



(11) **EP 2 276 406 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:  
**12.12.2018 Bulletin 2018/50**

(51) Int Cl.:  
**A61B 5/1477** <sup>(2006.01)</sup> **A61B 5/1455** <sup>(2006.01)</sup>  
**A61B 5/01** <sup>(2006.01)</sup> **G05F 1/00** <sup>(2006.01)</sup>  
**A61B 5/145** <sup>(2006.01)</sup> **A61B 5/00** <sup>(2006.01)</sup>

(21) Application number: **09730011.5**

(86) International application number:  
**PCT/US2009/037829**

(22) Date of filing: **20.03.2009**

(87) International publication number:  
**WO 2009/126422 (15.10.2009 Gazette 2009/42)**

(54) **APPARATUS AND METHODS FOR NON-INVASIVE MEASUREMENT OF A SUBSTANCE WITHIN A BODY**

GERÄT UND VERFAHREN ZUR NICHTINVASIVEN MESSUNG EINER SUBSTANZ IN EINEM KÖRPER

APPAREIL ET PROCÉDÉS DE MESURE NON INVASIVE D'UNE SUBSTANCE DANS UN CORPS

(84) Designated Contracting States:  
**AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO SE SI SK TR**

(74) Representative: **Lucas, Phillip Brian Lucas & Co.**  
**135 Westhall Road**  
**Warlingham, Surrey CR6 9HJ (GB)**

(30) Priority: **11.04.2008 US 101859**

(56) References cited:  
**WO-A1-2009/102549 WO-A2-2007/072300**  
**JP-A- 2007 195 653 US-A- 5 054 487**  
**US-A- 5 666 956 US-A- 6 025 597**  
**US-A1- 2005 043 630 US-A1- 2005 043 630**  
**US-A1- 2007 106 139 US-A1- 2007 197 885**

(43) Date of publication of application:  
**26.01.2011 Bulletin 2011/04**

(73) Proprietor: **GlucoVista Inc.**  
**Fairfield, NJ 07044 (US)**

(72) Inventor: **GERLITZ, Jonathan Herzliya (IL)**

**EP 2 276 406 B1**

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

**Description**

## FIELD OF THE INVENTION

**[0001]** The present invention relates to measurement of a substance, such as glucose, within a body, such as the human body.

## DESCRIPTION OF RELATED ART

**[0002]** Several patents suggest methods to non-invasively measure the concentration of a substance, such as glucose, in the bloodstream. Examples include U.S. Patent Nos. 5,313,941; 5,370,114; 5,515,847; 5,601,079; 5,615,672; 5,666,956; 6,949,070; 6,998,247; and 7,183,102. However, the methods disclosed in these patents do not adequately consider the body surface temperature at the point of measurement and the ambient temperature. Both of these parameters affect the accuracy of the substance concentration measurement in the mid to far infrared spectrum.

**[0003]** US 4054487 (Grant) discloses apparatus and methods for non-invasive material analysis in which a material (e.g., a liquid such as blood in a surface vein) is illuminated at a plurality of discrete wavelengths. The apparatus includes a multiple wavelength illumination source for illuminating a sample of the material, a wavelength specific detector array, and a reflection ratio analyzer. The illumination source can be a single multi-wavelength laser diode or a series of discrete diode elements, each emitting a distinct wavelength of light. The detector array detects light reflected from the sample, converts the reflected light into electrical signals indicative of the intensity of the reflected light at each wavelength and transmits the converted signals to the reflection ratio analyzer which processes the electrical signals and derives a reflectance ratio for at least two of the wavelengths transmitted. The analyzer then compares the calculated reflectance ratio with predetermined values to detect the presence of an analyte e.g. glucose in the material sample.

**[0004]** US 5666956 (Burchert) is said to be based on the discovery that natural infrared emission from the human body, especially from the tympanic membrane, is modulated by the state of the emitting tissue. Spectral emissivity of human infrared radiation from the tympanic membrane consists of spectral information of the blood analyte which can be directly correlated with the blood analyte concentration, e.g. glucose concentration. The detection system which is said to be the main embodiment of the invention consists, for example, of the dual element type P4488 series pyroelectric detector from the Hamamatsu Corporation, Bridgewater, N.J., with two pyroelectric sensing areas covered by a silicon window with a 5  $\mu\text{m}$  long pass filter to pass only infrared radiation that corresponds to emission in the range of the internal temperature of a human body. One of the sensing elements is covered by a negative correlation filter when the other

sensing area is covered by an appropriate attenuation filter which does not have spectral bands characteristic to the measured analyte. Spectrally modified infrared radiation from, for example, the tympanic membrane illuminates both windows, one with a negative correlating filter which blocks radiation in the absorption bands for the analyte to be measured and the other which passes through a neutral density filter capable of blocking radiation equally at all wavelengths in the range of interest to compensate for overall attenuation by the negative correlating filter in the first sensing area. The two sensing areas 11 and 12 of the detector 7, whose top view is shown on FIG. 4b, are connected so that their outputs are subtracted. Difference of the radiation intensity between the two radiation paths provides a measure proportional to the analyte concentration.

**[0005]** US 2005/043630 (Buchert) discloses a device that isolates and measures blood glucose levels from the eardrum using the body's natural heat emission. The device uses a method of determining a human body tissue analyte concentration (e.g. glucose in blood) by non-invasive measurement of emission spectral lines characteristic to a body tissue analyte in an infrared spectral region emitted naturally by a human body as heat, comprising: measuring a spectral intensity of said emission lines having a wavelength dependence of tissue constituents. detecting the emission spectral lines at a predetermined emission wavelength, analyzing the emission spectral lines in said infrared spectral region, measuring ambient temperature and humidity, measuring body temperature by means of heat conduction and also in a non-contact manner by means of radiation and correlating said spectral intensity of emission spectral lines, said ambient temperature and said optional humidity and said body temperature measured by means of conduction and means of radiation with body analyte concentrations. The detection system may comprise an infrared energy sensor which is a dual element pyroelectric or thermopile detector having two sensing areas in combination with a filter having areas, one of which blocks radiation in the absorption bands for the analyte to be measured and the other which passes through a neutral density filter capable of blocking radiation equally at all wavelengths in the range of interest. The two sensing areas are connected so that their outputs are subtracted. Difference of the radiation intensity between the two radiation paths provides a measure proportional to the analyte concentration which is then further processed.

## SUMMARY OF THE INVENTION

**[0006]** In one aspect, the invention provides a method for non-invasively measuring a concentration of a substance in a body, the method comprising the steps of:

measuring a first amount of infrared (IR) radiation absorbed or emitted from the body in a first IR wavelength band in which the substance emits and ab-

sorbs IR radiation;  
 measuring a second amount of IR radiation absorbed or emitted from the body in a second IR wavelength band different from the first IR wavelength band and which is either the entire spectrum in which the body emits and absorbs IR radiation in the far IR (FIR) spectrum or is a wavelength band or bands in which the substance has no or negligible emission and absorption of IR radiation;  
 measuring a temperature of a surface of the body;  
 measuring an ambient temperature;  
 operating a processor to (a) calculate a first normalized IR radiation measurement which is the first measured amount of IR radiation normalized against a first blackbody radiation in the first IR wavelength band, (b) calculate a second normalized IR radiation measurement which is the second measured amount of IR radiation normalized against a second blackbody radiation in the second IR wavelength band, and (c) calculate a normalized radiation parameter ratio value as the ratio of the normalized first radiation measurement value to the normalized second radiation measurement value;  
 storing in a memory data for a series of measurements across a statistically representative population at various concentrations of the substance taken according to a conventional invasive method and constructed into an empirically derived lookup table by taking, and storing for the measurements in said series body surface temperatures, ambient temperatures and normalized ratio parameters; and  
 operating the processor to calculate the concentration of the substance in the body using the empirically derived lookup table by correlating the concentration with the normalized ratio parameter, the body surface temperature, and the ambient temperature.

**[0007]** The invention also provides a system for non-invasively measuring a concentration of a substance in a body, the system comprising:

an infrared (IR) detector; and  
 a filter assembly including at least a first filter and a second filter configured to filter IR radiation transmitted to the detector;  
 wherein the first filter is configured to transmit only a first amount of IR radiation absorbed or emitted from the body in a first IR wavelength band in which the substance emits and absorbs IR radiation and the second filter is configured to transmit only a second amount of IR radiation absorbed or emitted from the body in a second IR wavelength band different from the first IR wavelength band and which is either the entire spectrum in which the body emits and absorbs IR radiation in the far IR (FIR) spectrum or is a wavelength band or bands in which the substance has no or negligible emission and absorption of IR radiation;

a first temperature sensor configured to measure a surface temperature of a surface of the body;  
 a second temperature sensor configured to measure an ambient temperature;  
 a processor configured to (a) calculate a first normalized IR radiation measurement which is the first measured amount of IR radiation normalized against a first blackbody radiation in the first IR wavelength band, (b) calculate a second normalized IR radiation measurement which is the second measured amount of IR radiation normalized against a second blackbody radiation in the second IR wavelength band, and (c) calculate a normalized radiation parameter ratio value as the ratio of the normalized first radiation measurement value to the normalized second radiation measurement value; and  
 a memory storing data for a series of measurements across a statistically representative population at various concentrations of the substance taken according to a conventional invasive method and constructed into an empirically derived lookup table (28) by taking, and storing for the measurements in said series body surface temperatures, ambient temperatures and normalized ratio parameters;  
 the processor being further configured to calculate the concentration of the substance in the body using the empirically derived lookup table by correlating the concentration with the normalized ratio parameter, the body surface temperature, and the ambient temperature.

