United States Patent [19]

Chance

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[54] **PHASE MODULATED SPECTROPHOTOMETRY**

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[73] Assignee: **Nim, Inc.**, Philadelphia, Pa.

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[22] Filed: **Feb. 6, 1989**

[51] **Int. Cl.**[5] **G06F 15/00**; A61B 5/00

[52] **U.S. Cl.** **364/550**; 128/633; 364/413.09

[58] **Field of Search** ..... 364/413.09, 497, 554, 364/575, 525, 550; 356/318, 319, 39, 40, 346, 333; 250/213 VT, 281; 455/611, 612; 128/633, 634, 637

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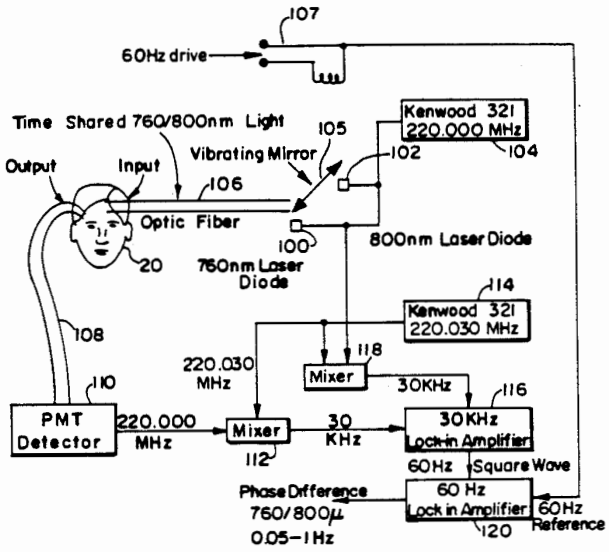
[57] **ABSTRACT**

The present invention to provides methods and apparatus for studying photon migration using signal modulation techniques such as time, frequency and phase modulation. The photon migration data may then be converted, using the principles of time-resolved spectroscopy, to determine the concentration of an absorptive constituent in a scattering medium, such as the concentration of hemoglobin in a brain of other tissue. The methods and apparatus of the present invention provide as a specific embodiment, a dual wavelength phase modulation system which allows the clinical application of time resolved spectroscopy in a commerically feasible embodiment.

