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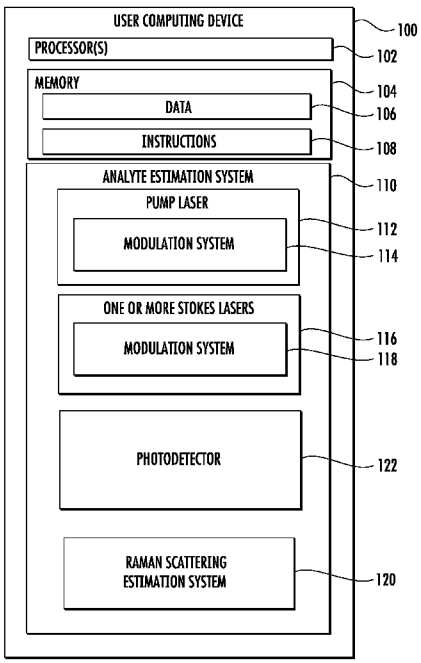


FIG. 3

(57) Abstract: The present disclosure provides methods, systems, and devices for estimating the presence of analytes in the tissue of a user. The system can include a Raman pump light source that emits pump light toward a tissue of the user at a pump wavelength. The system can include a Stokes light source that emits Stokes light toward the tissue at one or more Stokes wavelengths. The system can include a calibration light source that emits light towards the tissue at a calibration. The system can include a pulse controller that engages the Raman pump light source, the Stokes light source, and the calibration light source to generate a Raman signal and a non-Raman signal. The system can include a photodetector that measures light that emanates from the tissue. The system can include a processor that processes the measured light to provide an estimated analyte level of the analyte in the user.

WO 2025/136394 A1

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DIFFERENTIAL STIMULATED RAMAN SPECTROSCOPY WITH A CALIBRATION LIGHT SOURCE FOR BACKGROUND-FREE SIGNAL DETECTION

FIELD

[0001] The present disclosure relates generally to the non-invasive monitoring of molecules in the body of a user.

BACKGROUND

[0002] Many human medical conditions may result in a need to measure the amount of a particular molecule present in an individual. For example, some experts estimate that over 400 million adults currently have diabetes. For many of these individuals, periodic monitoring of the amount of glucose in their bloodstream is a part of everyday life to avoid serious medical complications. Traditionally, to measure the chemical makeup internal to a user's body, invasive measuring methods (e.g., such as sample tissue extraction or blood draw) have been used. Example techniques include finger-prick blood glucometry and transdermal continuous glucose monitoring (CGM). These systems are often painful and expensive to use. For users who have to take such measurements repeatedly, the pain and expense associated with glucose monitoring can significantly affect their quality of life.

SUMMARY

[0003] Aspects and advantages of embodiments of the present disclosure will be set forth in part in the following description, or may be learned from the description, or may be learned through practice of the embodiments.

[0004] One example embodiment includes a device for non-invasively measuring a level of an analyte in a user using Stimulated Raman Scattering. The device can include a Raman pump light source that emits pump light toward a tissue of the user at a pump wavelength. The device can include a Stokes light source that emits Stokes light toward the tissue at one or more Stokes wavelengths. The device can include a calibration light source that emits light towards the tissue at a calibration. The device can include a pulse controller that engages the Raman pump light source, the Stokes light source, and the calibration light source to generate a Raman signal and a non-Raman signal. The device can include a photodetector that measures light that emanates from the tissue to detect the Raman signal and the non-Raman signal. The device can include a processor that processes the measured light to provide an

estimated analyte level of the analyte in the user based on a comparison of the Raman signal and the non-Raman signal.

[0005] Another example aspect of the present disclosure is a computer-implemented method for non-invasively measuring a level of an analyte in a user using Stimulated Raman Scattering. The method comprises controlling, by a pulse controller, a Stokes light source, a calibration light source, and a Raman pump light source. The method further comprises emitting, from a Stokes light source and a calibration light source, Stokes light and calibration light toward a skin surface of the user during a first time. The method further comprises measuring, by a photodetector, light that emanates from the skin surface during the first time to produce a non-Raman signal. The method further comprises emitting, from a Stokes light source and a Raman pump light source in response to the pulse controller, Stokes light and Raman pump light toward a skin surface of the user during a second time. The method further comprises measuring, by a photodetector, light that emanates from the skin surface during the first time to produce a Raman signal. The method further comprises modifying, by a computing system including one or more processors, the Raman signal based on the non-Raman signal to generate a modified Raman signal. The method further comprises processing, by the computing system, the modified Raman signal to provide an estimated analyte level of the user.

[0006] Another example aspect of the present disclosure is an analyte estimation system. The system can include a Raman pump light source that emits pump light toward a tissue of the user at a pump wavelength. The system can include a Stokes light source that emits Stokes light toward the tissue at one or more Stokes wavelengths. The system can include a calibration light source that emits light towards the tissue at a calibration. The system can include a pulse controller that engages the Raman pump light source, the Stokes light source, and the calibration light source to generate a Raman signal and a non-Raman signal. The system can include a photodetector that measures light that emanates from the tissue to detect the Raman signal and the non-Raman signal. The system can include a processor that processes the measured light to provide an estimated analyte level of the analyte in the user based on a comparison of the Raman signal and the non-Raman signal.

[0007] Other example aspects of the present disclosure are directed to systems, apparatus, computer program products (such as tangible, non-transitory computer-readable media but also such as software which is downloadable over a communications network without necessarily being stored in non-transitory form), user interfaces, memory devices, and

electronic devices for measuring stimulated Raman scattering using an embedded computing system.

[0008] These and other features, aspects and advantages of various embodiments will become better understood with reference to the following description and appended claims. The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate embodiments of the present disclosure and, together with the description, serve to explain the related principles.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] A detailed discussion of embodiments directed to one of ordinary skill in the art are set forth in the specification, which refers to the appended figures, in which:

[0010] FIG. 1A illustrates an example analyte estimation system that includes a Raman pump light source, a Stokes light source, and a calibration light source in accordance with example embodiments of the present disclosure.

[0011] FIG. 1B illustrates an example analyte estimation system that includes a calibration light source in accordance with example embodiments of the present disclosure.

[0012] FIG. 2A illustrates a graph of the wavelength and intensity of light resulting from spontaneous Raman scattering when light is projected into a target material;

[0013] FIG. 2B illustrates a graph of the wavelength and intensity of light resulting from stimulated Raman scattering when light is projected into a target material;

[0014] FIG. 2C illustrates an example analyte estimation system for measuring the analyte in the arm of a user non-invasively in accordance with example embodiments of the present disclosure;

[0015] FIG. 2D illustrates an example analyte estimation system with multiple laser diodes for generating light at a particular wavelength within a Stokes range in accordance with an example embodiment of the present disclosure;

[0016] FIG. 2E illustrates an example analyte estimation system with a single tunable Stokes laser for generating light at different wavelengths within a Stokes range as needed in accordance with an example embodiment of the present disclosure;

[0017] FIG.3 illustrates an example computing environment including a user computing device in accordance with example embodiments of the present disclosure;

[0018] FIG. 4A illustrates an example of different types of photon scattering by matter in accordance with example embodiments of the present disclosure;

[0019] FIG. 4B illustrates an example of energy level changes of a molecule as a result of light scattering in accordance with example embodiments of the present disclosure;

[0020] FIG. 5 illustrates a relative amount of Rayleigh scattered light and Raman scattered light for a typical analyte;

[0021] FIG. 6 illustrates a graph representing the wavelengths of scattered light in accordance with example embodiments of the present disclosure;

[0022] FIG. 7 illustrates spontaneous Raman scattering;

[0023] FIG. 8 illustrates stimulated Raman scattering;

[0024] FIG. 9A illustrates an example graph representing the amount of light that is Raman scattered with spontaneous Raman scattering;

[0025] FIG. 9B illustrates an example graph representing the amount of light that is Raman scattered with stimulated Raman scattering;

[0026] FIG. 10A illustrates an example configuration of a system for detecting analytes in a user's skin in accordance with example embodiments of the present disclosure;

[0027] FIG. 10B illustrates an example configuration of a system for detecting analytes in the user's skin in accordance with example embodiments of the present disclosure;

[0028] FIG. 10C illustrates an example configuration of a system for detecting molecules in the user's skin in accordance with example embodiments of the present disclosure;

[0029] FIG. 10D illustrates an example configuration of a system 940 for detecting analytes in the user's skin in accordance with example embodiments of the present disclosure;

[0030] FIG. 11 illustrates an example system for detecting the presence of a molecule in the skin of the user in accordance with example embodiments of the present disclosure;

[0031] FIGS. 12A and 12B represent example molecule detection systems in accordance with example embodiments of the present disclosure;

[0032] FIG. 13 illustrates an example system for non-invasively measuring molecules within a user's body in accordance with example embodiments of the present disclosure;

[0033] FIG. 14 illustrates an example system with light sources and photodiodes in accordance with example embodiments of the disclosure;

[0034] FIG. 15 illustrates a layout of a plurality of light-producing sources in accordance with example embodiments of the present disclosure;

[0035] FIG. 16 illustrates an example analyte estimation system in accordance with example embodiments of the present disclosure;

[0036] FIG. 17 is a flowchart depicting an example process of detecting molecules within a target in accordance with example embodiments of the present disclosure;

[0037] FIG. 18 depicts a block diagram of an example data analysis model according to example embodiments of the present disclosure;

[0038] FIG. 19 is a flowchart depicting an example process of detecting analytes within a target tissue in accordance with example embodiments of the present disclosure;

[0039] FIG. 20 illustrates an example computing environment, including a computing device 2000 in accordance with example embodiments of the present disclosure;

[0040] FIG. 21 is an example of two diagrams representing the pulse intensity of different light sources at different points in time in accordance with example embodiments of the present disclosure;

[0041] FIG. 22A is an example graph of the strength of the Raman signal (or SRS signal) produced without using a calibration light source at different wavelengths in accordance with example embodiments;

[0042] Figure 22B is a graph of a modified Roman signal in accordance with example embodiments of the disclosure;

[0043] Figure 22C is a graph of a modified Raman signal in accordance with example embodiments of the disclosure; and

[0044] FIG. 23 is a flowchart depicting an example process of detecting analytes within a target tissue in accordance with example embodiments of the present disclosure.

DETAILED DESCRIPTION

[0045] Reference now will be made in detail to embodiments, one or more examples of which are illustrated in the drawings. Each example is provided by way of explanation of the embodiments, not limitation of the present disclosure. In fact, it will be apparent to those skilled in the art that various modifications and variations can be made to the embodiments without departing from the scope or spirit of the present disclosure. For instance, features illustrated or described as part of one embodiment can be used with another embodiment to yield a still further embodiment. Thus, it is intended that aspects of the present disclosure cover such modifications and variations.

[0046] Generally, the present disclosure is directed towards a system for improving the performance of an analyte measurement system that non-invasively monitors one or more analytes internal to a user's body. For example, an analyte estimation system for monitoring

analytes can estimate the amount of an analyte in a target material (e.g., the tissue of a user) using Raman spectroscopy. Specifically, the analyte estimation system can project light into a target material (e.g., user's body tissue) and measure the wavelengths and intensity of the light that is emitted out of the material. The analyte measurement system can determine the amount of Raman scattering of the light based on the increase of photons at a specific wavelength associated with the particular analyte or the loss of photons at the specific wavelength. In one aspect, the analyte measurement system can use a Stokes light source and a Raman pump light source and project them at the same portion of the user's tissue.

[0047] The amount of Raman scattering can be relatively small and may be difficult to distinguish from sources of noise in the light detected by a photodetector. To improve the analyte measurement system's ability to distinguish the portion of the detected light that results from Raman scattering from the portion of the detected light that results from one or more noise sources, the Raman-based analyte measurement system can take steps to identify and remove the noise from the detected signal.

[0048] In some examples, the analyte measurement estimation system can include a calibration light source in addition to a Raman pump light source and a Stokes light source. The calibration light source can be a third light source that generates and transmits light toward the target tissue of the user. The wavelength of light generated by the calibration light source can be calibrated such that it does not cause any Raman scattering when the calibration light source is activated at the same time as the Stokes light source. A pulse modulator can control the activation of the Raman pump light source, the Stokes light source, and the calibration light source. By controlling the pulses of these light sources, the analyte measurement system can ensure that during the first period of time, only the Stokes light source and the calibration light source are activated. During this time, a photodetector can detect any light that emanates from the tissue. Because the frequency of light generated by the calibration light source is chosen to ensure that no Raman scattering occurs, the detected light is entirely composed of a non-Raman scattered light and the signal produced by the photodetector can be referred to as a non-Raman signal.

[0049] . In some examples, the wavelength of the calibration light source is selected to be as close to the wavelength of the Raman pump light source as possible without causing Raman scattering. In this way, the conditions in which the calibration light source is activated are as similar as possible to the conditions when the Raman pump light source is activated. Having similar conditions will minimize the differences in the noise sources in both the non-

Raman signal and the Raman signal. For example, if the fixed wavelength of the calibration light source differs significantly enough from the wavelength of the Raman pump light source, the sources of the light noise and characteristics of the light noise may differ enough that analyzing the non-Raman signal may not be useful to remove noise from the Raman signal.

[0050] The analyte measurement system can identify one or more elements or features of the non-Raman signal. The pulse modulator can activate the Raman pump light source and the Stokes light source at a second time period. During the second time period, the photodetector can detect a signal that includes a portion of the signal generated by Raman scattering and a portion of the signal generated by noise sources. The analyte measurement system can compare the non-Raman signal generated when only the Stokes and the calibration light sources were activated with the Raman signal detected when the Raman pump light source and the Stokes light source were activated. The analyte measurement system can generate a modified Raman signal by removing the noise features identified from the non-Raman signal. In this way, the analyte measurement system can remove noise from the Raman signal to help isolate only that portion of the signal resulting from Raman scattering.

