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(71) Applicant *(for all designated States except US)*: **GLUCO-LIGHT CORPORATION** [US/US]; 115 Research Drive, Bethlehem, PA 18015 (US).

(72) Inventor: **SHURMAN, MATTHEW, J.**; 139 Hickory Road, Somerset, NJ 08873 (US).

(74) Agent: **BOOKS, GLEN, E.**; Lowenstein Sandler PC, 65 LIvingston Avenue, Roseland, NJ 07068 (US).

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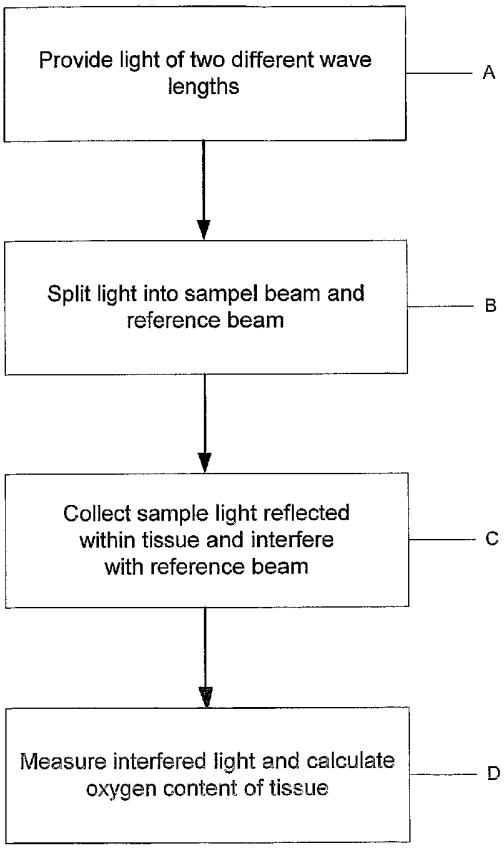
(54) Title: METHOD AND APPARATUS FOR TISSUE OXIMETRY



(57) Abstract: In accordance with the invention, the oxygenation of blood-profused tissue is measured by shining light into the profused tissue and analyzing the light reflected within the tissue. The light is reflected by cell walls in the tissue and is partially absorbed by hemoglobin in the blood. Since the extent of absorption is sensitive to the extent of hemoglobin oxygenation, measurement and processing of the reflected light provides a measure of the oxygenation of the blood. In one embodiment, the method is applied to measure the oxygenation of blood within the tympanic membrane (ear drum).

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METHOD AND APPARATUS FOR TISSUE OXIMETRY

Inventor: Matthew J. Schurman

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 60/485,761 filed by Matthew J. Schurman on July 9, 2003 and entitled *Method and Apparatus For Brain Oximetry*, which application is incorporated herein by reference.

FIELD OF THE INVENTION

The invention pertains to a method and apparatus for measuring the oxygenation of blood-profused biological tissue (tissue oximetry), and more specifically to a method and apparatus for tissue oximetry using low coherence interferometry or optical coherence tomography.

BACKGROUND OF THE INVENTION

Transmission pulse oximetry has long been used in the clinical setting to measure the oxgenation of blood. (See, T. L. Rusch et al, Computers in Biology and Medicine, 26, 143-159, (1996)). In a typical transmission pulse oximetry, two light emitting diodes (LEDs) with peak wavelengths of 660 nm and 940 nm are shone through one side of a finger, and the transmitted light is received via a photodetector positioned on the other side of the finger. The first LED has peak absorption for oxygenated hemoglobin (oxyhemoglobin). The second LED has peak absorption for deoxygenated hemoglobin (reduced hemoglobin or deoxyhemoglobin). As the heart beats, the time varying absorbance signal is recorded. The transmitted light will obey the Beers-Lambert law (Beers law) given by:

$$I_{trans} = I_{in} e^{-DC\alpha},$$

where: I_{trans} is the intensity of the transmitted light, I_{in} is the intensity of initial light, D is the distance the light travels, C is the concentration of the solution, and α is the absorption cross-section of the absorbing species. Fig. 1 graphically illustrates a typical transmission pulse oximetry signal.

In transmission pulse oximetry, hemoglobin is assumed to be composed of two substances: oxyhemoglobin and reduced hemoglobin. Since both species have different absorption cross-sections at the two differing wavelengths, the percentage of each substance in the blood can be calculated.

