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Sanyal et al.

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(54) **MULTIPLE SENSOR GLUCOSE CONCENTRATION DETERMINATION ANALYZER APPARATUS AND METHOD OF USE THEREOF**

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(22) Filed: **Nov. 22, 2019**

(65) **Prior Publication Data**

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Related U.S. Application Data

(63) Continuation-in-part of application No. 15/829,877, filed on Dec. 2, 2017, now abandoned, which is a (Continued)

(51) **Int. Cl.**

A61B 5/1455 (2006.01)
A61B 5/145 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61B 5/14532*** (2013.01); ***A61B 5/0053*** (2013.01); ***A61B 5/1455*** (2013.01); ***A61B 5/6832*** (2013.01); *G01J 3/00* (2013.01)

(58) **Field of Classification Search**
CPC A61B 5/1455; A61B 5/14551; A61B 5/14552; A61B 5/14532; A61B 5/6832; A61B 5/6843
See application file for complete search history.

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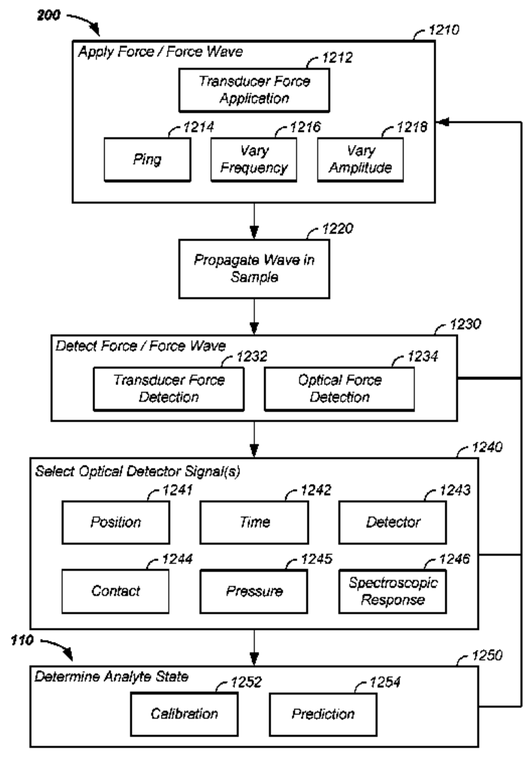
Primary Examiner — Eric F Winakur
(74) *Attorney, Agent, or Firm* — Kevin H. Hazen; Hazen Patent Group, LLC

(57) **ABSTRACT**

The invention comprises a method and apparatus for non-invasively determining state of a person, comprising the steps of: providing an analyzer comprising a first and second spectrometer unit and a main controller subsystem; replaceably attaching the first spectrometer unit to the person at a first illumination zone; the first spectrometer unit delivering first photons, from first illumination optics, along a first mean z-axis optical path normal to a first x/y-plane tangentially contacting the first illumination zone of the person; replaceably attaching a second spectrometer unit to the person at a second illumination zone; the second spectrometer delivering second photons, from second illumination optics, along a second mean z-axis optical path perpendicular to a second x/y-plane tangentially contacting the second illumination zone of the skin, the first x/y-plane noncoplanar
(Continued)



with the second x/y-plane; and the main controller processing detected signals to generate at least one measure of state of the person.

10 Claims, 10 Drawing Sheets

Related U.S. Application Data

continuation-in-part of application No. 15/636,073, filed on Jun. 28, 2017, now abandoned.

(60) Provisional application No. 62/355,507, filed on Jun. 28, 2016.

(51) **Int. Cl.**

A61B 5/00	(2006.01)
G01J 3/00	(2006.01)

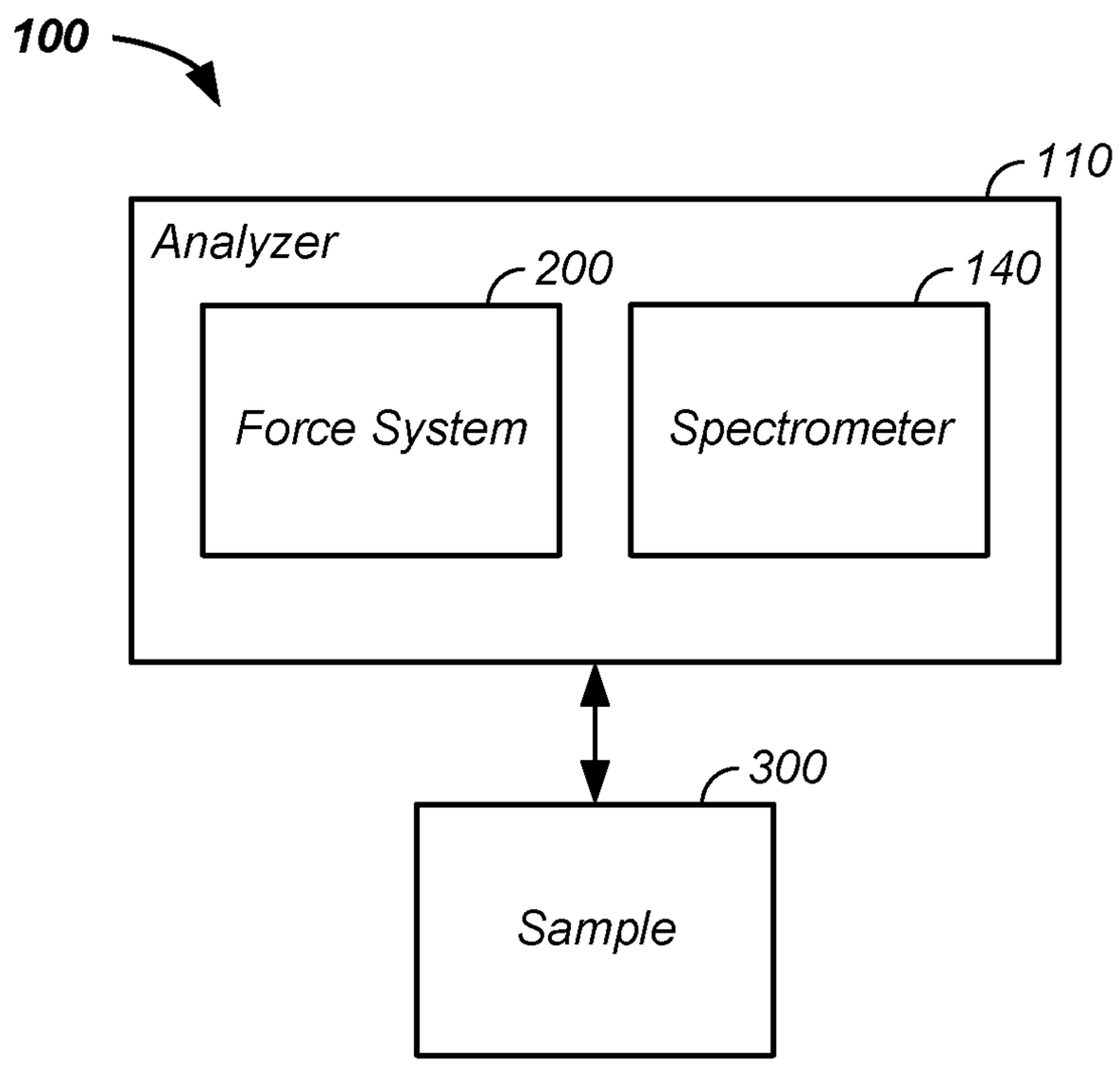

100
110
Analyzer
200
Force System
140
Spectrometer
300
Sample

FIG. 1

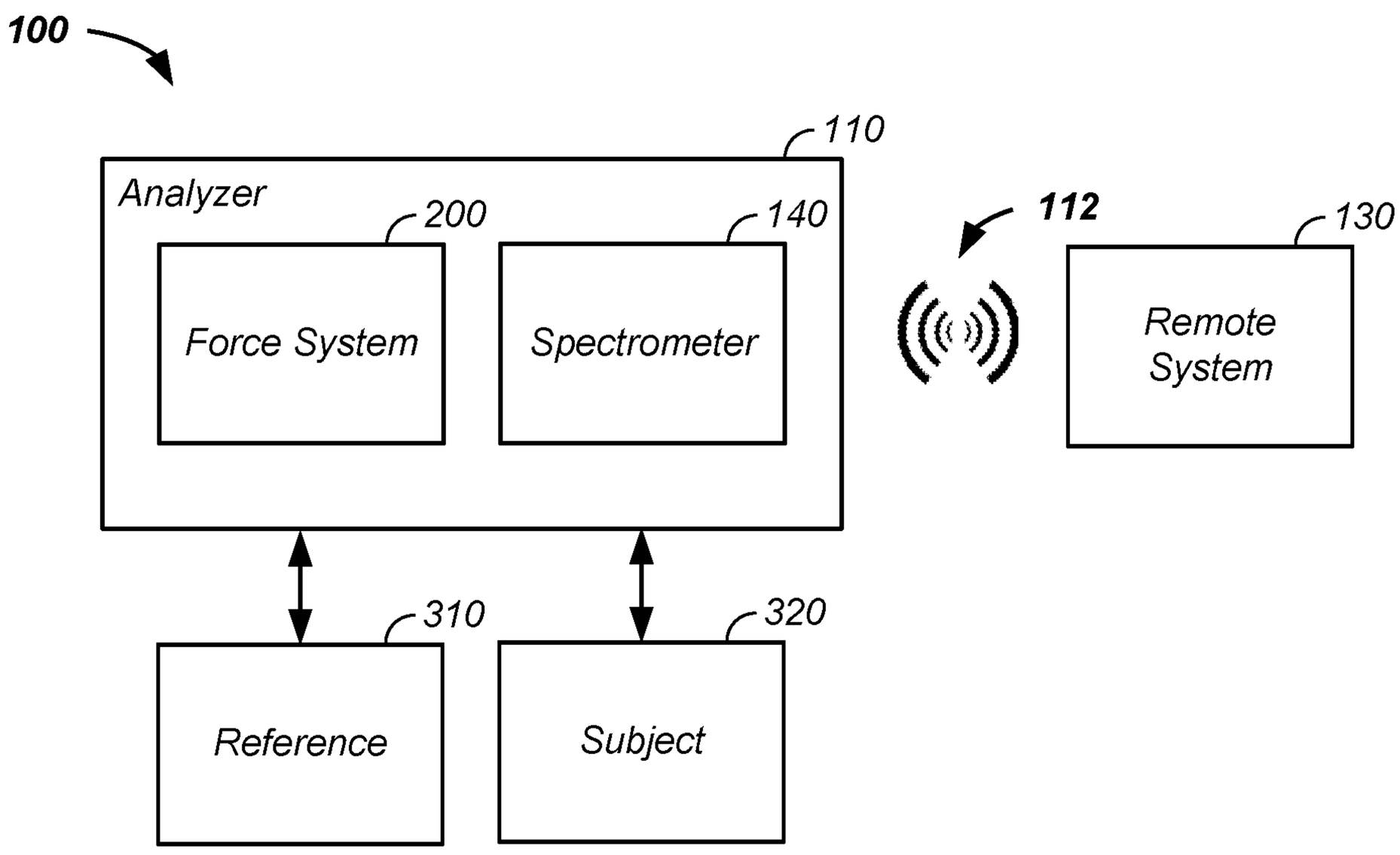

100
110
Analyzer
200
Force System
140
Spectrometer
112
130
Remote System
310
Reference
320
Subject