[0051] More specifically, Raman spectroscopy uses Raman scattering to determine whether an analyte is present in a particular target material (e.g., the tissue of a user). Raman scattering is an optical process where excitation light can be projected into a target sample by a light source (e.g., a pump laser). The incoming excitation light can excite molecules within the target sample to a higher energy state. The molecule that has been excited can emit a photon, thus lowering the energy of the molecule to a lower energy level. In some examples, the higher energy state can be a virtual excited state such that the molecule is never actually excited to that state. Instead, both the excitation and the relaxation (when the photon is emitted) occur simultaneously via the virtual state.

[0052] The specific wavelengths present in photons generated by Raman scattering can be determined by the vibrational modes of the chemical bonds of the molecule that was excited by the excitation light and the wavelength of the incoming light. A system that uses Raman scattering to determine the presence of an analyte can implement either spontaneous Raman scattering or stimulated Raman scattering. It should be noted that other types of Raman scattering can be used to perform the systems and methods described herein.

[0053] An analyte estimation system can be included in a computing device. The analyte estimation system can identify any of: the presence, amount, or density of a particular analyte in a user's tissue. In some examples, the analyte estimation system can be integrated into a wearable computing device. Such a wearable computing device can include a smartwatch, a fitness band, or any other wearable computing device. A wearable computing device can be worn such that the analyte estimation system can be placed directly against or directly facing the skin of a user. In this way, the analyte estimation system can unobtrusively measure an analyte without the user needing to take any particular action.

[0054] The analyte estimation system can include a Raman pump light source that projects light at a particular wavelength (e.g., 850 nanometers). A detector can measure light reflected at the wavelength of the Raman pump light source. The measured light can be the light that was not Raman scattered or noise associated light. This measured light can have the same wavelength as the light generated by the pump laser. The peak detected at the wavelength (e.g., 850 nanometers) emitted by the Raman pump light source can be referred to as a Rayleigh peak. Rayleigh scattering can refer to light emitted by the target sample with the same wavelength as the pump light. Rayleigh scattering is much more common than Raman scattering. Thus, the intensity of light at the Rayleigh peak can be higher than the intensity measured for light resulting from Raman scattering.

[0055] Raman scattered light can be detected at one or more particular wavelengths or within certain ranges of wavelengths (depending on the specific analytes to be measured). This light can result from spontaneous Raman scattering in which the light emitted by the target material has a different wavelength than the light produced by the pump laser. The range of wavelengths generated by Raman scattering by a particular molecule can be referred to as the Stokes range of that molecule for emitted photons that have a higher wavelength than the originally projected photons or the anti-Stokes range for photons that have a lower wavelength than the originally projected photons.

[0056] One or more Stokes lasers can be included in the analyte estimation system and can project light into the target material to increase the amount of Raman scattered light. In some examples, the Stokes source(s) can provide light over a wavelength range associated with an analyte. The Stokes source can be a broadband light source that provides light at all wavelengths within the wavelength range. As a result of the presence of one or more Stokes sources, the Raman response can be significantly higher. As a result, the presence of an analyte can more easily be identified.

[0057] In some examples, the light detected by the photodetector can also include light from one or more noise sources (such as thermal lensing (TL), optical self- and cross-phase modulations (SPM and XPM) and two-photon absorption (TPA)). An important factor in accurately detecting the presence of (or amount of) a particular analyte is distinguishing the portion of the measured light (or the signal generated based on the measured light) that is the result of Raman scattering from the portion of the measured light that is generated by noise sources. Methods for doing so can include measuring the signal produced by the measured light when no Raman scattering occurs and comparing it to the signal that is generated when Raman scattering occurs. By comparing the two signals, the analyte estimation system can identify the portions of the detected light that are attributable to noise and the portion that is attributable to Raman scattering.

[0058] Methods for generating a signal without Raman scattering can include using a calibration light source in the analyte estimation system. The calibration light source can produce light calibrated to have a wavelength that will not result in Raman scattering for particular analytes. The analyte estimation system can use a controller device (e.g., a pulse controller) to activate the calibration light source simultaneously with the Stokes light source during one or more time periods without activating the Raman pump light source. The photodetector can capture the light that emanates from the user's skin. This captured light can be used to generate a non-Raman signal. The non-Raman signal can be a signal that does not include Raman scattered light.

[0059] The analyte estimation system can analyze the non-Raman signal to identify one or more characteristics of the non-Raman signal that are associated with sources of noise. The analyte estimation system can use the controller to activate the Raman pump light source and the Stokes light source at the same time without activating the calibration light source. The photodetector can then detect the light emanating from the tissue of the user. The analyte estimation system can generate a Raman signal based on the detected light.

[0060] In some examples, the analyte estimation system can subtract the non-Raman signal from the Raman signal to generate a modified Raman signal. The modified Raman signal can contain significantly less noise and, as such, can be used to more accurately and reliably determine whether a particular analyte is present in the tissue of a user.

[0061] The pulse controller can target the light produced by the Raman pump light source, the Stokes light source, and the calibration light source at a particular portion of the tissue of the user. During a first time period the pulse controller can activate the Stokes light

source and the calibration light source. Once the first time period is complete, the pulse controller can deactivate the Stokes light source and the calibration light source. During a second time period, the pulse controller can activate the Stokes light source and the Raman pump light source.

[0062] During the first time period, the analyte estimation system can generate a non-Raman signal using a photodetector that measures the light emitted by the tissue. During the second time period, the analyte estimation system can generate a Raman signal using a photodetector that measures the light emitted by the tissue. The analyte estimation system can analyze the non-Raman signal to identify aspects, characteristics, or portions of the non-Raman signal that are associated with sources of light noise. In some examples, the analyte estimation system can compare the non-Raman signal to the Raman signal to identify which portions of the Raman signal are associated with light noise instead of Raman scattering.

[0063] The analyte estimation system (e.g., analyte estimation system in FIG. 20) can generate a modified Raman signal by removing portions determined to originate from light noise sources. The modified Raman signal can be analyzed to detect the presence of one or more analytes, as discussed above.

[0064] Embodiments of the disclosed technology provide a number of technical effects and benefits, particularly in the area of detecting analytes in the target material. In particular, embodiments of the disclosed technology provide improved techniques for detecting analytes in the tissue of a user. For example, it can be difficult to detect the Raman scattering signal in the light emanating from the tissue of a user. Including a calibration light source is a technical solution that overcomes this technical issue by helping the analyte estimation system to distinguish the Raman scattering signal from noise. As a result, the Raman scattering is easier to detect. Doing so increases the accuracy and effectiveness of the analyte estimation system. Improving the precision and effectiveness of the system results in a significant benefit to the users.

[0065] With reference to the figures, example embodiments of the present disclosure will be discussed in further detail.

[0066] FIG. 1A illustrates an example analyte estimation system that includes a Raman pump light source 134, a Stokes light source 132, and a calibration light source 136 in accordance with example embodiments of the present disclosure. In this example, the analyte measurement system can measure the analyte in the tissue of the arm 144 of the user. The analyte estimation system can include a Stokes light source 132, a Raman pump light source

134, and a calibration light source 136. All three light sources can be targeted at the same portion 162 of the tissue of the arm 144 of the user. In this example, the calibration light source 136 can be controlled such that it is activated when the Stokes light source 132 is activated and the Raman pump light source 134 is not activated. The wavelength of the light produced by the calibration light source 136 can be selected or determined such that it does not induce any Raman scattering. A photodetector can detect the light emanating from the portion 162 of the tissue of the arm 144 of the user.

[0067] When, during the first time, the calibration light source 136 and the Stokes light source are activated, the photodetector can detect light emanating from the tissue 162 of the user and, based on that emanated light, generate a signal. This signal will not include Raman scattered light (or very little Raman scattered light) and can be referred to as the non-Raman signal. During a second time, the Raman pump light source 134 can be activated when the Stokes light source 132 is activated but the calibration light source 136 is not. The photodetector can detect light emanating from the portion of the tissue 162 of the arm 144 of the user. The emanated light can include light that has been Raman scattered. When the Stokes light source 132 and the Raman pump light source 134 are activated, the photodetector can generate a signal based on the light that includes Raman scattered light. This signal can be referred to as the Raman signal.

[0068] In some examples, the analyte estimation system can analyze the non-Raman signal and compare it to the Raman signal to determine one or more portions of the Raman signal associated with a noise source instead of resulting from Raman scattering. For example, the non-Raman signal can include noise that is also present in the Raman signal. The elements of noise present in the non-Raman signal can be removed from the Raman signal to generate a modified Raman signal. The modified Raman signal can be analyzed to determine the amount of Raman scattered light and estimate the amount of a particular analyte in the tissue of a user. Removing one or more noise-based elements from the Raman signal can increase the accuracy of the analyte estimation system.

[0069] FIG. 1B illustrates an example analyte estimation system that includes a calibration light source 136 in accordance with example embodiments of the present disclosure. In this example, the analyte measurement system can include a Raman pump light source 134, a Stokes light source 132, and a calibration light source 136 to transmit light at a portion of the tissue of a user's body. Light can emanate back out of the portion of the tissue and can be measured by the photodetector 142. The photodetector 142 can generate a signal

based on the detected light. This signal can be analyzed to determine the presence of a particular analyte and, if the analyte is present, the density of the analyte.

[0070] As noted above, the signal produced by the photodetector 142 can include noise. Noise can be the result of a plurality of different factors. The amount of Raman scattering is relatively small, even when stimulated. As a result, the presence of noise can make identifying analytes based on the signal significantly more difficult and inaccurate for the analyte estimation system. The analyte estimation system can include a controller 140. The controller 140 can determine when each light source is activated to improve the ability of the analyte estimation system to distinguish between noise and signal. In some examples, the Stokes light source 132 and the calibration light source 136 can be activated simultaneously without activating the Raman pump light source 134. The wavelength of light produced by the Stokes light source 132 and the calibration light source 136 can be determined such that no Raman scattering is produced when those light sources are focused on the tissue of a user. Without Raman scattering, the light detected by the photodetector 142 can be a non-Raman signal and can include noise without any Raman scattering.

[0071] The non-Raman signal can be analyzed to identify the characteristics or portions of the signal that result from noise sources rather than Raman scattering. The controller 140 can activate the Raman pump light source 134 and the Stokes light source 132 at the same time without activating the calibration light source 136. When both the Raman pump light source 134 and the Stokes light source 132 are activated, the photodetector can produce a Raman signal. The Raman signal can include Raman scattered light as well as noise-based light. The analyte estimation system can compare the features and characteristics of the non-Raman signal to identify the noise characteristics and remove them from the Raman signal to produce a modified Raman signal. This modified Raman signal can be used to determine the amount of Raman scattering of the light based on the characteristics of the user's tissue. Based on this information, the analyte estimation system can determine the presence of one or more analytes.

[0072] FIG. 2A illustrates a graph of the wavelength 162 and intensity 160 of light resulting from spontaneous Raman scattering when light is projected into a target material. In this example, a pump laser 112 can project light at a particular wavelength (e.g., 850 nanometers). As seen in the example graph, light with high intensity is measured at the wavelength of the pump laser 112. This represents the light that was not Raman scattered and instead has the same wavelength as the light generated by the pump laser 112. The peak that

is detected at the particular wavelength (e.g., 850 nanometers) emitted by the Raman pump light source can be referred to as a Rayleigh peak. Rayleigh scattering can refer to light that is emitted by the target sample and has the same wavelength as the pump light. Rayleigh scattering is much more common than Raman scattering and thus the intensity of light at the Rayleigh peak can be higher than the intensity measured for light that is the result of Raman scattering.

[0073] In this particular example, Raman scattered light is detected between approximately the wavelengths of 900 nanometers and 1000 nanometers. However, other ranges of wavelengths can be measured depending on the specific analyte to be measured. This light is the result of spontaneous Raman scattering in which the light emitted by the target material has a different wavelength than the light produced by the pump laser 112. The range of wavelengths generated by Raman scattering by a particular molecule can be referred to as the Stokes range of that molecule for emitted photons that have a higher wavelength than the originally projected photons or the anti-Stokes range for photons that have a lower wavelength than the originally projected photons. The specific features of the detected Stokes range, including but not limited to the wavelengths at which peak intensity is measured, can be analyzed to generate a Raman signature for the molecule. The Raman signature can represent specific features of a detected Stokes range (e.g., peaks) that are associated with a particular molecule. In this manner, the Raman signature can allow a specific molecule to be identified by analyzing the Stokes range that results when the specific molecule is present in the target material. Not pictured is the anti-Stokes range which can occur on the other side of the Rayleigh peak and represents Raman scattering in which the emitted light has a wavelength lower than the light generated by the pump laser 112. Although much of the present disclosure will be described in terms of the Stokes range, it will be appreciated that the disclosed concepts may be utilized with wavelengths within the anti-Stokes range.

[0074] In FIG. 2A, three peaks (166, 168, and 170) are present in the Stokes range. This information, as well as other information about the Stokes range, can be used to determine whether a particular analyte is present in the target material and at what concentrations. However, the amount of Raman scattering that occurs with spontaneous Raman scattering is very low. As a result, the information needed to identify a molecule by its corresponding Stokes range or Raman signature can be difficult to detect.

[0075] FIG. 2B illustrates a graph of the wavelength 162 and intensity 160 of light resulting from stimulated Raman scattering when light is projected into a target material. In

addition to the pump laser 112, one or more Stokes lasers 116 can project light into a target material. In some examples, the Stokes laser(s) 116 can provide light over a wavelength range that is associated with an analyte. Traditionally, the Stokes source can be an LED that provides broadband light at all wavelengths within the wavelength range when the LED is turned on.

