invention, the characteristics of the emitted radiation source used again will depend on the particular analyte being examined. That is, the power, type of radiation, wavelength, and periodicity, for example, and will affect the properties of first and second radiation beams B_1 and B_2 emitted from first radiation source 126 and second radiation source 128, and these properties will each differently affect particular

analytes, and it is thus important to tailor these properties to maximize the ability of the optical apparatus to determine the concentration of the analyte. Different materials exhibit different reflectance, transmittance, and absorption properties. When performing optical measurements for determining the concentration of an analyte in a particular medium, the properties of both the analyte and the medium must be taken into consideration. The amount of radiation that is absorbed and scattered by the analyte is dependent on the power and wavelength of the radiation beams. Accordingly, it is desirable to emit radiation beams at a particular power and wavelength sufficient to produce a measurable amount of absorption and scatterings attributable to the analyte being examined, and differentiated from any surrounding mediums. For example, first and second radiation beams B_1 and B_2 will be emitted having predetermined wavelengths and a predetermined power. Consistent with embodiments of the present invention, the predetermined wavelengths and power may be the same or may be different, depending on the analyte being examined.

[0030] In a particular embodiment consistent with the present invention, first and second radiation beams B_1 and B_2 are emitted having predetermined wavelengths that are selected from a characteristic absorption band of the analyte being examined in a particular medium. In another embodiment, first and second radiation beams B_1 and B_2 are emitted at a wavelength which corresponds to a peak wavelength of an absorption band of the analyte being examined. In embodiments wherein first and second radiation beams B_1 and B_2 are emitted with different wavelengths, one beam B_1 or B_2 may have a wavelength which is greater than an absorption band peak of the analyte, and the other beam B_1 or B_2 may have a wavelength which is less than the absorption peak of the analyte. In specific embodiments, as will be described in further detail below, consistent with the present invention, a first radiation beam B_1 is emitted at a power of about 1-10 W and a wavelength of about 1550 nm, and a second radiation beam is emitted at a power of 0.1-1 W and a wavelength of about 1550-1690 nm.

[0031] As previously noted, first radiation source 126 and second radiation source 128 may comprise a pulsed radiation source. In embodiments using a pulsed radiation source, first and second radiation beams B_1 and B_2 may also be pulsed. For example, when using a pulsed source, first and second radiation beams B_1 and B_2 may be emitted as mono-pulses with a predetermined delay between the pulses. First and second radiation beams B_1 and B_2 may also be emitted as short pulses of quasi-continuous (QCW) light having an equal spacing therebetween, and a variable repetition rate. Furthermore, first and second radiation beams B_1 and B_2 may be emitted as a train of pulses, and having a variable frequency, a variable pulse power, a variable pulse duration, and a variable number of pulses. In a particular embodiment, noted below, second radiation beam B_2 is emitted as a short pulse having equal spacing, to periodically irradiate testing area 130.

[0032] Reference is now made to FIG. 2, which is a flowchart illustrating a method for determining a concentration of an analyte, consistent with the present invention. In an embodiment consistent with the present invention, the method illustrated in FIG. 2 may be performed using the optical apparatus illustrated in FIG. 1. For the purpose of illustrating such an embodiment, the steps of FIG. 2 will be described in conjunction with the operation of FIG. 1.

[0033] A probe, which may be optical components enclosure 104, is initially placed in contact with testing area 130 on surface 106 (S201). Consistent with the present invention, the probe may be in contact with testing area 130, or the probe may be near testing area 130. Further consistent with the present invention, testing area 130 may be at a surface 106, or may be below surface 106. Testing area 130 is irradiated with a first radiation beam B_1 emitted from first radiation source 126, which may be an exciter pulse (S202). Testing area 130 is subsequently irradiated with a second radiation beam B_2 emitted from second radiation source 128, which may be a probe pulse (S203).

[0034] Consistent with the present invention, second radiation source 128 may emit a plurality of second irradiation beams B_2, each beam emitted with a predetermined period therebetween. First and second radiation beams B_1 and B_2 will irradiate testing area 130, and a predetermined amount of radiation will be back scattered from the testing area, depending on the reflectivity of surface 106, illustrated as a first scattering D_1 and a second scattering D_2. Moreover, first and second radiation beams B_1 and B_2 may further cause periodic or non-periodic transient processes in surface 106 which may at least partially modulate scatterings of radiation D_1 and D_2.

[0035] Scatterings of radiation D_1 and D_2 may then be detected by detector 132 (S204). Detector 132 converts detected scatterings D_1 and D_2 into electrical signals for processing. Consistent with the present invention, the electrical signals may represent at least one of the amplitude, frequency, or decay time of any transient processes that may be produced in surface 106. The electrical signals are then transmitted from first and second peak detectors 118 and 120 to multiplexer 122. Multiplexer 122 combines the electrical signals from first and second peak detectors 118 and 120, and outputs a single combined electrical signal to analog to digital converter 124. Analog to digital converter 124 converts the input analog electrical signal into a digital electrical signal and outputs the digital electrical signal to processor 112.

[0036] Processor 112 receives the digital electrical signals and executes instructions, which may be stored in an internal memory (not shown), for performing calculations using the digital electrical signals. For example, processor 112 may calculate changes in the intensity of scatterings of radiation D_1 and D_2 (S205), the changes in the intensity being caused by repeated emission of

second radiation beams B_2, and any subsequent transient processes that may occur in surface 106 as a result of emitted first or second radiation beams B_1 and B_2. From the calculated changes in intensity, processor 112 will then execute instructions to perform an algorithm for calculating the concentration of an analyte present at testing area 130 (S206). Consistent with the present invention, the calculations may also be performed by an external processor, for example, a processor contained in PC 110. The calculated concentration may then be displayed for a user to view (S207). Consistent with the present invention, the concentration may be displayed on a display screen attached to electronics enclosure 102, or on computer 110. Moreover, the concentration may also be tabulated in computer 110 for trending and over-time analysis.

[0037] Consistent with the present invention, image analysis techniques may be used in conjunction with the optical apparatus described herein. In particular, image analysis techniques may be used to ensure that first and second radiation beams B_1 and B_2 are consistently incident on testing area 130, with no variation. Image analysis techniques may include video hardware and software, attached to and/or embedded on optical apparatus, which allows a user to accurately position optical apparatus such that radiation beams B_1 and B_2 are consistently incident on testing area. Consistent with the present invention, a portable video camera could be installed such that a real time video feed could show user positioning optical apparatus on surface 106. Markers could be placed at testing area 130 so that user could reliably, using the video feed, align the optical apparatus with testing area 130 to ensure incidence thereon.

[0038] FIG. 3 illustrates an embodiment of the optical components enclosure of FIG. 1. In this embodiment, optical components enclosure 104 of FIG. 1 is formed into a probe, or a probe head 304. Probe head 304 includes at least one radiation emitter, which may include first and second radiation emitters 126 and 128, at least one detector 132, which includes first and second scattered radiation detectors 332 and 334 having a different spacing with respect to surface 106 within detector 132. Probe head 304 may also include a first lens 306 for focusing radiation beams emitted from first and second radiation emitters onto test area 130. Probe head 304 may also include a second lens 308 and a third lens 310, for respectively focusing scattered radiation from surface 106 into second detector 334 and first detector 332. Although not shown in FIG. 3, probe head 304 may further be connected to other electronic processing components, such as those contained in electronics enclosure 102 shown in FIG. 1.

[0039] As shown in FIG. 3, in an embodiment consistent with the present invention, detector 132 is provided at a predetermined distance from surface 106. Consistent with the present invention second scattered radiation detector 334 may be provided in probe head 304 at a distance from surface 106 that is greater than the distance between first scattered radiation detector 332 and surface 106. By providing second scattered radiation detector 334 at a greater distance from surface 106 the optical apparatus is able to generate additional data points for performing a differential analysis on, and thus increasing the accuracy of the concentration readings. For example, for a given system excited by a first radiation beam B_1 and a second radiation beam B_2, the amplitude of detected scatterings at second scattered radiation detector 334 will be smaller than those detected at first scattered radiation detector 332, and can be used to calculate a relative amplitude between the detected scatterings at the two detectors. This relative amplitude can then be used to offset for an errors cause by positioning, pressure, or radiation source instability. Although the amplitude of the detected scatterings has been described as a detected parameter, the parameter may also be related to the frequency or decay time of the scatterings, consistent with the present invention.

[0040] In another embodiment of the present invention, probe head 304 may also include a gating sensor 302, which may be a contact, proximity, or pressure sensor. In embodiments using a contact sensor as gating sensor 302, the contact sensor must detect contact between probe head 304 and surface 106 before testing is allowed to begin, thus acting as a gate. In embodiments using a proximity sensor as gating sensor, the proximity sensor must detect that surface 106 is in a reasonable proximity to probe head 304. That is, in embodiments using a proximity sensor, the proximity sensor determines that there is a predetermined distance between surface 106 and probe head 304 before testing is allowed to begin.