**[0008]** Also disclosed is a method for creating an empirically derived lookup table by taking a series of measurements across a population. The method comprises the steps of

(a) directly measuring a concentration of a substance in the body for each member of the population,  
 (b) measuring a first amount of infrared (IR) radiation absorbed or emitted from the body in a first wavelength band for each member of the population, and  
 (c) measuring a second amount of IR radiation absorbed or emitted from the body in a second wavelength band for each member of the population.  
 In steps (d) and (e), respectively, simultaneously with steps (b) and (c) a temperature at a surface of the body is measured and an ambient temperature is measured. The method further comprises the step of  
 (f) calculating a normalized ratio parameter based on the first amount, the second amount, the body surface temperature and the ambient temperature. In step (g), steps a) through f) are repeated at a plurality of ambient temperatures and for a plurality of substance concentrations. In step (h) the empirically derived lookup table is created by plotting the body surface temperature, the ambient temperature and the normalized ratio parameter for each member of the population at each ambient temperature and for

each substance concentration.

#### BRIEF DESCRIPTION OF THE DRAWINGS

**[0009]** How the invention may be put into effect will now be described, by way of example, with reference to the accompanying drawings, in which like numerals indicate like parts, and in which:

Figure 1 is a plot of infrared (IR) radiation emitted from and absorbed by a hypothetical body across a given spectrum;

Figure 2 is a plot of far infrared (FIR) radiation emitted from and absorbed by a hypothetical body and a blackbody across a given spectrum;

Figure 3 is a conceptual perspective view of an empirically derived lookup table according to the present embodiments, the table having as axes a body surface temperature, an ambient temperature and a normalized ratio parameter;

Figure 4 is a schematic drawing of one embodiment of the present system for measuring a concentration of a substance in a body;

Figure 5 is a schematic drawing of another embodiment of the present system for measuring a concentration of a substance in a body;

Figure 6 is a schematic drawing of control electronics for the systems of Figures 4 and 5;

Figure 7 is a process flow chart illustrating one embodiment of the present method for measuring a concentration of a substance in a body; and

Figure 8 is a process flow chart illustrating one embodiment of the present method for constructing an empirically derived lookup table.

#### DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

**[0010]** Embodiments of the present system and methods are configured to determine a concentration of a substance in a body. In certain embodiments, the measured substance may be glucose in the bloodstream. However, those of ordinary skill in the art will appreciate that the present system and methods may be used to measure concentrations of other substances, such as cholesterol for example. The present system and methods are advantageously non-invasive, and therefore avoid the discomfort of skin punctures.

**[0011]** To determine the substance concentration, the present embodiments measure infrared (IR) radiation emitted and/or absorbed from the body in different wavelengths and normalize these measurements against IR radiation emitted and/or absorbed from a blackbody. The present embodiments also measure the ambient temperature and the body surface temperature simultaneously with the IR radiation measurements. Ambient temperature and body surface temperature affect the accuracy of the IR radiation measurements, because they affect

the equilibrium of heat transfer between the surrounding environment and the measured surface, and they also affect the probability of absorption or emission by the surface.

**[0012]** In certain embodiments the internal body temperature may be measured instead of, or in addition to, the body surface temperature. In the present disclosure and claims the term body surface temperature is used broadly to include either or both of the temperature at the body surface and the internal body temperature.

**[0013]** In the present embodiments, a ratio of the normalized IR radiation measurements results in a normalized ratio parameter. Using the normalized ratio parameter and measurements of the body surface temperature and the ambient temperature, the present system and methods return the substance concentration in the body by referencing an empirically derived lookup table. The empirically derived lookup table, and example methods for creating such a table, are discussed in further detail below.

**[0014]** All bodies and all substances absorb and emit IR radiation. The magnitude of IR radiation absorbed and emitted at a given wavelength varies according to the body's temperature and the ambient temperature. Figure 1 illustrates a sample plot of the IR emission spectrum for a hypothetical body, where the ambient temperature  $T_A$  is equal to  $x$  and the body temperature  $T_B$  is equal to  $y$ . As shown, the body more readily absorbs and emits IR radiation at certain wavelengths, represented by the peaks 20 in the curve 22.

**[0015]** In certain substances, IR absorption/emission is particularly distinctive in the far infrared (FIR). Glucose is one example. Thus, to measure the concentration of substances such as glucose in a body it is advantageous to measure the FIR radiation emitted by the body. As used herein, the term far infrared and the abbreviation FIR denote IR radiation at wavelengths greater than or equal to approximately 7 microns.

**[0016]** Embodiments of the present system and methods measure the FIR radiation absorbed or emitted by a body at different wavelength bands. The first wavelength band (or bands) is selected to be in a band (or bands) where the substance is known to have significant FIR absorption/emission. The second wavelength band is selected to be the entire FIR absorption/emission spectrum of the body. In an alternative embodiment, the second wavelength band (or bands) is selected to be in a band (or bands) where the substance is known to have no or negligible FIR absorption/emission. After normalizing each measurement, their ratio can be used to determine the concentration of the substance in the body, as discussed in detail below.

**[0017]** In the present embodiments, the FIR measurements are normalized against a blackbody. A blackbody, as those of ordinary skill in the art will appreciate, is one that absorbs and emits radiation with theoretical emissivity of one. Figure 2 illustrates a sample plot of the FIR absorption/emission spectrum for a hypothetical body

(solid curve 24) and for a blackbody (dashed curve 26). For both the body and the blackbody the ambient temperature  $T_A$  is the same. Similarly, for both the body and the blackbody the body/blackbody temperature  $T_B$  is the same. The dashed vertical lines represent a first wavelength band 27 in which the substance whose concentration is to be measured is known to have an FIR absorption/emission peak 29. For example, for glucose the selected band 27 may be between 9.3 microns and 9.9 microns.

**[0018]** In one embodiment of the present methods the FIR radiation absorbed/emitted by the body in the first wavelength band is measured and then normalized against the blackbody FIR radiation in the first wavelength band. The FIR radiation absorbed/emitted by the body over the entire FIR spectrum is then measured and normalized against the blackbody FIR radiation over the entire FIR spectrum. Measurements of the body surface temperature and the ambient temperature are taken simultaneously with the first and second FIR measurements. The ratio of the first and second normalized measurements yields a normalized ratio parameter. The concentration of the substance in the body is correlated with the normalized ratio parameter, the body surface temperature and the ambient temperature. In certain embodiments a logarithm, such as a natural logarithm ( $\ln$ ), of the normalized ratio parameter may be used in the correlation step. In the present embodiments, the correlation step includes referencing an empirically derived lookup table.

**[0019]** According to embodiments of the present system and methods, an empirically derived lookup table may be constructed by taking a series of measurements across a statistically representative population (hereinafter "the Group"). The measurements taken for each member of the Group include a concentration of the substance of interest (such as glucose) taken according to a conventional invasive method, a first amount of FIR radiation absorbed or emitted from the body in a first wavelength band, a second amount of FIR radiation absorbed or emitted from the body in a second wavelength band, a temperature at a surface of the body and an ambient temperature. The first wavelength band (which may comprise multiple bands) is selected to be in a band where the substance is known to have significant FIR absorption/emission. In one embodiment, the second wavelength band is selected to be the entire FIR absorption/emission spectrum of the body. In an alternative embodiment, the second wavelength band (or bands) is selected to be in a band (or bands) where the substance is known to have no or negligible FIR absorption/emission. The above measurement process is repeated in various ambient temperatures and for various substance concentrations.

**[0020]** The first and second FIR radiation measurements are normalized against a blackbody at the same temperature. The lookup table is then created by plotting three of the measured parameters against one another

for all members of the Group. The three parameters are the body surface temperature, the ambient temperature and the ratio of the first normalized FIR measurement to the second normalized FIR measurement, referred to herein as a normalized ratio parameter. In certain embodiments a logarithm, such as a natural logarithm ( $\ln$ ), of the normalized ratio parameter may be plotted against the body surface temperature and the ambient temperature. If the population size is large enough, an accurate reference table can be created that enables easy determination of the substance concentration in the body using only noninvasive measurements of FIR absorption/emission, ambient temperature and body surface temperature.

**[0021]** Figure 3 illustrates a conceptual embodiment of the present empirically derived lookup table 28. In the illustrated embodiment, the table 28 comprises three axes: the body surface temperature 30, the ambient temperature 32 and the normalized ratio parameter 34. To determine the concentration of a given substance within the body, three measurements, corresponding to the three axes, are taken from a body. The intersection 36 of the three measurements in the table 28 yields the substance concentration, as shown in Figure 3.

**[0022]** In alternative embodiments, the lookup table may comprise a database containing a plurality of data points. The illustrated Cartesian plot of Figure 3 is intended to help the reader visualize the relationships between the three parameters of the body surface temperature 30, the ambient temperature 32 and the normalized ratio parameter 34. However, those of ordinary skill in the art will appreciate that not all of the present embodiments need include a lookup table that is plotted in three-dimensional space.

**[0023]** The Applicant has not yet completed taking a series of measurements across a population in order to construct the empirically derived lookup table 28. These measurements are expected to yield a population distribution that will indicate to what extent FIR radiation readings will vary from one subject to the next under identical conditions (same substance concentration in bloodstream, same body surface temperature, same ambient temperature). If the results indicate that there is no or negligible variation, then embodiments of the present system 38 and methods can be used to determine the concentration of a substance in bloodstream without the need for any invasive measurements for each subject. However, if the results indicate that there is a substantial variation, then for each subject an initial measurement through conventional invasive methods may need to be taken in order to calibrate the system 38 and methods for that particular subject. Advantageously, however, only one or two invasive measurements are needed for the calibration.