[0076] As a result of the Stokes laser 116, the Raman response is significantly higher. As a result, the Stokes range, and therefore the Raman signature, of the molecule can more easily be detected and the analyte can more easily be identified.

[0077] FIG. 2C illustrates an example analyte estimation system for non-invasively measuring the analyte in the arm of a user in accordance with example embodiments of the present disclosure. A pump laser 188 (e.g., a first light source) can project light into the target material 180. In this example, the target material 180 is the skin and other tissue of the arm of a user. The projected light can be generated by the pump laser 188 at a first wavelength. The analyte estimation system can also include one or more Stokes lasers 189. To facilitate stimulated Raman scattering, the one or more Stokes lasers 189 can be configured to generate light at wavelengths associated with the Raman signature of a target analyte. The pump laser 188 and the one or more Stokes lasers 189 can be vertical-cavity surface-emitting lasers (VCSELs) and can be integrated into a printed circuit board (PCB) 184.

[0078] The one or more Stokes lasers 189 can be narrow-band light sources. The pump laser 188 also can be a narrow-band light source in some examples. As used herein, a narrowband light source can project light such that the photons have wavelengths that fall within a narrow range of wavelengths relative to the relevant wavelength range (e.g., Stokes range) associated with the Raman-scattered radiation for the analyte of interest. In some examples, a narrowband light source can be defined based on the percentage of that wavelength range that is generated at a particular point in time. For example, a narrowband laser can generate light that falls within a bandwidth that is 10% of the total wavelength range that the laser can project. For example, if a particular Stokes laser 189 is tunable such that it can generate light within the range of 500 nanometers to 1500 nanometers, a narrowband laser can project light such the wavelength of each photon falls within a 100-nanometer range (e.g., 10% of the total range of the laser). In another example, a narrowband laser can be defined as a laser that projects light with a wavelength bandwidth of 1% of the total wavelength range of the laser. With this definition, the narrowband laser can produce light

that falls within a 10-nanometer range (e.g., such that all the projected light has a wavelength within five nanometers of the target wavelength).

[0079] In some examples, the Stokes laser 189 can be a single tunable laser that can sweep a narrowband laser over the range of wavelengths that the tunable laser can produce. In some examples, the tunable laser can sweep over the wavelengths in the Stokes range of the target analyte. In another example, the Stokes laser 189 can include a plurality of laser diodes, each of which generates a narrowband of light centered around a wavelength in the Stokes range of the target analyte.

[0080] In some examples, the narrowband VCSEL light sources can be tunable over a relatively small range (e.g., approximately 5 nm range) using temperature and electrical current. In this way, the narrowband VSCEL light sources can be enabled to obtain a larger range without the extra components that are typically included in a tunable laser such as additional mechanical components integrated in the chip (e.g., MEMS mirrors) to allow for the wider tunability.

[0081] In some examples, other configurations can be used. For example, the analyte estimation system can include more than one pump laser combined with a tunable Stokes laser. Thus, the analyte estimation system can include two pump lasers 188 that are 20 nm apart, and a single tunable Stokes laser 189 that can be tuned over a 20 nm range, resulting in a total of 40 nm range of possible Raman shifts. Additionally, or alternatively, with 3 pump lasers 20 nm apart the range can be tripled. Additionally, or alternatively, one or more fixed wavelength Stokes lasers 189 and a tunable pump laser 188.

[0082] The light projected by the pump laser 188 can excite one or more molecules within the target material 180 (e.g., electrons within the molecules are raised to a higher energy level). The molecules can return to a lower energy level and emit one or more photons. A photodetector 182 can detect light emitted from the target material 180. The detected light can be represented in a graph of the intensity of the light at various wavelengths.

[0083] The detected light can form a Stokes range for the molecule that was excited by incident light. The spectral intensity at wavelengths across the Stokes range for a particular analyte can form a specific Raman signature. In some examples, a Raman signature can be associated with a specific pattern based on the wavelengths at which peaks are detected, the spacing between peaks, and/or the intensity of light that is detected at one or more

wavelengths. The features detected in the Stokes range can be compared to predetermined Raman signatures to determine one or more analytes present in the target material.

[0084] Data representing the Stokes range can include information representing the amount of light or intensity of light at each wavelength in a range of wavelengths included in the Stokes range. The data representing the Stokes range can be analyzed to determine one or more features, including peak wavelengths (e.g., wavelengths at which the measured intensity is higher than other nearby wavelengths), troughs, the distances between peaks, the distances between each peak wavelength, and the wavelength of the pump laser, and so on.

[0085] FIG. 2D illustrates an example analyte estimation system with multiple laser diodes generating light at one or more particular wavelengths within a Stokes range in accordance with an example embodiment of the present disclosure. As with FIG. 1C, a pump laser 188 can project light into a target material. A plurality of Stokes lasers (189-1, 189-2, and 189-3) can project narrowband light into the target material 180 with a center wavelength different from the center wavelength of the pump laser 188. Photodetectors 182 can be placed such that they measure light being emitted by analytes in the target material 180.

[0086] The Stokes lasers 189 can each generate narrow-band light (e.g., the light generated by the Stokes lasers falls within a particular wavelength band which can be represented as a percentage of the total wavelength range of the Stokes laser or as a specific wavelength number such as within 1 nanometer of the target wavelength) for a different wavelength within the Stokes range. In one example embodiment, the pump laser (e.g., the first light source) and the Stokes lasers (e.g., one or more second light sources) are VCSELs that each use 40 milliwatts of power. In other examples, different lasers that use different amounts of power can be used.

[0087] It should be noted that light can be measured based on its wavenumber rather than its wavelength. Wavenumber can represent the spatial frequency of an electromagnetic wave and can be measured relative to a base value (e.g., in this case, the light produced by the pump laser can be considered to have a wavenumber of 0 and the light produced by the one or more second sources can be given a wavenumber relative to the wavenumber of the light produced by the pump laser).

[0088] FIG. 2E illustrates an example analyte estimation system with a single tunable Stokes laser 189 generating light at different wavelengths within a Stokes range in accordance with an example embodiment of the present disclosure. As with FIG. 1C, a pump laser 188 can project light into a target material. A tunable Stokes laser 190 can generate light

that can project a narrowband of light into the target material 180 that can be adjusted to any wavelength within a Stokes range of interest. In some examples, the tunable laser can start with a narrowband of light at the low end of the Stokes range and adjust the wavelengths such that they sweep along the entire Stokes range without widening the narrowband of light wavelengths at any point. Photodetectors 182 can be placed such that they measure light being emitted by analytes in the target material 180.

[0089] FIG. 3 illustrates an example computing environment including a computing device 100 in accordance with example embodiments of the present disclosure. The computing device 100 can include an analyte estimation system for non-invasively determining the presence and amount of one or more analytes internal to a user. In some examples, the computing device 100 can be a user computing device such as a smartphone or a wearable computing device. In other examples, the computing device 100 can be a computing device intended for home use and not for portability. In this example, the user computing device 100 can include one or more processors 102, memory 104, and an analyte estimation system 110.

[0090] In more detail, the one or more processors 102 can be any suitable processing device for a computing device 100. For example, such a processor can include one or more of: one or more processor cores, a microprocessor, an ASIC, an FPGA, a controller, a microcontroller, etc. The one or more processors can be one processor or a plurality of processors that are operatively connected. The memory 104 can include one or more non-transitory computer-readable storage media, such as RAM, ROM, EEPROM, EPROM, flash memory devices, etc., and combinations thereof.

[0091] In particular, in some devices, memory 104 can store instructions 108 for implementing the analyte estimation system 110. It will be appreciated that the term "system" can refer to specialized hardware, computer logic that executes on a more general processor, or some combination thereof. Thus, a system can be implemented in hardware, application-specific circuits, firmware, and/or software controlling a general-purpose processor. In one embodiment, the system can be implemented as program code files stored on the storage device, loaded into memory, and executed by a processor or can be provided from computer program products, for example, computer-executable instructions, that are stored in a tangible computer-readable storage medium such as RAM, hard disk or optical or magnetic media.

[0092] Memory 104 can also include data 106 that can be retrieved, manipulated, created, or stored by the one or more processor(s) 102. In some example embodiments, such data can

be accessed and used as input to the analyte estimation system 110. In some examples, the memory 104 can include data used to perform one or more processes and instructions that describe how those processes can be performed.

[0093] In some examples, the analyte estimation system 110 can include a pump laser 112, one or more Stokes lasers 116, a photodetector 122, and a Raman scattering estimation system 120. Although not pictured, the analyte estimation system 110 can also include an optical filter and one or more optical lenses (e.g., micro lenses) to focus the lasers on the same area (e.g., the same portion of the user's skin). The pump laser 112 (e.g., a first light source) can be a laser diode that emits light (e.g., a stream of photons) within a narrow wavelength band such that the emitted light has a particular wavelength within a certain range of the target wavelength. In some examples, the pump laser can produce narrowband light with an average wavelength of 780 nanometers. Other wavelengths of a pump laser 112 may be used, with the wavelengths of the one or more Stokes lasers 116 being determined based, at least in part, on the wavelength of the pump laser 112. In some examples, the pump laser 112 can be a vertical-cavity surface-emitting laser (VCSEL) included in a semiconductor chip. In some examples, the wavelength of the light emitted by the pump laser 112 is 850 nanometers. Other wavelengths can be used.

[0094] The pump laser 112 can include (or be associated with) a modulation system 114. The modulation system 114 can include a waveform generator that can produce a waveform that can be used to modulate the light produced by the pump laser 112. The pump laser can be referred to as a first light source. By modulating the light produced by the pump laser 112, the analyte estimation system 110 can differentiate (e.g., using a filter or lock-in amplifier) between light that the target material emits after being excited by the light that originated from the pump laser 112 and the light that the target material emits after being excited by the light that originates from the one or more Stokes lasers 116.

[0095] The one or more Stokes lasers 116 can include a tunable laser that can produce light with a wavelength within a predetermined range as needed. Thus, the tunable laser can be adjusted such that the wavelength of the light produced by the light source can change within a range. For example, in some examples, the tunable laser can be adjusted to emit light with a wavelength that can vary from 910 nanometers to 980 nanometers. In some examples, the wavelength of the light produced by the tunable laser can be determined based on the Raman signature of a particular analyte that the analyte estimation system 110 is trying to

identify. In some examples, both the pump laser and the one or more Stokes lasers can use about 40 milliwatts of power to operate.

[0096] In some examples, the one or more Stokes lasers can include a modulation system 118. Thus, in some configurations, the one or more Stokes lasers 116 is modulated to distinguish the light produced by the pump laser 112 from the light produced by the one or more Stokes lasers 116. In other examples, the one or more Stokes lasers 116 are modulated to distinguish between the two light sources.

[0097] In some examples, the one or more Stokes lasers 116 can provide light with a wavelength tuned to the Raman signature of a particular analyte that the analyte estimation system 110 is trying to identify (e.g., glucose). By providing additional light (e.g., a stream of photons) with a wavelength determined based on the Raman signature of the analyte, the analyte estimation system 110 can enable stimulated Raman scattering to occur. Stimulated Raman scattering can result in the light provided by the one or more Stokes lasers 116 stimulating more Raman scattering than would be expected without the additional light provided by the one more Stokes lasers 116. Thus, introducing the light provided by the one or more Stokes lasers 116 can increase the detectability of a particular analyte in the sample material because the probability of Raman scattering is increased.

[0098] In some examples, the analyte estimation system 110 can include a photodetector 122. The photodetector 122 can be a sensor (e.g., a semiconductor device that converts light (e.g., photons) into electrical current) such as a photodiode. The photodiode can be configured to detect light over a range of wavelengths. In some example embodiments, light can be optically filtered such that only light within a specific wavelength range is detected by the photodetector. An amount of light can also be understood to be the number of photons detected and/or the intensity of the light measured at a particular wavelength.

[0099] In some examples, a filter can be employed to remove target-emitted light that is associated with the one or more Stokes lasers 116 such that only light originating from the pump laser 112 is detected. Similarly, an optical filter can filter out light with a wavelength associated with the pump laser 112 such that only target-emitted light that results from the Stokes lasers 116 or Raman scattering is detected by the photodetector. In some examples, a filter (or a lock-in amplifier) can remove modulated light, if the one or more Stokes lasers 116 were modulated, or unmodulated light, if the pump laser 112 was modulated.

[00100] The Raman scattering estimation system 120 can be used to detect the amount of light (e.g., the intensity of the light or the number of photons) generated by Raman scattering

associated with an analyte in the sample material. In some examples, the Raman scattering estimation system 120 can determine the amount of light (e.g., either the number of photons or the intensity of the light) that has been Raman scattered to identify an analyte in the target material. In a first example, the user computing device can determine the amount of light at the pump wavelength (e.g., a first wavelength) that is lost (stimulated Raman loss). Alternatively, the user computing device can determine the amount of light at the Stokes associated wavelength that is gained (e.g., stimulated Raman gain). Either measurement or their combination can be used to estimate the amount of a particular analyte in the target material (e.g., a user's skin). A detected Stokes range can be compared to a reference spectrum to non-invasively measure the presence or absence of a target analyte.

[00101] For example, the sample material can be a portion of a user's body. The analyte can be, for example, glucose. Based on the amount of light having the predetermined second wavelength, the Raman scattering estimation system 120 can estimate the amount of the analyte in the target sample. In some examples, the estimated amount of the analyte can be presented for display to a user.