FIG. 2

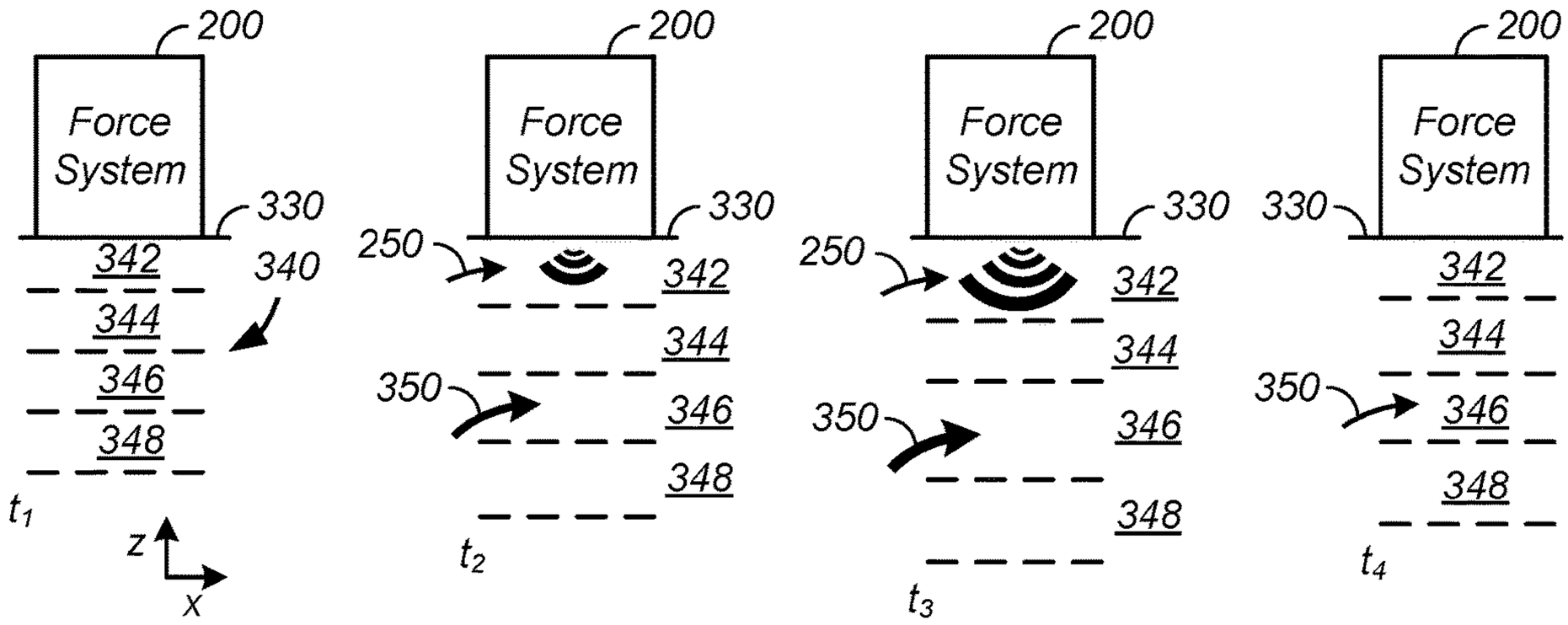


FIG. 3A

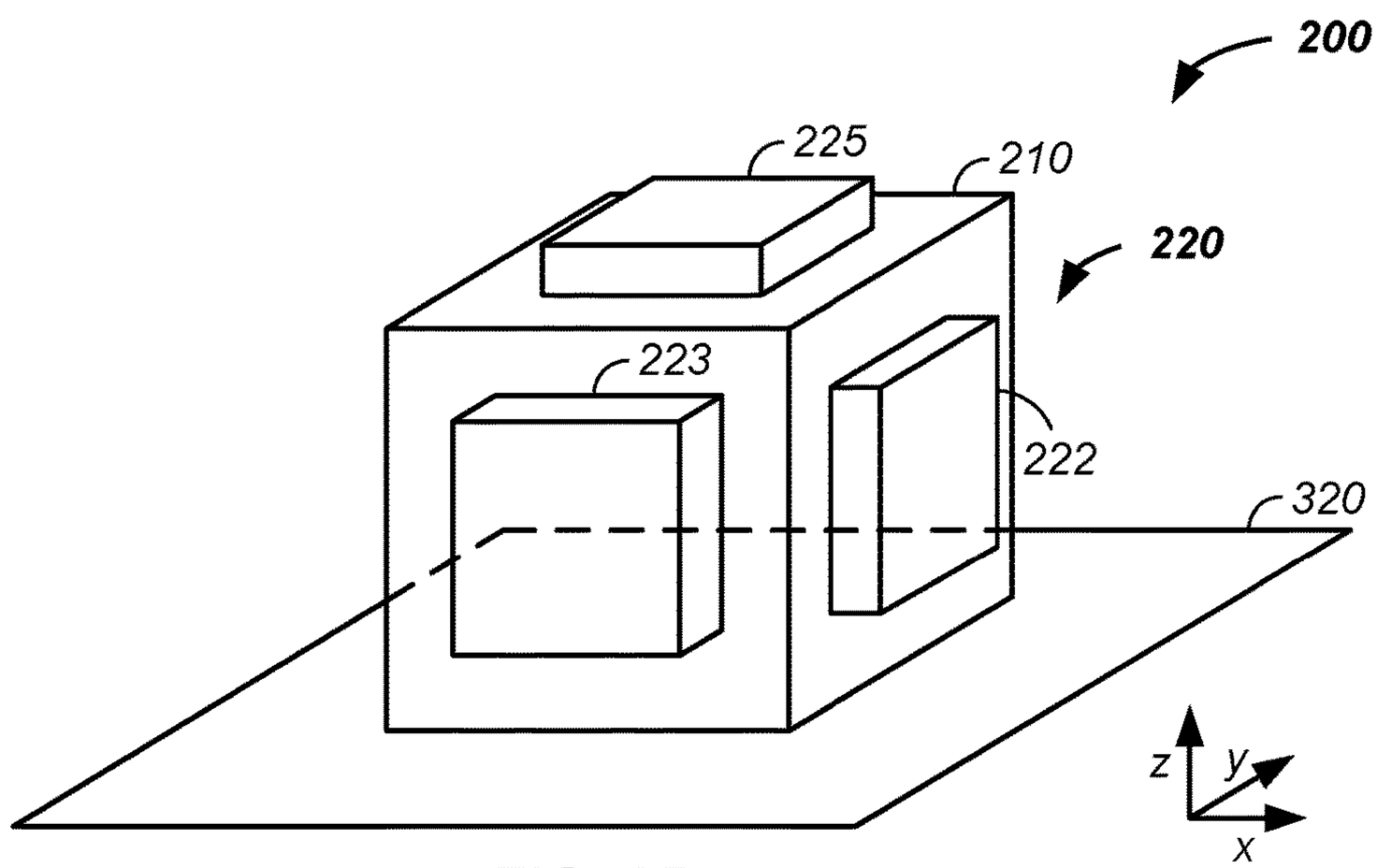


FIG. 3B

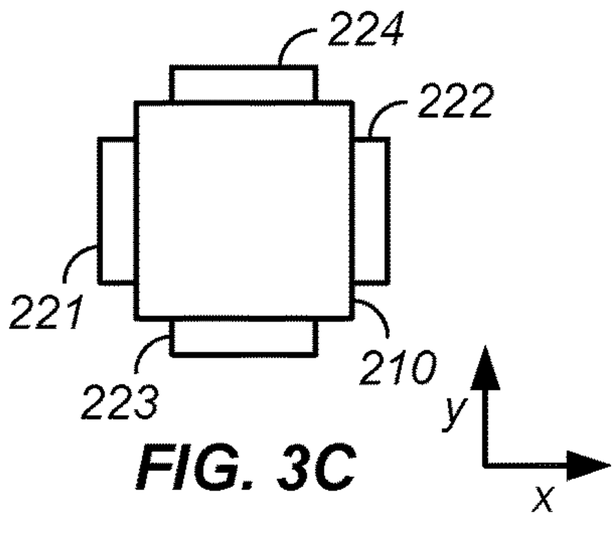


FIG. 3C

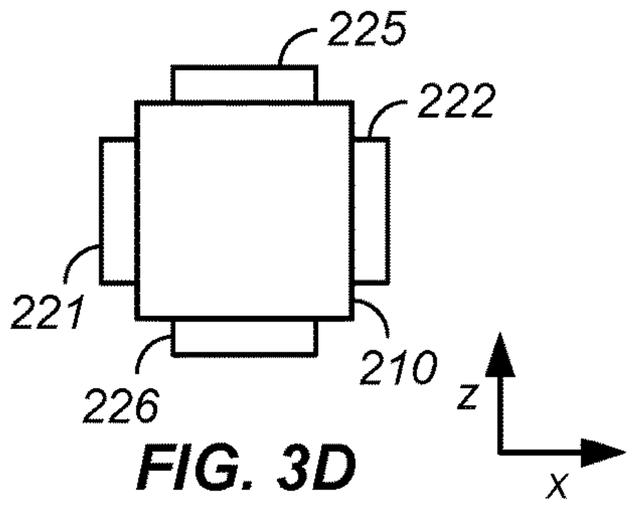


FIG. 3D

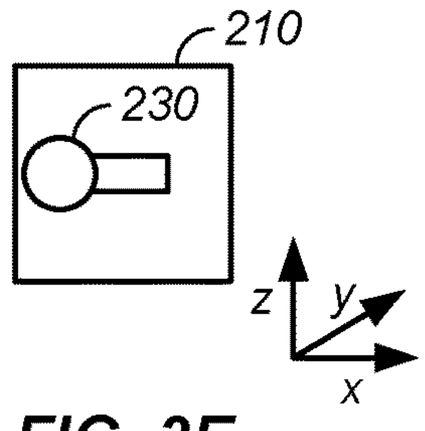


FIG. 3E

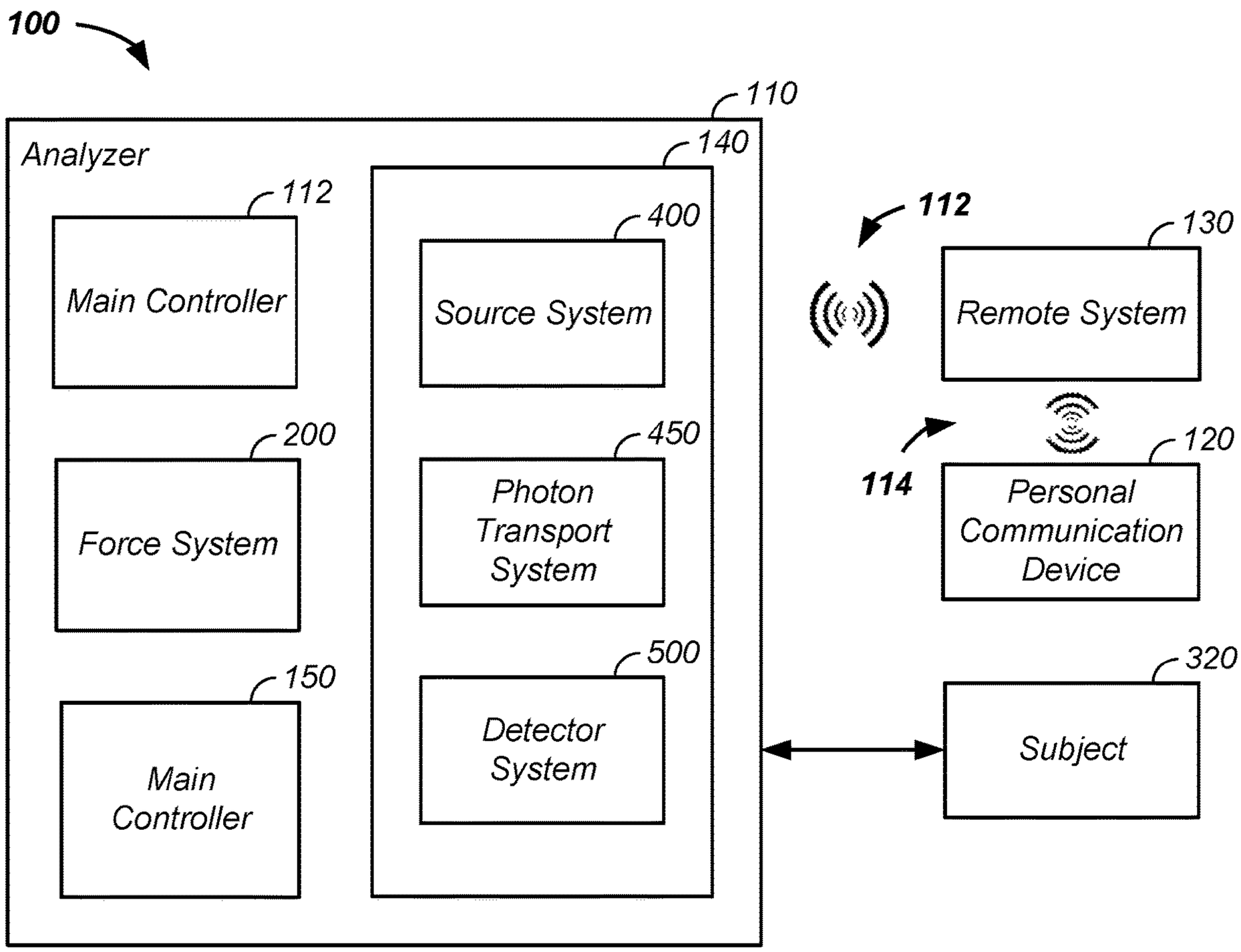


FIG. 4A

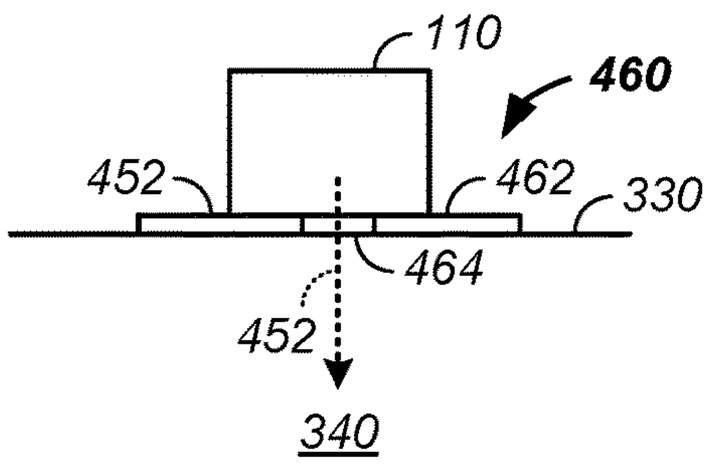


FIG. 4B

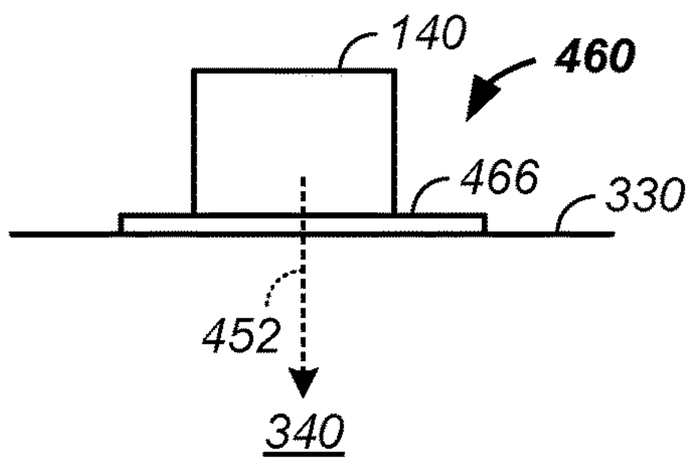


FIG. 4C

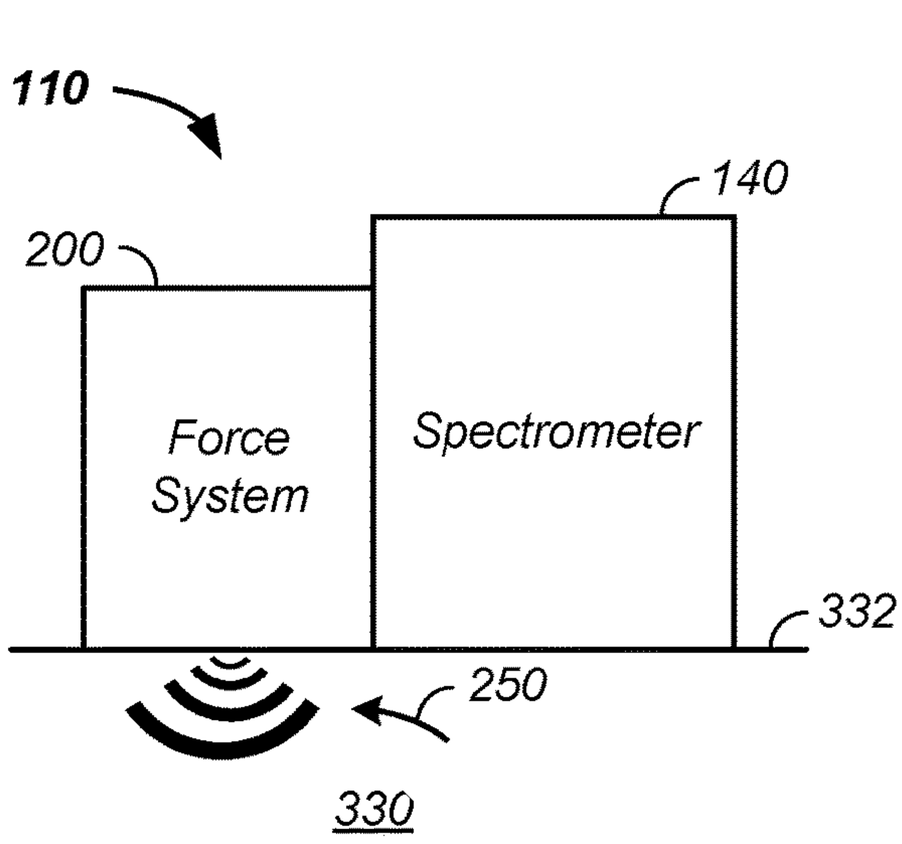


FIG. 5A

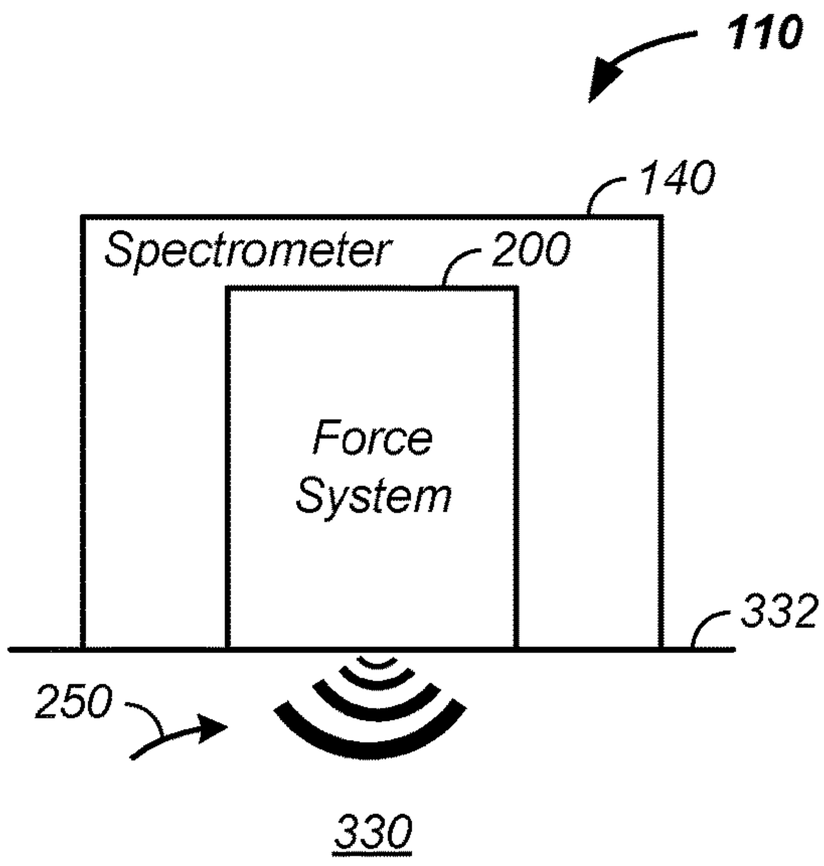


FIG. 5B

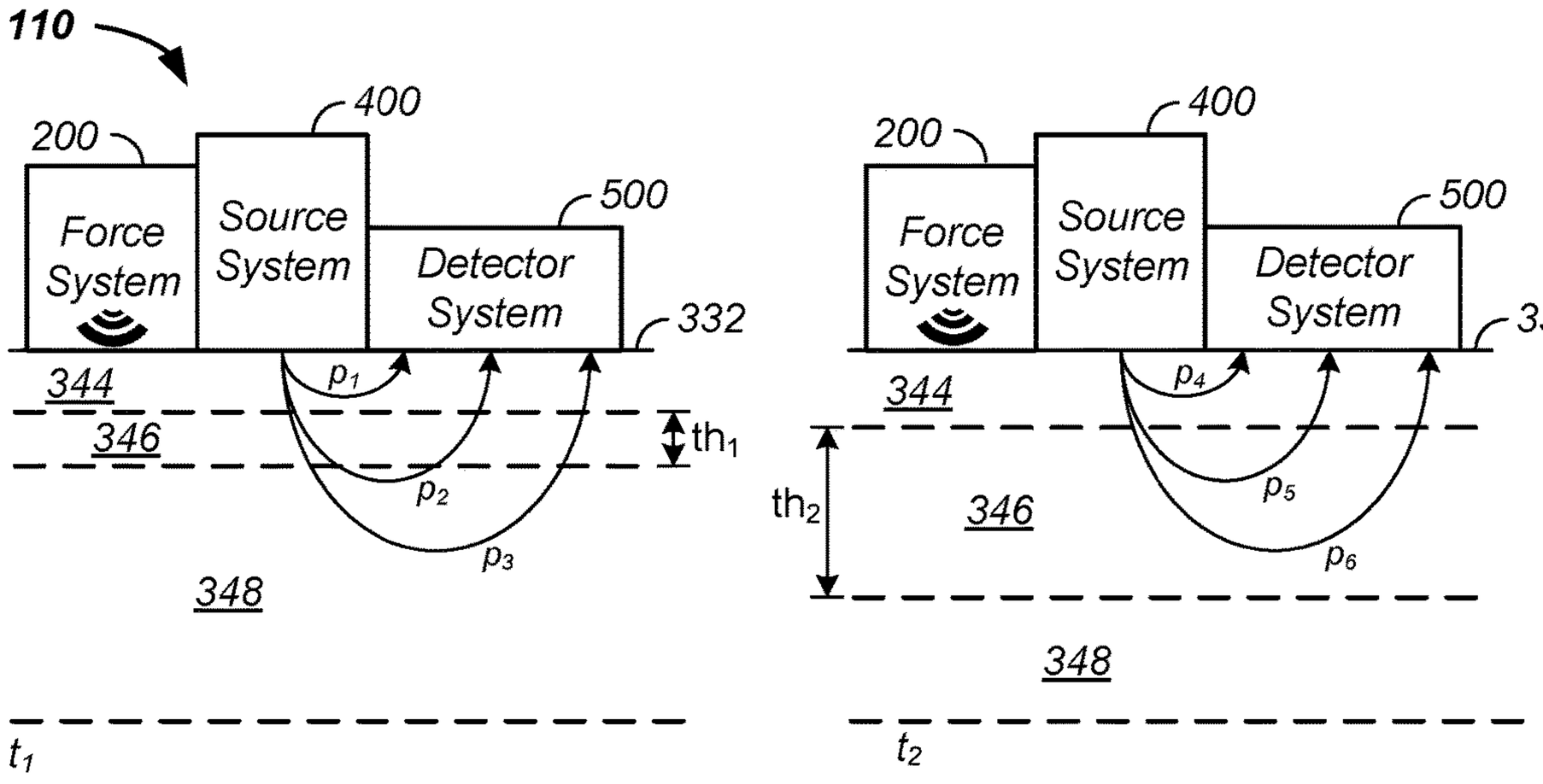


FIG. 6

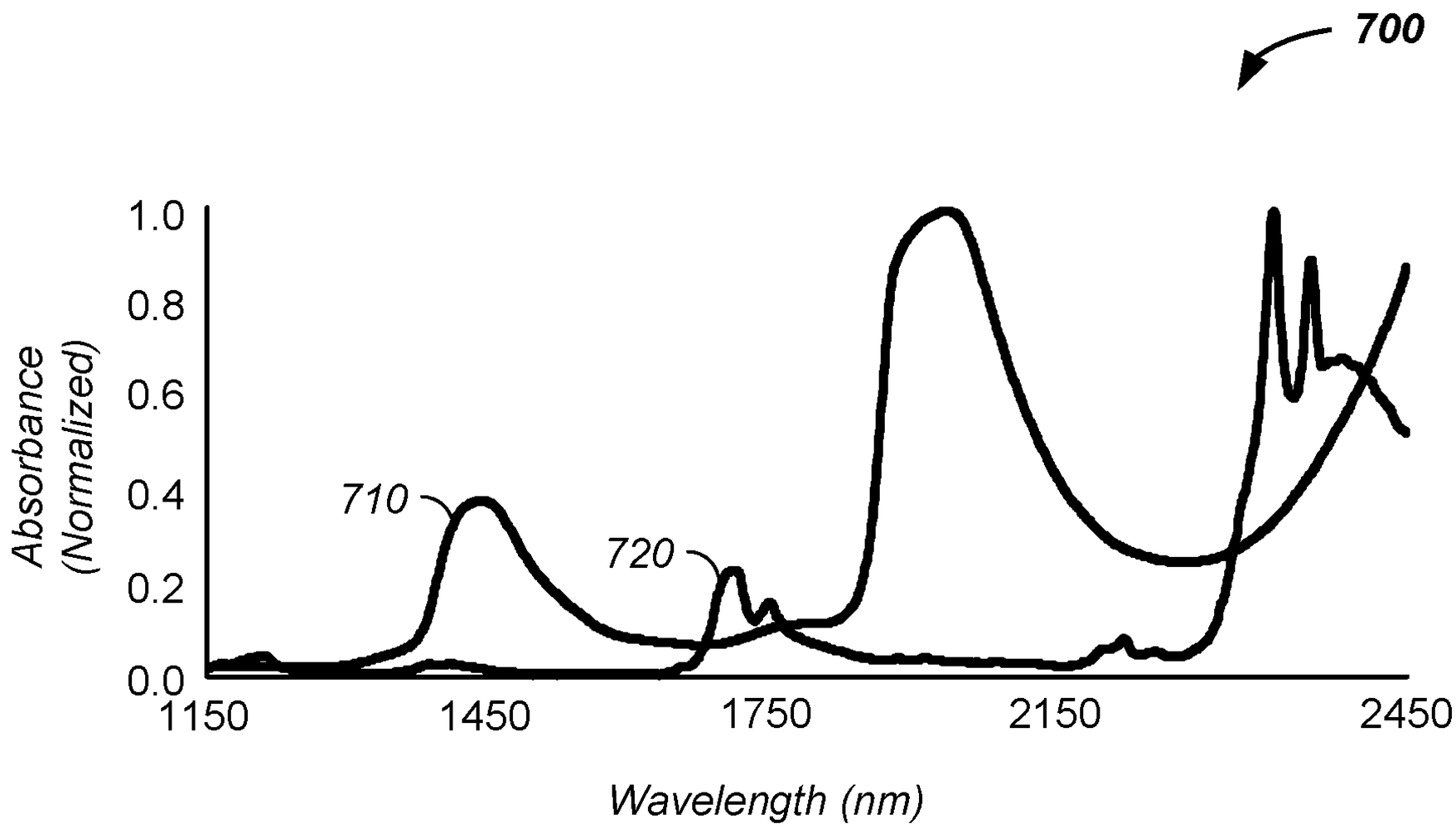

700
1.0
0.8
0.6
0.4
0.2
0.0
Absorbance (Normalized)