**[0024]** Figure 4 illustrates, schematically, one embodiment of the present system 38 for measuring a concentration of a substance in a body. Broadly, the illustrated embodiment of the present system 38 comprises an IR

radiation detector 40, an IR filter assembly 42, heating and/or cooling apparatus 44, and apparatus for measuring the ambient temperature 46. In the present embodiments the IR detector 40 measures the body surface temperature. However, those of ordinary skill in the art will appreciate that alternative apparatus for measuring the body surface temperature may be used.

**[0025]** In one embodiment the IR detector 40 is a thermopile with collimating optics. However, those of ordinary skill in the art will appreciate that the IR detector could comprise a different type of detector, such as a bolometer. The illustrated system 38 further comprises a display 48 for presenting information such as the substance concentration, the measured parameters and other information. In certain embodiments the display 48 may be a liquid crystal display (LCD).

**[0026]** With continued reference to Figure 4, the IR filter assembly 42 is positioned in front of the detector 40. In the illustrated embodiment, the IR filter assembly 42 comprises three filters 50, although those of ordinary skill in the art will appreciate that the IR filter assembly 42 could include any number of filters. A first one of the filters 50 transmits only the spectral band in which the substance exhibits significant absorption/emission of IR radiation. A second one of the filters 50 transmits part of the spectral band in which the substance has no or negligible absorption/emission. A third one of the filters 50 transmits all of the IR radiation related to the body's temperature. The third filter 50 may transmit, for example, all of the IR radiation between approximately 7 microns and approximately 15 microns.

**[0027]** In the illustrated embodiment, the IR filter assembly 42 includes a filter wheel or drive 52 and a motor 54. In certain embodiments, the motor 54 may comprise a solenoid. The motor 54 or solenoid is configured to provide a motive force for changing a position of the filter assembly 42 with respect to the IR detector 40. Activation of the motor 54 or solenoid enables the filters 50 to be sequentially positioned in front of the detector 40 as each IR radiation measurement is taken.

**[0028]** In an alternative embodiment of the present system 39 illustrated in Figure 5, the motor 54 and the filter assembly 42 are replaced with a plurality of fixed position IR detectors 56. In the illustrated embodiment, three IR detectors 56 are shown. However, those of ordinary skill in the art will appreciate that any number of IR detectors may be provided. In the embodiment of Figure 5, each IR detector 56 includes its own IR filter 58. The filters 58 may, for example, be substantially similar to the three filters 50 provided in the embodiment of Figure 4 with respect to the wavelengths of IR radiation that they transmit. In the embodiment of Figure 5, there are advantageously no moving parts in the detector/filter assembly, and all measurements may be made simultaneously.

**[0029]** With reference to Figures 4 and 5, the illustrated embodiments of the present system 38, 39 include apparatus for measuring ambient temperature 46. In certain embodiments the ambient temperature measuring appa-

ratus 46 may be a thermistor, such as a negative temperature coefficient (NTC) thermistor. For simplicity, the ambient temperature measuring apparatus will be referred to herein as a thermistor. However, those of ordinary skill in the art will appreciate that the ambient temperature measuring apparatus 46 may be any apparatus that is suitable for measuring ambient temperature, such as a thermocouple. While in the illustrated embodiments the thermistor 46 is attached to the IR detector 40, 56, those of ordinary skill in the art will appreciate that it need not be. In certain embodiments the thermistor 46 measures the temperature of a housing (not shown) of the IR detector 40, 56, which normally is equal to ambient temperature.

**[0030]** With continued reference to Figures 4 and 5, outputs 60, 62 of the IR detector(s) 40, 56 and the thermistor 46 and control inputs 64, 66 of the motor 54 and the heating/cooling apparatus 44 are connected to control electronics 68. Figure 6 illustrates further details of the control electronics 68, which include a processing unit 70 and memory 72. The memory 72 may include the lookup table 28 and/or other look up tables for calculating results of the measurements taken by the present system 38, 39. The processing unit 70 may comprise a central processing unit (CPU) running software and/or firmware. Alternatively, the processing unit 70 may comprise one or more application-specific integrated circuits (ASICs). The processing unit 70 processes signals from the IR detector(s) 40, 56 and the thermistor 46. The processing unit 70 also drives the display 48 to show results that may include the substance concentration, the measurements taken by the IR detector(s) 40, 56 and/or the thermistor 46, and other information. In the embodiment of Figure 6, the processing unit 70 also controls a motor drive 74, which in turn controls the motor 54 to change the position of the filter assembly 42 with respect to the IR detector 40.

**[0031]** With reference to Figure 6, the illustrated control electronics 68 include one or more switches 75 for switching between measurement channels. For example, the switches 75 might change between a first channel that carries a signal from the IR detector 40, 56 and a second channel that carries a signal from the thermistor 46. The processing unit 70 controls the switches 75.

**[0032]** With continued reference to Figure 6, the illustrated control electronics 68 further include an integrating amplifier 77. The integrating amplifier 77 amplifies a voltage generated by the IR detector 40, 56 to a measurable value. The voltage generated by the IR detector 40, 56 is proportional to the detected body radiation, and may be very small. The illustrated control electronics 68 further include a comparator 79. The comparator 79, together with the integrating amplifier 77 converts the voltage from the IR detector 40, 56 into a time interval that is inversely proportional to the input voltage and is measured by the processing unit 70.

**[0033]** With reference to Figures 4 and 5, in certain embodiments the heating/cooling apparatus 44 compris-

es a Peltier element 82 configured to provide a desired amount of heat or cold, a fan 84 to drive the heated or cooled air, and a funnel 86 to direct the heated or cooled air onto the body surface. Applying heat or cold to the skin surface stimulates the absorption or emission of IR radiation by the substance whose concentration is to be measured. In the case of glucose, for example, cooling the skin stimulates the absorption of IR radiation while heating the skin stimulates the emission of IR radiation. In another embodiment, a flow of ambient temperature air stimulates emission or absorption. In such an embodiment the heating/cooling apparatus 44 may be replaced with an airflow apparatus to drive the ambient air.

**[0034]** The process flowchart of Figure 7 illustrates one embodiment of the present methods for measuring the concentration of a substance within a body. At step S700 the IR radiation detector(s) and the heating/cooling/airflow apparatus are positioned with respect to the body. At step S702 the heating/cooling/airflow apparatus is activated to stimulate absorption/emission of IR radiation by the substance. At step S704 the absorption/emission of IR radiation, ambient temperature and body surface temperature are measured simultaneously. Step S704 is repeated to obtain IR radiation measurements in first and second wavelength bands, as discussed above. At step S706 the normalized ratio parameter is calculated from the IR radiation measurements. At step S708 the normalized ratio parameter is correlated with the ambient temperature and the body surface temperature using the lookup table 28. And at step S710 the substance concentration is displayed.

**[0035]** With either embodiment of the system 38, 39 shown in Figures 4 and 5, an alternative method of measuring the absorption/emission of IR radiation, the ambient temperature and the body surface temperature is to scan the body surface while taking multiple measurements at various points on the body surface. Software, for example, may then be used to identify the most desirable result from the plurality of measurements. Parameters for selecting the most desirable result may be, for example, repeatability, maximum signal, etc.

**[0036]** The process flowchart of Figure 8 illustrates one embodiment of the present methods for constructing an empirically derived lookup table 28. At step S800 a concentration of a substance of interest (such as glucose) is directly measured for each member of the Group. This step may, for example, involve drawing a sample of blood from each member and testing the blood according to any known method. At step S802 the IR radiation detector(s) and the heating/cooling/airflow apparatus are positioned with respect to the body of each member of the Group. At step S804 the heating/cooling/airflow apparatus is activated to stimulate absorption/emission of IR radiation by the substance for each member of the Group. At step S806 the absorption/emission of IR radiation, ambient temperature and body surface temperature are measured simultaneously for each member of the Group. Step S806 is repeated for each member of the Group to

obtain IR radiation measurements in first and second wavelength bands, as discussed above. At step S808 the normalized ratio parameter is calculated for each member of the Group from the IR radiation measurements. At step S810, steps S802, S804, S806 and S808 are repeated at various ambient temperatures and for various substance concentrations. At step S812 the body surface temperature, the ambient temperature and the normalized ratio parameter are plotted against one another and against the measured blood substance concentration for all members of the Group.

**[0037]** It will be appreciated that modifications may be made to the embodiments described above without departing from the invention, the scope of which is defined in the accompanying claims.

## Claims

1. A method for non-invasively measuring a concentration of a substance in a body, the method comprising the steps of:

measuring a first amount of infrared (IR) radiation absorbed or emitted from the body in a first IR wavelength band in which the substance emits and absorbs IR radiation;

measuring a second amount of IR radiation absorbed or emitted from the body in a second IR wavelength band different from the first IR wavelength band and which is either the entire spectrum in which the body emits and absorbs IR radiation in the far IR (FIR) spectrum or is a wavelength band or bands in which the substance has no or negligible emission and absorption of IR radiation;

measuring a temperature of a surface of the body;

measuring an ambient temperature;

operating a processor (70) to (a) calculate a first normalized IR radiation measurement which is the first measured amount of IR radiation normalized against a first blackbody radiation in the first IR wavelength band, (b) calculate a second normalized IR radiation measurement which is the second measured amount of IR radiation normalized against a first blackbody radiation in the second IR wavelength band, and (c) calculate a normalized ratio parameter value as the ratio of the normalized first radiation measurement value to the normalized second radiation measurement value;

storing in a memory (72) data for a series of measurements across a statistically representative population at various concentrations of the substance taken according to a conventional invasive method and constructed into an empirically derived lookup table (28) by taking, and

storing for the measurements in said series body surface temperatures, ambient temperatures and normalized ratio parameters; and operating the processor (70) to calculate the concentration of the substance in the body using the empirically derived lookup table by correlating the concentration with the normalized ratio parameter, the body surface temperature, and the ambient temperature.