[0041] In embodiments using a pressure sensor, sensor 302 must detect a predetermined pressure before proceeding with the test. As discussed above with reference to FIGS. 1 and 2, detected changes in the intensity of scattered beams D_1 and D_2 may be influenced by transient processes caused by first and second radiation beams B_1 and B_2. When placing probe head 304 in contact with surface 106, an additional transient process may be introduced into surface 106, further affecting changes in the intensity of scattered beams D_1 and D_2, and thus also affecting the calculated concentration of the analyte. A certain pressure imparted on surface 106 by probe, however, may be used as an offset such that when calculating the concentration of the analyte, the known pressure and its effects can be taken into consideration and corrected for. The pressure sensed by pressure sensor 302 between probe head 304 and surface 106 would have to be equal to a predetermined pressure before first radiation emitter 126 would emit a first radiation beam B_1. Pressure sensor 302 may comprise a fiber optic pressure probe.

[0042] Consistent with an embodiment of the present invention, probe head 304 comprises a fiber optic probe. In this embodiment, probe head 304 is made up of many optical fibers which are in optical communication with at least one radiation source and at least one detector. For

example, the optical fibers may be in optical communication with first radiation source 126, second radiation source 128, first detector 332, and second detector 334. The fiber optic bundles act as conduits or waveguides for transmitting radiation to and from surface 106. Consistent with such an embodiment, the many optical fibers may be arranged as shown in FIG. 7. The use of optical fibers allows for providing a probe head 304 which is small, lightweight, and easily able to be placed in contact with surface 106.

[0043] FIG. 7 illustrates examples of optical fiber arrangements consistent with the present invention. FIG. 7(a) illustrates an optical fiber arrangement which includes three fibers 726 for transmitting radiation from radiation source 126 and/or 128, and a plurality of pick-up fibers 732 for transmitting scattered radiation from surface 106 to a radiation detector, which may include radiation detector 132. FIG. 7(b) illustrates an optical fiber arrangement which includes two fibers 726 for transmitting radiation from radiation source 126 and/or 128, and a plurality of pick-up fibers 752 for transmitting scattered radiation from surface 106 to a radiation detector, which may include radiation detector 132. FIG. 7(c) illustrates an optical fiber arrangement which includes two fibers 726 for transmitting radiation from radiation source 126 and/or 128, and a plurality of near pick-up fibers 732 for transmitting scattered radiation from surface 106 to a radiation detector, which may include radiation detector 132 or 332, and a plurality of
distant pick-up fibers 734 for transmitting scattered radiation to radiation detector 334, as shown in FIG. 3.

[0044] The optical apparatus described herein, may be used in certain embodiments to detect the concentration of glucose in human tissue. Consistent with the present invention, an embodiment for detecting glucose in human tissue emits a short, high power radiation beam B_1 as an exciter pulse onto testing area 130 of surface 106, which in this embodiment, is tissue. Part of the radiation is absorbed by surface 106 and generates transient processes in surface 106 which change the optical, mechanical, and other physical and chemical properties of surface 106. The change in these properties subsequently also changes the amplitude, frequency, and decay time of scattered radiation D_1 and D_2, as well as the photoacoustic oscillations in surface 106.

[0045] After the initial emission of radiation beam B_1, second radiation source 128 periodically emits second radiation beam B_2, which acts as a probe pulse. According to the invention, these probe pulses are at a lower power than first radiation beam B_1, such that they only induce minimal transient processes in surface 106. The probe pulses serve to generate additional scatterings of radiation D_1 and D_2 that can be detected by detector 132 as surface 106 relaxes over time. As surface 106 relaxes from the initial high power radiation beam B_1, detector 132 will be able to obtain readings which can be processed to determine the amplitude of the scattered light from the initial exciter pulse, and the subsequent probe pulses, the change in amplitude of the scattered light over time, the amplitude and frequency of modulation occurring as a result of the introduced transient processes, a decay constant of surface 106, and a phase delay in amplitude modulation of light scattered from the probe pulses, which allows for calculation of the velocity of acoustical wave propagation in surface 106. From these processed values, the concentration of glucose present in surface 106 may be determined. Specific examples using optical apparatuses consistent with the present invention will be discussed in detail as follows.

EXAMPLE 1

[0046] In an embodiment consistent with the present invention, the optical apparatus as described above with respect to FIG. 1, for example, is used to determine the concentration of glucose in a human subject, such that surface 106 of FIG. 1 is human tissue. FIG. 4 is a graph illustrating the intensity and duration of the different types of radiation emitted by an optical apparatus consistent with this embodiment. For this embodiment, first and second radiation sources 126 and 128 are selected to correspond to a glucose absorption band having a peak around 1590 nm. In this embodiment the optical apparatus is provided such that first radiation source 126 is a laser emitting an exciter beam B_1 at a wavelength of 1550 nm, power of 1.0-10.0 W, and a pulse width of 100 ns. Second radiation source 128 is a laser provided to emit a plurality of periodic probe pulses B_2 at a wavelength of 1550 nm, a power of 0.1-1.0 W, and a pulse width of 80 ns.

[0047] In operation, exciter beam B_1, in accordance with opto-acoustical principles, generates mechanical changes and fast-faded oscillations in tissue 106. Exciter beam B_1 also generates an initial scattering of light D_1 or D_2. After exciter beam B_1 is emitted, probe pulses B_2 are periodically emitted, generating additional scatterings of light D_1 or D_2. Scatterings of light D_1 and D_2 are detected by detector 132, converted to electrical signals representative of the intensity of amplitude of scatterings of light D_1 and D_2, and sent to electronics enclosure 102 for processing.

[0048] Due to the mechanical changes and fast-faded oscillations in tissue 106, the amplitude of the additional scatterings of light D_1 or D_2 changes over time. CPU 112 processes the electrical signals representative of the changes in amplitude, and sends the results to PC 110. PC 110, using a proprietary algorithm, stores the electrical signals and calculates the concentration of glucose in tissue 106.

EXAMPLE 2

[0049] In another embodiment consistent with the present invention, the optical apparatus as described above with respect to FIG. 3, for example, is used to determine the concentration of glucose in a human subject, such that surface 106 of FIG. 3 is human tissue.

FIG. 5 is a graph illustrating the intensity and duration of the different types of radiation emitted by an optical apparatus consistent with this embodiment. For this embodiment, first and second radiation sources 126 and 128 are selected to correspond to a glucose absorption band having a peak around 1590 nm. In this embodiment the optical apparatus is provided such that first radiation source 126 is a laser emitting an exciter beam Bi at a wavelength of 1550 nm, power of 5 W, and a pulse width of 100 ns. Second radiation source 128 is a laser provided to emit a plurality of periodic probe pulses B2 at a wavelength of about 1610-1690 nm, a power of 0.25-0.5 W, and a pulse width of 80 ns.

[0050] Alternatively and consistent with the present invention, exciter beam Bi may be emitted at a wavelength of about 1550 nm and a power of 10 W, and periodic probe pulses B2 may be emitted from the same radiation source as exciter beam B1, at a wavelength of about 1550 nm and a power of about 0.25-0.5 W, with about periodic probe pulses B_2 being emitted such that there is about a 25 microsecond delay between each pulse.

[0051] In operation, probe head 304 is placed in contact with tissue 106. Gating sensor 302, which in this example comprises a pressure sensor, measures a pressure between probe head 304 and tissue 106. When pressure sensor 302 determines that the pressure between probe head 304 and tissue 106 is at an acceptable value, first radiation source emits an exciter beam. The exciter beam, in accordance with opto-acoustical principles, generates mechanical changes and fast-faded oscillations in tissue 106, and an initial scattering of light. After the exciter beam is emitted, probe pulses are periodically emitted by second radiation source 128, generating additional scatterings of light. The scatterings of light are detected by first and second detectors 332 and 334, converted to electrical signals representative of the intensity of amplitude of the scatterings of light, and sent to electronics enclosure 102 (shown in FIG. 1) for processing.

[0052] Due to the mechanical changes and fast-faded oscillations in tissue 106, the amplitude of the additional scatterings of light modulates over time. CPU 102 (shown in FIG. 1) processes the electrical signals representative of the changes in amplitude, and performs an algorithm for comparing the amplitudes of the scatterings of light with each other over time to look for differential changes in not only amplitude, but also frequency, decay time, and the velocity of acoustical oscillation diffusion. These differential changes are stored in an internal memory (not shown), and then used in an algorithm to calculate the concentration of glucose in tissue 106.