There are, however, several drawbacks to transmission pulse oximetry. First, it can only be applied to parts of the body where the optical signal can pass from one side of a body part to another side (such as through a finger on an adult, or through a foot on a newborn). Thus, the technique is limited to measuring oxygen saturation at the extremities. In the case of many major surgeries or in the case of trauma, the saturation of blood in the extremities does not reflect the saturation of oxygen at major organs such as the brain. Second, because transmission pulse oximetry relies on transmission through extremities, bright lights can saturate the detector so that the LED signals cannot be read. Third, the technique relies upon the pulsatile signal generated by the beating of the heart. If the blood profusion is low, the pulsatile signal will be small in relation to a baseline DC signal, which can lead to errors in the calculation of the oxygen saturation. Fourth, because the path lengths of the optical signals are not known in pulse transmission oximetry, only the oxygen saturation, and not the actual oxygen level of the blood, can be measured. Accordingly, there is a need for an improved method and apparatus for measuring the oxygenation of blood-profused biological tissue.

SUMMARY OF THE INVENTION

In accordance with the invention, the oxygenation of blood-profused tissue is measured by a method of comprising shining light into the profused tissue and analyzing the light reflected within the tissue. The light is reflected by cell membranes in the tissue and is partially absorbed by hemoglobin in the blood. Since the extent of absorption is sensitive to the extent of hemoglobin oxygenation, measurement and processing of the reflected light provides a measure of the oxygenation of the blood. In one embodiment, the method is applied to measure the oxygenation of blood within the tympanic membrane (ear drum).

Apparatus for measuring the oxygenation of blood-profused tissue comprises one or more light sources to provide light at wavelengths where absorption is sensitive to hemoglobin oxygenation. Light from the sources is directed into the blood-profused tissue, and the light reflected within the tissue is collected, analyzed and measured by an interferometer. A processor responsive to the light measurements then calculates the oxygenation level of the blood-profused tissue. Advantageously, the apparatus uses low coherence light emitting diodes (LEDs) or super luminescent diode light sources (SLEDs) and a low coherence interferometer (LCI).

BRIEF DESCRIPTION OF THE FIGURES

The advantages, nature and various additional features of the invention will appear more fully upon consideration of the illustrative embodiments now to be described in detail in connection with the accompanying drawings. In the drawings:

FIG. 1 shows a typical pulse oximetry signal;

FIG. 2 is a schematic diagram of a method of tissue oximetry in accordance with the invention;

FIG. 3 schematically illustrates apparatus useful for practicing the method of Fig. 2; and

FIG. 4 illustrates one embodiment of the Fig. 3 apparatus where a probe is inserted in an ear for providing a measure of brain oximetry.

It is to be understood that the drawings are for the purpose of illustrating the concepts of the invention, and except for the graphs, are not to scale.

DETAILED DESCRIPTION OF THE INVENTION

The invention is directed to devices and methods for measuring the oxygenation of blood-profused biological tissue. More specifically, the invention uses an interferometry technique, such as low coherence interferometry (LCI), optical coherence domain reflectometry (OCDR) or optical coherence tomography, to measure the oxygenation level of blood-profused biological tissue. The invention includes devices and methods of tissue oximetry which illuminate the blood-profused tissue (target tissue) with light, analyze the reflected light to measure hemoglobin absorption, and determine oxygenation from the absorption. In one embodiment, an interferometer is used to measure the reflection of light from an object. An interferometer is an instrument in which light from a source is split into two or more beams which are subsequently reunited after traveling over different paths and display interference.

Any well-known interferometer may be used in the invention. Suitable interferometers for use in the invention include, but are not limited to Michelson interfermeters and Mach-Zehnder interferometers. A preferred apparatus uses an interferometer with low coherence light sources to measure reflection of low coherence light from the tissue.

Due to the low optical coherence of the source, the interferogram can only be generated over a small volume whose position in the depth of the object is determined via the position of the reference mirror. Thus a high degree of localization of the measured scattering phenomena can be achieved. For example, for a typical light emitting diode (LED) operating at a 1.3 μm wavelength, a depth resolution of 10 μm is easily achieved in biological tissues. This has been adapted for use in high resolution imaging applications (J. M. Schmitt, IEEE Journal of Quantum Electronics, 5, 1205-1214 (1999)). Typically in biological tissues the scatter of the light occurs at the interface between the cell membrane and the fluid that surrounds the cell (i.e. blood or interstitial fluid).