- 2. The method of Claim 1, wherein the normalized ratio parameter is a logarithm of the ratio of the normalized first amount to the normalized second amount.
- 3. The method of claim 1 or 2, wherein the substance is glucose.
- 4. The method of any preceding claim, wherein the body is a human body.
- 5. The method of any preceding claim, further comprising the step of cooling the body surface to cause the substance to absorb IR, or heating the body surface to cause the substance to emit IR, or creating a flow of ambient air across the body surface.
- 6. A system for non-invasively measuring a concentration of a substance in a body, the system comprising:

an infrared (IR) detector (40); and a filter assembly (42) including at least a first filter and a second filter configured to filter IR radiation transmitted to the detector (40); wherein the first filter is configured to transmit only a first amount of IR radiation absorbed or emitted from the body in a first IR wavelength band in which the substance emits and absorbs IR radiation and the second filter is configured to transmit only a second amount of IR radiation absorbed or emitted from the body in a second IR wavelength band different from the first IR wavelength band and which is either the entire spectrum in which the body emits and absorbs IR radiation in the far IR (FIR) spectrum or is a wavelength band or bands in which the substance has no or negligible emission and absorption of IR radiation; a first temperature sensor configured to measure a surface temperature of a surface of the body; a second temperature sensor (46) configured to measure an ambient temperature; a processor (70) configured to (a) calculate a first normalized IR radiation measurement which is the first measured amount of IR radiation normalized against a first blackbody radiation in the first IR wavelength band, (b) calculate a second normalized IR radiation measurement

which is the second measured amount of IR radiation normalized against a first blackbody radiation in the second IR wavelength band, and (c) calculate a normalized ratio parameter value as the ratio of the normalized first radiation measurement value to the normalized second radiation measurement value; and a memory (72) storing data for a series of measurements across a statistically representative population at various concentrations of the substance taken according to a conventional invasive method and constructed into an empirically derived lookup table (28) by taking, and storing for the measurements in said series body surface temperatures, ambient temperatures and normalized ratio parameters; the processor (70) being further configured to calculate the concentration of the substance in the body using the empirically derived lookup table by correlating the concentration with the normalized ratio parameter, the body surface temperature, and the ambient temperature.

- 7. The system of Claim 6, further comprising temperature changing apparatus (82) operable to increase or decrease the surface temperature of the surface of the body.
- 8. The system of Claim 6 or 7, further comprising airflow apparatus (84) operable to create a flow of ambient air across the surface of the body.
- 9. The system of any of claims 6-8, wherein the substance is glucose and the body is a human body, and preferably wherein the first or second temperature sensor (46) comprises a thermistor.
- 10. The system of any of claims 6-9, wherein the IR detector (40) comprises a thermopile with collimating optics.
- 11. The system of any of claims 6-10, wherein the filter assembly (42) is movable to selectively position the first filter and the second filter with respect to the IR detector (40), and preferably further comprising drive apparatus (54) for positioning the filter assembly (42) with respect to the IR detector (46).
- 12. The system of any of claims 6-11, wherein the IR detector (46) comprises a first detector and a second detector, and the first filter is fixed relative to the first detector and the second filter is fixed relative to the second detector, and preferably, wherein the filter assembly comprises at least a third filter.
- 13. The system of any of claims 6-12, further comprising a display (48) configured to display the concentration of the substance in the body.

## Patentansprüche

1. Verfahren zum nicht-invasiven Messen von einer Konzentration einer Substanz in einem Körper, wobei das Verfahren die folgenden Schritte umfasst:

Messen von einer ersten Menge an Infrarot (IR)-Strahlung, die von dem Körper in einer ersten IR-Wellenlängenbande absorbiert oder emittiert wird, in welcher die Substanz IR-Strahlung emittiert oder absorbiert;

Messen von einer zweiten Menge an Infrarotstrahlung (IR), die von dem Körper in einer zweiten IR-Wellenlängenbande absorbiert oder emittiert wird, die sich von der ersten IR-Wellenlängenbande unterscheidet und die entweder das gesamte Spektrum ist, in welchem der Körper IR-Strahlung in dem langweiligen IR-Spektrum (FIR; für Englisch: "far IR") emittiert oder absorbiert, oder eine Wellenlängenbande oder -banden ist, in der oder denen die Substanz keine oder eine vernachlässigbare Emission und Absorption von IR-Strahlung aufweist;

Messen von einer Temperatur von einer Oberfläche des Körpers;

Messen von einer Umgebungstemperatur;

Betreiben von einer Verarbeitungseinheit (70), um (a) eine erste normalisierte IR-Strahlungsmessung zu berechnen, die die erste gemessene Menge an IR-Strahlung normalisiert gegen eine erste Schwarzkörperstrahlung in der ersten IR-Wellenlängenbande ist, (b) eine zweite normalisierte IR-Strahlungsmessung zu berechnen, die die zweite gemessene Menge an IR-Strahlung normalisiert gegen eine erste Schwarzkörperstrahlung in der zweiten IR-Wellenlängenbande ist, und (c) einen normalisierten Verhältnisparameterwert als das Verhältnis des normalisierten ersten Strahlungsmesswerts zu dem normalisierten zweiten Strahlungsmesswert zu berechnen;

Speichern in einem Speicher (72) von Daten für eine Reihe von Messungen über eine statistisch repräsentative Population an verschiedenen Konzentrationen der Substanz, die entsprechend einem herkömmlichen invasiven Verfahren gewonnen und in einer empirisch hergeleiteten Nachschlagetabelle (28) angelegt wurden, indem für die Messungen in der Reihe Körperoberflächentemperaturen, Umgebungstemperaturen und normalisierte Verhältnisparameter gewonnen und gespeichert wurden; und Betreiben von der Verarbeitungseinheit (70), um die Konzentration der Substanz in dem Körper unter Verwendung der empirisch hergeleiteten Nachschlagetabelle zu berechnen, indem die Konzentration mit dem normalisierten Verhältnisparameter, der Körperoberflächentempera-

tur und der Umgebungstemperatur korreliert wird.

2. Verfahren nach Anspruch 1, wobei der normalisierte Verhältnisparameter ein Logarithmus des Verhältnisses von der normalisierten ersten Menge zu der normalisierten zweiten Menge ist.
3. Verfahren nach Anspruch 1 oder 2, wobei die Substanz Glucose ist.
4. Verfahren nach einem der vorhergehenden Ansprüche, wobei der Körper ein menschlicher Körper ist.
5. Verfahren nach einem der vorhergehenden Ansprüche, ferner umfassend den Schritt des Kühlens von der Körperoberfläche, um die Substanz zu veranlassen IR zu absorbieren, oder des Erwärmens von der Körperoberfläche, um die Substanz zu veranlassen IR zu emittieren, oder des Erzeugens von einer Umgebungsluftströmung über die Körperoberfläche.
6. System zum nicht-invasiven Messen von einer Konzentration einer Substanz in einem Körper, wobei das System das Folgende umfasst:

einen Infrarot (IR)-Detektor (40); und eine Filteranordnung (42), die mindestens einen ersten Filter und einen zweiten Filter umfasst und konfiguriert ist, um IR-Strahlung zu filtern, die zu dem Detektor (40) übertragen wird; wobei der erste Filter konfiguriert ist, um nur eine erste Menge an IR-Strahlung zu übertragen, die von dem Körper in einer ersten IR-Wellenlängenbande absorbiert oder emittiert wird, in welcher die Substanz IR-Strahlung emittiert oder absorbiert, und wobei der zweite Filter konfiguriert ist, um nur eine zweite Menge an IR-Strahlung zu übertragen, die von dem Körper in einer zweiten IR-Wellenlängenbande absorbiert oder emittiert wird, die sich von der ersten IR-Wellenlängenbande unterscheidet und die entweder das gesamte Spektrum ist, in welchem der Körper IR-Strahlung in dem langweiligen IR-Spektrum (FIR; für Englisch: "far IR") emittiert oder absorbiert, oder eine Wellenlängenbande oder -banden ist, in der oder denen die Substanz keine oder eine vernachlässigbare Emission und Absorption von IR-Strahlung aufweist; einen ersten Temperatursensor, der konfiguriert ist, um eine Oberflächentemperatur von einer Oberfläche des Körpers zu messen; einen zweiten Temperatursensor (46), der konfiguriert ist, um eine Umgebungstemperatur zu messen; eine Verarbeitungsvorrichtung (70), die konfiguriert ist, um (a) eine erste normalisierte IR-Strahlungsmessung zu berechnen, die die erste ge-

messene Menge an IR-Strahlung normalisiert gegen eine erste Schwarzkörperstrahlung in der ersten IR-Wellenlängenbande ist, (b) eine zweite normalisierte IR-Strahlungsmessung zu berechnen, die die zweite gemessene Menge an IR-Strahlung normalisiert gegen eine erste Schwarzkörperstrahlung in der zweiten IR-Wellenlängenbande ist, und (c) einen normalisierten Verhältnisparameterwert als das Verhältnis des normalisierten ersten Strahlungsmesswerts zu dem normalisierten zweiten Strahlungsmesswert zu berechnen;  
 einen Speicher (72), der Daten für eine Reihe von Messungen über eine statistisch repräsentative Population an verschiedenen Konzentrationen der Substanz speichert, die entsprechend einem herkömmlichen invasiven Verfahren gewonnen und in einer empirisch hergeleiteten Nachschlagetabelle (28) angelegt wurden, indem für die Messungen in der Reihe Körperoberflächentemperaturen, Umgebungstemperaturen und normalisierte Verhältnisparameter gewonnen und gespeichert wurden; und wobei die Verarbeitungseinheit (70) ferner konfiguriert ist, um die Konzentration der Substanz in dem Körper unter Verwendung der empirisch hergeleiteten Nachschlagetabelle zu berechnen, indem die Konzentration mit dem normalisierten Verhältnisparameter, der Körperoberflächentemperatur und der Umgebungstemperatur korreliert wird.