710
720
1150
1450
1750
2150
2450
Wavelength (nm)

FIG. 7A

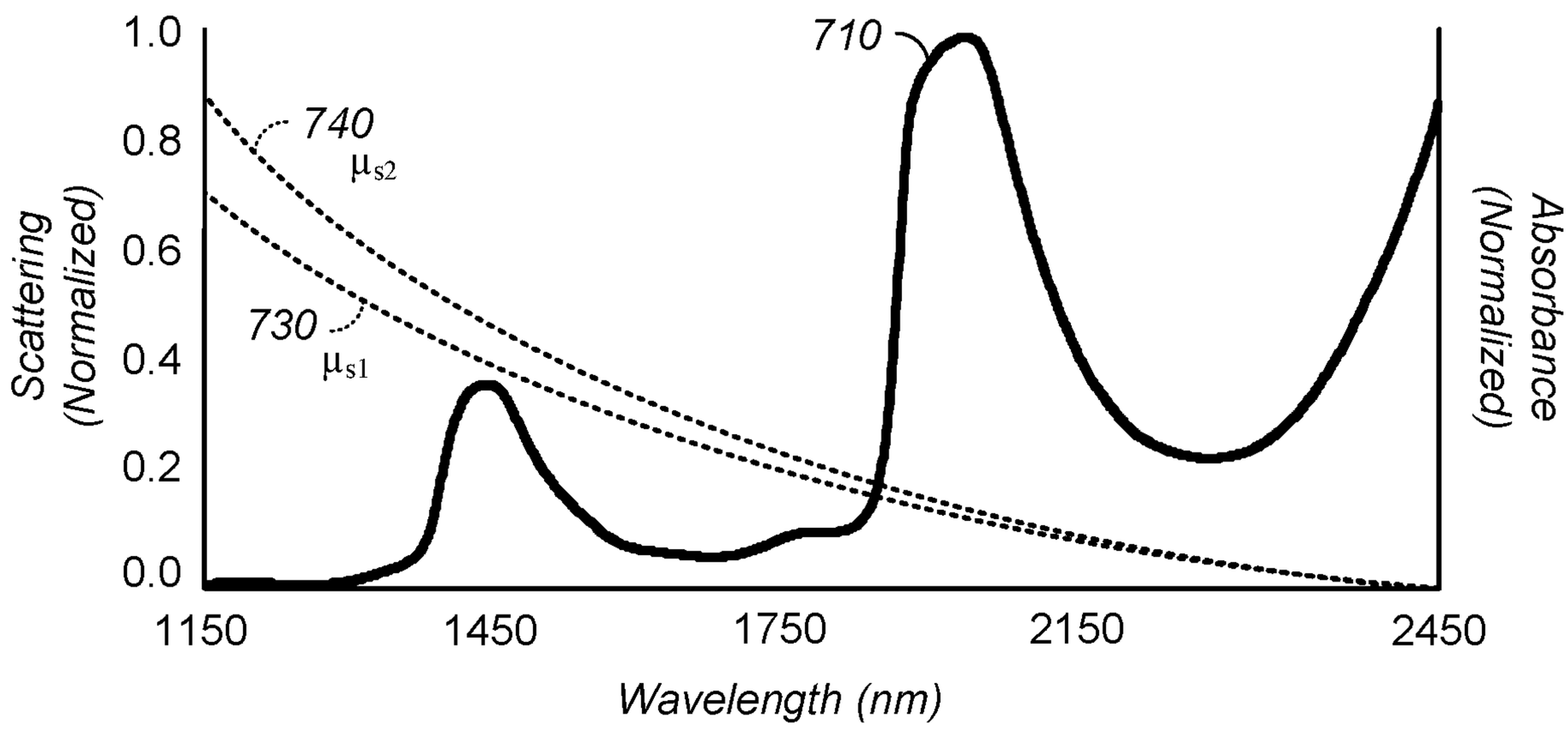

1.0
0.8
0.6
0.4
0.2
0.0
Scattering (Normalized)
740
μ_{s2}
730
μ_{s1}
710
Absorbance (Normalized)
1150
1450
1750
2150
2450
Wavelength (nm)

FIG. 7B

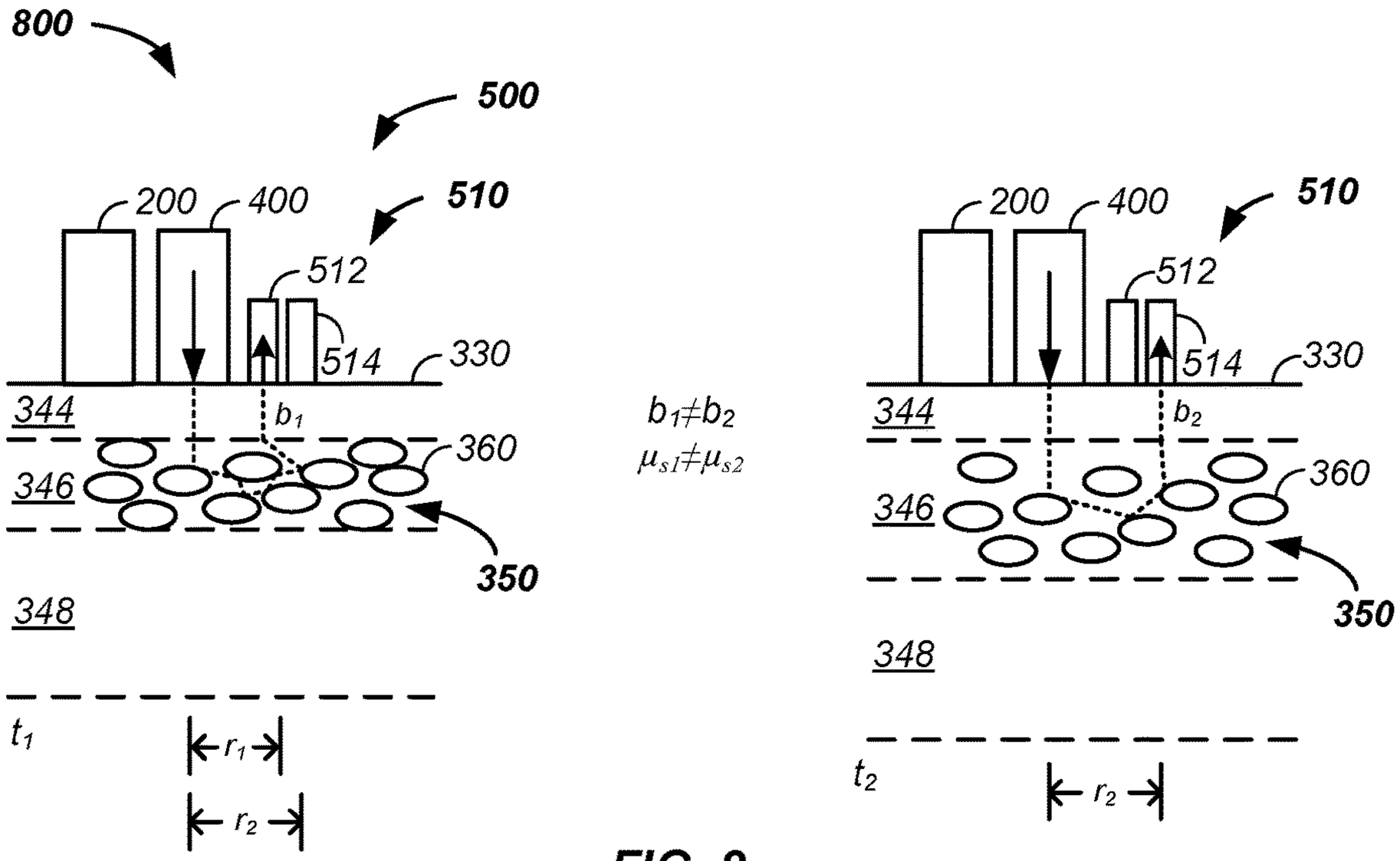

800
500
510
200
400
512
514
330
344
b_1
360
346
350
348
t_1
r_1
r_2
$b_1 \neq b_2$
$\mu_{s1} \neq \mu_{s2}$
510
200
400
512
514
330
344
b_2
360
346
350
348
t_2
r_2

FIG. 8

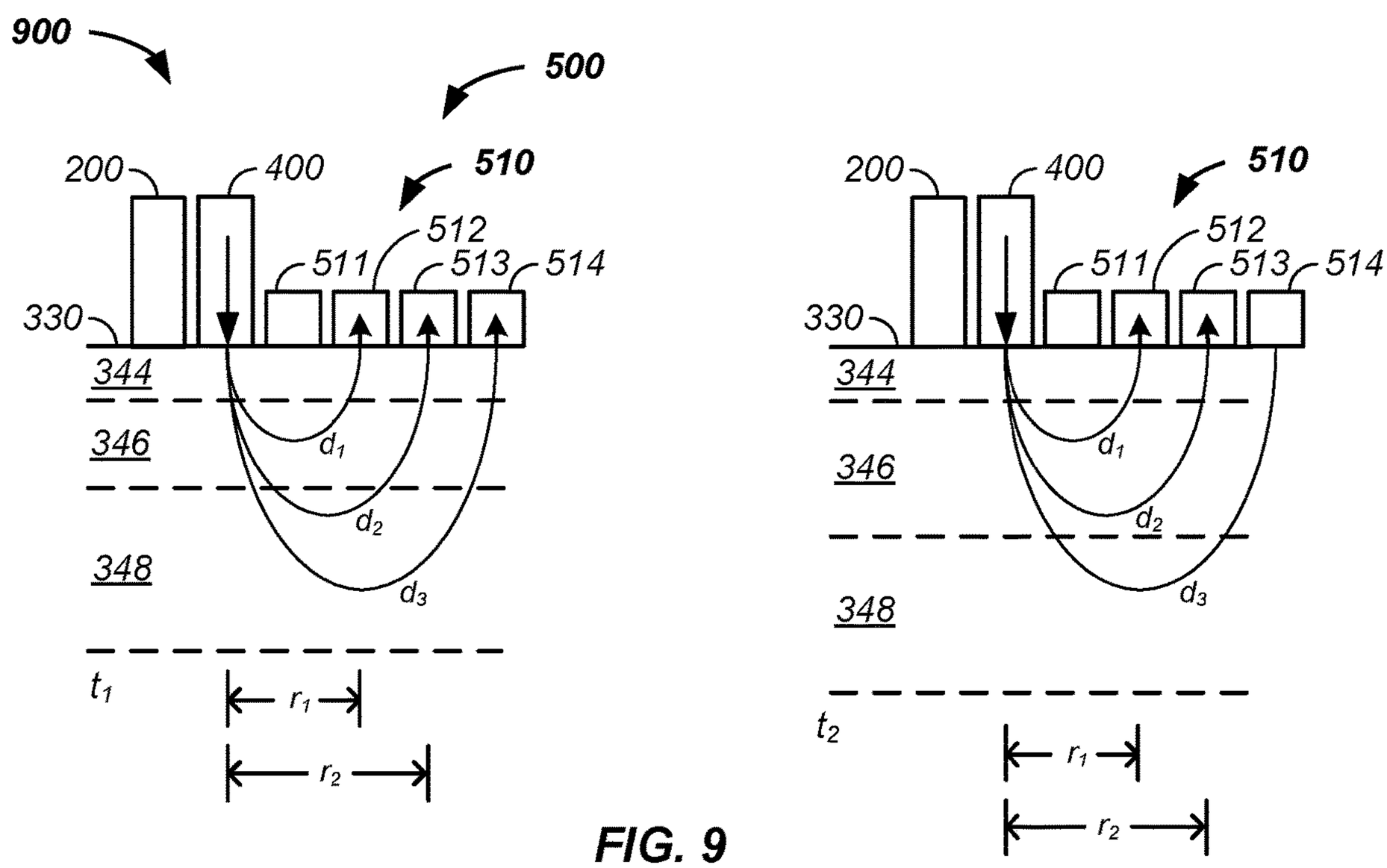

900
500
510
200
400
511
512
513
514
330
344
346
348
d_1
d_2
d_3
t_1
r_1
r_2
510
200
400
511
512
513
514
330
344
346
348
d_1
d_2
d_3
t_2
r_1
r_2