[00102] FIG. 4A illustrates an example of different types of photon scattering by matter. As seen in this example, an incoming photon (e.g., the incident light) can interact with a particular sample molecule. One or more photons of the incident laser can interact with the sample molecules (e.g., with electrons in the sample molecules), temporarily raising the electron's energy level. When the energy level of the electron returns to its lower level, a photon is emitted. In some examples, this process can be referred to as scattering. Scattering can include Rayleigh scattering and Raman scattering. In Rayleigh scattering (which is a type of elastic scattering), the emitted photons have the same energy (and thus the same wavelength) as the incident photon but with the trajectory of the photon potentially altered. In Raman scattering, the energy level of the electron is changed, such that when the photon is emitted, the energy level (and thus the wavelength) of the photon is different than the incident photon. As a result, the presence of a particular sample molecule can be determined based on the presence or absence of Raman scattered light with particular altered wavelengths.

[00103] In some examples, the energy level of the target molecule can increase, resulting in a decrease in the energy of the Raman scattered light (referred to as Stokes Raman scattered light), or the energy level of the target and molecule can decrease, resulting in an increase in the energy of the Raman scattered light (referred to as anti-Stokes Raman scattered light).

[00104] It should be noted that, if the incident light has a consistent wavelength, the Raman scattered light will result in a particular Stokes range. The Stokes range can have a consistent Raman signature which can enable an analyte estimation system to distinguish the Raman scattering that results from one analyte from the Raman scattering that results from a second analyte. Thus, identifying the presence of a particular Raman signature can be used to estimate the presence of the target analyte and may also be used to estimate the amount of that analyte in the target substance.

[00105] FIG. 4B illustrates an example of energy level changes of an analyte as a result of light scattering. As seen herein, an electron 304 can have a first energy level 306 (e.g., a base energy level). In response to interactions with the incident light, the energy level of the electron increases. After a period of time, the electron 304 can emit a photon and return to a lower first energy level 306.

[00106] In a first example 302, the electron 304 is initially at a first energy level 306 (a low energy level). In response to the incident light, the electron 304 gains energy to a second energy level 310 higher than the first energy level 306. The electron 304 can emit the light as Rayleigh scattered light 312. In this example 302, the energy of the Rayleigh scattered light 312 is the same as the incident light (and thus has the same wavelength). The electron 304 can return to the first energy level 306 such that the total energy level of the system is maintained.

[00107] In a second example 320, the electron 304 is initially at a first energy level 306 (a low energy level). In response to the incident light, the electron 304 gains energy to a second energy level 310 higher than the first energy level 306. However, in this example, some of the energy is gained by the molecule as vibrational energy. As a result, when the Raman scattered light is emitted by the electron 304 the energy (and thus wavelength) of the emitted photon 322 is reduced but does not fall back down to the first energy level 306. Instead, the electron remains at the third energy level 324 which is higher than the first energy level 306 but lower than the second energy level 310. Thus, the total energy of the system is maintained because the electron 304 ends up at a third energy level 324 which is higher than the first energy level 306 but the scattered photon 322 is at a lower energy level than the incident light.

[00108] In a third example 330, the electron 304 is initially at a fourth energy level 332 higher than the first energy level 306. In response to the incident light, the electron 304 gains energy to a fifth energy level higher than the second energy level 310. When the Raman

scattered light is emitted, the electron 304 returns to the first energy level 306 having lost energy from its initial starting position at the fourth energy level 332. The scattered light 334 (referred to as anti-Stokes Raman scattered light) can have a higher energy level than the incident light.

[00109] FIG. 5 illustrates a relative amount of scattered light. In this example, it is clear that the amount of Raman scattered light is a tiny fraction of the total amount of scattered light. Thus, if Rayleigh scattered light represents more than 99.99 percent of all the scattered light, Raman scattered light can represent as little as 0.000001 percent of the scattered light. As such, the amount of Raman scattered light is much less than the total amount of scattered light. As a result, any technique to increase the amount of Raman scattered light can result in significant improvements in the ability of the detection system to determine whether or not an analyte is present.

[00110] FIG. 6 illustrates a graph representing the wavelengths of scattered light in a Stokes range. In this example graph, the detected scattered light can be represented as a Stokes range that shows the wavelength of the detected light and its intensity. As can be seen, the majority of scattered light can be Rayleigh scattered light with the wavelength the same as the wavelength of the incident light generated by the pump laser. Thus, the peak at the 532-nanometer wavelength (wavenumber 0) is very high. Other peaks (e.g., at 800 nanometers and so on) can represent Stokes Raman scattered light (in which the light has lost energy) or anti-Stokes Raman scattered light (in which the light has gained energy) in a Stokes range associated with an analyte.

[00111] FIG. 7 illustrates spontaneous Raman scattering. For spontaneous Raman scattering, light generated by the first light source (or pump laser) can interact with a particular molecule. A small fraction of the photons that are emitted by the molecule(s) will have less energy and thus have a different wavelength than the incoming photons. As noted above, a particle in the molecule (e.g., an electron) can gain energy increasing from a ground level to a virtual level. In some cases, rather than returning to the ground level, one or more particles in the molecule can retain some energy as vibrational energy. Thus, the emitted photon has less energy than the incoming photon.

[00112] As a result, most of the emitted light retains the same wavelength as the incoming light. However, a small fraction of the incoming light is scattered such that the energy level of the scattered light and its wavelengths are different from the incoming light that excited

the molecule. As noted above, the Raman signature of the scattered light can be used to determine what analytes are present in the target material.

[00113] FIG. 8 illustrates stimulated Raman scattering. In the case of stimulated Raman scattering, two or more light sources can be used to amplify or increase the amount of light that is scattered in by Raman scattering, thus increasing the average intensity of the Stokes range. In some examples, a pump laser can generate light with a first wavelength (as with spontaneous Raman scattering). In addition, one or more Stokes lasers can generate light with a second wavelength. The second wavelength can be a wavelength associated with the Raman signature of a particular analyte.

[00114] The light with the first wavelength and the light with the second wavelength can be combined and projected towards a target sample. A dichroic mirror (or one or more optical lenses) can be used but is not required. The light with a second wavelength can cause coherently driven molecular vibrations that have the effect of increasing the amount of Raman scattered light. As a result, less light is needed from the pump laser to result in a detectable amount of Raman scattered light.

[00115] In some examples, if the generated light can be equally split between the first wavelength and the second wavelength, the light emitted by molecules in the target sample can have more light that has the second wavelength. The difference between the amount of light with the second wavelength that is generated by the one or more Stokes lasers and the amount of light with the second wavelength that is measured after emission can be the amount of light that has been emitted with a different wavelength due to stimulated Raman scattering.

[00116] The light generated by the pump laser (or first light source) can excite a particular molecule to a higher energy level. A small fraction of the photons that are emitted by the molecule will be emitted with less energy (e.g., a particle in the molecule can retain some energy as vibrational energy) and with a different wavelength. As noted above, a particle (e.g., an electron) in the molecule can gain energy increasing from a base level of energy to a higher virtual energy level. In some cases, rather than returning to the base level, the one or more particles in the molecule can retain some vibrational energy and thus the photon emitted when the energy level of the electron returns to a lower level has less energy than the incoming photon.

[00117] As a result, most of the emitted light retains the same wavelength as the incoming light. However, a small fraction of the incoming light is Raman scattered such that the

emitted light has a different energy level and thus a different wavelength. As noted above, the wavelength detected for the emitted light can be used to determine what analytes are present in the target material.

[00118] FIG. 9A illustrates an example graph representing the amount of light that is Raman scattered with spontaneous Raman scattering. As noted above, during spontaneous Raman scattering, a single light source can provide light with a first wavelength 802. A small portion of the light provided at the first wavelength 802 can excite a molecule to a higher energy level. Light with a second wavelength 804 can be emitted because some of the energy is retained by particles within one or more target molecules as vibrational energy.

[00119] FIG. 9B illustrates an example graph representing the amount of light that is Raman scattered with stimulated Raman scattering. In this example, a pump laser generates light at a first wavelength 802 and a Stokes laser can generate light whose wavelength is the second wavelength 804. As a result of resonance, the amount of Raman scattered light is increased by a first amount 806, making detection of the scattered light more efficient and requiring less power.

[00120] FIG. 10A illustrates an example configuration of a system 900 for detecting analytes in a user's skin in accordance with example embodiments of the present disclosure. In this example, the relevant portion of an analyte estimation system 110 includes two printed circuit boards (PCBs). A first PCB 902 can include two light sources (VCSELs). The first light source 904 can be a pump laser that produces light at one or more first wavelengths and the second light source 906 can be a Stokes laser that produces light at one or more second wavelengths. The second wavelength(s) can be associated with the Raman signature associated with a target analyte.

[00121] The second printed circuit board 908 can include one or more photodiodes 910 that are configured to detect light. The one or more photodiodes 910 can produce a signal based on the detected light. In some examples, the signal produced by the photodiode(s) can be processed to remove a modulated portion of the signal generated in response to light produced by the Stokes laser (second light source 906). In this manner, the processed signal can represent light produced by Raman scattering of the pump laser (first light source 904). The analyte estimation system 110 can be pressed against the skin 912 of a user such that the light is projected down into the skin of a user and molecules included in the skin and/or tissue of the user can emit light into the photodiode 910. It should be noted that two PCBs are used

in this example, but in some example embodiments, only a single PCB is used. If so, the photodiodes can be slightly raised from the surface.

[00122] The analyte estimation system 110 includes a single window 914 through which the light from both sources passes to interact with the skin 912 of a user. The light interacts with molecules in the user and in response light is emitted from the skin 912 of the user. The emitted light can pass through an optical filter 909 to the photodiode 910.

[00123] FIG. 10B illustrates an example configuration of a system 920 for detecting analytes in the user's skin in accordance with example embodiments of the present disclosure. In this example, the relevant portion of the computing system includes two printed circuit boards (PCBs). A first PCB 902 can include two light sources (VCSELs). A first light source 904 can include a pump laser that can produce light at one or more first wavelengths and a second light source 906 can include a Stokes laser that can produce light at one or more second wavelengths. The second wavelength(s) can be associated with the Raman signature of a target analyte. The light from both light sources passes through an optical element 922 (e.g., a lens) before passing through two or more windows 924.

[00124] The second printed circuit board 908 can include one or more photodiodes 910 that are configured to detect light. One or more optical filters can be used to filter the received light for one or more target frequencies. For example, a long pass optical filter can be used to pass Stokes frequencies and reject pump frequencies. The one or more photodiodes 910 can produce a signal based on the detected light. In some examples, the signal produced by the photodiode(s) can be processed to remove a modulated portion of the signal generated in response to light produced by the Stokes laser (second light source 906). In this manner, the processed signal can represent light produced by Raman scattering of the pump laser (first light source 904). The analyte estimation system 110 can be pressed against the skin 912 of a user such that the light is projected into the skin of a user and molecules included in the skin and/or tissue of the user can emit light into the photodiode 910.

[00125] In this example, the analyte estimation system 110 can include two or more windows 924. The light from both sources (first light source 904 and second light source 906) can be projected with beam divergence of 45 degrees through the two or more windows 924. Other angles can be used.

[00126] FIG. 10C illustrates an example configuration of a system 930 for detecting analytes in the user's skin in accordance with example embodiments of the present disclosure. In this example, the relevant portion of the computing system includes two printed

circuit boards (PCBs). A first PCB 902 can include two light sources (VCSELs). A first light source 904 can include a pump laser that can produce light at one or more first wavelengths and a second light source 906 can include a Stokes laser that can produce light at one or more second wavelengths. The second wavelength(s) can be associated with the Raman signature of a target analyte. The analyte estimation system 110 includes two or more windows and each source passes their associated light through a respective window (e.g., window 932 or window 934).

[00127] The second printed circuit board 908 can include one or more photodiodes 910 that are configured to detect light. The one or more photodiodes 910 can produce a signal based on the detected light. In some examples, the signal produced by the photodiode(s) can be processed to remove a modulated portion of the signal generated in response to light produced by the Stokes laser (second light source 906). In this manner, the processed signal can represent light produced by Raman scattering of the pump laser (first light source 904). The analyte estimation system 110 can be pressed against the skin 912 of a user such that the light is projected into the skin of a user and molecules included in the skin and/or tissue of the user can emit light into the photodiode 910.

[00128] FIG. 10D illustrates an example configuration of a system 940 for detecting analytes in the user's skin in accordance with example embodiments of the present disclosure. In this example, the relevant portion of the computing system includes two printed circuit boards (PCBs). A first PCB 902 can include two light sources (VCSELs). A first light source 904 can include a pump laser that can produce light at one or more first wavelengths and a second light source 906 can include a Stokes laser that can produce light at one or more second wavelengths. The second wavelength(s) can be associated with the Raman signature of a target analyte.

[00129] The second printed circuit board 908 can include one or more photodiodes 910 that are configured to detect light. The one or more photodiodes 910 can produce a signal based on the detected light. In some examples, the signal produced by the photodiode(s) can be processed to remove a modulated portion of the signal generated in response to light produced by the Stokes laser (second light source 906). In this manner, the processed signal can represent light produced by Raman scattering of the pump laser (first light source 904). The analyte estimation system 110 can be pressed against the skin 912 of a user such that the light is projected into the skin of a user and molecules included in the skin and/or tissue of the user can emit light into the photodiode 910.

[00130] The analyte estimation system 110 includes a single window 914 through which the light from both sources passes to interact with the skin 912 of a user and light emitted from the skin 912 of the user can pass through to the photodiode 910. Thus, the light is projected through the window towards a user's skin 912. Light can be emitted from the skin 912 of a user such that it passes through one or more filters to the photodiode 910. The width of the area in which the analyte estimation system 110 contacts the skin 912 is 5 millimeters.