7. System nach Anspruch 6, ferner umfassend einen Temperaturveränderungsapparat (82), der operabel ist, um die Oberflächentemperatur von der Oberfläche des Körpers zu erhöhen oder zu erniedrigen.
8. System nach Anspruch 6 oder 7, ferner umfassend einen Luftströmungsapparat (84), der operabel ist, um eine Umgebungsluftströmung über der Oberfläche des Körpers zu erzeugen.
9. System nach einem der Ansprüche 6-8, wobei die Substanz Glucose ist und der Körper ein menschlicher Körper ist und wobei vorzugsweise der erste oder zweite Temperatursensor (46) einen Thermistor umfasst.
10. System nach einem der Ansprüche 6-9, wobei der IR-Detektor (40) eine Thermosäule mit Kollimationsoptik umfasst.
11. System nach einem der Ansprüche 6-10, wobei die Filteranordnung (42) bewegbar ist, um den ersten Filter und den zweiten Filter in Bezug auf den IR-Detektor (40) selektiv zu positionieren, und vorzugsweise ferner einen Antriebsapparat (54) zum Positionieren der Filteranordnung (42) in Bezug auf den

IR-Detektor (46) umfasst.

12. System nach einem der Ansprüche 6-11, wobei der IR-Detektor (46) einen ersten Detektor und einen zweiten Detektor umfasst und wobei der erste Filter in Bezug auf den ersten Detektor feststehend ist und der zweite Filter in Bezug auf den zweiten Detektor feststehend ist und wobei vorzugsweise die Filteranordnung mindestens einen dritten Filter umfasst.
13. System nach einem der Ansprüche 6-12, ferner umfassend eine Anzeige (48), die konfiguriert ist, um die Konzentration der Substanz in dem Körper anzuzeigen.

### Revendications

1. Procédé de mesure non invasive d'une concentration d'une substance dans un corps, le procédé comprenant les étapes de :

mesure d'une première quantité de rayonnement infrarouge (IR) absorbé ou émis par le corps dans une première bande de longueur d'onde IR dans laquelle la substance émet ou absorbe un rayonnement IR ;

mesure d'une seconde quantité de rayonnement IR absorbé ou émis par le corps dans une seconde bande de longueur d'onde IR différente de la première bande de longueur d'onde IR et qui est soit le spectre entier dans lequel le corps émet et absorbe un rayonnement IR dans le spectre IR lointain (FIR) soit une ou des bandes de longueur d'onde dans laquelle ou lesquelles la substance ne présente pas ou peu d'émission et d'absorption de rayonnement IR ;

mesure d'une température d'une surface du corps ;

mesure d'une température ambiante ;

exploitation d'un processeur (70) pour (a) calculer une première mesure de rayonnement IR normalisée qui est la première quantité mesurée de rayonnement IR normalisée par rapport à un premier rayonnement de corps noir dans la première bande de longueur d'onde IR, (b) calculer une seconde mesure de rayonnement IR normalisée qui est la seconde quantité mesurée de rayonnement IR normalisée par rapport à un premier rayonnement de corps noir dans la seconde bande de longueur d'onde IR, et (c) calculer une valeur de paramètre de rapport normalisé en tant que rapport entre la première valeur de mesure de rayonnement normalisée et la seconde valeur de mesure de rayonnement normalisée ;

stockage dans une mémoire (72) de données pour une série de mesures sur une population

- statistiquement représentative à diverses concentrations de la substance prises selon une méthode invasive classique et construites dans une table de consultation dérivée empiriquement (28) en prenant et en stockant pour les mesures dans ladite série des températures de surface du corps, des températures ambiantes et des paramètres de rapport normalisés ; et exploitation du processeur (70) pour calculer la concentration de la substance dans le corps à l'aide de la table de consultation dérivée empiriquement en corrélant la concentration avec le paramètre de rapport normalisé, la température de surface du corps, et la température ambiante.
2. Procédé selon la revendication 1, dans lequel le paramètre de rapport normalisé est un logarithme du rapport entre la première quantité normalisée et la seconde quantité normalisée.
  3. Procédé selon la revendication 1 ou 2, dans lequel la substance est le glucose.
  4. Procédé selon l'une quelconque des revendications précédentes, dans lequel le corps est un corps humain.
  5. Procédé selon l'une quelconque des revendications précédentes, comprenant en outre l'étape de refroidissement de la surface du corps pour amener la substance à absorber de l'IR, ou de chauffage de la surface du corps pour amener la substance à émettre de l'IR, ou de création d'un flux d'air ambiant sur la surface du corps.
  6. Système de mesure non invasive d'une concentration d'une substance dans un corps, le système comprenant :
    - un détecteur d'infrarouge (IR) (40) ; et
    - un ensemble de filtres (42) comportant au moins un premier filtre et un deuxième filtre configurés pour filtrer un rayonnement IR transmis au détecteur (40) ;
    - dans lequel le premier filtre est configuré pour transmettre uniquement une première quantité de rayonnement IR absorbé ou émis par le corps dans une première bande de longueur d'onde IR dans laquelle la substance émet et absorbe un rayonnement IR et le deuxième filtre est configuré pour transmettre uniquement une seconde quantité de rayonnement IR absorbé ou émis par le corps dans une seconde bande de longueur d'onde IR différente de la première bande de longueur d'onde IR et qui est soit le spectre entier dans lequel le corps émet et absorbe un rayonnement IR dans le spectre IR lointain (FIR) soit une ou des bandes de longueur d'onde dans laquelle ou lesquelles la substance ne présente pas ou peu d'émission et d'absorption de rayonnement IR ;
    - un premier capteur de température configuré pour mesurer une température superficielle de la surface du corps ;
    - un second capteur de température (46) configuré pour mesurer une température ambiante ;
    - un processeur (70) configuré pour (a) calculer une première mesure de rayonnement IR normalisée qui est la première quantité mesurée de rayonnement IR normalisée par rapport à un premier rayonnement de corps noir dans la première bande de longueur d'onde IR, (b) calculer une seconde mesure de rayonnement IR normalisée qui est la seconde quantité mesurée de rayonnement IR normalisée par rapport à un premier rayonnement de corps noir dans la seconde bande de longueur d'onde IR, et (c) calculer une valeur de paramètre de rapport normalisé en tant que rapport entre la première valeur de mesure de rayonnement normalisée et la seconde valeur de mesure de rayonnement normalisée ; et
    - une mémoire (72) stockant des données pour une série de mesures sur une population statistiquement représentative à diverses concentrations de la substance prises selon une méthode invasive classique et construites dans une table de consultation dérivée empiriquement (28) en prenant et en stockant pour les mesures dans ladite série des températures de surface du corps, des températures ambiantes et des paramètres de rapport normalisés ;
    - le processeur (70) étant en outre configuré pour calculer la concentration de la substance dans le corps à l'aide de la table de consultation dérivée empiriquement en corrélant la concentration avec le paramètre de rapport normalisé, la température de surface du corps, et la température ambiante.
  7. Système selon la revendication 6, comprenant en outre un appareil de changement de température (82) opérationnel pour augmenter ou diminuer la température superficielle de la surface du corps.
  8. Système selon la revendication 6 ou 7, comprenant en outre un appareil de flux d'air (84) opérationnel pour créer un flux d'air ambiant sur la surface du corps.
  9. Système selon l'une quelconque des revendications 6 à 8, dans lequel la substance est le glucose et le corps est un corps humain, et dans lequel de préférence le premier ou second capteur de température (46) comprend un thermistor.