[0053] Consistent with the present invention, although not necessarily required, the optical apparatus illustrated in FIGS. 1 or 3 may be calibrated in order to provide optimal determinations of the concentration of an analyte. FIG. 6 is a flowchart illustrating a method for calibrating an optical apparatus consistent with the present invention. If the analyte being tested is glucose, as described above, it is important for the health of the user that the concentrations obtained are accurate, and in conformance with other accepted means of testing glucose concentration. Accordingly, in performing a calibration process, the results of a standard blood test is compared to the results of the optical apparatus, and the optical apparatus is offset to match the blood test. Although this calibration process has been summarized with respect to glucose testing, the calibration process described in detail below may also be used when using the optical apparatus consistent with the present invention to determine the concentration of analytes other than glucose.

[0054] First, a fluid sample is obtained (S401), and using a fluid concentration determining means, a first concentration of an analyte is determined (S402). This first concentration is recorded, and then the optical apparatus consistent with the present invention is used to take a concentration measurement (S403). The optical apparatus performs a method, such as illustrated in FIG. 2, and determines a second concentration of the analyte (S404). The first concentration and the second concentration are compared to one another to determine if they match within a predetermined degree of accuracy (S405). If the first concentration and the second concentration match, no further calibration is needed (S406). If, however, the first concentration and the second concentration do not match, the optical apparatus is offset by a predetermined amount such that the second concentration will match the first concentration (S407). After this step, the calibration is complete (S408). Consistent with embodiments of the present invention, a computer, external to the optical apparatus or on-board the optical apparatus, may perform the recordation of the concentrations, the match determination, and the offset.

[0055] While the methods and apparatus disclosed herein may or may not have been described with reference to specific hardware or software, the methods and apparatus have been described in a manner sufficient to enable persons of ordinary skill in the art to readily adapt commercially available hardware and software as may be needed to reduce any of the embodiments of the present invention to practice without undue experimentation and using conventional techniques. In addition, while the present invention has been described with reference to a few specific embodiments, the description is intended to be illustrative of the invention as a whole and is not to be construed as limiting the invention to the embodiments shown. It is appreciated that various modifications may occur to those skilled in the art that, while not specifically shown herein, are nevertheless within the scope of the invention.

[0056] Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. It is intended that the specification and examples be considered as exemplary only, with the scope of the invention being indicated by the following claims.

Claims

1. An apparatus for determining a concentration of an analyte in tissue, comprising:

   at least one radiation source (126, 128) operative to emit a first pulsed radiation beam (B_1) and at least one second pulsed radiation beam (B_2), the first pulsed radiation beam irradiating a testing area (130) of tissue with an exciter pulse and causing a first scattering of radiation (D_1), and the at least one second pulsed radiation beam having a lower intensity than the first radiation beam and subsequently periodically irradiating the testing area with probe pulses causing periodic second scatterings of radiation (D_2);
   at least one detector (132) comprising a first radiation detector (332) and a second radiation detector (334), wherein the first radiation detector and the second radiation detector are configured to detect the first scattering of radiation and the second scatterings of radiation and the radiation detectors are configured to convert the detected scatterings into electrical signals, and wherein the first radiation detector and the second radiation detector are located at different distances from the testing area of tissue enabling a relative amplitude between the detected scatterings to be calculated and used as an offset; and
   a processor (112) for determining the concentration of the analyte based on said electrical signals.

2. The apparatus according to claim 1, wherein:
   the first and second pulsed radiation beams (B_1, B_2) have predetermined wavelengths selected from a characteristic absorption band of the analyte in a predetermined medium.

3. The apparatus according to claim 1, wherein:

   the first and second radiation pulsed beams (B_1, B_2) have predetermined wavelengths,
   wherein the predetermined wavelength of the first radiation beam corresponds to a peak of an absorption band of the analyte in a predetermined medium, and wherein the first radiation beam interacts with the tissue causing at least one transient process dependent on the concentration of the analyte.

4. The apparatus according to any of the preceding claims, wherein the first and second pulsed radiation beams (B_1, B_2) have the same wavelength.

5. The apparatus according to any of claims 1-3 wherein the first and second pulsed radiation beams (B_1, B_2) have different wavelengths.

6. The apparatus according to claim 5, wherein one of the first and second radiation beams has a wavelength that is greater than an absorption band peak of the analyte in a predetermined medium, and one of the first and second pulsed radiation beams has a wavelength that is less than the absorption band peak of the analyte in a predetermined medium.

7. The apparatus according to any of the preceding claims, wherein the first pulsed radiation beam (B_1) excites at least one periodic or non-periodic transient process in the tissue, and wherein at least one of the first and second scatterings of radiation are at least partially modulated by the at least one transient process.

8. The apparatus according to claim 7, wherein the at least one transient process includes photo-acoustic oscillations.

9. The apparatus according to claim 7 or 8, wherein the electrical signals represent at least one of the amplitude, frequency, or decay time of the at least one transient process.

10. The apparatus according to any of the preceding claims, wherein the first and second pulsed radiation beams comprise mono-pulses having a delay between the pulses.

11. The apparatus according to any of claims 1-9, wherein the second pulsed radiation beam comprises substantially equally-spaced short pulses of quasi-continuous wave (QCW) having a variable repetition rate.

12. The apparatus according to any of claims 1-9, wherein the second pulsed radiation beam comprises a train of pulses having a variable frequency, variable pulse power, variable pulse duration, and variable number of pulses.

13. The apparatus according to any of the preceding claims, wherein the first and second pulsed radiation beams are focused on substantially the same point of the testing area.

14. The apparatus according to claim 1, further comprising one of the following features:

    the first pulsed radiation beam has a power of about 1-10 W;
    the first pulsed radiation beam has a power of about 5 W;
    the first pulsed radiation beam has a wavelength

of about 1550 nm;
the second pulsed radiation beam has a power of about 0.1-1 W;
the second pulsed radiation beam has a power of about 0.25 - 0.5 W;
the second pulsed radiation beam has a wavelength of about 1610 nm to 1690 nm;
the at least one radiation source comprises a pulsed laser diode;
the at least one radiation source comprises a fiber-coupled diode laser array;
the at least one radiation source comprises a pulsed optical fiber laser;
the at least one radiation source comprises an Er-glass rod or slab laser pumped by diode lasers or a flash lamp;
the at least one radiation source comprises a tunable Co:MgF2 laser;
the at least one radiation source comprises a Q-switched neodymium containing optical medium laser, and providing quasi-continuous wave generation giving equidistant short pulses having a variable duration, frequency, number and power; and
the analyte is glucose.

15. A method for determining a concentration of an analyte in tissue, comprising:

irradiating a testing area (130) of tissue with at least one radiation source (126, 128) emitting a first pulsed radiation beam (B_1) as an exciter pulse causing an initial back-scattering of radiation and subsequently emitting a second pulsed radiation beam (B_2) periodically irradiating the testing area with probe pulses causing periodic back-scatterings of radiation, wherein the second pulsed radiation beam has a lower intensity than the first pulsed radiation beam;
detecting the initial back-scattering caused by the first pulsed radiation beam and the periodic back-scatterings caused by the second pulsed radiation beam with a first radiation detector and a second radiation detector, wherein the first radiation detector and the second radiation detector are located at different distances from the testing area of tissue enabling a relative amplitude between the detected scatterings to be calculated and used as an offset;
converting the detected back-scatterings into electrical signals; and
determining the concentration of the analyte in response to said electrical signals.

Patentansprüche

1. Vorrichtung zum Bestimmen einer Konzentration eines Analyten in Gewebe, die Folgendes umfasst:

mindestens eine Strahlungsquelle (126, 128), die wirksam ist, um ein erstes gepulstes Strahlungsbündel (B_1) und mindestens ein zweites gepulstes Strahlungsbündel (B_2) auszustrahlen, wobei das erste gepulste Strahlungsbündel einen Prüfbereich (130) von Gewebe mit einem Erregerimpuls bestrahlt und eine erste Streuung von Strahlung (D_1) bewirkt, und das mindestens eine zweite gepulste Strahlungsbündel eine geringere Intensität aufweist als das erste Strahlungsbündel, und anschließend den Prüfbereich periodisch mit Sondenimpulsen zu bestrahlen, die periodische zweite Streuungen von Strahlung (D_2) verursachen;
mindestens einen Detektor (132), umfassend einen ersten Strahlungsdetektor (332) und einen zweiten Strahlungsdetektor (334), wobei der erste Strahlungsdetektor und der zweite Strahlungsdetektor dazu konfiguriert sind, die erste Streuung von Strahlung und die zweiten Streuungen von Strahlung zu erfassen, und die Strahlungsdetektoren dazu konfiguriert sind, die erfassten Streuungen in elektrische Signale umzuwandeln, und wobei sich der erste Strahlungsdetektor und der zweite Strahlungsdetektor in unterschiedlichen Entfernungen von dem Prüfbereich von Gewebe befinden, sodass eine relative Amplitude zwischen den erfassten Streuungen berechnet und als Offset verwendet werden kann; und
einen Prozessor (112) zum Bestimmen der Konzentration des Analyten basierend auf den elektrischen Signalen.