[00131] FIG. 11 illustrates an example system for detecting the presence of an analyte in the skin of the user in accordance with example embodiments of the present disclosure. The system can include a pump laser (e.g., a VCSEL) that produces light with a wavelength of 850 nanometers.

[00132] A second light source can be one or more Stokes lasers that can produce light in the range of 910 to 980 nanometers. Light from both the pump laser and the one or more Stokes lasers can be projected towards the skin of a user where it will encounter cells and blood vessels that contain a plurality of molecules. At least some of the light produced by the pump laser can excite a molecule in the skin of the users and be Raman scattered such that the photons emitted by the molecule have a different wavelength than the incoming light.

[00133] The system can include a bandpass filter that filters out light emitted from the epidermis of the user to remove light in a wavelength that is outside of the Stokes range. By filtering out wavelengths outside the Stokes range, the system can ensure that the measured light can be used to identify the Raman signature of any analytes in the skin and/or blood of the user. The nonfiltered light can then be sensed by a photodiode. The photodiode can generate an electrical signal. The electrical signal can be demodulated (e.g., using a lock-in amplifier) and amplified. In addition, if the Stokes lasers produce light at a plurality of wavelengths, the photodiode can assemble a spectrum from the various wavelengths. The amplified, demodulated, and assembled information can be analyzed to determine what molecules are present in the skin of the user and in what concentration.

[00134] FIG. 12A represents an example analyte estimation system 110 in accordance with example embodiments of the present disclosure. In this example, the analyte estimation system 110 can include a pump laser 1102. The pump laser 1102 can be referred to as a first light source. In some examples, the pump laser 1102 can produce light with a wavelength of 850 nanometers although other wavelengths may be used. In some examples, the pump laser 1102 can take the output of a waveform generator 1104 as input. The waveform generator 1104 can produce a signal to modulate the amplitude of the light produced by the pump laser

1102. In this way, the light produced by the pump laser 1102 can be distinguished from light produced from other light sources. Thus, the analyte estimation system 110 can determine whether the wavelength of particular light is the result of Raman scattering based on the modulation.

[00135] The light produced by the pump laser 1102 can pass through a bandpass filter 1106. The bandpass filter 1106 can ensure that only light within a particular frequency (e.g., the frequency associated with 850 nanometers) passes through the filter to the sample tissue. For example, the bandpass filter can ensure that only light with a wavelength of 850 nanometers passes through the filter to the sample tissue. The analyte estimation system 110 can also include a Stokes laser 1108 (e.g., referred to as a second light source) that produces light at a narrowband around one or more second wavelengths.

[00136] In some examples, the Stokes laser 1108 can be a tunable light source. A tunable light source can be controlled to produce light at a narrowband of wavelengths around any wavelength (e.g., within 0.1 nanometers of the target wavelength) within a given predetermined range. In some examples, the tunable light source can be controlled to produce a narrowband light that sweeps through a range of wavelengths from 910 nanometers to 980 nanometers. In another example, the Stokes laser 1108 can include a plurality of different light sources (e.g., laser diodes or other light-emitting diodes), each configured to output light with a particular wavelength associated with a Raman signature of a particular analyte. For example, the Stokes lasers 1108 can include a set of VCSELs, each tuned to provide light at a different wavelength within a Stokes range of an analyte.

[00137] In some examples, the plurality of Stokes lasers 1108 can be activated one at a time such that only one Stokes laser 1108 is activated at any particular point. In other examples, a plurality of Stokes lasers 1108 can be activated simultaneously.

[00138] In this example, respective Stokes lasers 1108 at different respective light wavelengths can be amplitude-modulated at different respective time frequencies, and then the response for each different respective light wavelength can be extracted from the combined-wavelength measured signal using time-based Fourier transform or other demodulation techniques, Exemplary time modulation frequencies for amplitude-modulating the different Stokes lasers 1108 can be in the range of 10 kHz-1 MHz, although the scope of the present teachings is not so limited.

[00139] The analyte estimation system 110 can include a dichroic mirror 1110 that is configured to ensure that light emitted from the pump laser 1102 and the Stokes laser 1108 is

projected in the same direction. The dichroic mirror 1110 can, for example, allow light from either the pump laser 1102 or the Stokes laser 1108 to pass through while reflecting the light from the other source. By orienting the dichroic mirror 1110 correctly, the light from both sources can be projected in the same direction.

[00140] The analyte estimation system 110 can include a focusing lens 1112 that causes the light from both the pump laser 1102 and the Stokes laser 1108 to be focused and ensure it is directed towards the target sample. Once the light from the pump laser 1102 and the Stokes laser 1108 has interacted with the sample 1114, the sample 1114 can emit light that can be filtered by one or more filters 1116. For example, the emitted light can pass through a long pass filter, which can filter out light with the first wavelength that was produced by the pump laser 1102 and allow light with the second wavelength(s) to pass through. In this way, the light from the Stokes laser 1108 and any light from the pump laser 1102 that has been Raman scattered can be passed through the filter 1116.

[00141] The analyte estimation system 110 can include a photodiode 1120 that detects light that passes through the long-pass filter. In some examples, the photodiode 1120 can be configured to measure light at any wavelength within a predetermined range of wavelengths. The light detected by the photodiode 1120 can be used to generate an electrical signal. The electrical signal can retain characteristics of the light based on which it was generated. For example, if a portion of the detect light is modulated by amplitude, the resulting electrical signal can include both a direct current portion (e.g., associated with the unmodulated light) and an alternating current (AC) portion, associated with the modulated light).

[00142] In some examples, the amount of Raman scattering can be determined by using a lock-in amplifier to distinguish the modulated portion of the electrical signal from the unmodulated portion of the electric signal. The modulated portion of the light can be determined to be associated with stimulated Raman gain (SRG) that represents the amount of light from the pump laser 1102 that was scattered (e.g., emitted from the target material at a different wavelength than the light generated by the pump laser) through Raman scattering such that the emitted light has a different wavelength than the incoming light.

[00143] The remaining electrical signal can be passed from the lock-in amplifier 1124 to the rest of the computing device for analysis. Removing the light generated by the pump laser 1102 can allow the analyte estimation system 110 to accurately calculate the stimulated Raman gain. In some examples, the stimulated Raman gain can be calculated using a signal analysis system 1152. This method can allow noninvasive measurement of a variety of

different analytes including but not limited to glucose, ethanol, lipids, hemoglobin, lactate, cortisol, and so on. In other examples, a spectrograph is not used.

[00144] FIG. 12B represents an example analyte estimation system 110 in accordance with example embodiments of the present disclosure. In this example, the Stokes laser 1108 is modulated, rather than the pump laser 1102. Similar to the configuration in FIG. 11A, the light from the pump laser 1102 and the modulated light from the Stokes laser 1108 can pass through a dichroic mirror 1110 and a focusing lens 1112 into the sample material 1114.

[00145] In this configuration, the system includes a short pass filter 1150, which can filter out light with the second wavelength(s) (e.g., light from the Stokes laser 1108) and allow light with the first wavelength from the pump laser 1102 to pass through.

[00146] The light detected by the photodiode 1120 can be used to generate an electrical signal. The electrical signal can be passed to a signal analysis system 1152 for analysis. The electrical signal is generated based on Rayleigh scattered light emitted from the target material. As noted above, the Rayleigh scattered light has the same wavelength as light generated by the pump laser 1102. As the Stokes laser 1108 is modulated, the intensity of the Rayleigh scattered light can vary. In one specific example, if the amplitude of the Stokes laser 1108 is at a low point (e.g., when the modulated amplitude reaches zero), the amount of Rayleigh scattered light emitted by the target material can reach a high intensity level (because less light is Raman scattered without the Stokes laser 1108). Similarly, when the amplitude of the Stokes laser 1108 reaches its high value during modulation, the intensity of Rayleigh scattered light emitted by the target material at the wavelength associated with the pump laser 1102 may reach a low point (as more light is Raman scattered with the Stokes laser 1108 being at peak intensity). The electrical signal that represents the intensity of light at the pump wavelength (because other wavelengths are filtered out by the short pass filter) can be measured at the high point (e.g., when the intensity of the Rayleigh scattered light is at its maximum) and at the low point (e.g., when the intensity of the Rayleigh scattered light is at its minimum).

[00147] The difference in the electric signal between the high point and the low point can be measured by the signal analysis system 1152 to determine the amount of light that is Raman scattered. This amount can be referred to as the stimulated Raman loss (SRL). The stimulated Raman loss can represent the amount of light that, after exciting a molecule to a higher energy level in the target tissue, was emitted with a different wavelength.

[00148] FIG. 13 illustrates an example system for non-invasively measuring analytes within a user's body in accordance with some example embodiments of the present disclosure. In accordance with example embodiments of the present disclosure. In this example, the analyte estimation system 110 can include two light sources. The first light source can be a pump laser 112 that can generate light with a first wavelength. The second light source can be one or more Stokes lasers 116. In FIG. 12, the Stokes laser 116 can be a single tunable laser that can generate a narrowband of light around any wavelength in a range of wavelengths. In another example, the Stokes lasers 116 can include a plurality of different laser diodes that each generate light at a particular wavelength and can be selectively turned on and off as needed during the detection process.

[00149] A pump laser controller 1202 can be associated with a pump laser 112. The pump laser controller 1202 can determine when the pump laser 112 is turned on and how long it remains on. A Stokes laser controller 1204 can be associated with the Stokes laser 116 and can control when the Stokes laser is 1204 turned on and, if the Stokes laser 116 is a tunable laser, what wavelength of light the Stokes laser 116 is outputting at any particular time.

[00150] A waveform generator 1206 can generate a waveform that is provided to the Stokes laser controller 1204. This waveform can be used to modulate the light produced by the Stokes laser 116. Modulating the output of the Stokes laser 116 can ensure that the light emitted by the Stokes laser 116 and the light emitted by the pump laser 112 can be separated from one another at a later point in the process.

[00151] A temperature controller 1210 can control a thermoelectric cooler 1212. The thermoelectric cooler 1212 can adjust the output of the pump laser 112 as directed by the temperature controller 1210. An XY adjuster 1214 can control the direction of the light emitted by the pump laser 112 and allow a fiber coupler 1216 to provide the light generated by the pump laser 112 into a bifurcated fiber bundle associated with the Stokes laser 116.

[00152] The light combined in the bifurcated fiber bundle 1218 can be projected towards the target sample 1220 which in this case is a participant's hand. The light can be emitted from the participant's hand towards a spectral measurement system 1222. The spectral measurement system 1222 can include one or more photodiodes 1224. In some examples, the photodiodes 1224 have an associated optical filter 1226. The optical filter 1226 can remove wavelengths of light that are not needed by the spectral measurement system 1222. The output of the spectral measurement system 1222 is provided to a bias module 1228. The

biased module has a DC power supply 1230. A lock-in amplifier 1232 can remove modulated light such that the unmodulated light can be isolated and analyzed.

[00153] The output of the lock-in amplifier can be provided to a computer 1240. The computer 1240 can analyze the data to determine the presence or absence of molecules of interest in the target tissue which is, in this case, the participant's hand.

[00154] FIG. 14 illustrates an example system with light sources and photodiodes in accordance with example embodiments of the disclosure. As can be seen, the two light sources can include a pump laser 112 and a Stokes laser 116 that are positioned to project light through a fiber 1302 in a detecting unit. The light passes forward through the opening into the skin of a user. The skin of a user can emit light towards the sensor unit. The sensing unit includes an optical filter 1304 that can filter out light of certain wavelengths. The plurality of photodiodes can then detect the emitted light that has not been filtered. Information gathered by the photodiodes can be transmitted back to a computing system to be analyzed to determine the contents of the tissue into which the light was projected.

[00155] FIG. 15 illustrates a layout of a plurality of light-producing sources in accordance with some example embodiments of the present disclosure. A plurality of pump lasers can be centered in the middle providing light at a consistent wavelength. A pump laser and one or more Stokes lasers can be arranged in a pattern such that the Stokes lasers provide a plurality of different wavelengths of light. In some examples, the wavelengths of light provided by the Stokes lasers are associated with molecules of interest.

[00156] FIG. 16 illustrates an example analyte estimation system 110 in accordance with some example embodiments of the present disclosure. The analyte estimation system 110 can include a pump laser 112 (e.g., a VCSEL) and two Stokes lasers 116 (e.g., an off-peak Stokes laser 116-1 and an on-peak Stokes laser 116-2). However, in other configurations, the Stokes laser 116 can include a plurality of Stokes lasers, each one configured to generate light with a particular wavelength. One or more outputs of the pump laser 112 and/or the Stokes lasers 116 may be modulated using a square wave at 10 kilohertz or higher. In general, a higher frequency is better when using modulation to distinguish light from different sources. A multiplexer (MUX) 1502 can be used to sequentially activate the two or more Stokes lasers 116.

[00157] Thus, the pump laser 112 consistently produces light at 850 millimeters and the two or more Stokes lasers 116 can be sequentially activated to produce light with a narrowband centered around specific wavelengths. The light from the pump lasers 112 and

two or more Stokes lasers 116 are projected forward through a focusing lens 1504 to the tissue of a user 1506. The tissue of a user can emit light that passes through one or more filters 1508. For example, the light can pass through a bandpass filter 1508 that restricts the light that passes through to a predefined band of wavelengths or a long pass filter that filters out one or more wavelengths of light.