Referring to the drawings, Fig. 2 is a schematic block diagram of an exemplary method of performing tissue oximetry on a human or animal subject. The first step, shown in Block A, is to provide light of at least two different wavelengths,. The two different wavelengths should have measurably different absorption and reflectivity from oxygenated and deoxygenated hemoglobin, respectively. Typically the light is provided from two or more sources such as low coherence LEDS at 660 nm and 940 nm. Alternatively it could be provided from a single multiwavelength source or from a single broadband source appropriately notch filtered. The light is advantageously directed in a single beam.

The next step, Block B, is to split the light into a sample beam and a reference beam; directing the sample beam toward the tissue of the subject to illuminate the tissue and directing the reference beam over an adjustable phase path.

The third step of Block C is to collect sample light reflected from within the illuminated tissue and to interfere the reflected light with reference beam light from the adjustable phase path.

The final step (Block D) is to measure the constructively interfered light at the different wavelengths and to process the measurements to provide a measurement of the oxygen content of hemoglobin in the tissue.

Figure 3 schematically shows exemplary apparatus **300** for practicing the method of Fig. 1. The apparatus **300** comprises a fiber optics-based low coherence interferometer (LCI). A 2 x 2 fiber optic splitter **301** forms the basic interferometer. An optical input from light source **306** is split between a sample arm **302** and a reference arm **304**. Reflected signals from arms **302** and **304** interfere and are presented to photodetector **307** for measurement. Preferably, the end of the sample arm **302** can contain imaging optics **303** to tailor the spot size according to the tissue being measured. Advantageously, imaging optics **303** can provide high coupling efficiency between the optical system and the tissue.

The tissue volume with which the light interacts (referred to as the interaction volume) is determined by the spot size of the imaging optics (surface area) and the coherence length of the light (depth) Reference arm **304** of the interferometer determines the phase shift applied to the reference beam and thus which reflected light from the sample will constructively interfere with the shifted reference beam. The reference arm **300** thus determines the depth within the interaction volume from which scattered light will be measured. The arm **304** can have either a fixed or scanning reflector **305** (such as a mirror). This can allow for a fixed sensor depth, adjustable sensor depth, or scan of multiple depths within the tissue. LCI is thus sensitive to the intensity of the reflected light localized in a small volume of tissue. Determination of the depth and interaction volume permits more accurate calculation of both the oxygen concentration and the oxygen saturation of the blood.

Light passing through turbid biological tissue is subject to wavefront distortion that produces coherent noise or "speckle". The use of two different wavelengths helps to reduce the effect of speckle. In addition is it advantageous to rapidly change the

interaction region being illuminated as by vibrating the illumination fiber or vibrating a lens directing the illumination beam. Such change reduces the random effect of speckle by spatial averaging.

The effect of speckle is also minimized by appropriate processing of the reflected light. Appropriate processing measures the envelope of the interferogram which contains the intensity information with speckle averaged out (as opposed to measuring absorption from the interferogram itself which would have full speckle noise). Further details concerning such processing are described in "Speckle in Optical Coherence Tomography", J. Biomed. Optics, January 1999, pp. 95-105.

The light source **306** can be a light emitting diode (LED) or a super luminescent diode (SLED), both of which are semiconductor based light emitters whose wavelengths can be chosen to give the best contrast in absorption between oxygenated and deoxygenated hemoglobin. Typically these wavelengths are in the red / near infrared (RNIR) region of the spectrum (600 nm to 1600 nm) however, longer and shorter wavelengths can be used for enhanced sensitivity. A unique property of these sources is a wide (>10nm) spectral bandwidth upon which the low coherence measurement can be based. For the oximetry measurements, two or more light sources are advantageous and can share the same optical paths through the interferometer.

One of the wavelengths can be chosen to have peak absorption for oxygenated hemoglobin e.g. 940 nm; the other wavelength can be chosen to have peak absorption for deoxygenated hemoglobin e.g. 660 nm. Light of the two wavelengths is differently absorbed by the respective hemoglobin species. This differential absorption differentially reduces the intensity of the scattered (reflected) light. Light reflected off the cellular membrane is partially absorbed by the respective hemoglobin species for that wavelength. Where the term "light is reflected from the blood" is used, it is understood to refer to light reflected from the cells in and around the blood vessels and the

hemoglobin in the blood absorbs some of the light according to the wavelength and oxygenation of the blood.