2. Vorrichtung nach Anspruch 1, wobei:
das erste und das zweite gepulste Strahlungsbündel (B_1; B_2) vorbestimmte Wellenlängen aufweisen, die aus einem charakteristischen Absorptionsband des Analysten in einem vorbestimmten Medium ausgewählt sind.

3. Vorrichtung nach Anspruch 1, wobei:

das erste und das zweite gepulste Strahlungsbündel (B_1; B_2) vorbestimmte Wellenlängen aufweisen,
wobei die vorbestimmte Wellenlänge des ersten Strahlungsbündels einem Peak eines Absorptionsbands des Analyten in einem vorbestimmten Medium entspricht, und wobei das erste Strahlungsbündel und das Gewebe aufeinander einwirken, sodass mindestens ein transienter Vorgang abhängig von der Konzentration des Analyten verursacht wird.

4. Vorrichtung nach einem der vorangehenden An-

sprüche, wobei das erste und das zweite gepulste Strahlungsbündel (B_1; B_2) die gleiche Wellenlänge aufweisen.

5. Vorrichtung nach einem der Ansprüche 1-3, wobei das erste und das zweite gepulste Strahlungsbündel (B_1; B_2) unterschiedliche Wellenlängen aufweisen.

6. Vorrichtung nach Anspruch 5, wobei eines von dem ersten und dem zweiten Strahlungsbündel eine Wellenlänge aufweist, die größer als ein Absorptionsband-Peak des Analyten in einem vorbestimmten Medium ist, und eines von dem ersten und dem zweiten gepulsten Strahlungsbündel eine Wellenlänge aufweist, die geringer ist als der Absorptionsband-Peak des Analyten in einem vorbestimmten Medium.

7. Vorrichtung nach einem der vorangehenden Ansprüche, wobei das erste gepulste Strahlungsbündel (B_1) mindestens einen periodischen oder nicht periodischen transienten Vorgang in dem Gewebe erregt, und wobei die erste und/oder die zweite Streuung von Strahlung von dem mindestens einen transienten Vorgang mindestens teilweise moduliert werden.

8. Vorrichtung nach Anspruch 7, wobei der mindestens eine transiente Vorgang fotoakustische Schwingungen umfasst.

9. Vorrichtung nach Anspruch 7 oder 8, wobei die elektrischen Signale mindestens eine von Amplitude, Frequenz oder Abfallzeit des mindestens einen transienten Vorgangs darstellen.

10. Vorrichtung nach einem der vorangehenden Ansprüche, wobei das erste und das zweite gepulste Strahlungsbündel Monoimpulse mit einer Verzögerung zwischen den Impulsen aufweisen.

11. Vorrichtung nach einem der Ansprüche 1-9, wobei das zweite gepulste Strahlungsbündel im Wesentlichen gleichmäßig beabstandete kurze Impulse einer quasikontinuierlichen Welle (QCW) mit variabler Wiederholrate umfasst.

12. Vorrichtung nach einem der Ansprüche 1-9, wobei das zweite gepulste Strahlungsbündel eine Folge von Impulsen mit einer variablen Frequenz, variablen Impulsleistung, variablen Impulsdauer und variablen Zahl von Impulsen umfasst.

13. Vorrichtung nach einem der vorangehenden Ansprüche, wobei das erste und das zweite gepulste Strahlungsbündel auf im Wesentlichen denselben Punkt des Prüfbereichs fokussiert sind.

14. Vorrichtung nach Anspruch 1, die weiter eines der folgenden Merkmale umfasst:

das erste gepulste Strahlungsbündel weist eine Leistung von etwa 1-10 W auf;
das erste gepulste Strahlungsbündel weist eine Leistung von etwa 5 W auf;
das erste gepulste Strahlungsbündel weist eine Wellenlänge von etwa 1550 nm auf;
das zweite gepulste Strahlungsbündel weist eine Leistung von etwa 0,1-1 W auf;
das zweite gepulste Strahlungsbündel weist eine Leistung von etwa 0,25-0,5 W auf;
das zweite gepulste Strahlungsbündel weist eine Wellenlänge von etwa 1610 nm bis 1690 nm auf;
die mindestens eine Strahlungsquelle umfasst eine Impulslaserdiode;
die mindestens eine Strahlungsquelle umfasst ein Array von fasergekoppelten Diodenlasern;
die mindestens eine Strahlungsquelle umfasst einen Impulsfaserlaser;
die mindestens eine Strahlungsquelle umfasst einen Er-Glasstab- oder -plattenlaser, der von Diodenlasern oder einer Blitzlampe gepumpt wird;
die mindestens eine Strahlungsquelle umfasst einen abstimmbaren Co:MgF2-Laser;
die mindestens eine Strahlungsquelle umfasst einen gütegeschalteten Laser mit neodymhaltigem optischem Medium und stellt eine quasikontinuierliche Wellenerzeugung bereit, die äquidistante kurze Impulse von variabler Dauer, Frequenz, Zahl und Leistung liefert; und
bei dem Analyten handelt es sich um Glukose.

15. Verfahren zum Bestimmen einer Konzentration eines Analyten in Gewebe, das Folgendes umfasst:

Bestrahlen eines Prüfbereichs (130) von Gewebe mit mindestens einer Strahlungsquelle (126, 128), die ein erstes gepulstes Strahlungsbündel (B_1) als einen Erregerimpuls ausstrahlt, der eine anfängliche rückwärtige Streuung von Strahlung verursacht, und anschließendes Ausstrahlen eines zweiten gepulsten Strahlungsbündels (B_2), das den Prüfbereich mit Sondenimpulsen periodisch bestrahlt, die periodische rückwärtige Streuungen von Strahlung verursachen, wobei das zweite gepulste Strahlungsbündel eine geringere Intensität aufweist als das erste gepulste Strahlungsbündel;
Erfassen der von dem ersten gepulsten Strahlungsbündel verursachten anfänglichen rückwärtigen Streuung und der von dem zweiten gepulsten Strahlungsbündel verursachten periodischen rückwärtigen Streuungen mit einem ersten Strahlungsdetektor und einem zweiten Strahlungsdetektor, wobei sich der erste Strah-

lungsdetektor und der zweite Strahlungsdetektor in unterschiedlichen Entfernungen von dem Prüfbereich von Gewebe befinden, sodass eine relative Amplitude zwischen den erfassten Streuungen berechnet und als Offset verwendet werden kann;
Umwandeln der erfassten rückwärtigen Streuungen in elektrische Signale; und
Bestimmen der Konzentration des Analysten als Reaktion auf die elektrischen Signale.

Revendications

1. Appareil de détermination d'une concentration d'un analyte dans un tissu, comprenant :

au moins une source de radiation (126, 128) permettant d'émettre un premier faisceau de radiation à impulsions (B_1) et au moins un second faisceau de radiation à impulsions (B_2), le premier faisceau de radiation à impulsions irradiant une surface d'essai (130) d'un tissu avec une impulsion d'excitation et provoquant une première diffusion de radiation (D_1), et l'au moins un second faisceau de radiation à impulsions ayant une intensité inférieure à celle du premier faisceau de radiation, puis irradiant périodiquement la surface d'essai avec des impulsions de sonde provoquant des secondes diffusions périodiques de radiation (D_2) ;
au moins un détecteur (132) comprenant un premier détecteur de radiation (332) et un second détecteur de radiation (334), le premier détecteur de radiation et le second détecteur de radiation étant configurés pour détecter la première diffusion de radiation et les secondes diffusions de radiation, et les détecteurs de radiation étant configurés pour convertir les diffusions détectées en signaux électriques, et le premier détecteur de radiation et le second détecteur de radiation étant situés à des distances différentes de la surface d'essai du tissu, permettant le calcul et l'utilisation, en tant que décalage, d'une amplitude relative entre les diffusions détectées ; et
un processeur (112) pour déterminer la concentration de l'analyte sur la base desdits signaux électriques.

2. Appareil selon la revendication 1, dans lequel :
les premier et second faisceaux de radiation à impulsions (B_1, B_2) ont des longueurs d'onde prédéterminées sélectionnées dans une bande d'absorption caractéristique de l'analyte dans un milieu prédéterminé.