10. Système selon l'une quelconque des revendications 6 à 9, dans lequel le détecteur d'IR (40) comprend une thermopile avec une optique de collimation.
11. Système selon l'une quelconque des revendications 6 à 10, dans lequel l'ensemble de filtres (42) est mobile pour positionner sélectivement le premier filtre et le deuxième filtre par rapport au détecteur d'IR (40), et comprenant en outre de préférence un appareil d'entraînement (54) pour positionner l'ensemble de filtres (42) par rapport au détecteur d'IR (46). 5 10
12. Système selon l'une quelconque des revendications 6 à 11, dans lequel le détecteur d'IR (46) comprend un premier détecteur et un second détecteur, et le premier filtre est fixe par rapport au premier détecteur et le deuxième filtre est fixe par rapport au second détecteur, et dans lequel, de préférence, l'ensemble de filtres comprend au moins un troisième filtre. 15 20
13. Système selon l'une quelconque des revendications 6 à 12, comprenant en outre un afficheur (48) configuré pour afficher la concentration de la substance dans le corps. 25

30

35

40

45

50

55

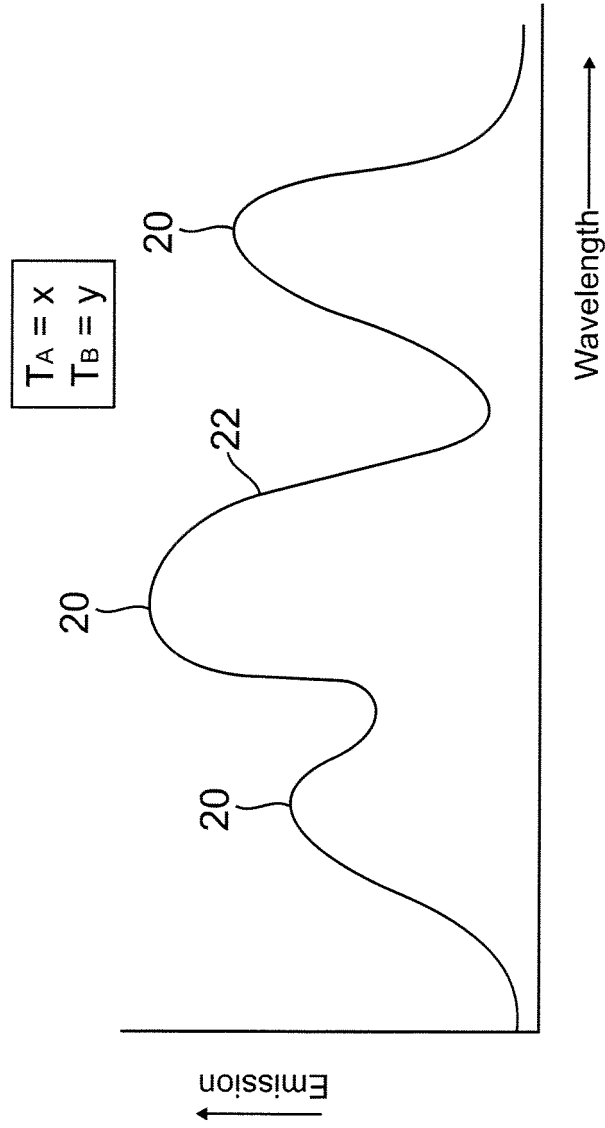


FIG. 1

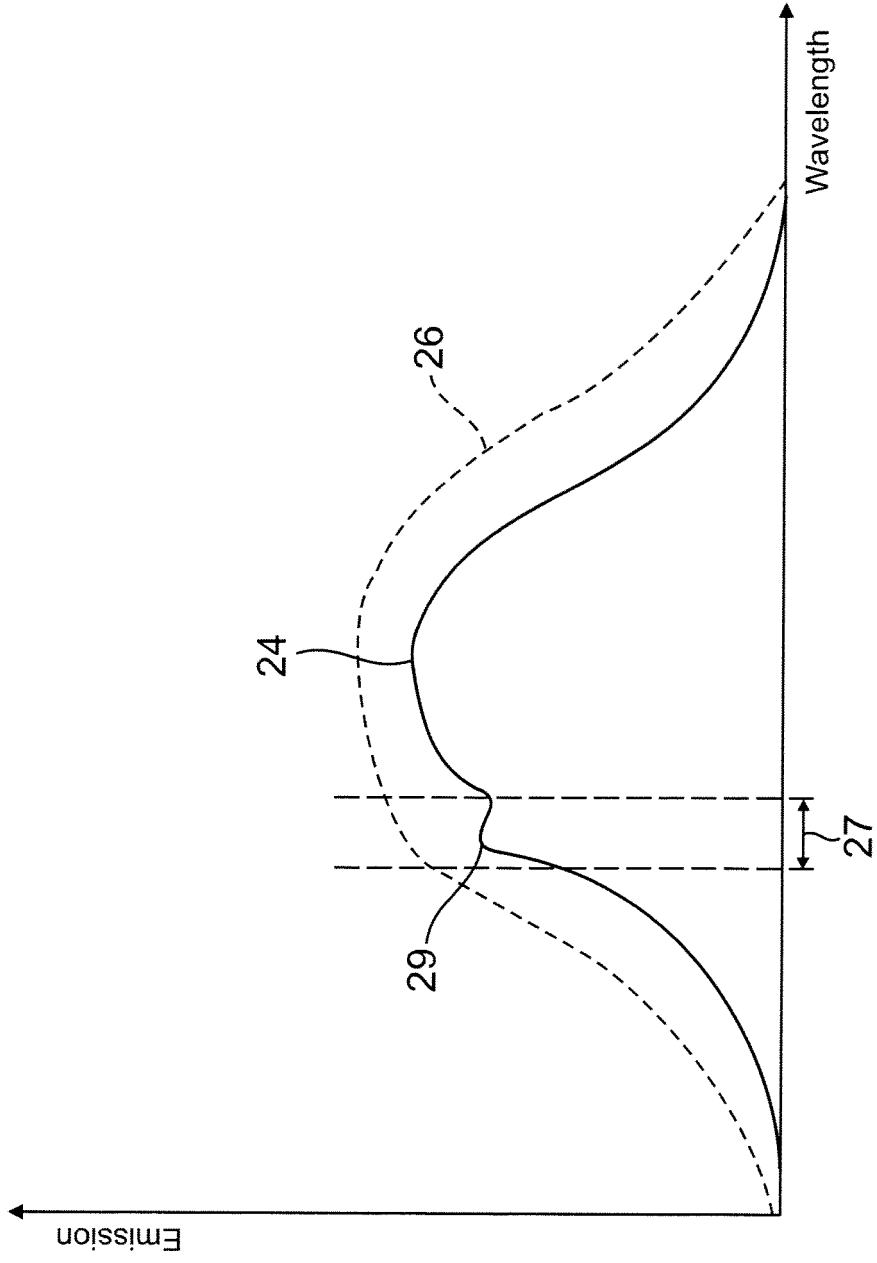


FIG. 2

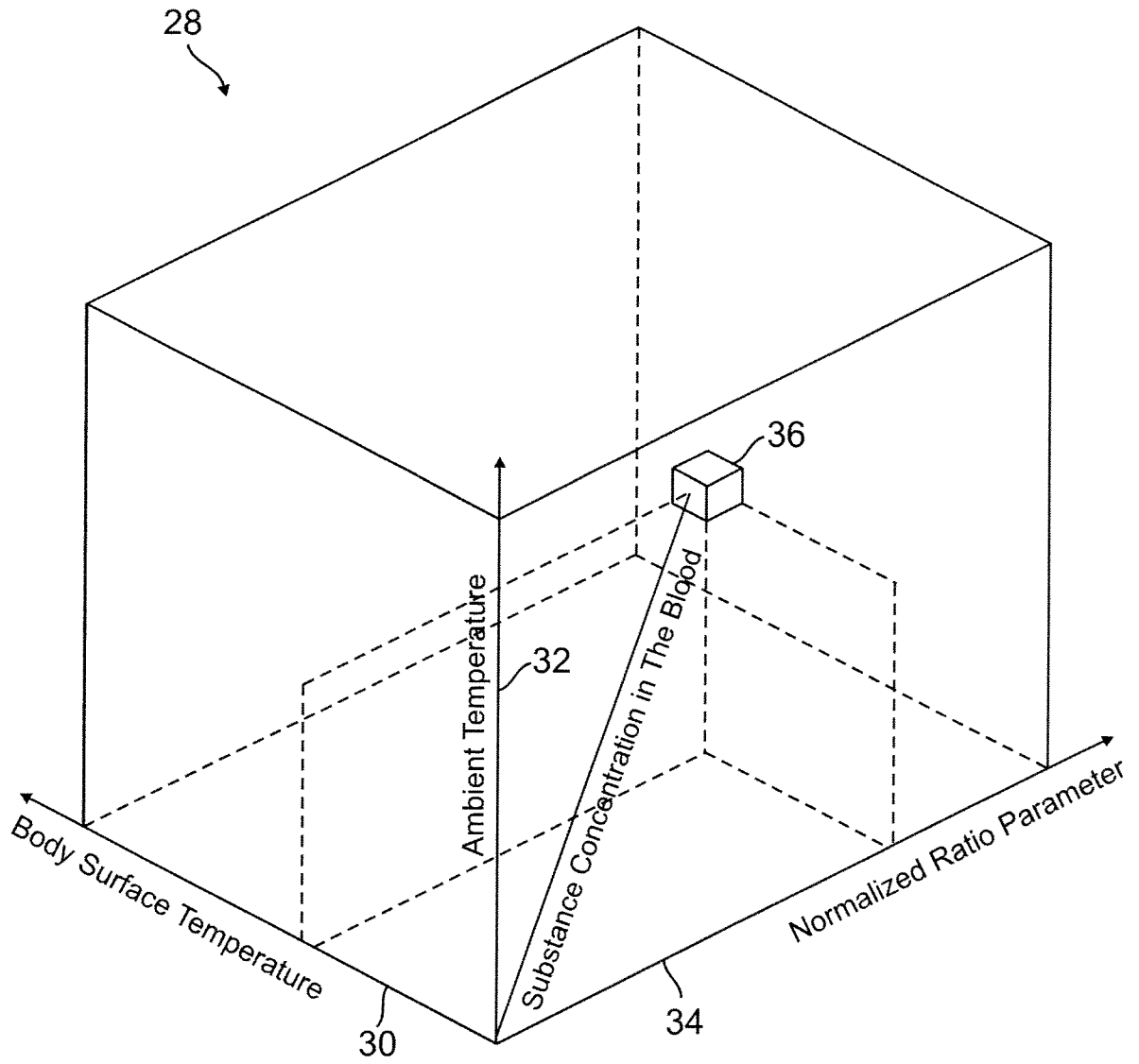


FIG. 3

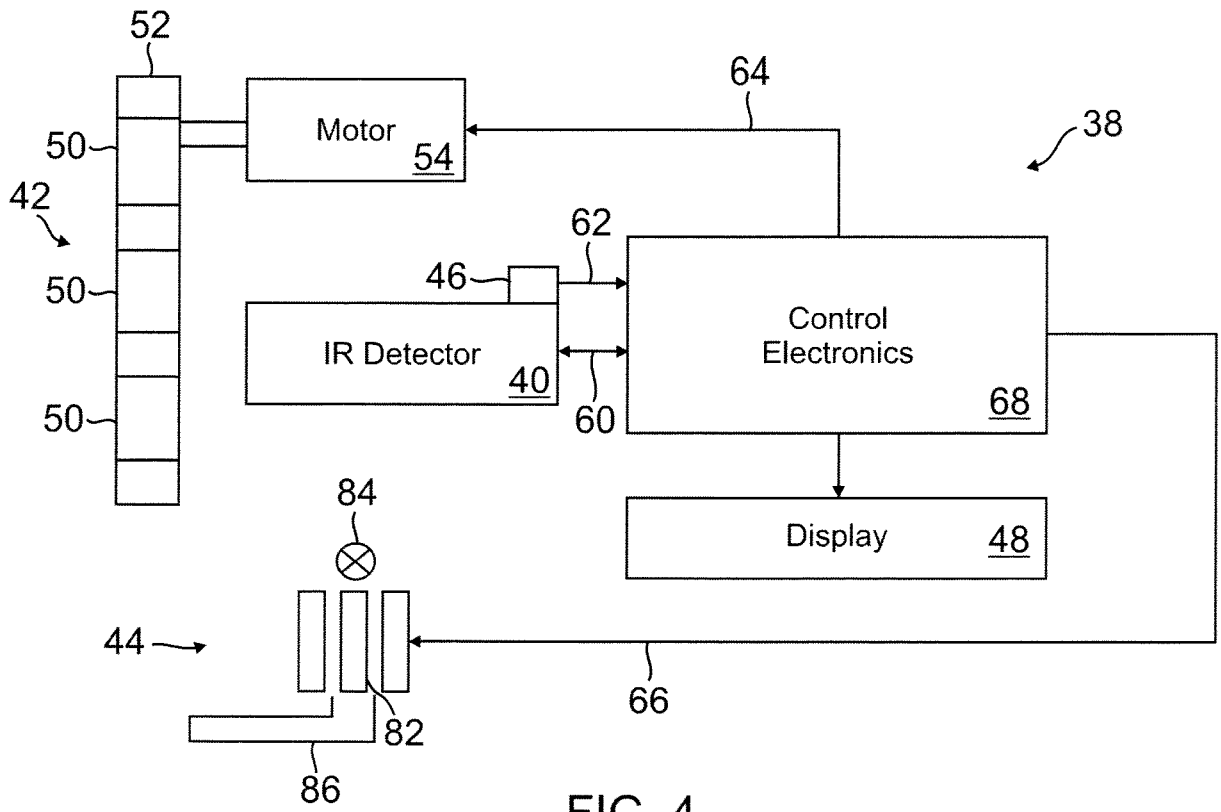


FIG. 4

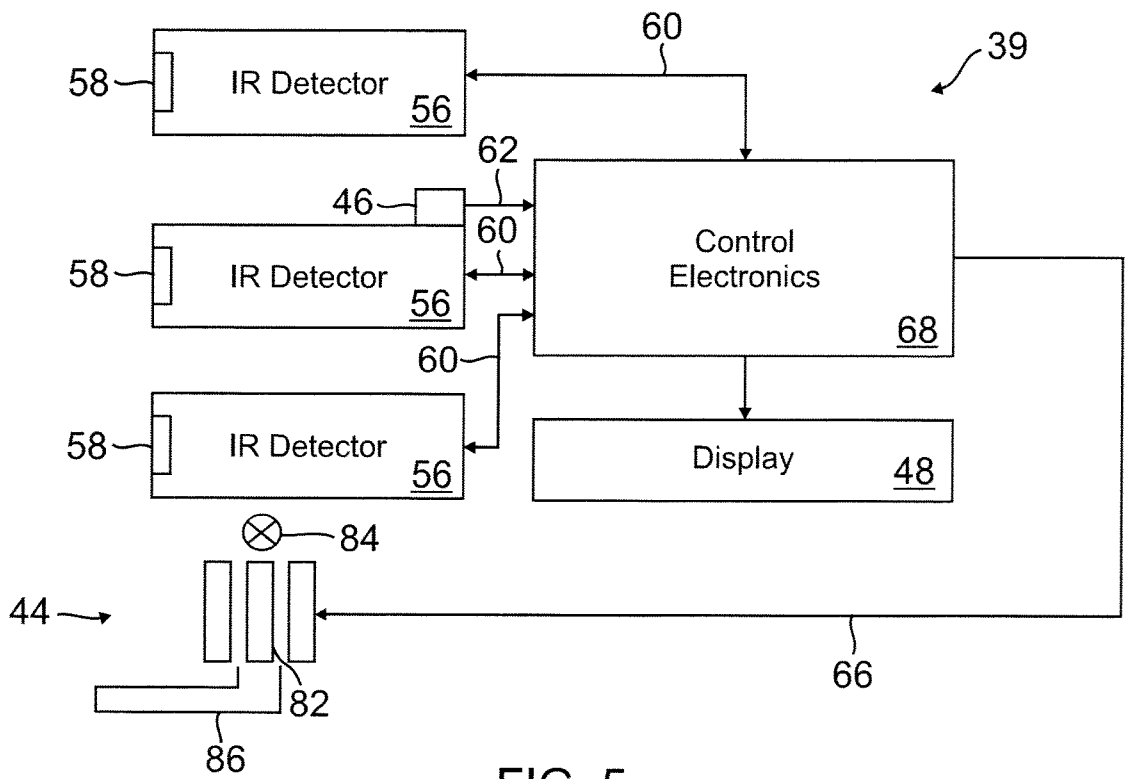


FIG. 5

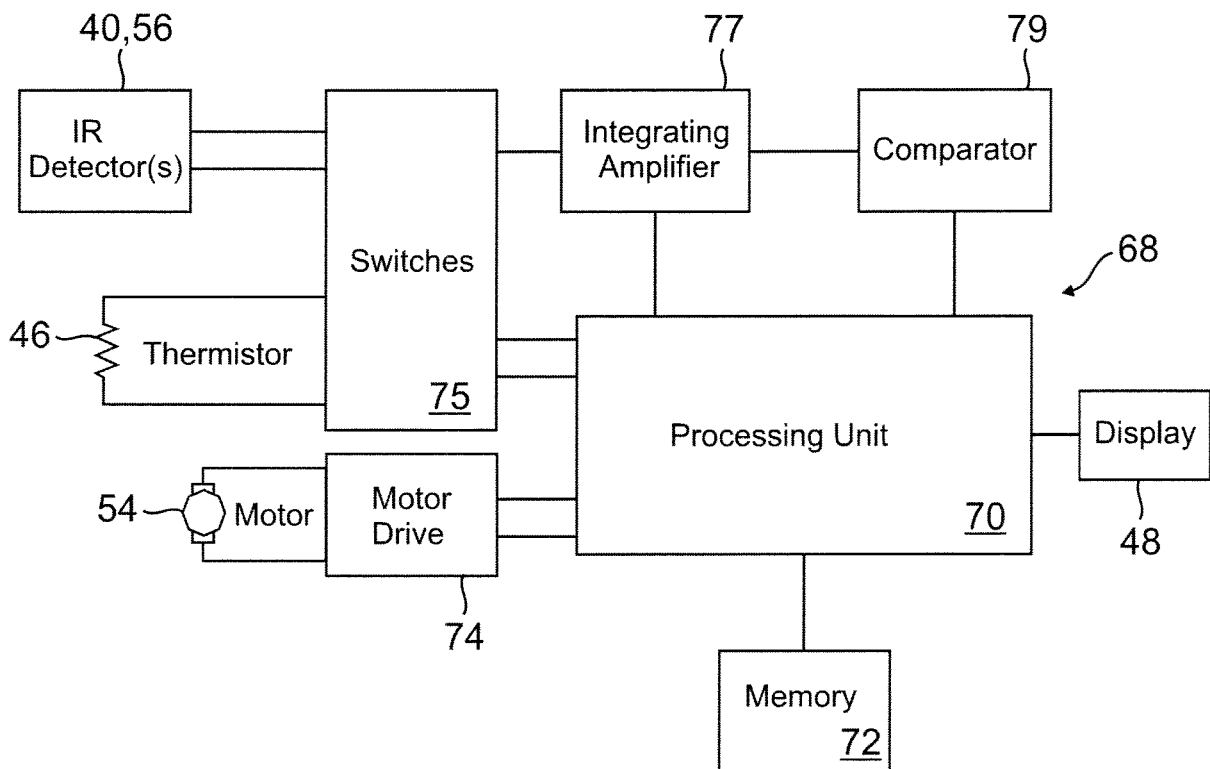


FIG. 6

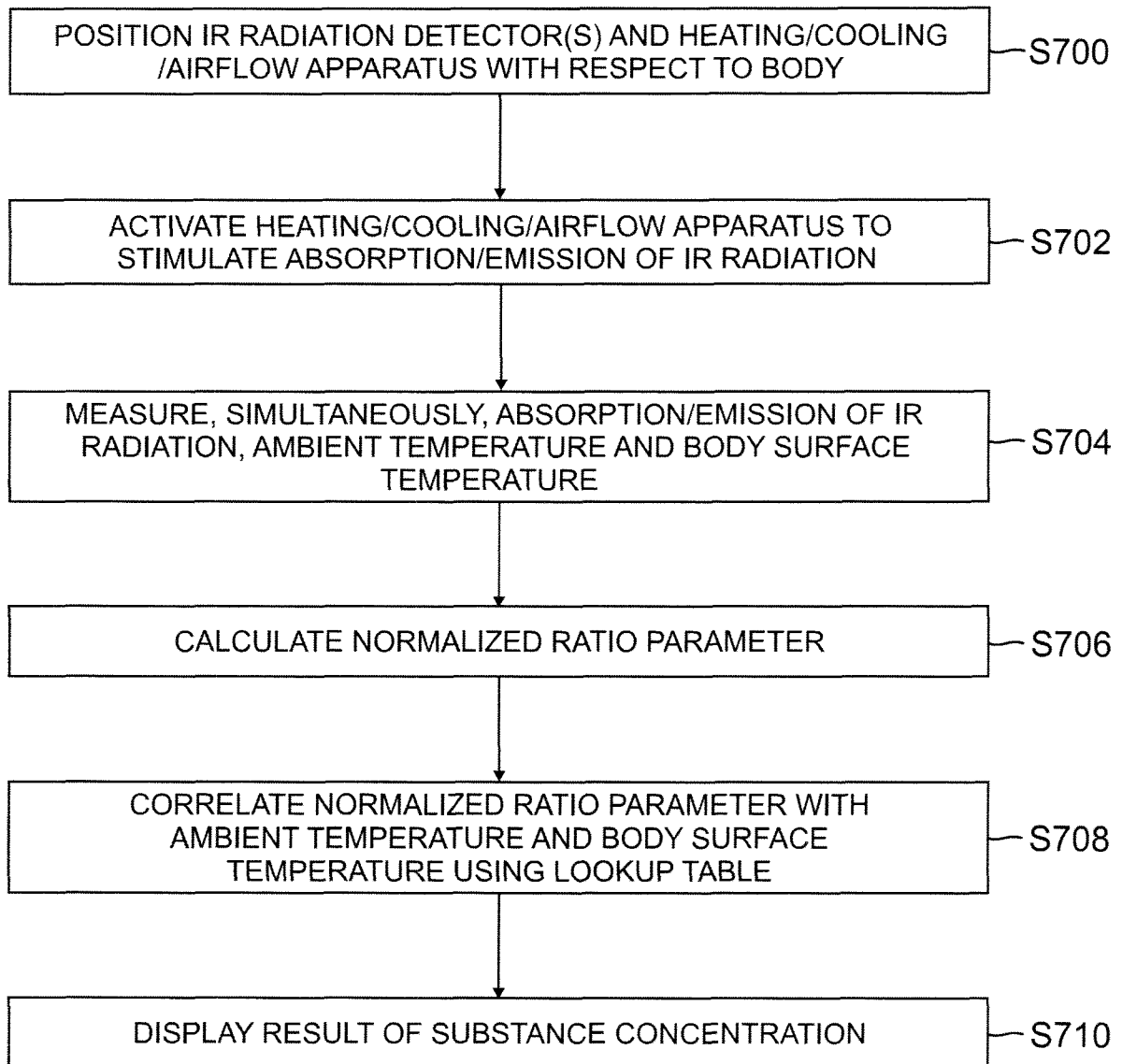


FIG. 7

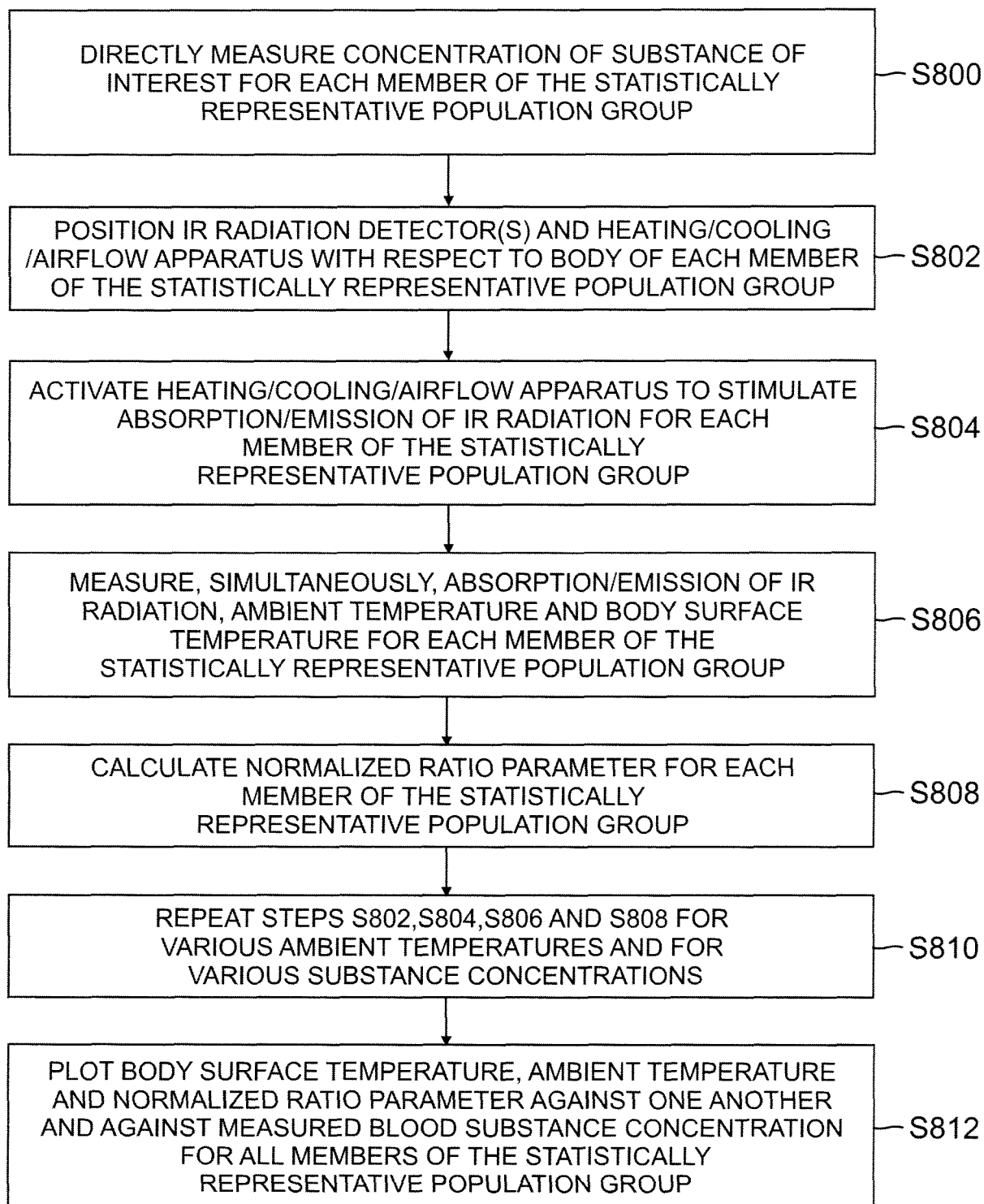


FIG. 8

**REFERENCES CITED IN THE DESCRIPTION**

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

**Patent documents cited in the description**

- US 5313941 A [0002]
- US 5370114 A [0002]
- US 5515847 A [0002]
- US 5601079 A [0002]