16 Claims, 3 Drawing Sheets



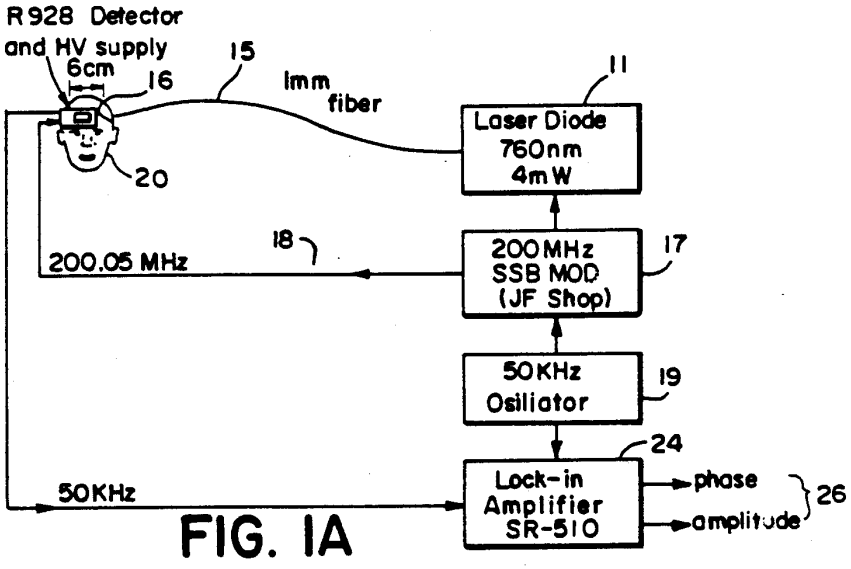


FIG. 1A

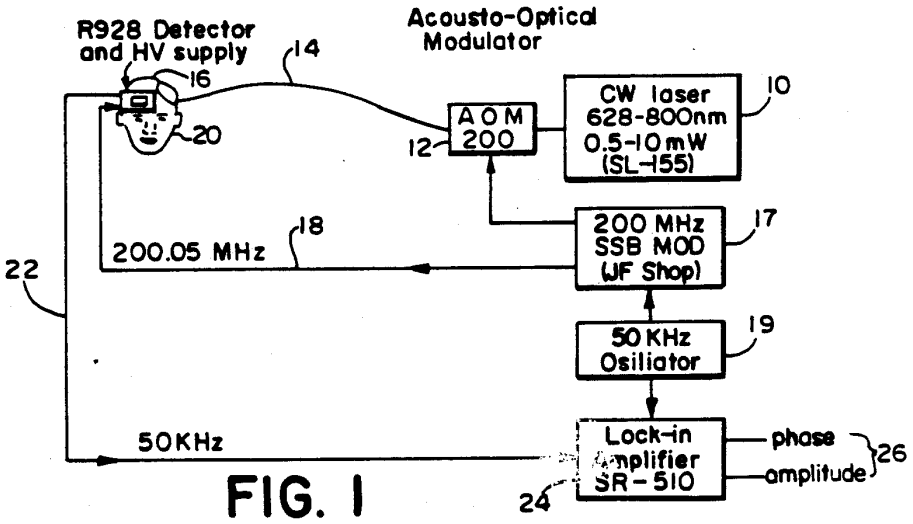


FIG. 1

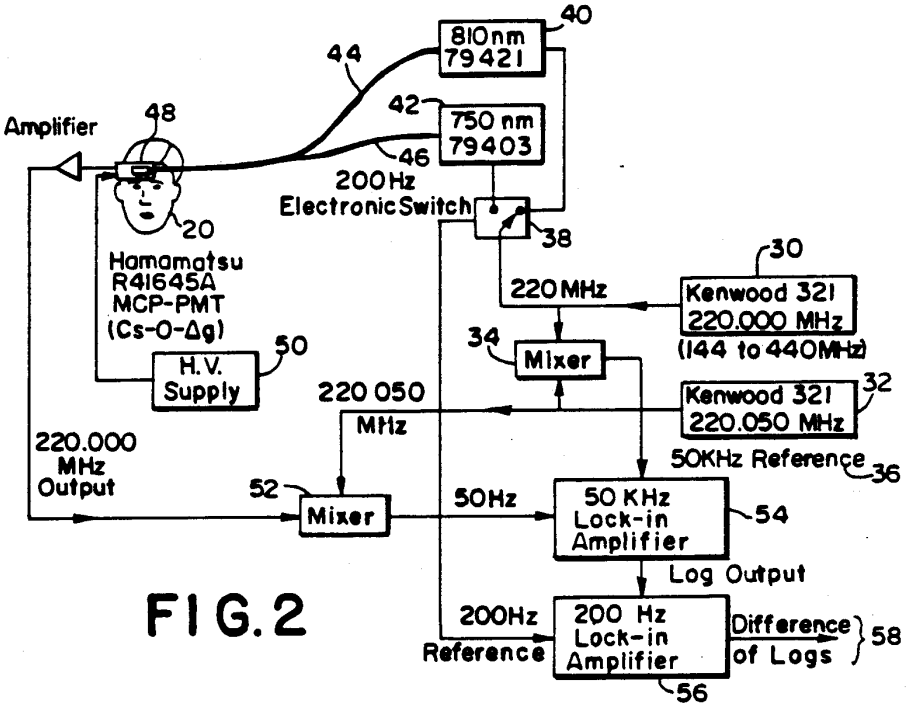


FIG. 2

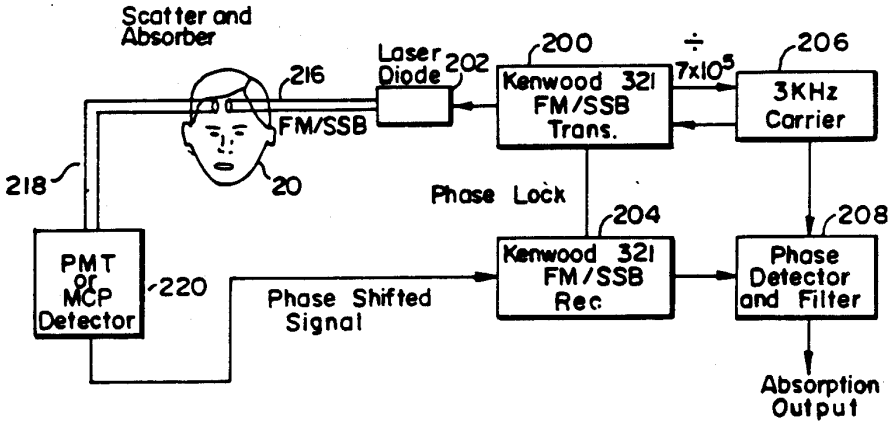


FIG. 4

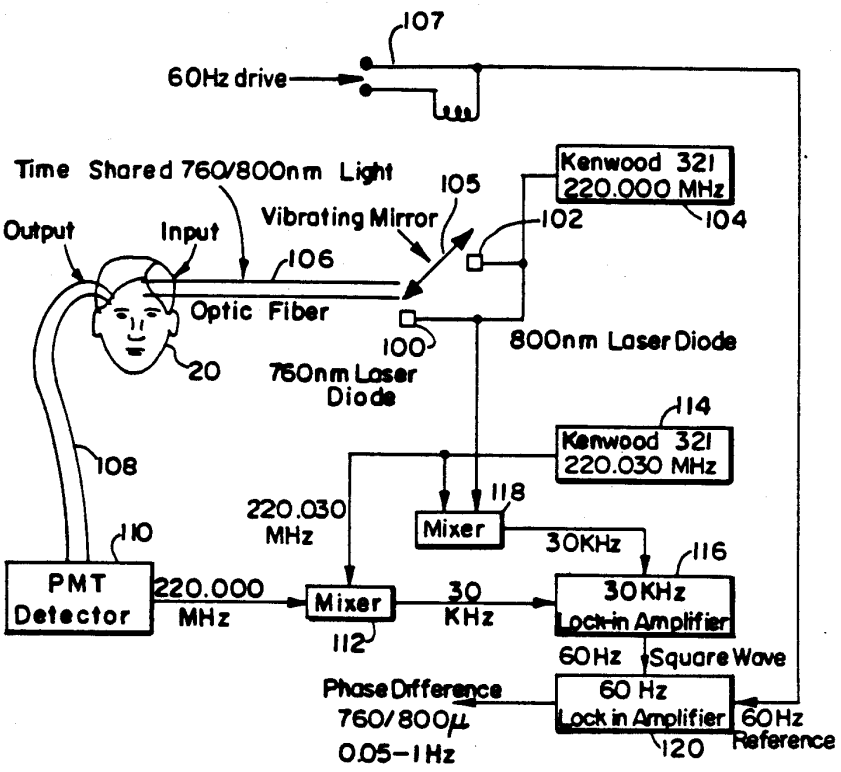


FIG. 3

PHASE MODULATED SPECTROPHOTOMETRY

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is related to co-pending applications, Ser. No. 266,166, filed Nov. 2, 1988, in the name of Britton Chance, entitled, "Optical Coupling System for Use in Monitoring Oxygenation State Within Living Tissue", which is hereby incorporated by reference as if fully set forth herein; Ser. No. 266,019, filed Nov. 2, 1988, in the name of Britton Chance, entitled, "A User-Wearable Hemoglobinometer For Measuring the Metabolic Condition of a Subject", which is hereby incorporated by reference as if fully set forth herein; and Ser. No. 287,847, filed Dec. 21, 1988, in the name of Britton Chance, entitled, "Methods and Apparatus For Determining the Concentration of a Tissue Pigment Of Known Absorbance, In Vivo, Using the Decay Characteristics of Scattered Electromagnetic Radiation", which is hereby incorporated by reference as if fully set forth herein.