Finally a photodetector **307** (such as a photodiode) can be used to measure the interference of the light from both the sample arm **303** and the reference arm **305**. One or more photodetectors **307** may be used along with optical filters (not shown) designed for each of the light sources **306** used in the measurement.

For oximetry, the phase adjusting path of the interferometer may be set to correspond to a fixed depth within tissue comprising blood or a depth profile comprising blood may be scanned. If a depth profile can be scanned, however, the rate of the scan needs to be sufficiently high in order to collect multiple depth scans along a typical heart beat (see Fig. 1). The heart typically beats at 60 beats / minute, however this rate can climb as high as 200 beats / minute. This implies that a minimum of 7 depth scans per second can be needed to satisfy the Nyquist condition for approximating analog signals via digital signal processing. By measuring the intensity of the resulting backscatter signal envelopes, at the different wavelengths, the concentration of oxygenated hemoglobin can be determined utilizing the same well known algorithms that are used in standard transmission pulse oximetry.

As one exemplary application, it is notoriously difficult to measure the oxygenation of blood feeding the brain. The apparatus of Fig. 3 can make such challenging measurements. There should be substantial equivalence between the oxygenation of tympanic blood with the oxygenation of the blood that feeds the brain. The invention can measure the oxygenation of tympanic membrane blood, to determine the oxygenation of blood in the brain (brain oximetry). In the case of brain oximetry, as shown in Fig. 4, the optics head **405** can be placed in the ear **401** near the tympanic membrane **402** (ear drum). This can be achieved by threading the optics head **405** through an earplug **404** that can then be placed in the ear canal **403** in proximity to the tympanic membrane. Optical fiber **406** connects the optics head to the splitter. The

reference arm delay can be adjusted to get the strongest absorption profile so that the surface reflections are being collected from the tympanic membrane by probe **405** (comprising the sample arm). The fixed depth, or depth scan, can then be set from this base line.

It can now be seen that the invention includes a tissue oximetry method comprising the steps of illuminating tissue containing blood with light, analyzing the reflected light to measure hemoglobin absorption, and determining oxygenation from the absorption. In an advantageous embodiment, light reflected from the tympanic membrane is interfered with reference light and the interfered reflected light is measured and processed to provide a measure of the oxygenation of the blood flowing into the brain. Preferably the light reflected within the blood is measured by low coherence interferometry.

In a preferred embodiment, the method comprises the steps of providing a low coherence interferometer having a sample arm, a reference arm, a reference arm reflector and one or more detectors. Light of first and second wavelengths is provided for illuminating both the sample arm and the reference arm reflector. The sample arm is used as a probe to illuminate blood-profused tissue and to sample the light reflected from the tissue. The light reflected from the tympanic membrane is interfered with the light from the reference arm reflector to select the light reflected within the blood, and the constructively interfered light is detected and processed to yield a measurement of tissue oxygenation. The processing can be done by a computer. Also, the reference arm can be phase adjusted for the strongest absorption profile.

In another embodiment, an apparatus for tissue oximetry of an animal or human subject comprises one or more sources of light providing light at two different wavelengths whose absorption in hemoglobin is sensitive to hemoglobin oxygenation. Light guides direct a beam of light from the sources onto blood-profused tissue of the subject and also serve to receive light reflected from within the tissue. An interferometer

interferes the reflected light with a phase adjusted sample of the beam, the phase adjustment chosen to select by constructive interference, the light reflected from blood within the tissue. One or more photodetectors measure the constructively interfered light; and a processor (computer or microprocessor) determines the oxygenation of the blood from the measurements.

The apparatus can comprise a low coherence interferometer. The interferometer can comprise a beam splitter for splitting the light into a sample beam and a reference beam, light guides for directing a beam of light from the sources onto the tissue and for receiving light reflected from within the tissue, and light guides for directing a sample of the light from the sources to a reference arm and reference reflector.

Further, the splitter can be a 2X2 optical splitter. The reflector can be a mirror. And, the reference arm delay can be phase adjustable. The photodetector can comprise a photodiode. And, the light source can be a light emitting diode (LED), or a super luminescent diode (SLED).