FIG. 9

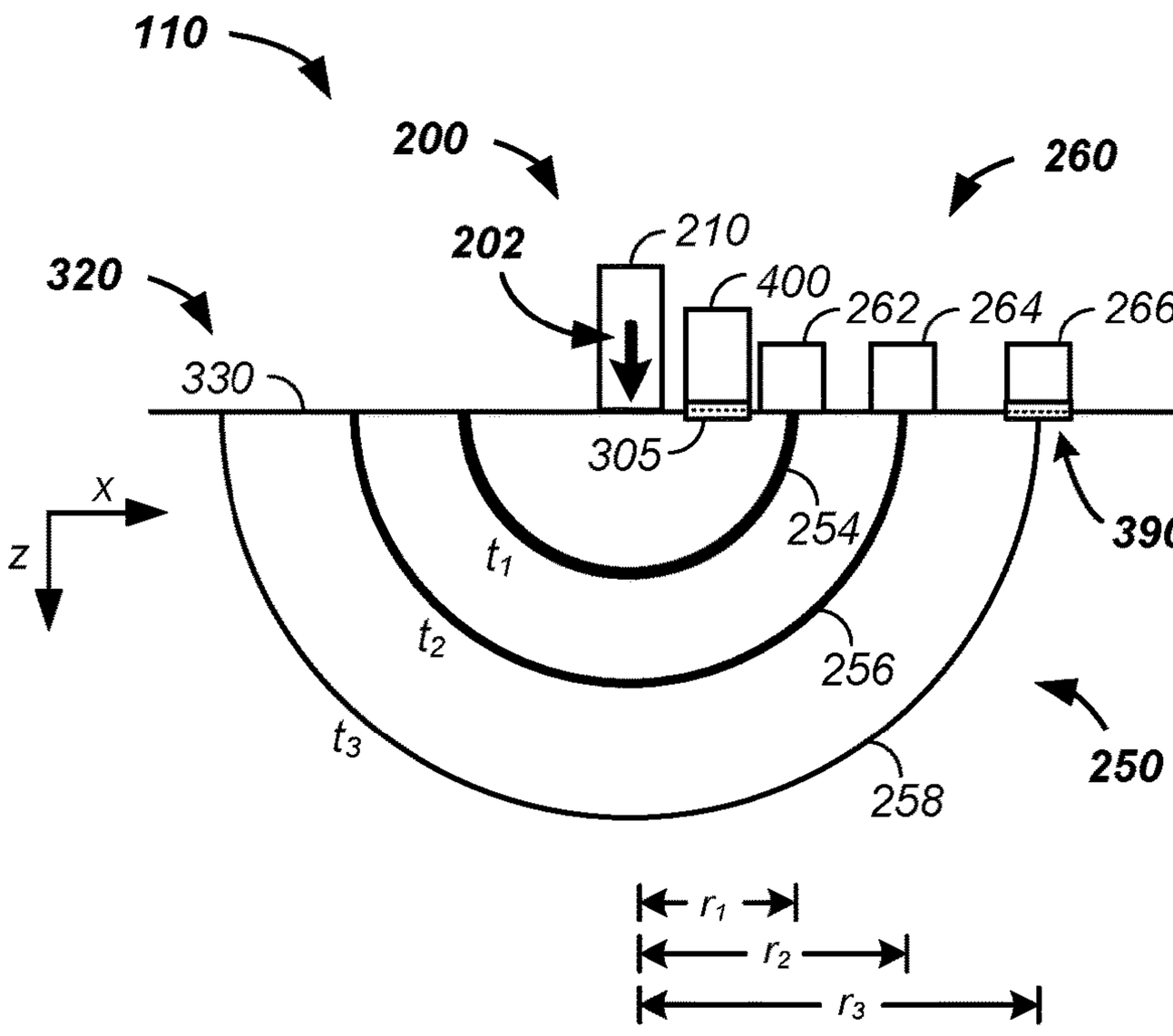


FIG. 10A

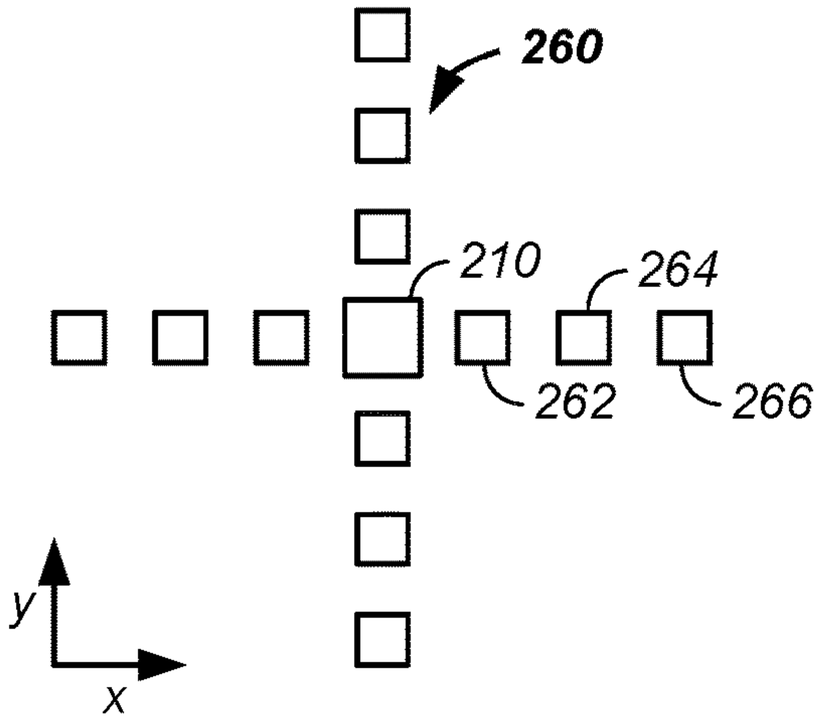


FIG. 10B

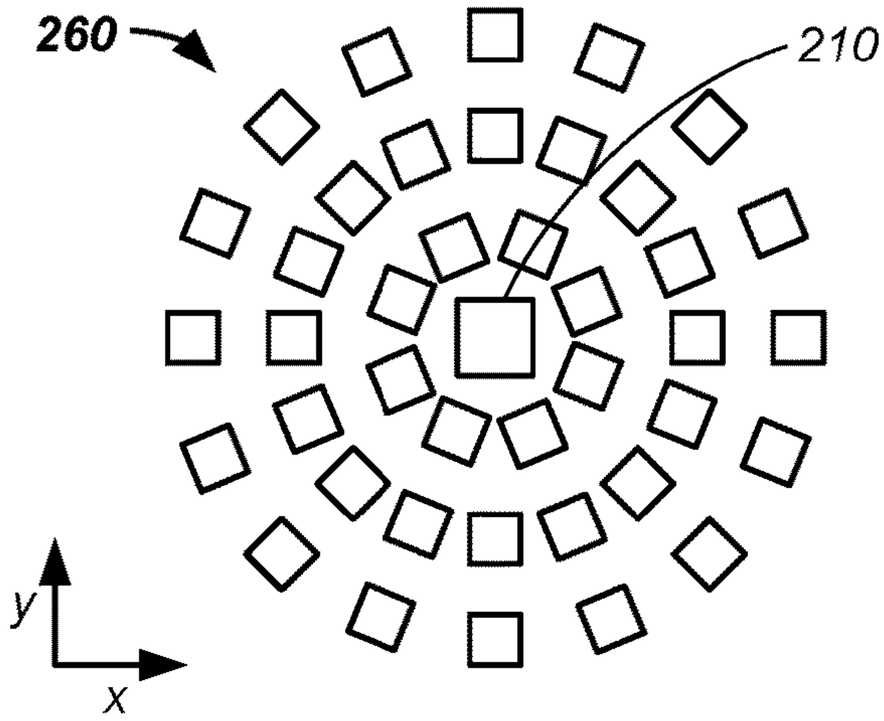


FIG. 10C

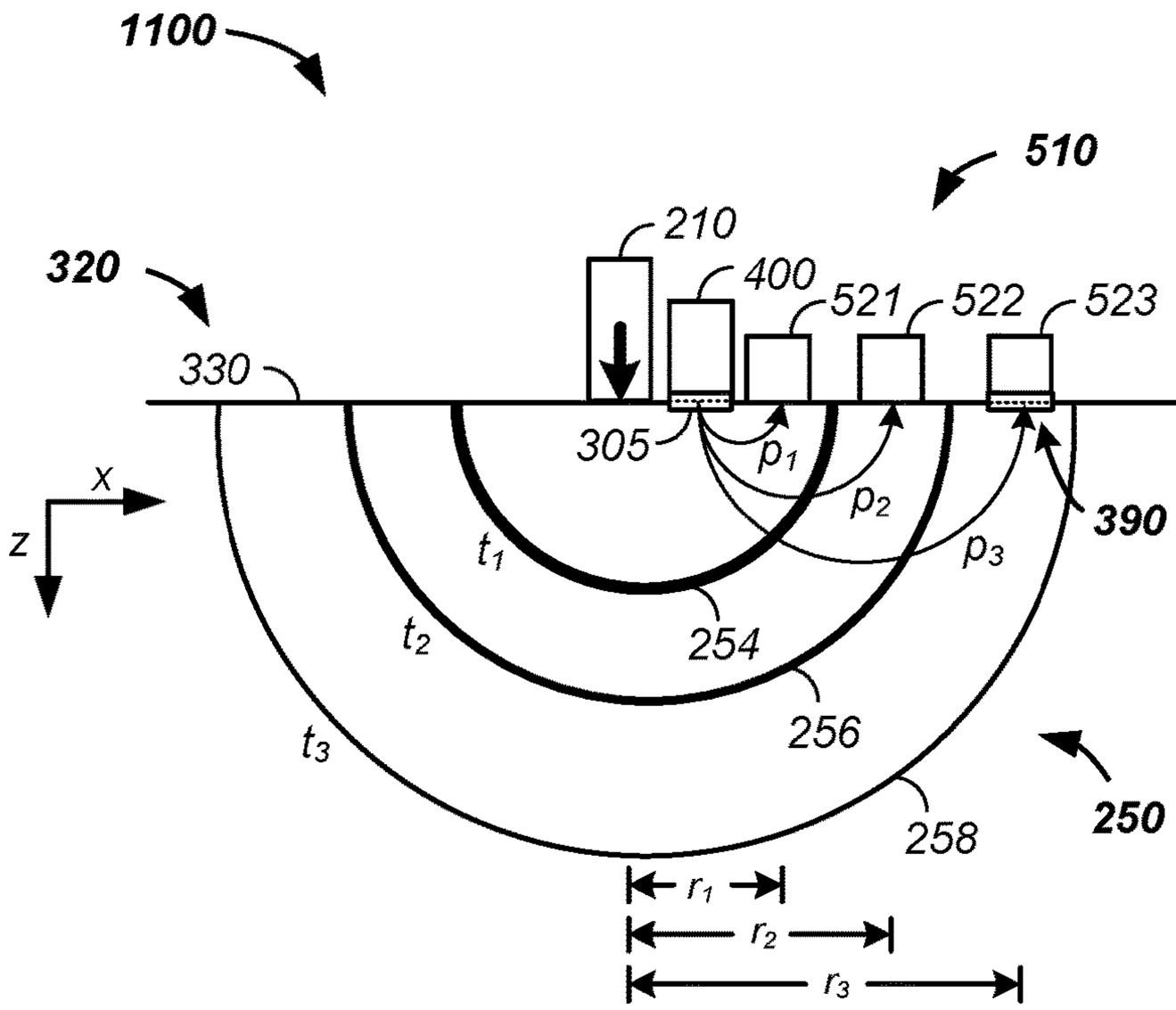


FIG. 11A

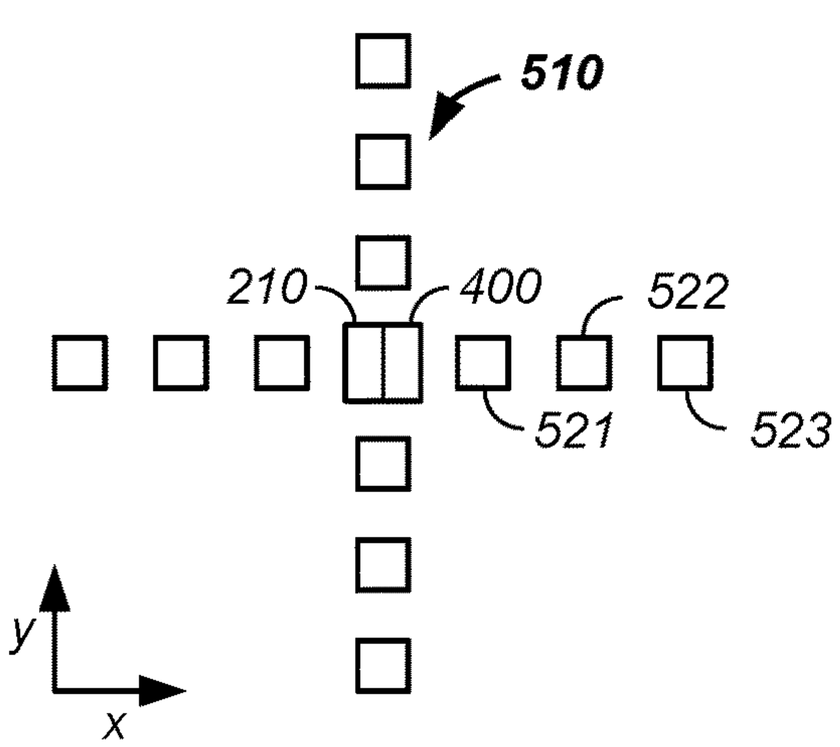


FIG. 11B

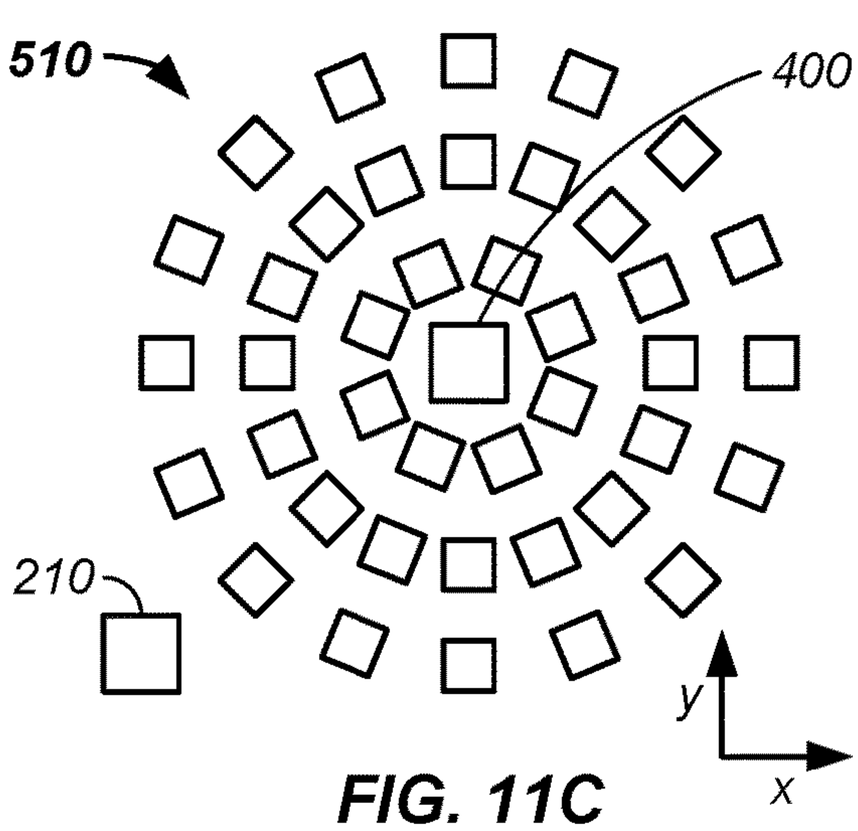


FIG. 11C

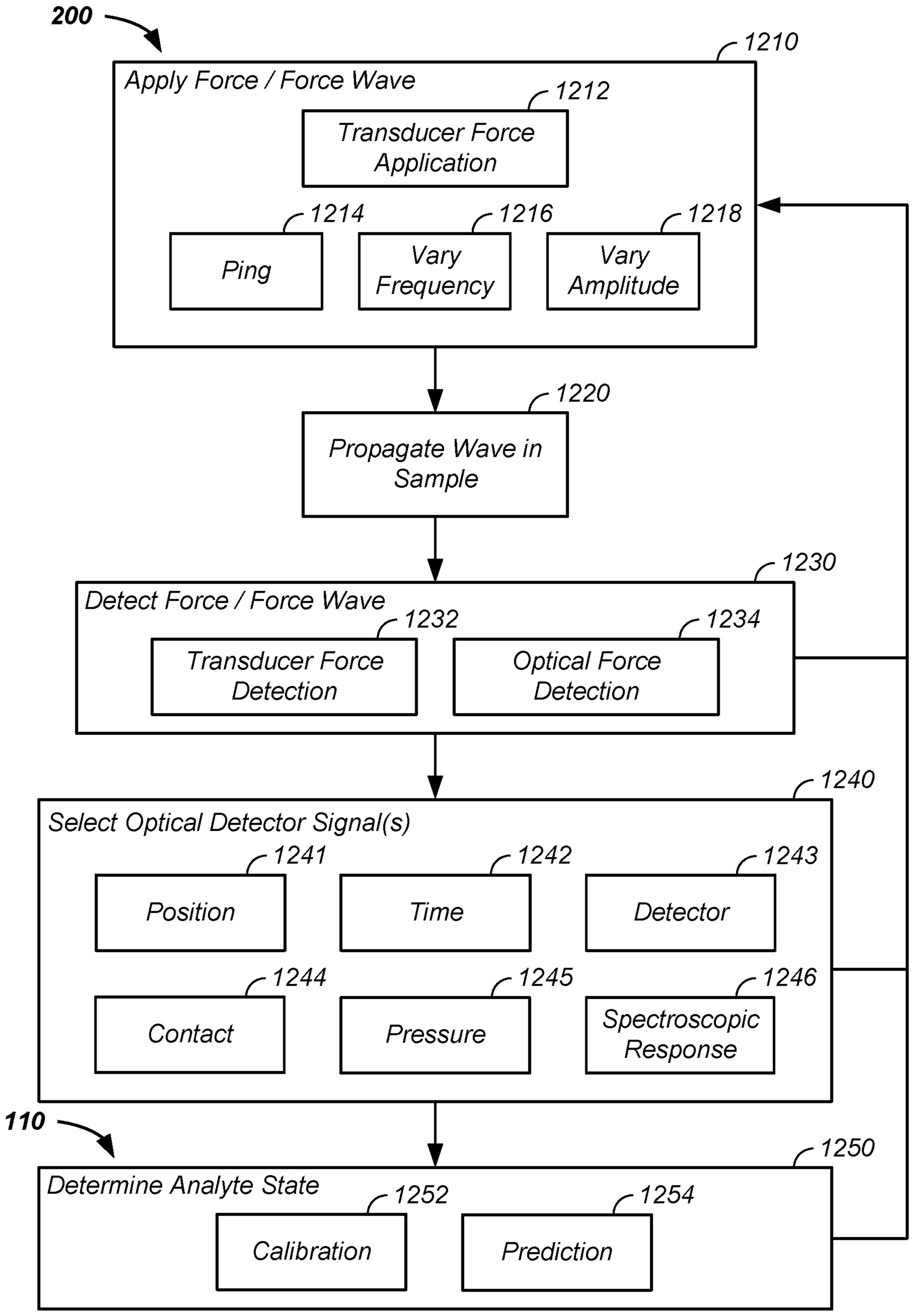

200
1210
Apply Force / Force Wave
1212
Transducer Force Application
1214
Ping
1216
Vary Frequency
1218
Vary Amplitude
1220
Propagate Wave in Sample
1230
Detect Force / Force Wave
1232
Transducer Force Detection
1234
Optical Force Detection
1240
Select Optical Detector Signal(s)
1241
Position
1242
Time
1243
Detector
1244
Contact
1245
Pressure
1246
Spectroscopic Response
110
1250
Determine Analyte State
1252
Calibration
1254
Prediction

FIG. 12

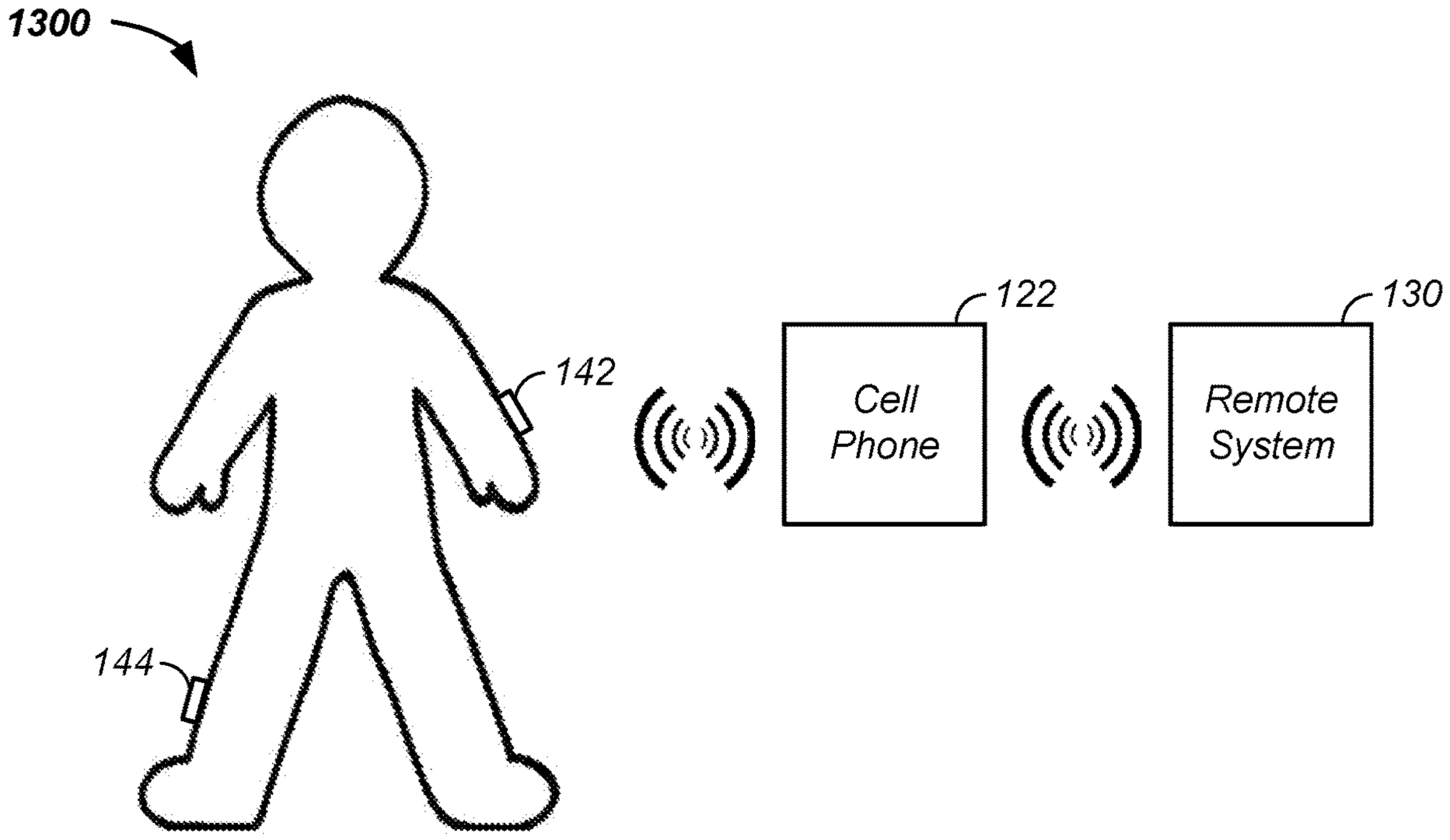


FIG. 13A

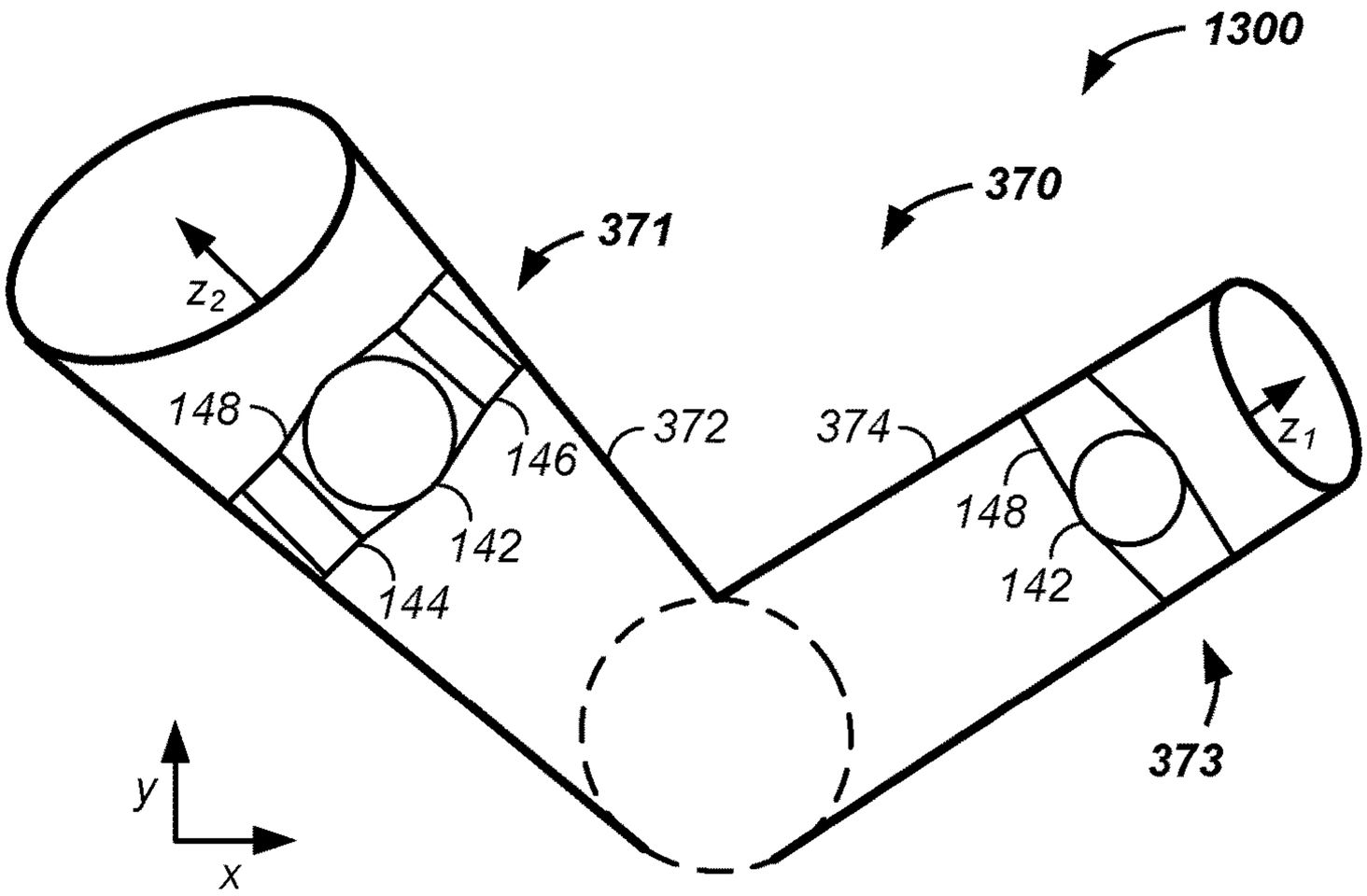


FIG. 13B

MULTIPLE SENSOR GLUCOSE CONCENTRATION DETERMINATION ANALYZER APPARATUS AND METHOD OF USE THEREOF

CROSS-REFERENCES TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. patent application Ser. No. 15/829,877 filed Dec. 2, 2017, which is a continuation-in-part of U.S. patent application Ser. No. 15/636,073 filed Jun. 28, 2017, which claims benefit of U.S. provisional patent application No. 62/355,507 filed Jun. 28, 2016.

BACKGROUND OF THE INVENTION

Field of the Invention

The invention relates generally to noninvasively determining glucose concentration in a living body using an optical analyzer, such as a visible/near-infrared noninvasive glucose concentration determination analyzer.

Discussion of the Prior Art

There exists in the art a need for noninvasively determining glucose concentration in the human body.

SUMMARY OF THE INVENTION

The invention comprises a noninvasive glucose concentration analyzer apparatus and method of use thereof.

DESCRIPTION OF THE FIGURES

A more complete understanding of the present invention is derived by referring to the detailed description and claims when considered in connection with the Figures, wherein like reference numbers refer to similar items throughout the Figures.

FIG. **1** illustrates use of an applied force-optic analyzer;

FIG. **2** illustrates a noninvasive analyzer;

FIG. **3**A illustrates an applied force system, FIG. **3**B illustrates a transducer,

FIG. **3**C illustrates transducer movement normal to an optical axis, FIG. **3**D illustrates a z-axis transducer, and FIG. **3**E illustrates a multi-axes off-center spinning mass transducer;