[00158] Once the light has passed through the filters, one or more photodiodes 1510 can detect the light (e.g., detecting the intensity of light with a particular wavelength or the number of photons with a particular wavelength). The photodiodes can generate electrical signals based on the interaction of photons with the photodiode 1510. The electrical signals can be demodulated, amplified, and transmitted to the computing device that can assemble an entire spectrum of light by wavelength. The spectrum can be analyzed to determine, based on the amounts of light at various points in the spectrum (e.g., the Raman signature), whether one or more analytes are present in the tissue of the user. As noted above, if a plurality of laser diodes are simultaneously activated and provide light at a respective plurality of Stokes frequencies, each laser diode can be modulated at a different respective frequency. The resulting signal can be analyzed using a Fourier transform (e.g., fast Fourier transform) to determine the intensity of light at each different wavelength.

[00159] FIG. 17 is a flowchart depicting an example process of detecting molecules within a target in accordance with example embodiments of the present disclosure. One or more portion(s) of the method can be implemented by one or more computing devices such as, for example, the computing devices described herein. Moreover, one or more portion(s) of the method can be implemented as an algorithm on the hardware components of the device(s) described herein. FIG. 17 depicts elements performed in a particular order for purposes of illustration and discussion. Those of ordinary skill in the art, using the disclosures provided herein, will understand that the elements of any of the methods discussed herein can be adapted, rearranged, expanded, omitted, combined, and/or modified in various ways without deviating from the scope of the present disclosure. The method can be implemented by one or more computing devices, such as one or more of the computing devices depicted in FIGS. 1, 11-14.

[00160] The computing device can project light from a first light source and a second light source towards a portion of a user's body. The first light source can project, at 1714, light with the first wavelength, and the one or more second light sources can generate light with a second wavelength. The light sources (e.g., lasers) can project the generated light onto the

skin of a user. The light can interact with molecules in the skin. The molecules in the skin can emit light to the system. In some examples, the light is Raman scattered by interacting with the molecules in the user's skin.

[00161] The computing device can detect, at 1716, using a photodiode, an intensity of emitted light with a particular wavelength. For example, the photodiode can measure the intensity of light in the second wavelength. The computing device can, at 1718, determine, based on the emitted light, the concentration of each of a plurality of molecules in a user's body.

[00162] The computing device can generate, at 1724, based on the concentration of each of the plurality of molecules in the user's body, a user profile. For example, the computing device can determine the relative concentrations of hemoglobin, glucose, lipids, and so on in a particular user's body based on information from the photodiodes. This information can be compiled into a standard user profile format.

[00163] In some examples, with the user's permission, the computing device can access locally stored user profiles or user profiles available via a computer network. The computing system can compare, at 1726, the user profile to a plurality of stored user profiles to identify the user. For example, the specific concentrations of various molecules and chemicals in the user's body can serve as a fingerprint to uniquely identify each user. However, in consideration of user privacy, no profile will be generated, and no comparison be made unless the user has consented.

[00164] In some examples, once the system has determined the identity of the user based on the matching user profile, the computer system can access data associated with the user account and provide that information and services to the user.

[00165] FIG. 18 depicts a block diagram of an example machine-learned data analysis model 1810 according to example embodiments of the present disclosure. A machine-learned data analysis model can take information about the intensity of late at a variety of wavelengths as input 1842. For example, the machine-learned data analysis model 1810 can identify the values at the expected wavelengths for glucose. Once trained, the machine-learned data analysis model can achieve a good accuracy of R2=0.84, which corresponds to approximately 30 mg/dl mean absolute error. Thus, machine-learned data analysis model 1810 can output 1844 information describing whether a particular analyte is present and in what concentration.

[00166] In some examples, glucose concentrations found in human blood (<300 mg/dl, usually <140 mg/dl), result in glucose peaks that are not easily separable from the background noise due to the fact that the Raman signal is very weak. The model picks up the important features which align with some of the expected Raman peaks of Glucose at wavenumbers 514, 1060, 1025, 1366 cm 1, which can be clearly visible for the spectrum measured for very high Glucose concentration (> 5000 mg/dl). This model can then be used to predict the glucose level for 200 new measurements with an R2 of 0.84. This corresponds to approximately 30 mg/dl mean absolute error.

[00167] In some examples, the machine-learned data analysis model 1810 can otherwise include various machine-learned models such as neural networks (e.g., deep neural networks), other types of machine-learned models, including non-linear models, and/or linear models, or binary classifiers. Neural networks can include feed-forward neural networks, recurrent neural networks (e.g., long short-term memory recurrent neural networks), convolutional neural networks, or other forms of neural networks.

[00168] A variety of training techniques can be used to train the machine-learned data analysis model 1810. Specifically, the machine-learned data analysis model 1810 can be trained using one of a plurality of semi-supervised training techniques. The machine-learned data analysis model 1810 can also be trained using a supervised training technique, such as, for example, backward propagation of errors. For example, a loss function can be backpropagated through the model(s) to update one or more parameters of the model(s) (e.g., based on a gradient of the loss function). Various loss functions can be used such as mean squared error, likelihood loss, cross-entropy loss, hinge loss, and/or various other loss functions. Gradient descent techniques can be used to iteratively update the parameters over several training iterations. In some implementations, performing backward propagation of errors can include performing truncated backpropagation through time. Generalization techniques (e.g., weight decays, dropouts, etc.) can be performed to improve the generalization capability of the models being trained.

[00169] FIG. 19 is a flowchart depicting an example process of detecting analytes within a target tissue in accordance with example embodiments of the present disclosure. One or more portion(s) of the method can be implemented by one or more computing devices such as, for example, the computing devices described herein. Moreover, one or more portion(s) of the method can be implemented as an algorithm on the hardware components of the device(s) described herein. FIG. 19 depicts elements performed in a particular order for purposes of

illustration and discussion. Those of ordinary skill in the art, using the disclosures provided herein, will understand that the elements of any of the methods discussed herein can be adapted, rearranged, expanded, omitted, combined, and/or modified in various ways without deviating from the scope of the present disclosure. The method can be implemented by one or more computing devices, such as one or more of the computing devices depicted in FIGS. 1, 11-14.

[00170] A computing device for non-invasively measuring glucose levels in a user using Stimulated Raman Scattering can comprise a Ramp pump laser, a Stokes laser, and a photodetector. The computing device can, at 1902, using a pump laser emit pump light into the skin surface of the user, the pump light being at a fixed wavelength. It should be noted that while the light can be directed towards the surface of the skin, the light can be focused at a subdermal area of the user such that the light is more likely to interact with the molecules in the blood of a user. Thus, when the present disclosure indicates that light is directed to or received from the surface of the skin of a user, the target of the light can be below the surface of the skin of the user. The computing device can, at 1904, using a Stokes laser, emit Stokes light into the skin surface at a plurality of Stokes wavelengths within a window of Raman measurement wavelengths.

[00171] The Stokes source can comprise a variable wavelength narrowband laser swept continuously from one end to the other end of the window of Raman measurement wavelengths during said non-invasive glucose measuring. In some examples, the Stokes source can comprise a plurality of fixed-wavelength narrowband laser sources, each having a different center wavelength lying within the window of Raman measurement wavelengths.

[00172] In some examples, the Raman pump light source and the fixed-wavelength narrowband laser sources of the Stokes source are VCSELs, and wherein no optical fibers or mirrors are used anywhere in the device. The computing device can, at 1906 and using a photodetector, measure light that is emanating back out the skin surface.

[00173] In some examples, the photodetector can detect light across a range of wavelengths including both said Raman pump light source wavelength and said window of Raman measurement wavelengths, and wherein time modulation of Raman pump light source, time modulation of said Stokes source, and/or different time modulations of both said Raman pump light source and said Stokes source are used to allow differentiation of Raman pump wavelength light from the light having the wavelengths lying within the window of Raman measurement wavelengths.

[00174] In some examples, the photodetector is a photodiode that detects light across the entire window of Raman measurement wavelengths, and wherein the plurality of fixed-wavelength narrowband laser sources are activated one-at-a-time during said non-invasive glucose measuring.

[00175] The computing device can, at 1908, process the measured light to provide an estimated glucose level of the user. In some examples, the Stokes source emits light that is narrowband relative to said window of Raman measurement wavelengths, wherein said Stokes light comprises a plurality of emissions of said narrowband light at a respective plurality of center wavelengths ranging across said window of Raman measurement wavelengths.

[00176] FIG. 20 illustrates an example computing environment, including a user computing device 2000 in accordance with example embodiments of the present disclosure. The user computing device 2000 can include an analyte estimation system for non-invasively determining the presence and amount of one or more analytes internal to a user. In some examples, the user computing device 2000 can be a user computing device such as a smartphone or a wearable computing device. In other examples, the computing device 2000 can be a computing device intended for home use and not for portability. In this example, the user computing device 2000 can include one or more processors 102, memory 104, and an analyte estimation system 110.

[00177] In more detail, the one or more processors 102 can be any suitable processing device for the computing device 2000. For example, such a processor can include one or more of: one or more processor cores, a microprocessor, an ASIC, an FPGA, a controller, a microcontroller, etc. The one or more processors can be one processor or a plurality of processors that are operatively connected. The memory 104 can include one or more non-transitory computer-readable storage media, such as RAM, ROM, EEPROM, EPROM, flash memory devices, etc., and combinations thereof.

[00178] In particular, memory 104 can store instructions 108 for implementing the analyte estimation system 110. It will be appreciated that the term "system" can refer to specialized hardware, computer logic that executes on a more general processor, or some combination thereof. Thus, a system can be implemented in hardware, application-specific circuits, firmware, and/or software controlling a general-purpose processor. In one embodiment, the system can be implemented as program code files stored on the storage device, loaded into memory, and executed by a processor. The program code files can be provided from

computer program products, for example, computer-executable instructions, that are stored in a tangible computer-readable storage medium such as RAM, hard disk or optical or magnetic media.

[00179] Memory 104 can also include data 106 that can be retrieved, manipulated, created, or stored by the one or more processor(s) 102. In some example embodiments, such data can be accessed and used as input to the analyte estimation system 110. In some examples, the memory 104 can include data used to perform one or more processes and instructions that describe how those processes can be performed.

[00180] In some examples, the analyte estimation system 110 can include a pump laser 112, one or more Stokes lasers 116, a calibration laser 130, a controller 156, a photodetector 122, a signal analysis system 152, and an analyte detection system 154. Although not pictured, the analyte estimation system 110 can also include an optical filter and one or more optical lenses (e.g., micro lenses) to focus the lasers on the same area (e.g., the same portion of the user's skin).

[00181] The pump laser 112 (e.g., a first light source) can be a laser diode that emits light (e.g., a stream of photons) within a narrow wavelength band such that the emitted light has a particular wavelength within a certain range of the target wavelength. In some examples, the pump laser can produce narrowband light with an average wavelength of 780 nanometers. Other wavelengths of a pump laser 112 may be used, with the wavelengths of the one or more Stokes lasers 116 being determined based, at least in part, on the wavelength of the pump laser 112. In some examples, the pump laser 112 can be a vertical-cavity surface-emitting laser (VCSEL) included in a semiconductor chip. In some examples, the wavelength of the light emitted by the pump laser 112 is 850 nanometers. Other wavelengths can be used.

[00182] The pump laser 112 can include (or be associated with) a modulation system. The modulation system can include a waveform generator that can produce a waveform that can be used to modulate the light produced by the pump laser 112. The pump laser can be referred to as a first light source. By modulating the light produced by the pump laser 112, the analyte estimation system 110 can differentiate (e.g., using a filter or lock-in amplifier) between the light that the target material emits after being excited by the light that originated from the pump laser 112 and the light that the target material emits after being excited by the light that originates from the one or more Stokes lasers 116 or the light that originates from the calibration laser 130.

[00183] The one or more Stokes lasers 116 can include a tunable laser that can produce light with a wavelength within a predetermined range as needed. Thus, the tunable laser can be adjusted such that the wavelength of the light produced by the light source can change within a range. In some examples, the tunable laser can be adjusted to emit light with a wavelength that can vary from 910 nanometers to 980 nanometers. In some examples, the wavelength of the light produced by the tunable laser can be determined based on the Raman signature of a particular analyte that the analyte estimation system 110 is trying to identify. In some examples, the pump laser 112, the calibration laser 130, and the one or more Stokes lasers can use about 40 milliwatts of power to operate.

[00184] In some examples, the one or more Stokes lasers 116 can include a modulation system. Thus, in some configurations, the one or more Stokes lasers 116 are modulated to distinguish the light produced by the one or more Stokes lasers 116 from the light produced by the pump laser 112 and the light produced by the calibration laser 130.

[00185] In some examples, the one or more Stokes lasers 116 can provide light with a wavelength tuned to the Raman signature of a particular analyte that the analyte estimation system 110 is trying to identify (e.g., glucose). By providing additional light (e.g., a stream of photons) with a wavelength determined based on the Raman signature of the analyte, the analyte estimation system 110 can enable stimulated Raman scattering to occur. Stimulated Raman scattering can result in the light provided by the one or more Stokes lasers 116 stimulating more Raman scattering than would be expected without the additional light provided by the one more Stokes lasers 116. Thus, introducing the light provided by the one or more Stokes lasers 116 can increase the detectability of a particular analyte in the sample material because the probability of Raman scattering is increased.

[00186] In some examples, the analyte estimation system 110 can include a calibration laser 130. The calibration laser 130 can be referred to as a third light source or a calibration light source. The calibration laser 130 can be tuned such that the light produced by the calibration laser 130 will not result in Raman scattering in the wavelengths associated with the current target analyte. The calibration laser 130 can have a fixed wavelength, or the calibration laser 130 can be tunable. The calibration laser 130 can also include a modulation system as described above with respect to the pump laser 112 and the one or more Stokes lasers 116.