It is understood that the above-described embodiments are illustrative of only a few of the many possible specific embodiments, which can represent applications of the invention. Numerous and varied other arrangements can be made by those skilled in the art without departing from the spirit and scope of the invention.

We claim:

1. A method of tissue oximetry on a human or animal subject comprising the steps of:

providing light of at least two different wavelengths, the light of the two wavelengths having different absorption and different reflectivity from oxygenated hemoglobin and deoxygenated hemoglobin, respectively;

splitting the light into a sample beam and a reference beam;

illuminating tissue of the subject with the sample beam;

collecting reflected light from within the illuminated tissue;

interfering the reflected light with reference light from the reference beam; and

measuring the interfered light and processing the measurements to determine the oxygen content of hemoglobin in the tissue.

2. The method of claim 1 wherein the light is provided by one or more low coherence sources.

3. The method of claim 2 wherein the reference light is adjusted in phase to constructively interfere with reflected light that is reflected from within the tissue.

4. The method of claim 1 further comprising the step of moving the sample beam to vary the region of the tissue being illuminated so as to reduce the effect of speckle.

5. A method of tissue oximetry on a subject comprising the steps of:

providing a low coherence interferometer comprising a sample arm, a sample arm probe coupled to the sample arm, a reference arm, a reference arm reflector and one or more detectors;

providing a light source for illuminating tissue of the subject and the reference arm;

positioning the sample arm probe, to sample the light reflected from within the tissue;

interfering light reflected from the tissue and light from the reference arm reflector to select light reflected within tissue comprising blood; and

detecting and processing the interfered light to yield a measurement of blood oxygenation.

6. The method of claim 5 wherein processing comprises processing by computer or microprocessor.

7. The method of claim 5 further comprising the step of increasing the absorption profile by adjusting the pathlength of the reference arm.

8. An apparatus for tissue oximetry of an animal or human subject comprising:

one or more sources of light to provide light at two different wavelengths that respectively absorb and reflect differently from oxygenated hemoglobin;

a first light path to direct a beam of light from the sources onto the tissue of the subject and to receive reflected light from the tissue;

a second light path to direct a beam of reference light from the sources through a phase adjuster;

an interferometer to interfere the reflected light with the phase adjusted reference light, the phase adjustment of the reference light chosen to select by constructive interference, the light reflected from tissue comprising blood;

one or more photodetectors to measure the interfered light; and

a processor to determine the oxygenation of the blood from the measurements,.

9. The apparatus according to claim 8 wherein the sources are low coherence sources and the interferometer comprises a low coherence interferometer.

10. The apparatus according to claim 8 wherein the interferometer comprises:

a beam splitter to split the light into a sample beam and a reference beam, sample light guides to direct a beam of light from the sources onto the tissue of the subject and to receive light reflected from within the tissue, and a reference light path to direct the reference beam into interference with the reflected light.