FIG. **4**A illustrates spectrometer components, FIG. **4**B illustrates an affixing layer, and FIG. **4**C illustrates a coupling fluid enhanced affixer;

FIG. **5**A illustrates a force system coupled to a spectrometer and FIG. **5**B illustrates a force system embedded in a spectrometer;

FIG. **6** illustrates photons interacting with applied force wave(s) in tissue;

FIG. **7**A illustrates absorbance of skin constituents and FIG. **7**B illustrates scattering;

FIG. **8** illustrates detector selection;

FIG. **9** illustrates changing detector selection with tissue change;

FIG. **10**A illustrates a transducer force applicator and FIG. **10**B and FIG. **10**C illustrate transducer force detectors in lines and arcs respectively;

FIG. **11**A illustrates radial optical detection of force waves, FIG. **11**B illustrates an array of optical detectors, and FIG. **11**C illustrates arcs of optical detectors;

FIG. **12** illustrates optical probes observing tissue modified by force waves in a noninvasive glucose concentration determination system/analyzer; and

FIG. **13**A and FIG. **13**B illustrate a multi-sensor analyzer system.

Elements and steps in the figures are illustrated for simplicity and clarity and have not necessarily been rendered according to any particular sequence. For example, steps that are performed concurrently or in different order are illustrated in the figures to help improve understanding of embodiments of the present invention.

Problem

There remains in the art a need for a noninvasive glucose concentration analyzer.

DETAILED DESCRIPTION OF THE INVENTION

The invention comprises a method and apparatus for noninvasively determining state of a person, comprising the steps of: providing an analyzer comprising a first and second spectrometer unit and a main controller subsystem; replaceably attaching the first spectrometer unit to the person at a first illumination zone; the first spectrometer unit delivering first photons, from first illumination optics, along a first mean z-axis optical path normal to a first x/y-plane tangentially contacting the first illumination zone of the person; replaceably attaching a second spectrometer unit to the person at a second illumination zone; the second spectrometer delivering second photons, from second illumination optics, along a second mean z-axis optical path perpendicular to a second x/y-plane tangentially contacting the second illumination zone of the skin, the first x/y-plane noncoplanar with the second x/y-plane; and the main controller processing detected signals to generate at least one measure of state of the person.