3. Appareil selon la revendication 1, dans lequel :
les premier et second faisceaux de radiation à impulsions (B_1, B_2) ont des longueurs d'onde prédéterminées,
la longueur d'onde prédéterminée du premier faisceau de radiation correspondant à un pic d'une bande d'absorption de l'analyte dans un milieu prédéterminé, et le premier faisceau de radiation interagissant avec le tissu pour provoquer au moins un processus transitoire qui dépend de la concentration de l'analyte.

4. Appareil selon l'une quelconque des revendications précédentes, dans lequel les premier et second faisceaux de radiation à impulsions (B_1, B_2) ont la même longueur d'onde.

5. Appareil selon l'une quelconque des revendications 1 à 3, dans lequel les premier et second faisceaux de radiation à impulsions (B_1, B_2) ont des longueurs d'onde différentes.

6. Appareil selon la revendication 5, dans lequel un des premier et second faisceaux de radiation a une longueur d'onde qui est supérieure à un pic de bande d'absorption de l'analyte dans un milieu prédéterminé, et un des premier et second faisceaux de radiation à impulsions a une longueur d'onde qui est inférieure au pic de bande d'absorption de l'analyte dans un milieu prédéterminé.

7. Appareil selon l'une quelconque des revendications précédentes, dans lequel le premier faisceau de radiation à impulsions (B_1) excite au moins un processus transitoire périodique ou non périodique dans le tissu, et dans lequel au moins une des première et secondes diffusions de radiation est au moins en partie modulée par l'au moins un processus transitoire.

8. Appareil selon la revendication 7, dans lequel l'au moins un processus transitoire inclut des oscillations photoacoustiques.

9. Appareil selon la revendication 7 ou 8, dans lequel les signaux électriques représentent au moins un paramètre parmi l'amplitude, la fréquence ou la durée de suppression de l'au moins un processus transitoire.

10. Appareil selon l'une quelconque des revendications précédentes, dans lequel les premier et second faisceaux de radiation à impulsions comprennent des monoimpulsions ayant un délai entre les impulsions.

11. Appareil selon l'une quelconque des revendications 1 à 9, dans lequel le second faisceau de radiation à impulsions comprend des impulsions courtes sensiblement équidistantes d'une onde quasi-continue

(QCW) ayant un taux de répétition variable.

12. Appareil selon l'une quelconque des revendications 1 à 9, dans lequel le second faisceau de radiation à impulsions comprend un train d'impulsions ayant une fréquence variable, une puissance d'impulsion variable, une durée d'impulsion variable et un nombre d'impulsions variable.

13. Appareil selon l'une quelconque des revendications précédentes, dans lequel les premier et second faisceaux de radiation à impulsions sont focalisés sur sensiblement le même point de la surface d'essai.

14. Appareil selon la revendication 1, comprenant en outre une des caractéristiques suivantes :

le premier faisceau de radiation à impulsions a une puissance d'environ 1 à 10 W ;
le premier faisceau de radiation à impulsions a une puissance d'environ 5 W ;
le premier faisceau de radiation à impulsions a une longueur d'onde d'environ 1550 nm ;
le second faisceau de radiation à impulsions a une puissance d'environ 0,1 à 1 W ;
le second faisceau de radiation à impulsions a une puissance d'environ 0,25 à 0,5 W ;
le second faisceau de radiation à impulsions a une longueur d'onde d'environ 1610 nm à 1690 nm ;
l'au moins une source de radiation comprend une diode laser à impulsions ;
l'au moins une source de radiation comprend un réseau de lasers à diode couplés à une fibre ;
l'au moins une source de radiation comprend un laser à fibre optique à impulsions ;
l'au moins une source de radiation comprend une tige de verre d'erbium ou un laser en plaques pompé par des lasers à diode ou une lampe-éclair ;
l'au moins une source de radiation comprend un laser Co:MgF2 accordable ;
l'au moins une source de radiation comprend un laser déclenché à milieu optique contenant du néodyme, et assurant une génération d'ondes quasi-continues donnant de courtes impulsions équidistantes ayant une durée, une fréquence, un nombre et une puissance variables ; et
l'analyte est du glucose.

15. Procédé de détermination d'une concentration d'un analyte dans un tissu, comprenant les étapes consistant à :

irradier une surface d'essai (130) d'un tissu avec au moins une source de radiation (126, 128) émettant un premier faisceau de radiation à impulsions (B_1) en tant qu'impulsion d'excitation provoquant une rétrodiffusion initiale de radiation, puis émettant un second faisceau de radiation à impulsions (B_2) irradiant périodiquement la surface d'essai avec des impulsions de sonde provoquant des rétrodiffusions périodiques de radiation, le second faisceau de radiation à impulsions ayant une intensité inférieure à celle du premier faisceau de radiation à impulsions ;
détecter la rétrodiffusion initiale provoquée par le premier faisceau de radiation à impulsions et les rétrodiffusions périodiques provoquées par le second faisceau de radiation à impulsions avec un premier détecteur de radiation et un second détecteur de radiation, le premier détecteur de radiation et le second détecteur de radiation étant situés à des distances différentes de la surface d'essai du tissu, permettant le calcul et l'utilisation, en tant que décalage, d'une amplitude relative entre les diffusions détectées ;
convertir les rétrodiffusions détectées en signaux électriques ; et
déterminer la concentration de l'analyte en réponse auxdits signaux électriques.

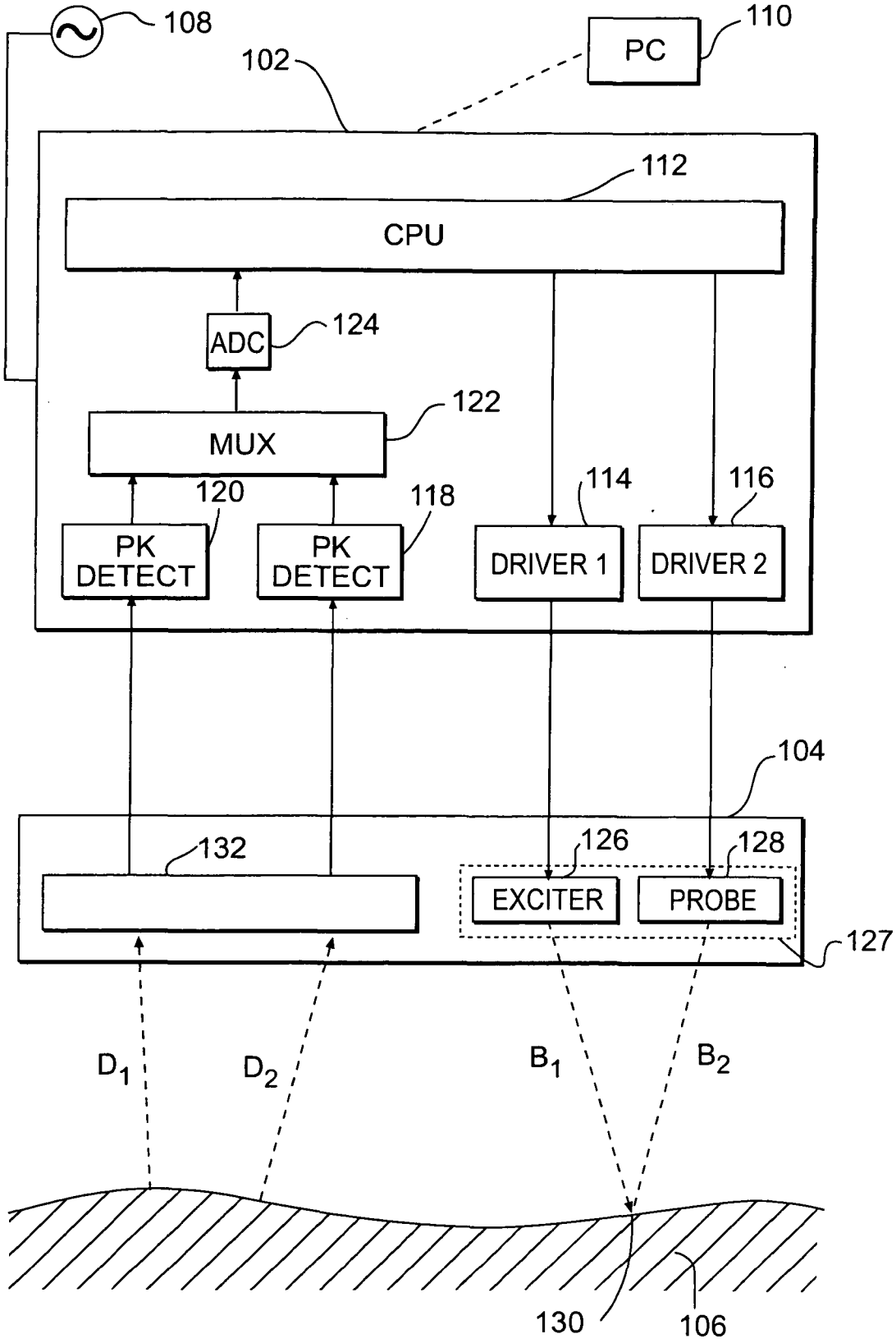
108
102
PC
110
112
CPU
ADC
124
MUX
122
120
118
114
116
PK DETECT
PK DETECT
DRIVER 1
DRIVER 2
104
132
126
128
EXCITER
PROBE
127
D1
D2
B1
B2
130
106