11. The apparatus of claim 8 wherein the beam splitter comprises a 2X2 optical splitter.

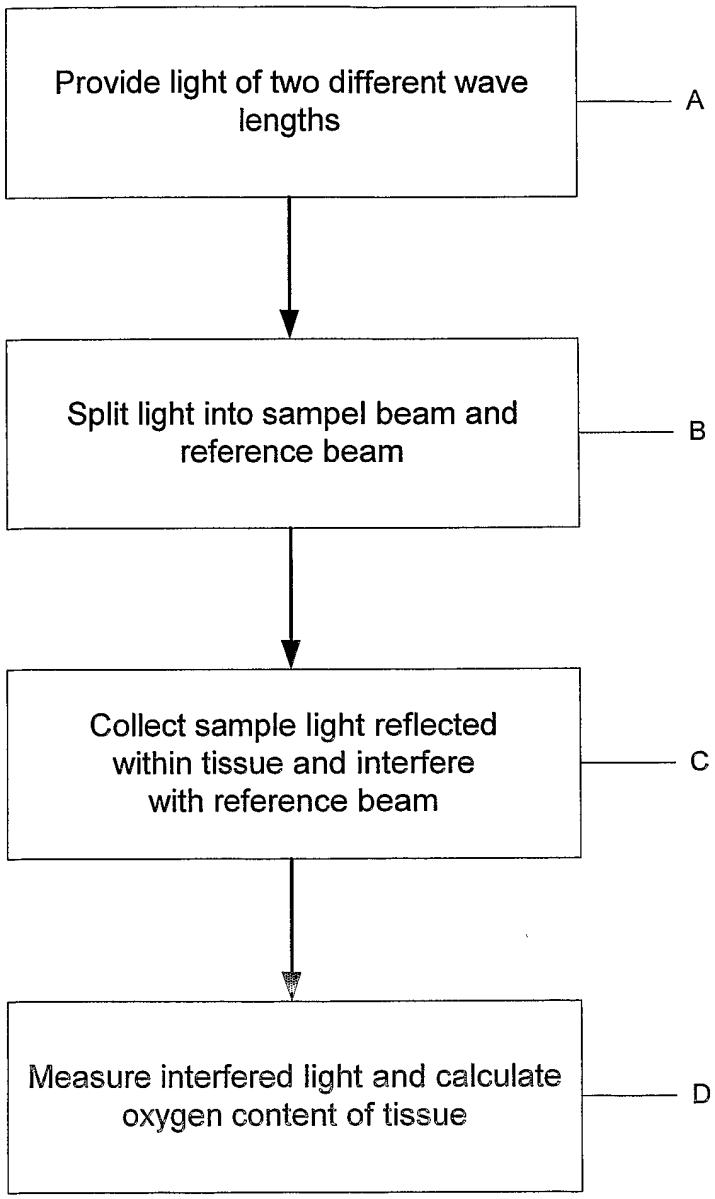
12. The apparatus of claim 8 wherein the reference light path comprises a reflector to adjust the path length.

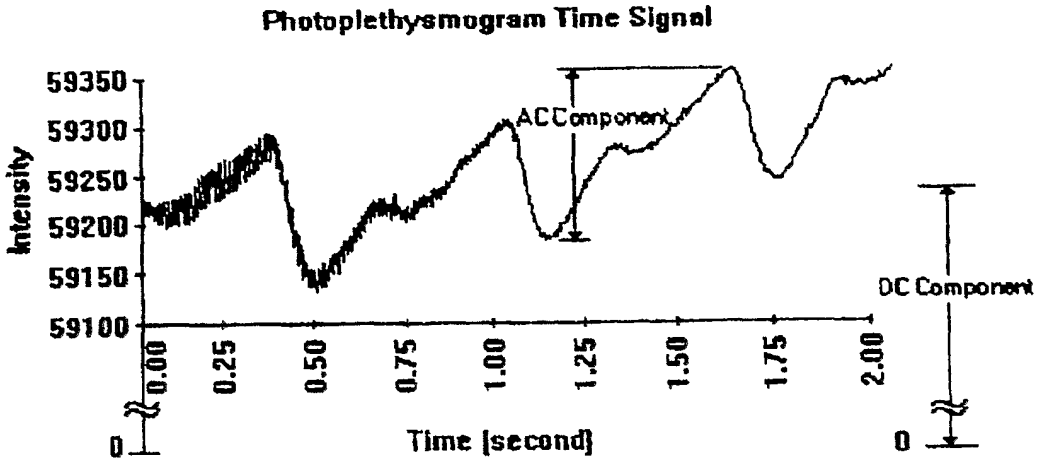
13. The apparatus of claim 8 further comprising a photodetector to measure the interfered light.

14. The apparatus of claim 13 where the photodetector comprises a photodiode.

15. The apparatus of claim 8 wherein at least one light source comprises a light emitting diode (LED) or a superluminescent diode (SLED)..

Fig. 1


Provide light of two different wave lengths
A
Split light into sampel beam and reference beam
B
Collect sample light reflected within tissue and interfere with reference beam
C
Measure interfered light and calculate oxygen content of tissue
D


Photoplethysmogram Time Signal
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59300
59250
59200
59150
59100
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0.00
0.25
0.50
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1.00
1.25
1.50
1.75
2.00
Time (second)
AC Component
DC Component
0