Herein, generally, when describing an optical portion of the applied force-optic analyzer, a z-axis is aligned with a mean direction of the photons in a given sub-portion of the analyzer, such as along a longitudinal path of the photons into skin of a subject, and x- and y-axes form a plane perpendicular to the z-axis, such as at an interface point of incident photons into the skin of the subject. At the point of contact of the applied force-optic analyzer with the biological sample, the z-axis is normal/perpendicular to the sample and the x/y-plane tangentially contacts the sample. For instance, the light moves dominantly along the z-axis along vectors approaching perpendicular to an upper arm of a subject or a patient and the x/y-plane tangentially touches the upper arm along the z-axis. In particular cases, a second x,y,z-axis system is used to describe the sample itself, such as a z-axis being along the longitudinal length of a body part, such as along a digit or a finger or along the length of an arm section and the x/y-plane in this case is a cross-section plane of the body part.

A sample is optionally any material responding to an applied physical force in a manner observed by a probing optical system. However, for clarity of presentation and without loss of generality, the sample is described as a person, subject, patient, and/or a living tissue, such as skin and/or a portion of a human or animal. While the analyzer is described as a noninvasive analyzer probing into and optionally through the outer layers of skin, the noninvasive analyzer is optionally used as and or in conjunction with a

minimally invasive glucose concentration analyzer and/or in conjunction with an invasive glucose concentration analyzer.

Herein, an illumination zone and/or an imaging zone is a point, region, or area of intersection of the illumination/imaging beam and/or pulse with an incident surface of the sample to yield a spectrum and/or an image of a desired volume of the sample. Herein, a detection zone is a point, region, or area of the sample sampled and/or visualized by one or more detectors. Similarly, herein an applied force zone is an incident point, region, or area of intersection at which an applied force is applied to the sample and a detected force zone is a point, region, or area of the sample interfacing with a force detector.

Applied Force-Optic Analyzer

Referring now to FIG. **1**, a noninvasive analysis system **100** using an analyzer **110**, such as an applied force-optic analyzer system is illustrated. Generally, an optional force system **200** is used to apply one or more applied forces, physical distortions, and/or force waves to a sample **300**. The applied force travels with a wave front, as a wave, in a pattern of compression and rarefication, and/or as a traveling displacement through the sample **300** or portions thereof. With or without application of the force waves, a spectrometer **140** is used to noninvasively collect spectra of the sample **300** and photometrically determine one or more properties of the sample, such as a glucose concentration. As described infra, the applied force is optionally in the form of an acoustic wave. However, the applied force is optionally and preferably a physical displacement of a portion of skin of a person, where the physical displacement is caused by movement of a mechanical object relative to the body to yield a time varying displacement of skin and/or constituents of the skin by the mechanical object. As described, infra, a variety of force provider technologies are available to variably displace the skin in a controlled manner. For clarity of presentation and without loss of generality, a transducer is used as an example to represent an applied force section of the force system **200**, where a transducer comprises a device that receives a signal/force in the form of one type of energy and converts it to a signal/force in another form. Again for clarity of presentation and without loss of generality, a piezoelectric actuator is used to represent a transducer and an off-center spinning mass is used to represent a transducer. Hence, again for clarity of presentation and without loss of generality, a piezoelectric-optical analyzer or simply a piezo-optic analyzer, a transducer, and/or a transducer force applicator is used to describe any and all applied force electromechanical sources in the force system **200**.

Referring now to FIG. **2**, use of the analyzer **110** is described. Generally, the analyzer **110** is optionally calibrated using a reference **310** and is used to measure a subject **320**, where the subject **320** is an example of the sample **300**. Optionally and preferably, the analyzer **110** and/or a constituent thereof communicates with a remote system **130** using a wireless communication protocol **112** and/or a wired communication protocol.

Force System

Referring now to FIGS. **3**(A-E), the force system **200** is further described. Generally, the force system **200** comprises a force delivery transducer that directly and/or indirectly contacts the sample **300**, such as an outer skin surface **330** of the subject **320** and/or a patient. The subject **320** has many skin layers **340**. For clarity of presentation, the skin layers **320** are represented as having a first skin layer, such as a stratum corneum **342**; a second skin layer, such as an epidermis **344** or epidermal layer; a third skin layer, such as a dermis **346** or dermis layer; and a fourth layer, such as subcutaneous fat **348** or a subcutaneous fat layer. It is recognized that skin is a complex organ with many additional layers and many sub-layers of the named layers that vary in thickness and shape with time. However, for clarity of presentation and without loss of generality, the stratum corneum, epidermis, dermis, and subcutaneous fat layers are used to illustrate impact of the force delivery transducer on the skin layers **340** of the subject **320** and how the applied force waves alter optical paths of probing photons in the spectrometer **140** of the analyzer **110** in the noninvasive analysis system **100**.

Still referring to FIG. **3**A, at a first time, t_1, the tissue layers **340** are in a first state. As illustrated, the tissue layers **340** are in a compressed state **340**, such as a result of mass of the force system **200** sitting on the skin surface **330**, as a result of dehydration of the subject **320**, and/or as a result of a physiological and/or environmental force on the tissue layers **340** of the subject. At a second time, t_2, the force system **200** applies a force wave **250** to the skin surface **330** of the patient **320**, which sequentially propagates into the stratum corneum **342**, epidermis **344**, dermis **346**, and given enough force into the subcutaneous fat **348**. In additional to the force wave propagating into the skin layers **340** along the z-axis, the force wave propagates radially through the skin layers, such as along the x/y-plane of the skin layers. As illustrated at the second time, t_2, as the force wave **250** propagates into the tissue layers **340**, the tissue layers expand and/or rarefy, such that the thickness of the epidermis **344** and/or the dermis **346** layers expands. The rarefication of the epidermis **344** and particularly the dermis **346** allows an increased and/or enhanced perfusion of blood **350** into the rarefied layers. The increased prefusion increases water concentration in the perfused layers, increase and/or changes distance between cells in the perfused layers, and/or changes shapes of cells in the perfused layers, such as through osmolarity induced changes in concentration in and/or around blood cells, such as red blood cells. Generally, scattering coefficients of the epidermis layer and/or especially the dermis layer changes, which is observed by the spectrometer **140** in the range of 400 to 2500 nm with larger changes at smaller wavelengths in the visible, 400 to 700 nm, and/or near-infrared, 700 to 2500 nm, regions. As illustrated at the third time, t_3, as the force wave **250** continues propagation in the tissue layers **340**, the perfusion **350** continues to increase, such as to a maximum perfusion. As illustrated at the fourth time, t_4, after discontinuation of the force wave **250**, the skin layers **340** revert toward the initial state of the non-force wave induced perfusion to a local minimum perfusion, which may match the initial perfusion, is likely higher than the initial perfusion, and is at times less than the initial perfusion due to changes in state of the environment, such as temperature, and/or generalized state of the subject **320**, such as hydration, localized hydration of skin, such as due to food intake, insulin response to food intake, exercise level, blood pressure, and/or the like. Generally, the tissue layers **340** of the subject increase in thickness and/or rarefy during application of the transducer applied force wave **250** and decrease and/or compress after termination of the transducer applied force wave **250** to the skin surface **330** of the subject **320**. The process of applying the force wave **250** is optionally and preferably repeated n times, where n is a positive integer of greater than 1, 2, 5, 10, 100, 1000, or 5000 times in a measurement period of an analyte of the subject **320**, such as a glucose concentration. Generally, the cycle of applying the force wave **250** results in a compression-rarefication cycle of the tissue that alters

an observed scattering and/or absorbance of probing photons in the visible and near-infrared regions. The force wave **250** is optionally and preferably applied as a single ping force in a tissue state classification step, as multiple pings in a tissue classification step, and/or as a series of waves during a tissue measurement step. Individual waves of a set of force waves are optionally controlled and varied in terms of one or more of: time of application, amplitude, period, frequency, and/or duty cycle.

Still referring to FIG. **3**A and referring now to FIGS. **3**(B-D), a force wave input element **210** of the force system **200** is illustrated. As illustrated, the force wave input element **210** is equipped with one or more transducers: a left transducer **221**, a right transducer **222**, a front transducer **223**, a back transducer **224**, a top transducer **225**, and/or a bottom transducer **226**. For instance, the left and/or right transducers **221**, **222** move the force wave input element **210** left and/or right along the x-axis; the front and/or back transducers **223**, **224** move the force wave input element **210** forward and/or back along the y-axis; and/or the top and bottom transducers **225**, **226** move the force wave input element **210** up and/or down along the z-axis along and/or into the skin surface **330** of the subject **320**, which moves the skin, skin layers **340**, and/or skin surface **330** of the subject relative the spectrometer **140** and/or is a source of the force wave **250** moving, in the skin layers **340**, along the z-axis into the skin, and/or radially outward from an interface zone of the force wave input element **210** of the force system **200**. A transducer itself is optionally used as the force wave impulse element **210**. Referring now to FIG. **3**E, one or more off-center mass elements **230** is optionally spun or rotated, such as with an electric motor, along one or more of the x,y,z-axes to move the force wave input element **210** relative to the skin surface **330** of the subject **320** resulting movement of the skin of the subject **320** relative to the spectrometer **140** and/or cycling and/or periodic displacement of the tissue layers **340** of the subject **320** due to movement of the force wave input element **210** resulting in the force wave(s) **250**. Generally, the force system **200** induces a movement of a sampled zone of skin of the subject **320**, applies a displacement of a sampled zone of the skin of the subject **320**, and/or applies a propagating force wave into and/or through a sample zone of tissue layers **340** of the subject, where the sampled zone is probed using photons from the spectrometer **140** and/or is measured using a set of detection zone transducers, described infra. The force wave(s) are optionally and preferably applied as a single input ping wave, a set of input ping waves, and/or are applied with a frequency of 0.01 Hz to 60 Hz. Optionally and preferably, the force waves **250** are applied with a frequency greater than 0.01, 0.02, 0.05, 0.1, or 1 Hz. Optionally and preferably, the force waves **250** are applied with a frequency of less than 200, 100, 50, 40, 30, or 20 Hz. Optionally and preferably, the force waves **250** are applied with a frequency within 5, 10, 25, 50, or 100 percent of 2, 4, 6, 8, 10, 12, 15, and 20 Hz.

Optical System

Referring now to FIG. **4**A, the spectrometer **140** of the analyzer **110** is further described. The spectrometer **140** comprises a source system **400**, which provides photons **452** in the visible and/or infrared regions to the subject **320**, such as via a photon transport system **450**, at an illumination zone. After scattering and/or absorbance by the tissue layers **340** of the subject **320**, a portion of the photons are detected at a detection zone by a detector system **500**. The source system **400** includes one or more light sources, such as any of one or more of a light emitting diode, a laser diode, a black body emitter, and/or a white light source, that emits at any wavelength, range of wavelengths, and/or sets of wavelengths from 400 to 2500 nm. Each source system photon source is optionally controlled in terms of time of illumination, intensity, amplitude, wavelength range, and/or bandwidth. The photon transport system **450** comprises any fiber optic, light pipe, air interface, air transport path, optic, and/or mirror to guide the photons from the light source to one or more illumination zones of the skin surface **330** of the subject **320** and/or to guide the photons from one or more detection zones of the skin surface **330** of the subject **320** to one or more detectors of the detector system **500**. Optionally and preferably, the photon transport system **450** includes one or more optical filters and/or substrates to selectively pass one or more wavelength regions for each source element of the source system **400** and/or to selectively pass one or more wavelength ranges to each detector element of the detector system **500**. Herein, the reference **310** is optionally an intensity and/or wavelength reference material used in place of the sample and/or is used in a optical path simultaneously measured by the analyzer **110**.

Still referring to FIG. **4**A and referring now to FIG. **4**B and FIG. **4**C, the subject **320** optionally and preferably wears the analyzer **110** in the physical form of a watch head, band, and/or physical element attached to the body with a band and/or an adhesive. For example, the analyzer **110**, the spectrometer **140**, the source system **400**, and/or the photon transport system **450** is optionally attached to the subject **320**, such as at the wrist or upper arm, using thin affixing layer **460**, such as a double sided adhesive **462**. Referring now to FIG. **4**B, the double sided adhesive **462** optionally contains an aperture **464** therethrough.

The photons **452** optionally and preferably pass through the aperture **452** to the skin surface **330** of the subject. The force wave **250** optionally moves the skin surface **330** through the aperture into intermittent contact with the analyzer **110**. Optionally, referring now to FIG. **4**C, a thin affixing layer **466**, such as less than 1, 0.5, or 0.25 mm thick, is continuous in nature in front of the incident surface and/or incident photon coupling zone and/or is continuous in nature in front of the detection zone, where photons exiting the skin surface **330** are detected by the detector system **500**. The affixing layer **466** is optionally permeated with a fluid, such as a coupling fluid, an air displacement medium, an optical coupling fluid, a fluorocarbon liquid, a fluorocarbon gel, an index of refraction matching medium, and/or any fluid that increases a percentage of photons from the source system **400** entering the skin surface **330** compared to an absence of the fluid and/or is any fluid that increases a percentage of photons from the tissue layers **340** exiting the detection zone and reaching the detector system **500** as compared to a case where the fluid is not embedded into the affixing layer. Hence, the affixing layer serves several purposes: attaching the analyzer or a portion thereof to the skin surface **330** of the subject **320**, coupling forces from the force system **200** to the skin surface **330** of the subject **320**, forming a constant sampling interface location on the skin surface **330** of the subject, and/or altering a coupling efficiency, angular direction, and/or reproducibility of coupling of photons enter the skin of the subject **320** and/or exiting the skin surface **330**.

Coupled Force System/Spectrometer

Referring now to FIG. **5**A and FIG. **5**B, the force system **200** is illustrated working in conjunction with the spectrometer **140**. Referring now to FIG. **5**A, the analyzer **110** is illustrated with the force system **200** being attached to and/or within 1, 2, 3, 5, 10, 20, or 50 mm of the spectrometer **140**. Referring now to FIG. **5**B, the analyzer **110** is illustrated with the force system **200** being integrated into the

spectrometer **140**, such as within 20, 10, 5, 2, or 1 mm of the source system **400** of the analyzer **110** and/or in a single housing unit of the analyzer **110**.

Several examples are provided that illustrate how the force system **200** alters the tissue layers **340** of the subject **320** and how a selection of detected signals from the spectrometer **140** is performed as a function of time and respective radial separation between the one or more illumination zones and the one or more detection zones, such as using water signal, fat signal, and/or protein signal to determine the correct detection signals to use for noninvasive glucose concentration determination.

EXAMPLE I

Referring now to FIG. **6**, a first example of the analyzer **110** using the force system **200** and the source system **400** at the same time and/or within less than 60, 30, 15, 10, 5, or 1 second of each other is provided. In this example, the force system **200** applies a force to the tissue layers **340** at a first time, t_1, when the dermis has a first mean z-axis thickness, th_1. Optionally and preferably, the analyzer **110** acquires signals representative of the tissue layers **340** of the subject **320** using the source system **400** and the detector system **500**. Illustrated are three representative photon pathways, $p_{1\text{-}3}$, reaching the detector system **500**, such as at a first detector element, a second detector element, and a third detector element, respectively, at the first time, t_1, and/or within less than 60, 30, 15, 10, 5, or 1 second from the first time, t_1. Notably, at the first time, the first photon pathway, p_1, has an average path that does not penetrate into the dermis **346**, while the second and third photon pathways, $p_{2\text{-}3}$, have mean pathways that penetrate through the dermis into the subcutaneous fat **348**. In at least one preferred use of the analyzer, noninvasive glucose concentration determination is performed using a mean photon pathway that penetrates into the dermis **346** and not into the subcutaneous fat **348** and/or uses signal from a detector element at a first/minimal radial distance from the illumination zone, where the first/minimal radial distance is the smallest radial distance observing an increase in a fat signal/dominantly fat related signal, such as from the subcutaneous fat **348**, compared to a water signal/dominantly water related signal from skin layers **340** closer to the skin surface **332** than that subcutaneous fat **348**. Examples of wavelengths containing dominantly water absorbing signals are wavelengths correlating with the peaks of the water absorbance bands **710**, FIG. **7**A, and examples of wavelengths containing an increased fat absorbance to water absorbance ratio when a mean photon path enters the subcutaneous fat **348** are at the fat absorbance bands **720**. Still referring to FIG. **6**, at a second time, t_2, the force wave **250** from the force system **200** has expanded the dermis layer to a second thickness, th_2, which is at least 0.1, 0.2, 0.3, 0.5, 1, 2, 5, 10, 20, or 50% thicker than the first thickness, th_1, and/or has an increased water absorbance, as measure by the first, second, and/or third detector element of the detector system **500**, representative of the first through third photon pathway, $p_{1\text{-}3}$, in the condition of the larger dermis thickness at the second time, t_2, as represented by a fourth, fifth, and sixth photon pathway, $p_{4\text{-}6}$. Notably, the fifth and sixth photon pathways, $p_{5,6}$, with the same illumination zone to detection zone radial distance as the first and second photon pathways, $p_{1\text{-}2}$, have mean photon pathways that penetrate into the dermis **346** and not into the subcutaneous fat **348**. Thus, the water-to-fat ratio of the observed signal continues to increase with radial distance for the second and third detectors after the force system **200** increased the thickness of the dermis **346** to the second thickness, th_2. Again, at least one preferred measurement is a measurement with a higher water-to-fat absorbance ratio. In this example, at the second time, the water-to-fat absorbance ratio of the fifth optical path, p_5, is greater than observed with the second optical path, p_2, despite have the same source zone-to-detector zone radial distance. Further, in this example a preferred optical signal is from the sixth optical path, th_6, at the second time, t_2, with a largest ratio of mean pathlength in the dermis **346** to total mean detected pathlength. FIG. **7**B illustrates increased scattering with decreasing wavelength at a first scattering coefficient, μ_{s1}, **730** and a second scattering coefficient, μ_{s2}, **740**.