- US 5615672 A [0002]
- US 5666956 A [0002] [0004]
- US 6949070 B [0002]
- US 6998247 B [0002]
- US 7183102 B [0002]
- US 4054487 A [0003]
- US 2005043630 A [0005]

专利名称(译)	用于非侵入式测量身体内物质的装置和方法		
公开(公告)号	<a href="#">EP2276406A2</a>	公开(公告)日	2011-01-26
申请号	EP2009730011	申请日	2009-03-20
[标]申请(专利权)人(译)	格鲁科威斯塔有限公司 GERLITZ JONATHAN		
申请(专利权)人(译)	GLUCOVISTA有限责任公司 GERLITZ , JONATHAN		
当前申请(专利权)人(译)	GLUCOVISTA INC.		
[标]发明人	GERLITZ JONATHAN		
发明人	GERLITZ, JONATHAN		
IPC分类号	A61B5/1477 A61B5/145 A61B5/01 G05F1/00 A61B5/00		
CPC分类号	A61B5/1455 A61B5/01 A61B5/14532 A61B5/14546 A61B2560/0252		
优先权	12/101859 2008-04-11 US		
其他公开文献	EP2276406B1 EP2276406A4		
外部链接	<a href="#">Espacenet</a>		

#### 摘要(译)

本系统和方法的实施方案测量体内物质(例如葡萄糖)的浓度。本实施例测量在第一波长带中从身体吸收或发射的第一量的红外(IR)辐射,以及在第二波长带中从身体吸收或发射的第二量的IR辐射。本实施例还测量身体表面的温度和环境温度。从四次测量计算归一化比率参数,并且通过使用经验导出的查找表将归一化比率参数与体表温度和环境温度相关联来计算体内物质的浓度。还公开了用于创建经验导出的查找表的方法。