Fig. 2

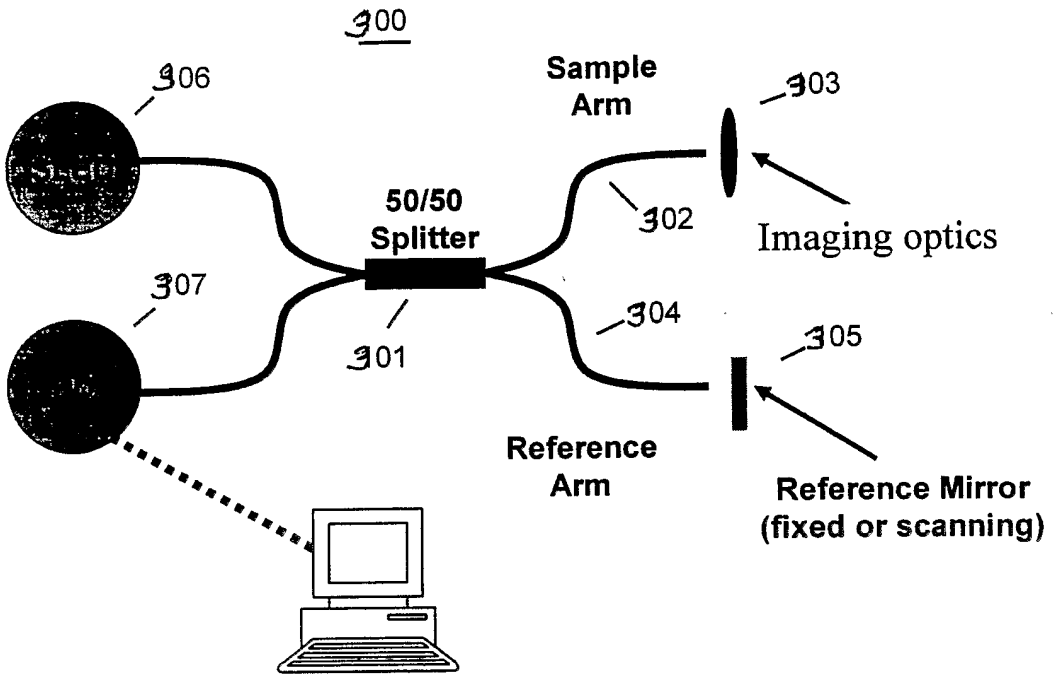
300
306
Sample
Arm
303
50/50
Splitter
302
Imaging optics
307
304
305
301
Reference
Arm
Reference Mirror
(fixed or scanning)

Fig. 3

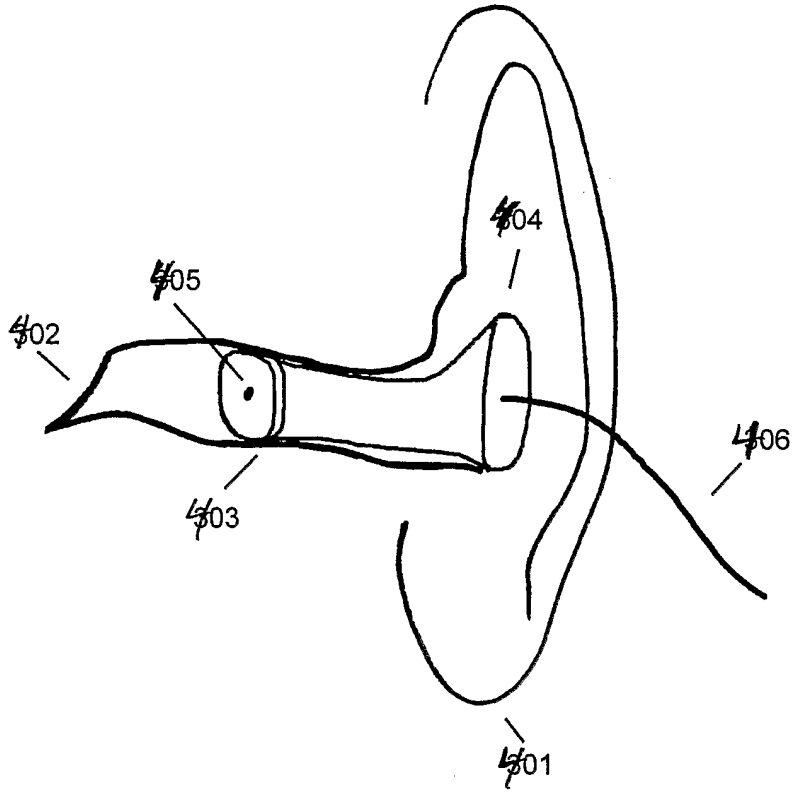

Fig. 4