EXAMPLE II

Referring now to FIG. **8**, a second example is provided where the analyzer **110** uses the force system **200** to alter the sample **300** to enhance a noninvasive analyte property determination using the spectrometer **140**. As above, the force system **200** provides one or more force waves **250** into the subject **320**, which alters positions of cells **260** in the dermis **346** relative to the illumination zone of the illumination system **400** and or relative to one or more detection zones associated with a single element detector and/or one or more detectors of an array of detector elements **510**. As illustrated, the cells **360** have a first average intercellular distance at a first time, t_1, which is altered by application of the force wave **250** to a second average intercellular distance at a second time, t_2, where the net change in cell position alters detected spectrophotometric absorbance signals at a give detector element of the detector system **500** by greater than 0.01, 0.02, 0.05, 0.1, 0.5, 1, 2, 5, or 10 percent, such as by a change in observed scattering and/or observed absorbance at a fixed radial distance between an illumination zone and a detection zone. Similarly, the average percentage volume of the intercellular fluid **350** in the dermis layer differs by greater than 0.01, 0.02, 0.05, 0.1, 0.5, 1, 2, 5, or 10 percent as a result of the applied force wave(s) **250**. All of a change in thickness, change in observed mean pathlength, change in radial distance of detection, change in mean intercellular spacing, change in scattering, and change in water concentration, related to perfusion, are illustrated between the first time, t_1, and the second time, t_2, as a result of the applied force wave **250**. Notably, a selected detector signal from the array of detectors **510** changed from a second detector element **512** at a first radial distance, r_1, from the illumination zone to a fourth detector element **514** at a second radial distance, r_2, from the illumination zone based on the above described larger observed water signal-to-observed fat signal ratio and/or as the second pathlength, b_2, is longer than the first pathlength, b_1, in the dermis layer. Similarly, absorbances of skin constituents, such as protein, albumin, globulin, keratin, and/or elastin increase relative to fat absorbance for the second pathlength, b_2, as the mean pathlength spends more time in the dermis layer compared to the subcutaneous fat layer **348**, as described supra.

EXAMPLE III

Referring now to FIG. **9**, a third example of using the force system **200** to alter properties of the subject **330** to enhance performance of a noninvasive glucose concentration determination using the spectrometer **140** is provided. In this example, the detector array **510** of the detector system **500** contains n detector elements at differing radial distances from a time correlated illumination zone. For clarity of

presentation, the detector array **510** is illustrated with four detector elements: a first detector element **511**, a second detector element **512**, a third detector element **513**, and a fourth detector element **514**. At a first time, t_1, the large water absorbance, protein absorbance, and/or protein and water absorbance-to-fat ratio is observed using the second detector element **512** having a first illumination zone-to-detection zone radial distance, r_1, and a first mean optical pathway, d_1, penetrating into the dermis **346** with minimal to no mean penetration into the subcutaneous fat **348**. However, at a second time, t_2, after the provided force wave **250** has altered the skin of the subject **320**, the third detector element is observed, at a selected detection point in time, to have the largest metric for detector selection, such as a smoothly falling observed intensity with radial distance at a fat absorbance wavelength, where a sudden decrease in observed intensity at the fat absorbance wavelength indicates mean penetration of the observed optical pathway into the subcutaneous fat **348**, such as at the second radial distance, r_2. Notably, the largest radial distance is selected for a given water, protein, and/or fat based metric as at the larger radial distance a difference between a shortest possible pathlength between the illumination zone and the detection zone, the radial distance, is closest to the largest possible observed pathlength, which is based upon a maximum observable absorbance by a detector type for a fixed number of photons. For example, if the maximum observable absorbance is 3.9 and the absorbance per millimeter is 1.3, then a maximum observable pathlength is 3.0 mm. If the observed radial pathlength is 1.5 mm then a first range of observed pathlengths is 1.5 to 3.0 mm with a difference of 1.5 mm. Hence, a first ratio of observed pathlength difference to radial distance is 1:1 (1.5 mm:1.5 mm), which is a 100% error. However, if the observed radial pathlength is 2.5 mm, then a second range of observed pathlengths is 2.5 to 3.0 mm with a difference of 0.5 mm. Hence, a second ratio of observed pathlength difference-to-radial distance is 1:5 (0.5 mm:2.5 mm), which is a second pathlength error of 20% or one-fifth of the pathlength error of the first case. In general, the largest radial distance yielding and intensity-to-noise ratio beyond a threshold, such as 0.5, 1, 1.5 or 2, is preferred as error in a range of observed pathlengths decreases, which reduces the error in b, in Beer's Law: equation 1,

$$A = \text{molar absorptivity} * b * C \quad \text{(eq. 1)}$$

where b is pathlength and C is concentration, which is central to visible and near-infrared absorbance and/or scattering models used to determine an analyte property, such as a noninvasive glucose concentration as measured using photons optically probing skin.

Skin State Classification

Skin state is optionally classified using a single force pulse or single impulse function, also referred to herein as a ping. Generally, an applied force, such as the force wave **250** provided by the force system **200**, takes time to propagate through the subject **320**. The travel time of the force wave varies as a function of state of the body, such as hydration, temperature, glucose concentration, triglyceride concentration, hematocrit and/or any constituent of skin, blood, and/or interstitial fluid. Hence, the amount of time to travel radial distances to force wave detectors is optionally used to classify the state of the subject and/or to map the state of the subject in regions probed by the force wave. For clarity of presentation and without loss of generality, two example of force wave detection are provided here using: (1) a transducer force detector and/or (2) an optical force wave classifier.

EXAMPLE I

Referring now to FIGS. **10**(A-C), transducer force detectors are optionally used to detect transit times of the force wave **250** from the force wave input element **210** to one or more detectors of a set of transducer force detectors **260**. Generally, a transducer force detector converts mechanical motion, such as passage of the force wave **250** and/or skin movement into a measured electrical signal. Referring now to FIG. **10**A, for clarity of presentation and without loss of generality, a first transducer force detector **262**, a second transducer force detector **264**, and a third transducer force detector **266** are illustrated that represent n transducer based force detectors, where n is a positive integer of greater than 1, 2, 3, 5, 10, or 20. As illustrated in FIGS. **10**B and **10**C, the n transducer based force detectors are optionally positioned in a linear array, in a two-dimensional array, and/or along arcs, such as at differing radial distances from one or more light sources in the source system **400**. Referring still to FIG. **10**A, as illustrated, at a first time, t_1, the force wave **250** has propagated to the first transducer force detector **262** as a first wave front position **254**; at a second time, t_2, the force wave **250** has propagated to the second transducer force detector **264** as a second wave front position **256**; and at a third time, t_3, the force wave **250** has propagated to the third transducer force detector **266** as a third wave front position **258**. Timing of each wave front to each transducer based force wave detector allows: (1) generation of a sub-surface tissue map of constituents of the skin of the subject **320** using mathematical techniques used for seismic mapping known to those skilled in the art of seismic mapping and/or (2) a classification of state of the subject **320** versus a calibration set of classifying states of force wave propagation radial translation times. For instance, the classification is as simple as slow, medium, or fast translation times to a given transducer detector or a more involved combination of translation times for one or more of: (1) responses at a single detector position and (2) responses at a set of detector positions and/or responses to varying inputs of the force wave, such as time, direction, amplitude, and/or frequency of one or more pings from the force wave input elements and/or time varying induced applied pressure and/or displacement of a portion of the skin of the subject **320** by the force system **200**.

EXAMPLE II

Referring now to FIGS. **11**(A-C), propagation of the force wave(s) **250**, such as force wave fronts **254**, **256**, **258** is detected using a set of optical detectors and using the results in a manner similar to detecting the force wave **250** using the set of transducer based wave detectors. For instance, as the force wave **250** propagates through the tissue layers **340**, the density, absorbance, and/or scattering of voxels of the skin of the subject **320** change, which alters an observed mean optical path between a given source of photons and a photon/photonic detector. One or more sources of the source system **400** coupled to the array of optical detector elements **510** via the subject **320** is optionally used to detect propagation times of the force wave(s) **250**. For clarity of presentation and without loss of generality, a first optical detector **521**, a second optical detector **522**, and a third optical detector **523** are illustrated that represent n optical

detectors, where n is a positive integer greater than 0, 1, 2, 3, 5, 10, 15, 16, 20, 25, 100, 500, 1000, and 5000. As illustrated in FIGS. **11**B and **11**C, the n optical detectors are optionally positioned in a linear array, in a two-dimensional array, and/or along arcs, such as differing radial distances from one or more light sources in the source system **400** and/or from one or more force wave sources. Notably, one or more detectors of the array of optical detector elements **510** are optionally and preferably used to detect photons from the source system **400** during a measurement phase of an analyte and/or tissue property with or without a tissue classification step. As illustrated, the first optical detector **521** detects a first optical signal, modified by the force wave **250**, with a first pathlength, p_1, at a given point in time; the second optical detector **522** detects a second optical signal, modified by the force wave **250**, with a second pathlength, p_2, at the given point in time; and the third optical detector **523** detects a third optical signal, modified by the force wave **250**, with a third pathlength, p_3, at the given point in time. Each detected optical signal contains absorbances due to any sample constituent, such as water, protein, fat, and/or glucose and/or is representative of state of the tissue, such as a measure of scattering and/or temperature. As the force wave(s) propagate through the tissue, the first, second, and third pathlengths, p_1, p_2, p_3, vary. Hence, the state of the subject **320** is optionally characterized and/or mapped in a manner similar to the transducer wave detection classification and/or mapping; however, optical signals with chemical meaning are used in the process, such as detected intensity, absorbance, and/or scattering related to temperature, one or more tissue layer properties, collagen, elastin, water, albumin, globulin, protein, fat, hematocrit, and/or glucose, such as a concentration, change in tissue state, or a physical structure.

Referring again to FIG. **11**A and FIG. **12**A, the applied pressure/force wave/displacement optionally generates a gap and/or varies an applied pressure at a first interface **305** of the source system **400** and the skin surface **330** and/or at a second interface **390** of the detector system **500** and/or any element thereof and the skin surface **330**. A resulting air gap between the analyzer **110** and the subject **320** and/or a time varying change between an air gap and contact between the analyzer **110** and the subject **320** is used to determine times of contact/relative contact, which is in turn optionally and preferably used in a selection of detected signals step, described infra. For example, loss of optical contact yields a sudden increase in observed intensity in a wavelength region of high absorbance, such at as region dominated by water absorbance in the range of 1350 to 1550 nm, 1400 to 1500 nm, and/or within 5, 10, 15, 25, and/or 50 nm of 1450 nm. Removal of non-contacting signals aids in the development of an outlier analysis algorithm and/or in determining state of the tissue and/or in determination of a degree of applied force from the source system **400**, detector system **500**, and/or analyzer **110** to the skin surface **330** of the subject **320** as a function of time and/or position.

Force Wave/Optical Probe Analyte State Determination

Referring now to FIG. **12**, a process of determining an analyte property, such as a glucose concentration, using one or more optical signals optionally and preferably modified by an applied force, force wave, and/or displacement is provided.

Referring still to FIG. **12**, in a process, such as a first process or a second process, a force is applied **1210**, such as in the form of a force wave and/or displacement induced force wave. For example, the force wave/displacement is generated with a transducer to generate application of a transducer force **1212**, which is a single ping **1214**/displacement and/or a series of pings and/or is a force/displacement varied in frequency **1216** and/or varied in amplitude **1218**, such as via a controller, such as a main controller of the analyzer **110**. Subsequently, the force wave **250**/tissue displacement induced pressure propagates in the sample **1220**.

Referring still to FIG. **12**, in another process, such as a first or second process, a result of the tissue displacement induced force wave is measured and/or detected **1230**, such as through a transducer force detection **1232** and/or an optical force detection **1234**.

Referring still to FIG. **12**, in still another process, such as a second and/or third process, selection of a sub-set of detected signals **1240** is performed, such as a function of position **1241**, time **1242**, detector **1243**, contact **1244**, pressure **1245**, and/or spectroscopic response **1246** and an analyte state is determined **1250**, such as via generation of a calibration **1252** and/or use of a generated calibration in a prediction step **1254**.

Multiple-Sensor System

Referring again to FIG. **4**A and referring now to FIG. **13**A, the analyzer **110** optionally comprises multiple sub-sensor systems that operate independently to collect data but operate in concert for determination of state of the subject **320**. For instance the spectrometer **140** optionally comprises a first spectrometer version/system **142** connected/affixed to a first part of the subject **320**, such as on the arm of the subject **320**, and a second spectrometer system/version **144** connected/affixed to a second part of the subject **320**, such as on the leg of the subject **320**. Optionally, the spectrometer **140** is affixed to any part of the body, such as an ear lobe, webbing of the hand, forehead, torso, limb, arm, or leg.

Still referring to FIG. **13**A, generally, the spectrometer **140** refers to n spectrometers/analyzers, where each of the n spectrometers optionally and preferably collects data independently, where n is a positive integer, such as 1, 2, 3, 4, 5, or more. Optionally, each of the n spectrometers collect and analyze data independently. However, preferably, each of the n spectrometers collect data and after little or no pre-processing, collected data is sent to the analyzer **110**, a central processor, a personal communication device, such as a cell phone **122**, and/or to the web for further processing, which allows a central system to process data from the multiple sub-spectrometer systems.

Still referring to FIG. **13**A, optionally, each of the n spectrometers are of the same type and design. However, preferably, each of the n spectrometers are distinct in type and/or design. For instance, the first spectrometer version **142** comprises first sources, optics, and detectors that are directed to measurement of a first constituent/property of the subject **320** and the second spectrometer version **144** comprises second sources, optics, and detectors that are directed to measurement of a second constituent/property of the subject **320**.

Still referring to FIG. **13**A, for example, the n spectrometer systems are optionally and preferably configured to interface to separate portions of the body and/or to measure separate and/or overlapping properties/constituents of the subject **320**, such as percent oxygen saturation, heart rate, heart rate variability, glucose concentration, protein concentration, fat, muscle, protein concentration, albumin concentration, globulin concentration, respiration rate, an electrocardiogram, blood pressure, and/or body temperature and/or environmental temperature and/or acceleration of the subject **320**, such as to indicate a fall of the subject **320** and/or an interfering movement of the subject **320** that affects the measurements of the one or more spectrometers **140**.

Still referring to FIG. **13**A, herein, for clarity of presentation and without loss of generality, the spectrometer **140** is illustrated as a noninvasive glucose concentration analyzer. However, the spectrometer **140** optionally measures any constituent of the body noninvasively, in a minimally invasive manner, and/or operates in conjunction with a noninvasive, minimally invasive, and/or invasive reference system, such as for calibration and quality control procedures. Examples of a first spectrometer version **142** and a second spectrometer version **144** determining an analyte property is provided, infra.

EXAMPLE I

Referring still to FIG. **13**A and referring now to FIG. **13**B, an example of interfacing **1300** the analyzer **110** to an arm **370** of the subject **320** is illustrated. As illustrated, a first analyzer/spectrometer version **371** of the analyzer **110** is coupled to a section of an upper arm **372** of the subject's arm and a second analyzer/spectrometer version **373** of the analyzer **110** is coupled to a forearm/wrist **374** of the patient's arm **320**. Notably, the first analyzer version **371** interfaces to the subject **320** at a first interface zone along a first z-axis perpendicular to a first x/y-axis plane that is tangential to the subject **320** and that is independent and different from a second interface of the second analyzer version **373**, which interfaces to the subject **320** along a second z-axis perpendicular to a second x/y-axis system that is tangential to a second interface zone of the subject. Generally, n analyzers **110**, optionally linked to a single main controller **112**, interface to n interface zones of the subject **320**, where the main controller **112** is optionally and preferably electrically, mechanically, and/or communicatively linked with any and preferably all subsystems of the analyzer **110** and is used to control the analyzer **110**, such as via computer hardware and associated software.