FIG. 1

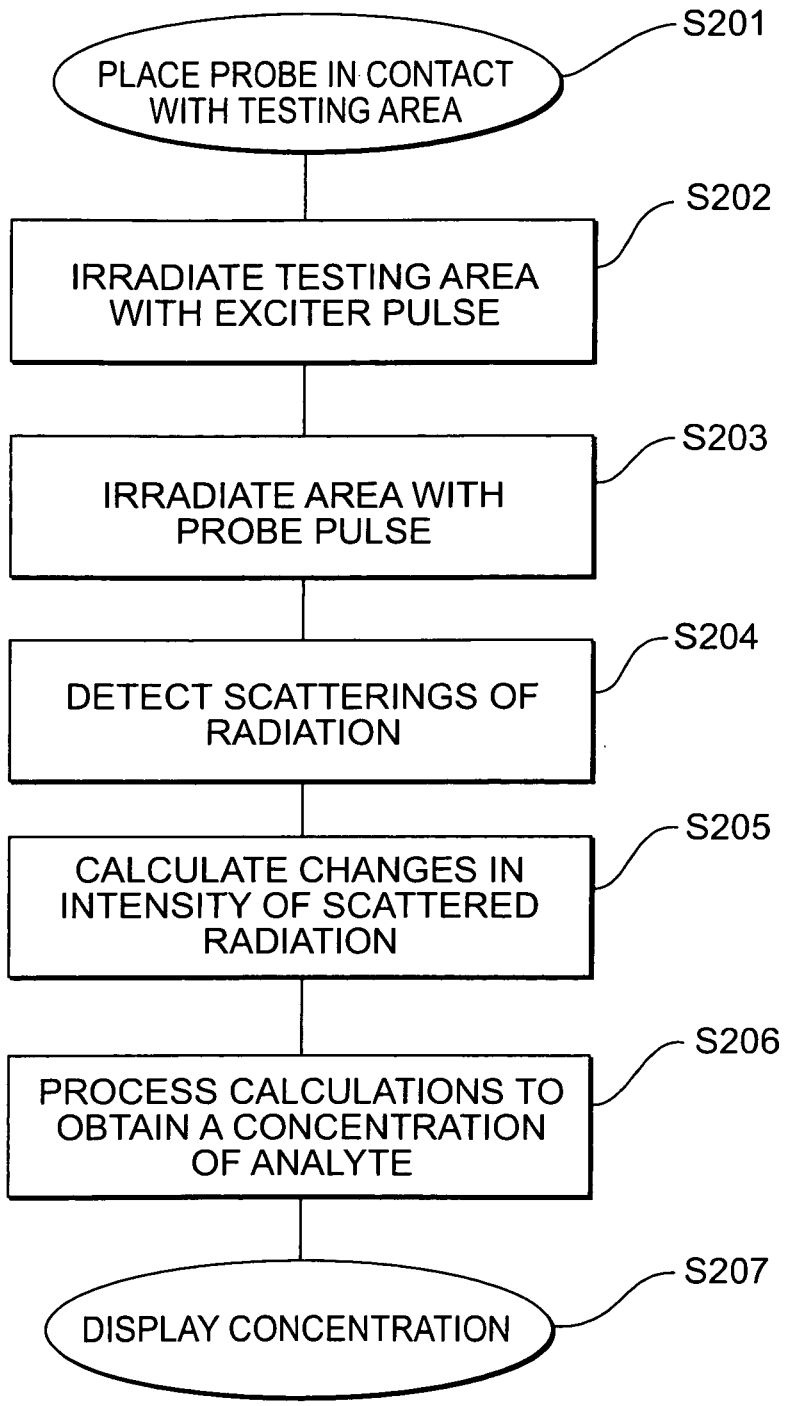
S201
PLACE PROBE IN CONTACT WITH TESTING AREA
S202
IRRADIATE TESTING AREA WITH EXCITER PULSE
S203
IRRADIATE AREA WITH PROBE PULSE
S204
DETECT SCATTERINGS OF RADIATION
S205
CALCULATE CHANGES IN INTENSITY OF SCATTERED RADIATION
S206
PROCESS CALCULATIONS TO OBTAIN A CONCENTRATION OF ANALYTE
S207
DISPLAY CONCENTRATION