[00187] In some examples, the analyte estimation system 110 can include a controller 156 (this may also be referred to as a pulse controller). The controller 156 can be connected to the

pump laser 112, the one or more Stokes lasers 116, and the calibration laser 130. Through this connection, the controller 156 can determine which light source is activated at which time. In this way, the controller 156 can ensure that the lasers needed to generate Raman scattering (e.g., the pump laser 112 and one or more Stokes lasers 116) can be activated simultaneously at some times. When these lasers are activated, the detected signal can include Raman scattering and can be referred to as the Raman signal.

[00188] Similarly, the controller 156 can control lasers that are not associated with Raman scattering and activate them simultaneously during one or more periods. For example, the controller 156 can simultaneously activate the one or more Stokes lasers 116 and the calibration laser 130. The wavelength produced by these lasers can be such that no Raman scattering is induced. Alternatively, these lasers can have wavelengths determined such that no Raman scattering occurs in the wavelengths associated with the analyte that is currently being analyzed. In some examples, because the controller 156 activates specific lasers (one or more Stokes lasers 116 and the calibration laser 130) to ensure that no Ra man scattering occurs, the resulting signal can be a non-Raman signal. The non-Raman signal can comprise noise signals from one or more noise sources.

[00189] In some examples, the analyte estimation system 110 can include a photodetector 122. The photodetector 122 can be a sensor (e.g., a semiconductor device that converts light (e.g., photons) into electrical current) such as a photodiode. The photodiode can be configured to detect light over a range of wavelengths. In some example embodiments, light can be optically filtered such that only light within a specific wavelength range is detected by the photodetector. An amount of light can also be understood to be the number of photons detected and/or the intensity of the light measured at a particular wavelength.

[00190] In some examples, a filter can be employed to remove target-emitted light that is associated with the one or more Stokes lasers 116 such that only light originating from the pump laser 112 is detected. Similarly, an optical filter can filter out light with a wavelength associated with the pump laser 112 such that only light that originated from the Stokes lasers 116 or was Raman scattered is detected by the photodetector when it emanates from the target. In some examples, a filter (or a lock-in amplifier) can remove modulated light (if the one or more Stokes lasers 116 were modulated) or unmodulated light (if the pump laser 112 was modulated).

[00191] As noted above, the signal produced by the photodetector when the light emanating from the tissue of the user is the result of both the one or more Stokes light sources

and the Raman pump light source being activated simultaneously and can be referred to as a Raman signal. Conversely, the signal produced by the photodetector when the calibration laser 130 and the one or more Stokes light sources 116 are activated can be referred to as a non-Raman signal. The photodetector 122 can produce both of these signals when the appropriate light sources are activated by the controller 156.

[00192] The signal analysis system 152 can analyze both the Raman and the non-Raman signals. In some examples, the signal analysis system 152 can identify one or more features within the non-Raman signal that are associated with noise. In some examples, the signal analysis system 152 can modify the Raman signal to remove one or more features found in both the Raman signal and the non-Raman signal. The signal analysis system 152 can subtract the non-Raman signal from the Raman signal, resulting in a modified Raman signal. The modified Raman signal can have less noise than the original Raman signal because one or more noise characteristics are removed from the original Raman signal. The modified Raman signal can provide information that can be used to more accurately determine the amount of an analyte within the tissue of the user.

[00193] The analyte detection system 154 can be used to detect the amount of light (e.g., the intensity of the light or the number of photons) generated by Raman scattering associated with an analyte in the sample material. In some examples, the analyte detection system 154 can determine the amount of light (e.g., either the number of photons or the intensity of the light) that has been Raman scattered to identify an analyte in the target material based on the data included in the modified Raman signal. In a first example, the user computing device can determine the amount of light at the pump wavelength (e.g., a first wavelength) that is lost (stimulated Raman loss) based on an analysis of the modified Raman signal.

[00194] Alternatively, the user computing device 2002 can determine the amount of light at the wavelength associated with the one or more Stokes lasers 116 that is gained (e.g., stimulated Raman gain) based on an analysis of the modified Raman signal. Either measurement or their combination can be used to estimate the amount of a particular analyte in the target material (e.g., a user's skin). A detected Stokes range can be compared to a reference spectrum to non-invasively measure the presence or absence of a target analyte.

[00195] For example, the sample material can be a portion of a user's body. The analyte can be, for example, glucose. Based on the amount of light having the predetermined second wavelength based on an analysis of the modified Raman signal, the analyte detection system

154 can estimate the amount of the analyte in the target sample. In some examples, the estimated amount of the analyte can be presented for display to a user.

[00196] FIG. 21 is an example of two diagrams representing the pulse intensity of different light sources at different points in time in accordance with example embodiments of the present disclosure. For example, the diagrams illustrate the pulse intensity of a Raman pump light source, a Stokes light source, and a calibration light source. The first graph 2104 represents the pulse intensity of the Stokes light source at different times (e.g., between 0 and 500 nanoseconds).

[00197] The second graph 2102 represents the pulse intensity of the Raman pump light source and the calibration light source at different times. Note that only one of the two light sources is activated at any given time. A controller can time the activation of the Raman pump light source and the calibration light source such that they are activated during at least one pulse of the Stokes light source but never activated during the same period. In one example, a controller can activate the Stokes source and simultaneously activate the Raman pump source during a first time window 2012 (e.g., a time window around 300 nanoseconds). Both the Stokes light source and the Raman pump light source are simultaneously activated to a pulse intensity of 1 during the first time window 2012 and simultaneously deactivated after a short period of time. The light detected as emanating from the user's tissue during this time can be referred to as the Raman signal or stimulated Raman scattering (SRS) signal. Because both the Raman pump light source and the Stokes light source are activated simultaneously and targeted at the same area of tissue, the chance of Raman scattering occurring is significantly increased.

[00198] During a second time window 2010 (e.g., around 350 nanoseconds), the Stokes light source is activated again. During the second time window 2010 the calibration light source is activated rather than the Raman pump light source (which was activated during the first time window 2012). Both the Stokes light source and the calibration light source are simultaneously activated, remain active for a short time, and are then deactivated. During the second time window 2010, both the Stokes light source and the Raman pump light source reach a pulse intensity of one. The photodetector associated with the analyte estimation system can capture light emanating from the user's tissue during this time. A photodetector can generate a signal based on the captured light. This signal can be referred to as a non-Raman signal. A non-Raman signal does not include Raman scattered light. As a result, the non-Raman signal primarily comprises noise from various light noise sources. The Raman

signal and the non-Raman signal can be compared and analyzed together to generate a modified Raman signal in which some or all of the portion of the Raman signal that is associated with noise sources is removed from the Raman signal.

[00199] FIG. 22A is an example graph 2202 of the strength of the Raman signal (or SRS signal) produced without using a calibration light source at different wavelengths in accordance with example embodiments. In this example, the intensity of the light within a range of wavelengths includes a peak 2204 at 769 millimeters and a baseline noise signal 2206 that exists at all wavelengths. As a result, the peak 2204 at 769 millimeters is less distinct from the other wavelengths. The calibration light source allows some or all of this extra noise to be removed when generating a modified Raman signal.

[00200] Figure 22B is a graph 2210 of a modified Roman signal in accordance with example embodiments of the disclosure. As seen here, the intensity or strength of the signal at different wavelengths is displayed in a graph 2210. In this example, the Raman pump light source can have a tunable wavelength. For example, the Raman pump light source can be tuned between 764 nm and 773 nm.

[00201] The intensity of detected light in the modified Raman signal can have one or more peaks at different wavelengths depending on the particular analytes present in the tissue of the user. As can be seen, at least one peak 2212 can have a wavelength between 769 nm and 770 nm. This specific wavelength can be represented by Ω in the following calculation:

$$\frac{1}{\lambda_{Raman\ Pump}} - \frac{1}{\lambda_{Stokes}} = \Omega$$

[00202] $\lambda_{Raman\ Pump}$ can represent the wavelength of the light produced by the Raman pump light source and λ_{Stokes} can represent the wavelength of the light produced by the Stokes light source.

[00203] The modified Raman signal can include less noise than the original Raman signal (e.g., as seen in FIG. 22A). Thus, most or all of the non-Raman background present in the original Raman signal can be removed from the modified Raman signal. Doing so allows the light generated by Raman scattering to be significantly easier to detect and identify.

[00204] Figure 22C is a graph 2220 of a modified Raman signal in accordance with example embodiments of the disclosure. As seen here, the intensity or strength of the signal at different wavelengths is displayed in a graph. In this example, the Stokes light source can

have a tunable wavelength. For example, the Stokes light source can be tuned between 831 nm and 842 nm.

[00205] The intensity of detected light in the modified Raman signal can have one or more peaks at different wavelengths as well as troughs at different wavelengths depending on the particular analytes that are present in the tissue of the user. In this example, the signal peak 2224 occurs at approximately 835 nm. This specific wavelength can be represented by Ω in the following calculation:

$$\frac{1}{\lambda_{Raman\ Pump}} - \frac{1}{\lambda_{Stokes}} = \Omega$$

[00206] $\lambda_{Raman\ Pump}$ can represent the wavelength of the light produced by the Raman pump light source and λ_{Stokes} can represent the wavelength of the light produced by the Stokes light source.

[00207] A trough 2226 can also occur at approximately 839 nm. This specific wavelength can be represented by Ω in the following calculation:

$$\frac{1}{\lambda_{Calibration}} - \frac{1}{\lambda_{Stokes}} = \Omega$$

[00208] $\lambda_{Calibration}$ can represent the wavelength of the light produced by the calibration light source and λ_{Stokes} can represent the wavelength of the light produced by the Stokes light source.

[00209] The modified Raman signal can include less noise than the original Raman signal (e.g., as seen in FIG. 22A). Thus, most or all of the non-Raman background present in the original Raman signal can be removed from the modified Raman signal. Doing so allows the light generated by Raman scattering to be significantly easier to detect and identify.

[00210] FIG. 23 is a flowchart depicting an example process of detecting analytes within a target tissue in accordance with example embodiments of the present disclosure. One or more portion(s) of the method can be implemented by one or more computing devices such as, for example, the computing devices described herein. Moreover, one or more portion(s) of the method can be implemented as an algorithm on the hardware components of the device(s) described herein. FIG. 23 depicts elements performed in a particular order for purposes of illustration and discussion. Those of ordinary skill in the art, using the disclosures provided herein, will understand that the elements of any of the methods discussed herein can be

adapted, rearranged, expanded, omitted, combined, and/or modified in various ways without deviating from the scope of the present disclosure. The method can be implemented by one or more computing devices, such as one or more of the computing devices depicted in FIGS. 3 and 20.

[00211] The method can be implemented by an analyte estimation system (e.g., analyte estimation system 110 in FIG. 20). The analyte estimation system (e.g., analyte estimation system 110 in FIG. 20) can include a pump light source, one or more Stokes light sources, a calibration light source, a pulse controller, a photodetector, a signal analysis system, and an analyte detection system. The pulse controller can, at 2302, control the Stokes light source, the calibration light source, and the Raman pump light source. The pulse controller can modulate the calibration light source and the one or more Stokes light sources at different frequencies.

[00212] In some examples, the calibration light source has a fixed wavelength. For example, the fixed wavelength of the calibration light source is selected to meet an off-resonance condition. In some examples, the one or more Stokes lasers include a tunable-wavelength Stokes laser, the Raman pump light source is a fixed wavelength laser, and the calibration light source is a fixed wavelength laser.

[00213] . In some examples, the fixed wavelength is selected to be as close to the wavelength of the Raman pump light source as possible without causing Raman scattering. In this way, the conditions in which the calibration light source is activated are as similar as possible to the conditions when the Raman pump light source is activated. Having similar conditions will minimize the differences in the noise sources in both the non-Raman signal and the Raman signal. For example, if the fixed wavelength of the calibration light source differs significantly enough from the wavelength of the Raman pump light source, the sources of the light noise and characteristics of the light noise may differ enough that analyzing the non-Raman signal may not be useful to remove noise from the Raman signal.

[00214] The analyte estimation system (e.g., analyte estimation system 110 in FIG. 20) can cause the Stokes light source and the calibration light source to, at 2304, emit (in response to the pulse controller), Stokes light and calibration light toward a skin surface of the user during a first time period. The calibration light source can be phase-modulated relative to the Raman pump light source. In some examples, the calibration light source can be phase-modulated 180 degrees relative to the Raman pump light source.

[00215] The analyte estimation system (e.g., analyte estimation system 110 in FIG. 20) can, at 2306, measure, using the photodetector, light that emanates from the skin surface during the first time period to produce a non-Raman signal. In some examples, the photodetector can be a broad-range photodiode.

[00216] The analyte estimation system (e.g., analyte estimation system 110 in FIG. 20) can generate the non-Raman signal based on the detected light that emanates from the tissue while the one or more Stokes light sources and the calibration light source are activated, and the Raman pump light source is not activated. In some examples, the pulse controller can periodically activate the one or more Stokes light sources and the calibration light source simultaneously.

[00217] The analyte estimation system (e.g., analyte estimation system 110 in FIG. 20) can, at 2308, emit, from a Stokes light source and a Raman pump light source (based on instructions received from the pulse controller), Stokes light and Raman pump light toward a skin surface of the user during a second time period. The analyte estimation system (e.g., analyte estimation system 110 in FIG. 20) can, at 2310, measure, using the photodetector, light that emanates from the skin surface during the second time period to produce a Raman signal. The analyte estimation system (e.g., analyte estimation system 110 in FIG. 20) can generate the Raman signal based on the detected light that emanates from the tissue while the Raman pump light source and the Stokes light source are activated at the same time.

[00218] The analyte estimation system (e.g., analyte estimation system 110 in FIG. 20) can, at 2312, modify the Raman signal based on the non-Raman signal to generate a modified Raman signal. In some examples, the analyte estimation system (e.g., analyte estimation system in FIG. 20) can identify one or more noise features of the non-Raman signal. The analyte estimation system (e.g., analyte estimation system 110 in FIG. 20) can generate the modified Raman signal by removing the identified noise features from the Raman signal.