EXAMPLE II

Still referring to FIG. **13**B, each of the analyzers interfacing to the subject **320** optionally comprise any system of the analyzer **110**. As illustrated, the first analyzer version **371**, which is an example of the analyzer **110** comprises three analyzer versions, illustrated as the first spectrometer version **142**, the second spectrometer version **144**, and the third spectrometer version **146**. As illustrated, the first spectrometer version **142**, optionally in the form of a watch head, interfaces to the subject **320** along a first z-axis perpendicular to a first x/y-plane, which tangentially touches the upper arm **372** at a first interface point; the second spectrometer version **144** has the form of a watch band link and interfaces to the subject **320** along a second z-axis perpendicular to a second x/y-plane, which tangentially touches the upper arm **372** at a second interface point; and the third spectrometer version **146**, optionally in the form of a watch band attachment, interfaces to the subject **320** along a third z-axis perpendicular to a third x/y-plane, which tangentially touches the upper arm **372** at a third interface point. Each of the three spectrometer versions **142**, **144**, **146** are optionally attached to the upper arm **146** via double-sided adhesives and are thus attached in the manner of a sticker. As illustrated, the three spectrometer versions **142**, **144**, **146** are attached to the upper arm **372** with a flexible band **148**, such as a watch band or an elastic band. The individual spectrometer versions **142**, **144**, **146** are optionally connected using one or more hinge components and or rotating connectors. The individual spectrometer versions **142**, **144**, **146** are optionally replaceably connected to the subject along separate planes forming angles therebetween of greater than 1, 2, 5, 10, 15, 25, or 25 degrees. The hinge allows tangential interfacing of illumination zones of the respective spectrometer version along a curved surface of the subject **320**. Optionally, the hinge allows for rotation of a first spectrometer unit relative to a second spectrometer unit to maintain tangential contact of the illumination zones with the subject **320** as the skin of the subject moves, such as by allowing a rotation of greater than 0.1, 0.5, 1, 2, or 5 degrees. The multiple planes of attachment of the analyzer **110** to the subject **320** allow attachment of multiple sources and/or detectors to the subject **320** along a curved skin surface of the subject **320**, such as around the upper arm **372** and/or the lower arm **374**, as illustrated with the second analyzer/spectrometer version **373** attached to the wrist of the subject **320**, with minimal applied tissue deformation forces at each of the analyzer/subject interface zones. Reduced forces, such as an applied mass, stress, and/or strain aids precision and/or accuracy of the analyzer **110** by reducing movement of fluids within the tissue layers **340** of the subject **320**, reducing changes in pathlength, and/or reducing changes in pressure induced scattering of light.

EXAMPLE III

Still referring to FIG. **13**B, in a first case, each of the first spectrometer version **142**, second spectrometer version **144**, and third spectrometer version **146** optionally contain all of the functionality of the analyzer **110**. However, optionally, one or more optical sources are in one interfacing aspect of the first analyzer version **371**, such as in the second spectrometer version **144**, without any functional optical detectors in the second spectrometer version **144**. In this case, the optical detectors are in a second interfacing aspect of the first analyzer version **371**, such as in the first spectrometer version **142**. For clarity of presentation and without loss of generality, a particular example is provided. In this example, the detector system **500** is positioned in the analyzer **110** in the first spectrometer version **142** along with optional illuminators of the source system **400**. However, the source system also includes photon sources in the second spectrometer version **144**, such as in a watch band link position. In this manner, photonic illuminators with short optical distances to the detector system **500** are positioned in the first spectrometer version **142**, such as in close proximity to the detector system **500**. For instance, photonic sources emitting in wavelength ranges: (1) with an optical absorbance of greater than one unit per millimeter of pathlength and/or (2) in the 1350 to 1560 nm range, such as within 25 mm of 1510, 1520, 1530, or 1540 nm are positioned near the detector system **500**, such as in the same housing as the detector system **500**, in the first spectrometer version **142**, and/or with a radial distance between an illumination zone and a detection zone of less than 10, 8, 6, 5, 4, 3, 2, 1.5, or 1 millimeters. However, photonic sources emitting in lower absorbance regions, such as from 400 to 1350 nm and/or 1565 to 1800 and/or in regions of absorbance by skin at a level of less than one absorbance unit per millimeter of pathlength are positioned in the second spectrometer version **144**, thus giving the photons a longer pathlength to the detector system **500** in the first spectrometer version **142**. The longer selected pathlength, as selected by a detector element of the detector system **500**, from a given source reduces a range of observed pathlengths by photons from the given source, as described supra. Further, each spectrometer version **142**, **144**, **146** allows an independent mean photon

path entering the skin of the subject **320** to be perpendicular to the subject **320** despite the radius of curvature of the skin of the subject **320** as the differing spectrometer versions **142**, **144**, **146** are each positioned with an x/y-plane interface tangential to the local curvature of the skin of the subject **320**, such as at different positions on a watch band equivalent. Optionally and preferably, the x/y-planes tangential to the subject **320** at local sample interface sites for the n interface points of the analyzer **110**, such as the first interface location of the first spectrometer version **142**, the second interface location of the second spectrometer version **144**, and the third interface location of the third spectrometer version **146** are separated by greater than 5, 6, 7, 8, 9, 10, 12, 14, 16, 18, or 20 millimeters as measured along the skin surface. Hence, second photon sources for providing second wavelengths for measuring oxygen and/or scattering of light, such as from 400 to 1300 nm, are optionally placed in a second housing along a second position of the watch band while first photon sources for providing first wavelengths, such as at glucose absorbing wavelengths from 1500 to 2400 nm, are optionally placed in a first housing proximate detector elements, where the detector elements in the first housing detect photons from second, third, . . . , n^{th} housings, such as along a circumferential band around a curved body part, where n is a positive integer greater than 1, 2, or 3.

EXAMPLE IV

In the first spectrometer version **371** of the analyzer **110**, three sample interface zones are used, a first sample interface zone, such as the back of a watch zone where the source system **400**, force system **200**, and/or a first set of optics, such as in the first spectrometer version **142**, interface to the subject **320**; a second interface zone, such as where a second set of optics, such as in the second spectrometer version **144**, interface to the subject **320**; and a third interface zone, such as where a third set of optics, such as in a third spectrometer version **146**, interface to the subject **320**. Generally, any number n of sets of optics interface to the subject **320** to yield n sets of data on a state of the subject **320** where n is a positive integer, such as 1, 2, 3, 4, 5 or more. Optionally, the n sets of optics generate simultaneous data on a single state of the subject **320**. However, each sub-set of optics in the n sets of optics are optionally configured to measure the same analyte and/or different analytes, such as one of more of percent oxygen saturation, heart rate, heart rate variability, glucose concentration, protein concentration, fat, muscle, protein concentration, albumin concentration, globulin concentration, respiration rate, an electrocardiogram, blood pressure, body temperature, environmental temperature, and acceleration of the subject **320**.

Acousto-Optic Analyzer vs. (1) UPI and (2) an AOTF

An applied force-optic analyzer is described herein. Optionally and preferably, the applied force results in a mechanical disturbance of the tissue resulting in a force being applied to the sample. However, in a sub-case of the applied force-optic analyzer, the applied force comprises an acoustic force yielding an acousto-optic analyzer. Notably, in the sub-case of the applied force-optic analyzer being an acousto-optic analyzer, as used herein an acousto-optic analyzer starkly contrasts with both: (1) an ultrasonic photoacoustic imaging (UPI) system and (2) an acousto-optic tunable filter (AOTF) spectrometer, as described infra.

Acousto-Optic Analyzer

As described, an acousto-optic analyzer (AOA) introduces an acoustic vibration wave to the sample to impact the state of the sample, such as tissue, and the state of the sample is measured using an optical probe.

Photoacoustic Imaging

In stark contrast, according to Wikipedia, ultrasonic photoacoustic imaging, also referred to as (UPI), photoacoustic imaging (PI), and/or optoacoustic imaging, delivers non-ionizing laser pulses to biological tissue, which results in absorbed energy and resultant heat in the form of transient thermoelastic expansions detected as wideband megaHertz ultrasonic emissions detected by ultrasonic transducers. The detected signals are used to produce images. As optical absorbance relationships exist with physiological properties, such as hemoglobin concentration and oxygen saturation, the detected pressure waves may be used to determine hemoglobin and oxygen concentration.

Hence, an acousto-optic analyzer starkly contrasts with photoacoustic imaging. Stated again, while the acousto-optic analyzer described herein may induce a heat wave like in photoacoustic imaging, in photoacoustic imaging the sound wave is detected whereas photons, from an external source, are detected in the acousto-optic analyzer described are detected after interacting with the sample being displaced/heated/disturbed by the sound wave.

Acousto-Optic Tunable Filter

According to Wikipedia, an acousto-optic tunable filter (AOTF), diffracts light based on an acoustic frequency. By tuning the frequency of the acoustic wave, the desired wavelength of the optical wave can be diffracted acousto-optically.

Hence, an acousto-optic analyzer (AOA) starkly contrasts with an acousto-optic tunable filter (AOTF) as, while the input sound wave of the AOA may diffract light, the separation of the input light is not the primary use of the sound wave. Indeed, a narrow-band light emitting diode (LED) is optionally used in conjunction with a broadband detector in the acousto-optic analyzer making any separation of the narrow band light source pointless. Further, in the AOA, the sound wave is used to change the state of the biological sample itself, whereas in the AOTF the sound wave is introduced to a birefringent crystal in a wavelength separation module of the spectrometer and is not introduced into the sample.

Still yet another embodiment includes any combination and/or permutation of any of the elements described herein.

The main controller, a localized communication apparatus, and/or a system for communication of information optionally comprises one or more subsystems stored on a client. The client is a computing platform configured to act as a client device or other computing device, such as a computer, personal computer, a digital media device, and/or a personal digital assistant. The client comprises a processor that is optionally coupled to one or more internal or external input device, such as a mouse, a keyboard, a display device, a voice recognition system, a motion recognition system, or the like. The processor is also communicatively coupled to an output device, such as a display screen or data link to display or send data and/or processed information, respectively. In one embodiment, the communication apparatus is the processor. In another embodiment, the communication apparatus is a set of instructions stored in memory that is carried out by the processor.

The client includes a computer-readable storage medium, such as memory. The memory includes, but is not limited to, an electronic, optical, magnetic, or another storage or transmission data storage medium capable of coupling to a processor, such as a processor in communication with a touch-sensitive input device linked to computer-readable

instructions. Other examples of suitable media include, for example, a flash drive, a CD-ROM, read only memory (ROM), random access memory (RAM), an application-specific integrated circuit (ASIC), a DVD, magnetic disk, an optical disk, and/or a memory chip. The processor executes a set of computer-executable program code instructions stored in the memory. The instructions may comprise code from any computer-programming language, including, for example, C originally of Bell Laboratories, C++, C#, Visual Basic® (Microsoft, Redmond, Wash.), Matlab® (MathWorks, Natick, Mass.), Java® (Oracle Corporation, Redwood City, Calif.), and JavaScript® (Oracle Corporation, Redwood City, Calif.).

Herein, any number, such as 1, 2, 3, 4, 5, is optionally more than the number, less than the number, or within 1, 2, 5, 10, 20, or 50 percent of the number.

Herein, an element and/or object is optionally manually and/or mechanically moved, such as along a guiding element, with a motor, and/or under control of the main controller.

The particular implementations shown and described are illustrative of the invention and its best mode and are not intended to otherwise limit the scope of the present invention in any way. Indeed, for the sake of brevity, conventional manufacturing, connection, preparation, and other functional aspects of the system may not be described in detail. Furthermore, the connecting lines shown in the various figures are intended to represent exemplary functional relationships and/or physical couplings between the various elements. Many alternative or additional functional relationships or physical connections may be present in a practical system.

In the foregoing description, the invention has been described with reference to specific exemplary embodiments; however, it will be appreciated that various modifications and changes may be made without departing from the scope of the present invention as set forth herein. The description and figures are to be regarded in an illustrative manner, rather than a restrictive one and all such modifications are intended to be included within the scope of the present invention. Accordingly, the scope of the invention should be determined by the generic embodiments described herein and their legal equivalents rather than by merely the specific examples described above. For example, the steps recited in any method or process embodiment may be executed in any order and are not limited to the explicit order presented in the specific examples. Additionally, the components and/or elements recited in any apparatus embodiment may be assembled or otherwise operationally configured in a variety of permutations to produce substantially the same result as the present invention and are accordingly not limited to the specific configuration recited in the specific examples.

Benefits, other advantages and solutions to problems have been described above with regard to particular embodiments; however, any benefit, advantage, solution to problems or any element that may cause any particular benefit, advantage or solution to occur or to become more pronounced are not to be construed as critical, required or essential features or components.

As used herein, the terms "comprises", "comprising", or any variation thereof, are intended to reference a non-exclusive inclusion, such that a process, method, article, composition or apparatus that comprises a list of elements does not include only those elements recited, but may also include other elements not expressly listed or inherent to such process, method, article, composition or apparatus. Other combinations and/or modifications of the above-described structures, arrangements, applications, proportions, elements, materials or components used in the practice of the present invention, in addition to those not specifically recited, may be varied or otherwise particularly adapted to specific environments, manufacturing specifications, design parameters or other operating requirements without departing from the general principles of the same. Although the invention has been described herein with reference to certain preferred embodiments, one skilled in the art will readily appreciate that other applications may be substituted for those set forth herein without departing from the spirit and scope of the present invention. Accordingly, the invention should only be limited by the Claims included below.

The invention claimed is:

1. A method for noninvasively determining a state of a person having skin, comprising the steps of:

providing an analyzer, comprising: a first spectrometer unit, a second spectrometer unit, and a main controller subsystem;

attaching said first spectrometer unit to the person at a first illumination zone;

said first spectrometer unit delivering first photons, from first illumination optics, along a first mean z-axis optical path normal to a first x/y-plane tangentially contacting the first illumination zone of the skin of the person;

attaching said second spectrometer unit to the person at a second illumination zone;

said second spectrometer delivering second photons, from second illumination optics, along a second mean z-axis optical path perpendicular to a second x/y-plane tangentially contacting the second illumination zone of the skin of the person, said first x/y-plane noncoplanar with said second x/y-plane;

said main controller processing detected signals from a detector mounted in said first spectrometer unit, the detected signals resultant from illumination from said first illumination optics and said second illumination optics, to generate at least one measure of the state of the person; and

a hinge, of said analyzer, connecting said first spectrometer unit to said second spectrometer unit rotating about at least one rotation axis by greater than one degree in response to movement of the skin of the person.

2. The method of claim **1**, further comprising the step of:

a detector system of said first spectrometer unit, configured to optically view a detection zone of said first x/y-plane, detecting the second photons delivered to the second illumination zone along the second mean z-axis optical path perpendicular to the second x/y-plane, the first x/y-plane and the second x/y-plane forming an angle therebetween of greater than five degrees.

3. The method of claim **1**, further comprising the steps of:

affixing an electro-mechanical transducer, of said analyzer, to the skin of the subject; and

said main controller driving said electro-mechanical transducer with a voltage waveform to induce displacement of the skin and generate a pressure wave in the skin during said step of delivering the first photons.

4. The method of claim **3**, said step of driving said electro-mechanical transducer further comprising the step of:

an input transducer applying a ping force to the skin tissue, driven by the applied voltage waveform persisting for less than one second, to yield a single displacement of the skin tissue.

5. The method of claim 4, further comprising the step of:

repeating said step of applying said ping force at least ten times during a measurement period of said analyzer.

6. An apparatus for noninvasively determining a state of a person having skin, comprising:

an analyzer, comprising:

a first spectrometer unit attached to the person at a first illumination zone during use, said first spectrometer unit comprising first illumination optics configured to deliver first photons along a first mean z-axis optical path through a first x/y-plane tangentially contacting said first illumination zone of the skin of the person;

a second spectrometer unit attached to the person at a second illumination zone during use, said second spectrometer unit comprising second illumination optics configured to deliver second photons along a second mean z-axis optical path through a second x/y-plane tangentially contacting said second illumination zone of the skin of the person, said first x/y-plane noncoplanar with said second x/y-plane;

a main controller configured to process detected signals from a detector mounted in said first spectrometer unit, the detected signals resultant from illumination from said first illumination optics and said second illumination optics, to generate at least one measure of the state of the person; and

a flexible band connecting said first spectrometer unit to said second spectrometer unit.

7. The apparatus of claim 6, said first x/y-plane and said second x/y-plane forming an angle therebetween of greater than ten degrees.

8. The apparatus of claim 6, said analyzer further comprising:

a hinge component connecting said first spectrometer unit to said second spectrometer unit.

9. The apparatus of claim 6, said first illumination zone and said second illumination zone separated by at least eight millimeters as measured along a shortest curved surface path of the skin of the person.

10. The apparatus of claim 6, said analyzer further comprising:

a permeable substrate between said first illumination optics and the first illumination zone, said permeable substrate infused with at least one of a fluorocarbon and a chlorofluorocarbon.

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