FIG. 2

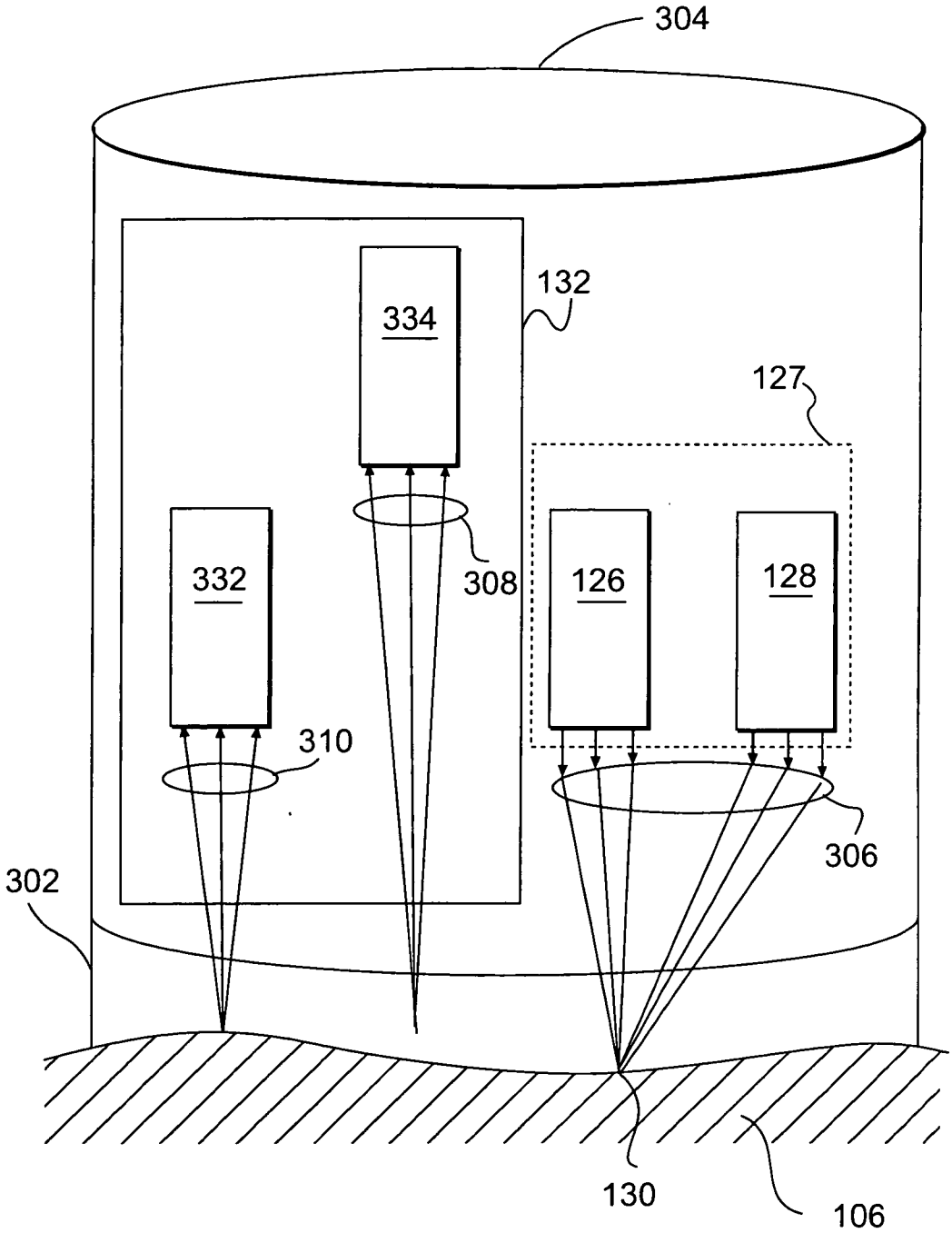

FIG. 3

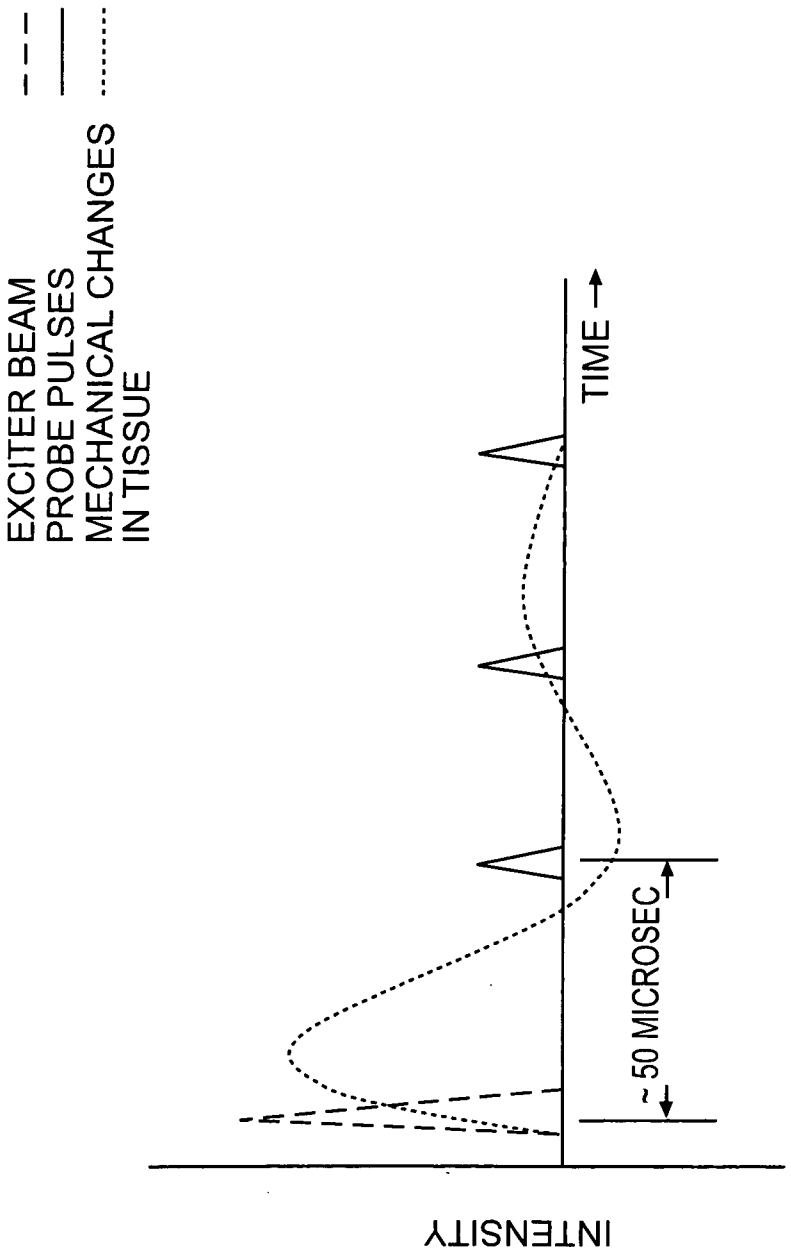
EXCITER BEAM
PROBE PULSES
MECHANICAL CHANGES
IN TISSUE
TIME
~ 50 MICROSEC
INTENSITY

FIG. 4

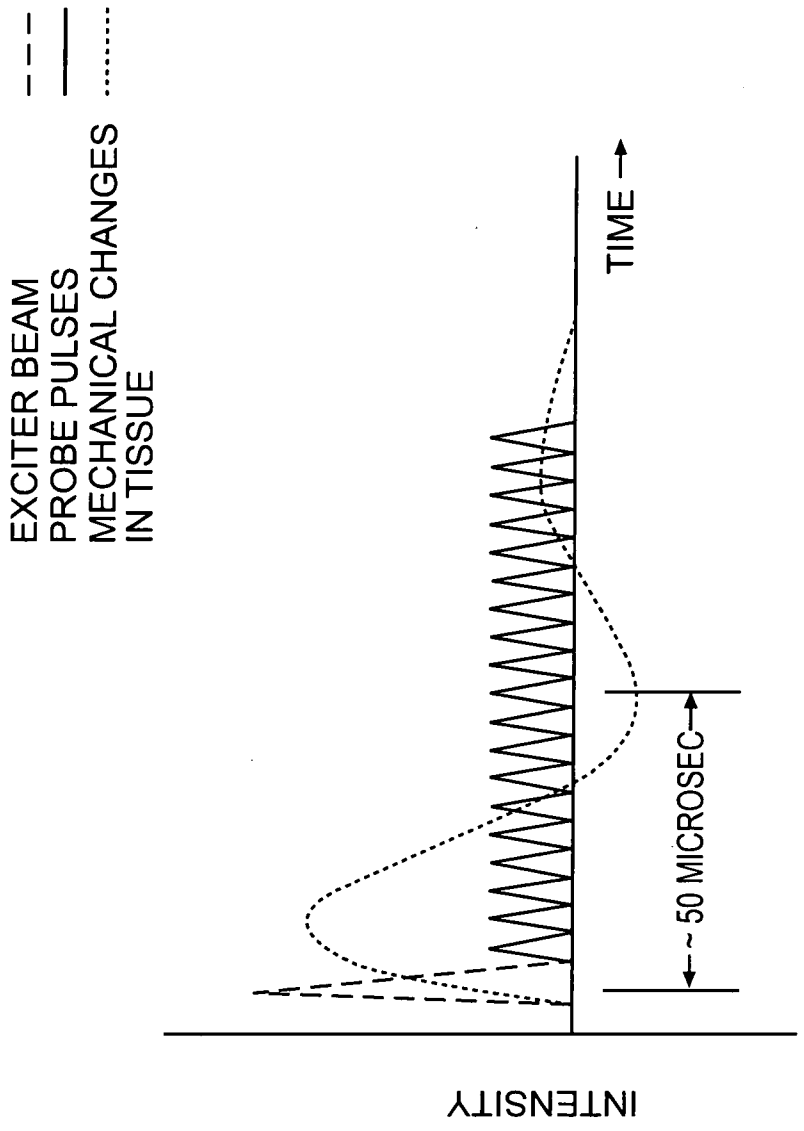
EXCITER BEAM
PROBE PULSES
MECHANICAL CHANGES
IN TISSUE
TIME
~ 50 MICROSEC
INTENSITY