BACKGROUND OF THE INVENTION

The application of the basic dual wavelength principle to detect hemoglobin and myoglobin changes in tissue began with the work of G.A. Millikan in his studies of the cat soleus muscle, and the work of Millikan and Pappenheimer who detected hemoglobin deoxygenation in the human ear lobe. Multiwavelength instruments have been developed; these instruments use either a multiwavelength laser diode light source or a time shared filter technique, in which high precision is sought through various algorithms which deconvolute background signals, oxidized and reduced cytochrome signals, and oxy- and deoxyhemoglobin signals. Such instruments are oxy-complex and often have difficulty obtaining light sources with wavelengths appropriate to the algorithms that have been developed, or they have such low light levels that photon counting is necessary. They are generally in the price range of $80,000 and have produced much experimental data in the literature on neonates and adults. The basic problem of such methods is that the optical pathlength is not known ab initio but is calculated by reference to animal models where the hemoglobin can be removed and cytochrome directly studied. Transferability of such data from the animal model to the human is one difficulty that had to be overcome prior to the invention of time-resolved spectroscopy, where the pathlength is measured directly. See U.S. Pat. Application Ser. No. 266,166, filed Nov. 2, 1988, "Optical Coupling System for Use in Monitoring Oxygenation State Within Living Tissue," fully referenced above.

Continuous wave spectroscopy (CWS) of tissue hemoglobin has the demonstrated advantages of great simplicity and sensitivity, as well as affording an "early warning" of tissue hypoxia. The application of picosecond-pulse time-resolved spectroscopy (TRS) to tissue in order to determine optical pathlengths, quantify the changes in hemoglobin concentration, and determine the actual concentration values of hemoglobin and cytochrome has great applicability to clinical studies of tissue hypoxia. Moreover, time-resolved spectroscopy used in conjunction with continuous light spectrophotometry offers a means of calibrating the optical pathlength which photons travel as they migrate through tissue. While trend indication can be of great value in many situations, the capability to quantify hemoglobin concentration for both continuous and pulsed light techniques greatly extends their applicability to clinical studies. See U.S Pat. Application Ser. No. 266,166, filed Nov. 2, 1988, "Optical Coupling System for Use in Monitoring Oxygenation State Within Living Tissue"; and U.S. Application Ser. No. 287,847, filed Dec. 21, 1988, "Methods and Apparatus For Determining the Concentration of a Tissue Pigment Of Known Absorbance, In Vivo, Using the Decay Characteristics of Scattered Electromagnetic Radiation", both of which are fully referenced above.

SUMMARY OF THE INVENTION

It has now been found that the principles of dual wavelength spectrophotometry may be applied to time-resolved spectrophotometry choosing a carrier frequency at a value in which the time characteristic is compatible with the time delay of photon migration from input to output through a scattering medium.

The present invention provides methods and apparatus whereby a modulated waveform is transmitted to a scattering medium and detected after migration therethrough. The detected waveform will have been altered and may thus be compared to the initial waveform. For example, a waveform is phase shifted by the delay in migration through the scattering medium. Thus, in a preferred embodiment, the phase of the waveform is modulated and the phase shift is detected. The difference in phase shift between two waveforms of emitted electromagnetic radiation having different, known wavelengths can then be processed to determine the concentration of an absorptive constituent such as hemoglobin.

It is an object of the present invention to provide methods and apparatus for studying photon migration using signal modulation techniques such as time, frequency and phase modulation. It is a specific object of the present invention to provide methods and apparatus whereby phase modulated spectrophotometry (PMS) may be utilized in conjunction with continuous wave spectrometry (CWS) to determine the critical value of an absorptive pigment such as hemoglobin, at the point the PCr/P_I ratio begins to decrease. It is another object of the present invention to provide as a specific embodiment, a dual wavelength phase modulation system which will allow the clinical application of the advantages of time resolved spectroscopy in an economical and commercially feasible embodiment.

BRIEF DESCRIPTION OF THE DRAWING

FIG. 1A illustrates a simplified single wavelength phase modulated spectrophotometer made in accordance with the present invention.

FIG. 1 is a block diagram of another embodiment of a single wavelength phase modulated spectrophotometer made in accordance with the present invention.

FIG. 2 is a block diagram of another embodiment of a phase modulated spectrophotometer made in accordance with the present invention.

FIG. 3 is a block diagram of the preferred embodiment of the spectrophotometer of the present invention.

FIG. 4 is a block diagram of an alternate embodiment of the spectrophotometer of the present invention.

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