FIG. 5

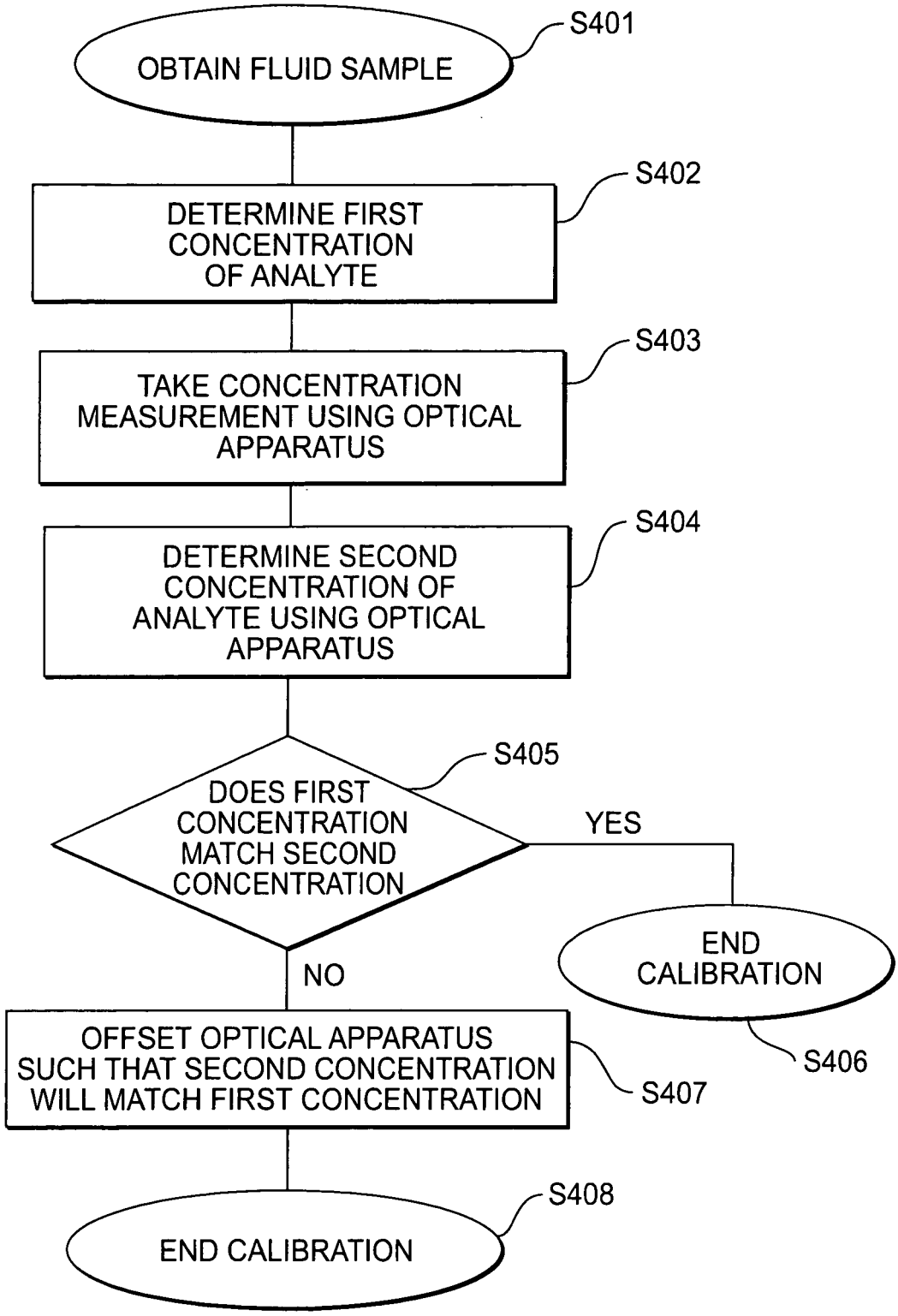
OBTAIN FLUID SAMPLE
S401
DETERMINE FIRST CONCENTRATION OF ANALYTE
S402
TAKE CONCENTRATION MEASUREMENT USING OPTICAL APPARATUS
S403
DETERMINE SECOND CONCENTRATION OF ANALYTE USING OPTICAL APPARATUS
S404
DOES FIRST CONCENTRATION MATCH SECOND CONCENTRATION
S405
YES
NO
END CALIBRATION
S406
OFFSET OPTICAL APPARATUS SUCH THAT SECOND CONCENTRATION WILL MATCH FIRST CONCENTRATION
S407
END CALIBRATION
S408

FIG. 6

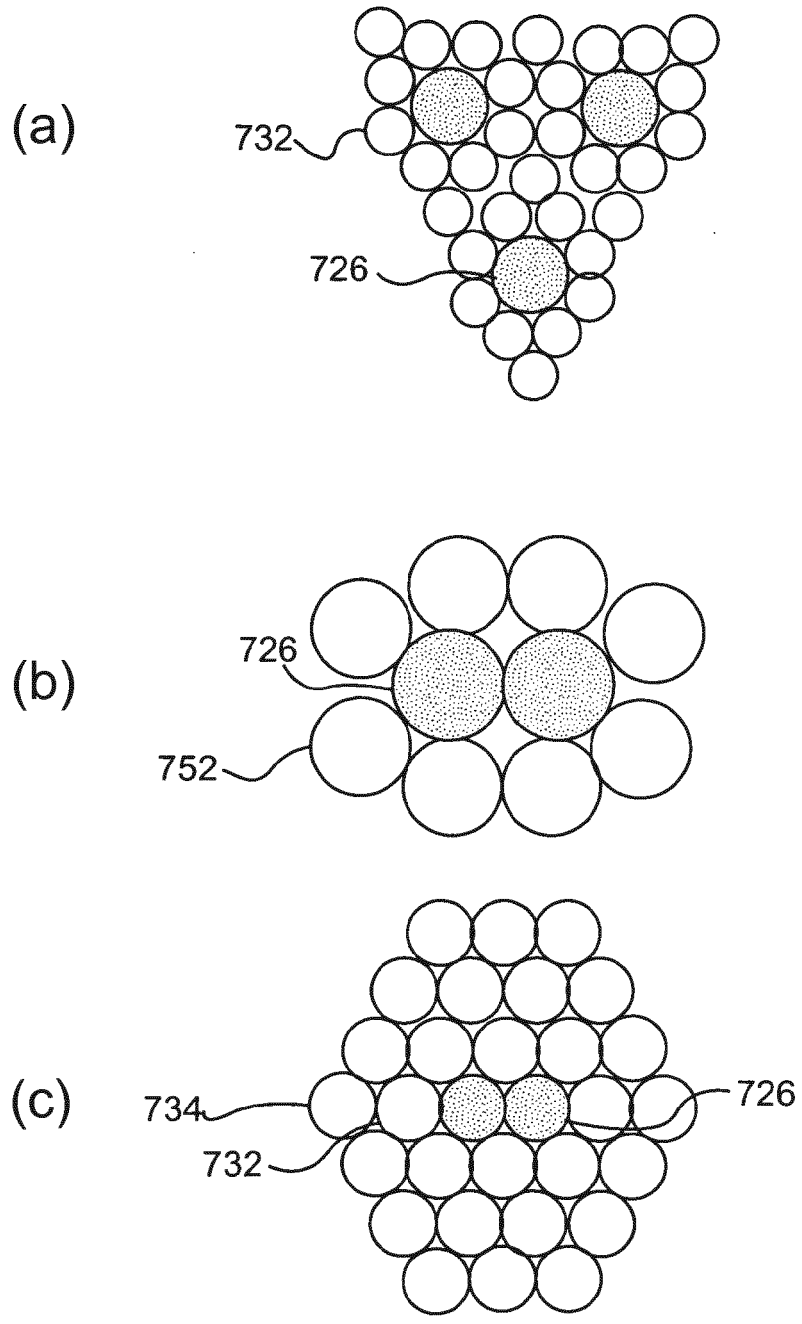

FIG. 7

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

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- US 6049728 A **[0010]**
- US 6833540 B, MacKenzie **[0011]**
- US 6466806 B, Geva **[0013]**
- WO 9702781 A **[0015]**

专利名称(译)	用于确定分析物浓度的光学传感器		
公开(公告)号	EP2207474B1	公开(公告)日	2018-08-22
申请号	EP2008846768	申请日	2008-10-31
申请(专利权)人(译)	生物传感器，INC.		
当前申请(专利权)人(译)	生物传感器，INC.		
[标]发明人	SCHULTZ PETER AMOSOV ARKADY IZVARINA NATALIA KRAVETZ SERGEY		
发明人	SCHULTZ, PETER AMOSOV, ARKADY IZVARINA, NATALIA KRAVETZ, SERGEY		
IPC分类号	G01N21/49 G01N21/17 A61B5/00 A61B5/1455 A61B5/145		
CPC分类号	A61B5/0059 A61B5/14532 A61B5/1455 A61B5/7239 G01N21/1717 G01N21/49 G01N2021/1725		
优先权	61/001960 2007-11-05 US		
其他公开文献	EP2207474A2		
外部链接	Espacenet		

摘要(译)

提供了一种使用光学激发和检测来非侵入性地确定受试者中葡萄糖浓度的方法和装置。该方法包括发射激励束（B1）以照射对象的组织的一部分（130），引起表面的物理和化学变化，并引起光的初始反向散射（D1）。该方法还包括周期性地发射探测光束（B2），该探测光束照射组织的一部分并引起光的周期性后向散射（D2）。检测初始和周期性后向散射并将其转换成至少物理和化学变化的幅度，频率或衰减时间的电信号，后向散射由物理和化学变化调制。通过随时间区分物理和化学变化的幅度，频率或衰减时间中的至少一个，可以确定葡萄糖的浓度。

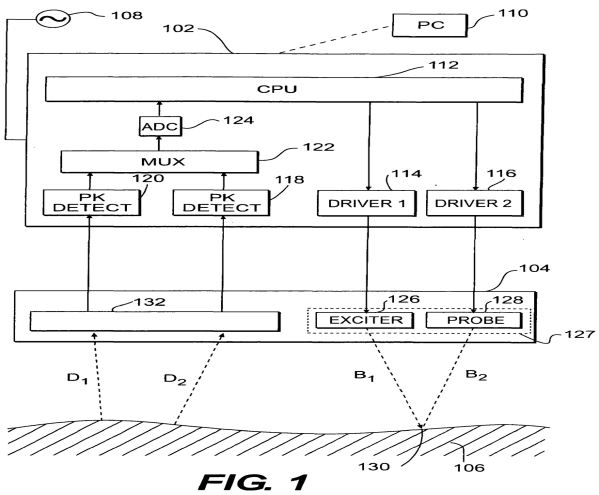

FIG. 1