[00219] The analyte estimation system (e.g., analyte estimation system in FIG. 20) can, at 2314, process the modified Raman signal to provide an estimated analyte level of the user. In some examples, the analyte estimation system (e.g., analyte estimation system in FIG. 20) can generate an estimated analyte level based on the Raman fingerprint for the skin surface of the user. In some examples, the analyte can be glucose.

[00220] The technology discussed herein refers to servers, databases, software applications, and other computer-based systems, as well as actions taken, and information sent to and from such systems. One of ordinary skill in the art will recognize that the inherent

flexibility of computer-based systems allows for a great variety of possible configurations, combinations, and divisions of tasks and functionality between and among components. For instance, server processes discussed herein may be implemented using a single server or multiple servers working in combination. Databases and applications may be implemented on a single system or distributed across multiple systems. Distributed components may operate sequentially or in parallel.

[00221] While the present subject matter has been described in detail with respect to specific example embodiments thereof, it will be appreciated that those skilled in the art, upon attaining an understanding of the foregoing may readily produce alterations to, variations of, and equivalents to such embodiments. Accordingly, the scope of the present disclosure is by way of example rather than by way of limitation, and the subject disclosure does not preclude inclusion of such modifications, variations and/or additions to the present subject matter as would be readily apparent to one of ordinary skill in the art.

WHAT IS CLAIMED IS:

1. A device for non-invasively measuring a level of an analyte in a user using Stimulated Raman Scattering, comprising:

a Raman pump light source that emits pump light toward a tissue of the user at a pump wavelength;

a Stokes light source that emits Stokes light toward the tissue at one or more Stokes wavelengths;

a calibration light source that emits light towards the tissue at a calibration;

a pulse controller that engages the Raman pump light source, the Stokes light source, and the calibration light source to generate a Raman signal and a non-Raman signal;

a photodetector that measures light that emanates from the tissue to detect the Raman signal and the non-Raman signal; and

a processor that processes the measured light to provide an estimated analyte level of the analyte in the user based on a comparison of the Raman signal and the non-Raman signal.

2. The device of claim 1, the calibration light source being phase modulated relative to the Raman pump light source.

3. The device of claim 2, the calibration light source being phase-modulated 180 degrees relative to the Raman pump light source.

4. The device of claim 1, the pulse controller periodically activating the Stokes light source and the calibration light source simultaneously.

5. The device of claim 4, the photodetector calibrated to:

generate the non-Raman signal based on the detected light that emanates from the tissue while the Stokes light source and the calibration light source are activated and the Raman pump light source is not activated.

6. The device of claim 4, the photodetector being calibrated to:

generate the Raman signal based on the detected light that emanates from the tissue while the Raman pump light source and the Stokes light source are activated at the same time.

7. The device of claim 1, estimating the analyte level of the analyte in the user further comprising:

identifying one or more noise features of the non-Raman signal; and

generating a modified Raman signal by removing the identified noise features from the Raman signal.

8. The device of claim 1, the pulse controller modulating the calibration light source and the Stokes light source at different frequencies.

9. The device of claim 1, the pulse controller modulating the calibration light source and the Raman pump light source at the same frequency.

10. The device of claim 1, the pulse controller modulating the Stokes light source at double the frequency of the calibration light source and the Raman pump light source.

11. The device of claim 1, the Raman pump light source, the Stokes light source, and the calibration light source being VCSELs.

12. The device of claim 1, the photodetector being a broad-range photodiode.

13. The device of claim 1, the analyte being glucose.

14. The device of claim 1, wherein the calibration light source has a fixed wavelength.

15. The device of claim 14, wherein the fixed wavelength of the calibration light source is selected to meet an off-resonance condition.

16. The device of claim 1, wherein the one or more Stokes light sources include a tunable-wavelength Stokes laser, the Raman pump light source is a fixed wavelength laser, and the calibration light source is a fixed wavelength laser.

17. A computer-implemented method for non-invasively measuring a level of an analyte in a user using Stimulated Raman Scattering, comprising:

controlling, by a pulse controller, a Stokes light source, a calibration light source, and a Raman pump light source;

emitting, from a Stokes light source and a calibration light source, Stokes light and calibration light toward a skin surface of the user during a first time;

measuring, by a photodetector, light that emanates from the skin surface during the first time to produce a non-Raman signal;

emitting, from a Stokes light source and a Raman pump light source in response to the pulse controller, Stokes light and Raman pump light toward a skin surface of the user during a second time;

measuring, by a photodetector, light that emanates from the skin surface during the first time to produce a Raman signal;

modifying, by a computing system including one or more processors, the Raman signal based on the non-Raman signal to generate a modified Raman signal; and

processing, by the computing system, the modified Raman signal to provide an estimated analyte level of the user.

18. The computer-implemented method of claim 17, wherein estimating the analyte level of the analyte in the user further comprising:

identifying one or more noise features of the non-Raman signal; and

generating a modified Raman signal by removing the identified noise features from the Raman signal.

19 The computer-implemented method of claim 17, wherein the pulse controller modulates the calibration light source and the Stokes light source at different frequencies.

20. An analyte estimation system, the system comprising:

a Raman pump light source that emits pump light toward a tissue of a user at a pump wavelength;

a Stokes light source that emits Stokes light toward the tissue at one or more Stokes wavelengths;

a calibration light source that emits light towards the tissue at a calibration;

a pulse controller that engages the Raman pump light source, the Stokes light source, and the calibration light source to generate a Raman signal and a non-Raman signal;

a photodetector that measures light that emanates from the tissue to detect the Raman signal and the non-Raman signal; and

a processor that processes the measured light to provide an estimated analyte level of the analyte in the user based on a comparison of the Raman signal and the non-Raman signal.

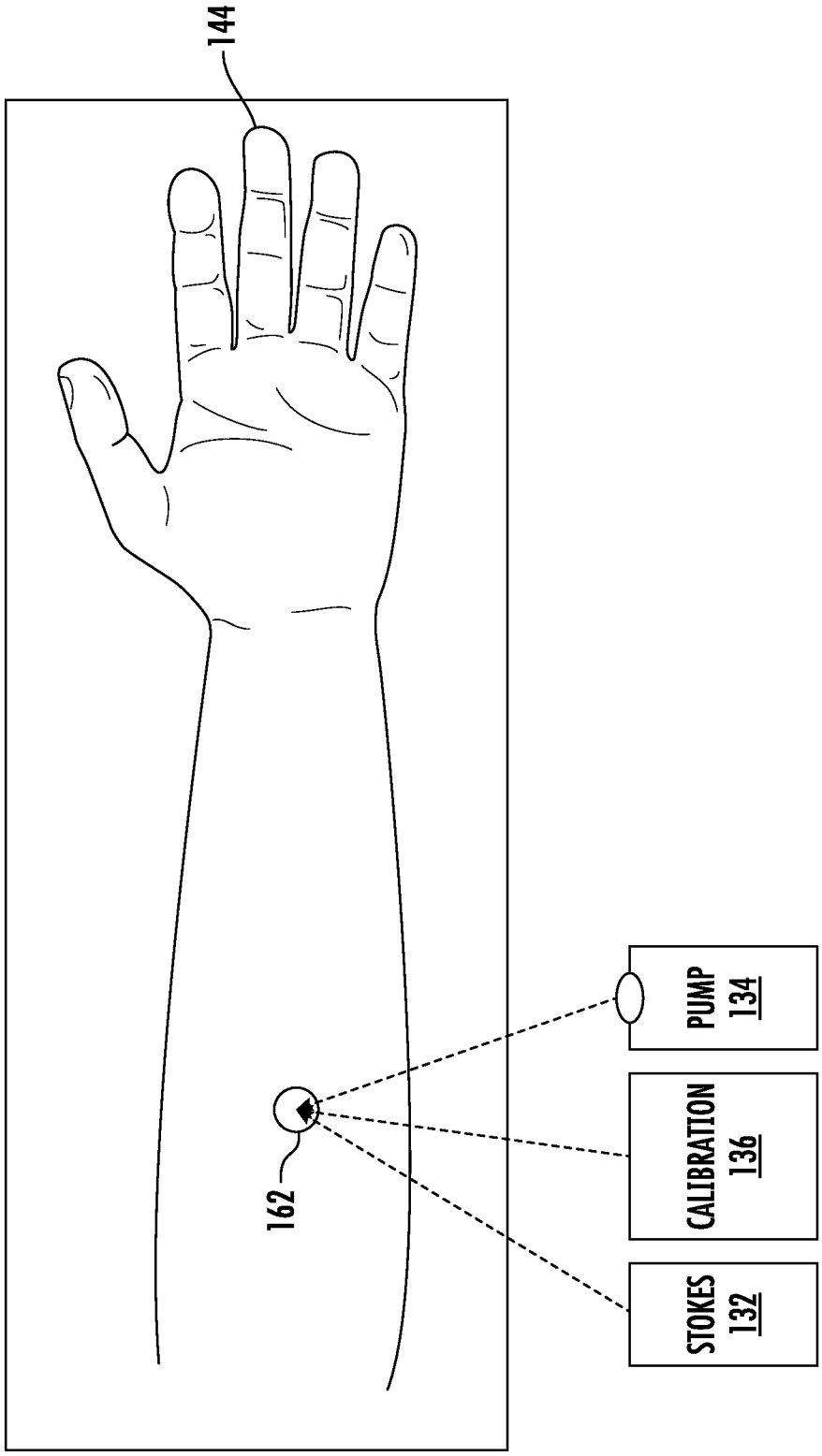


FIG. 1A

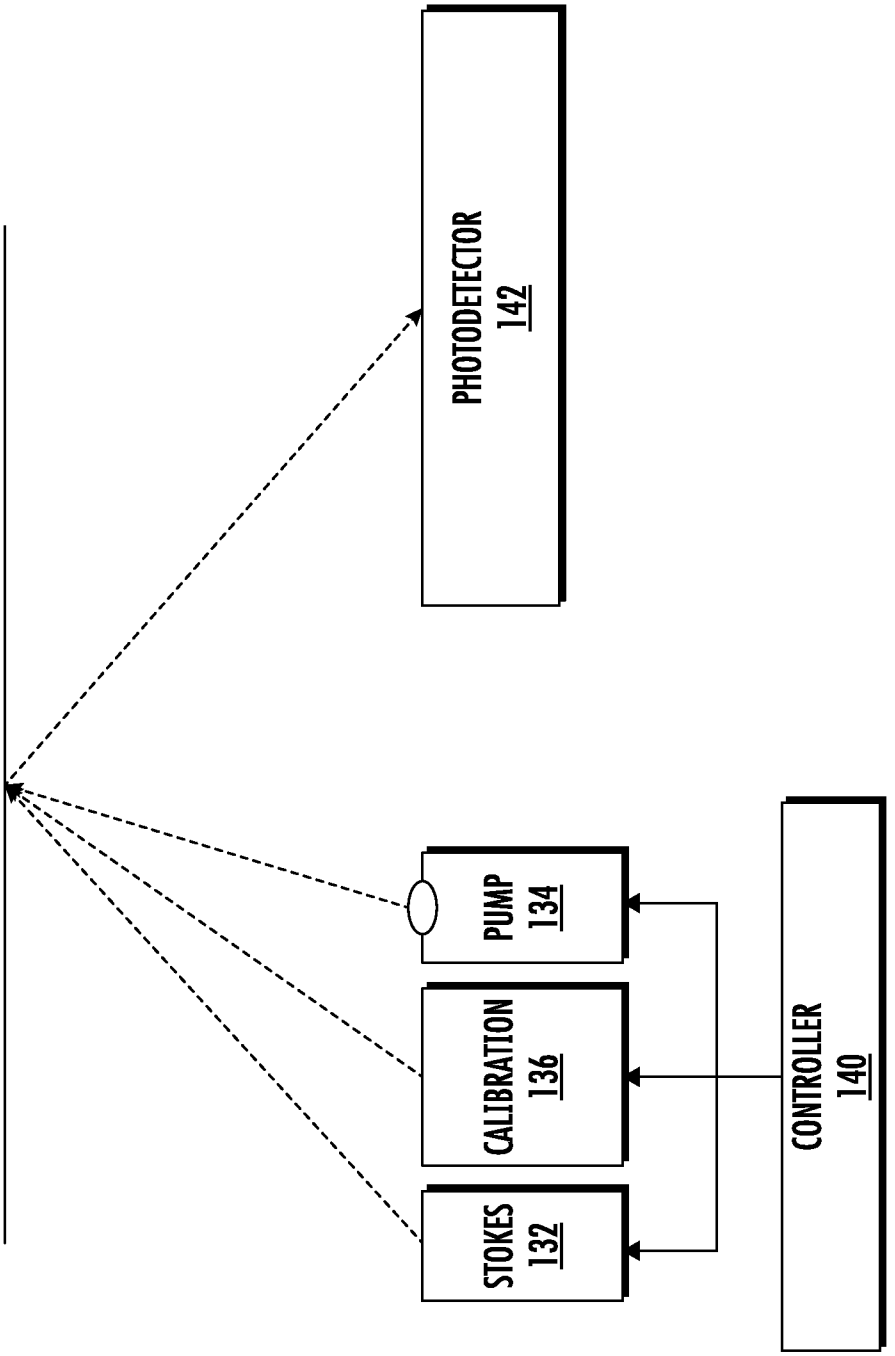

PHOTODETECTOR
142
PUMP
134
CALIBRATION
136
STOKES
132
CONTROLLER
140

FIG. 1B

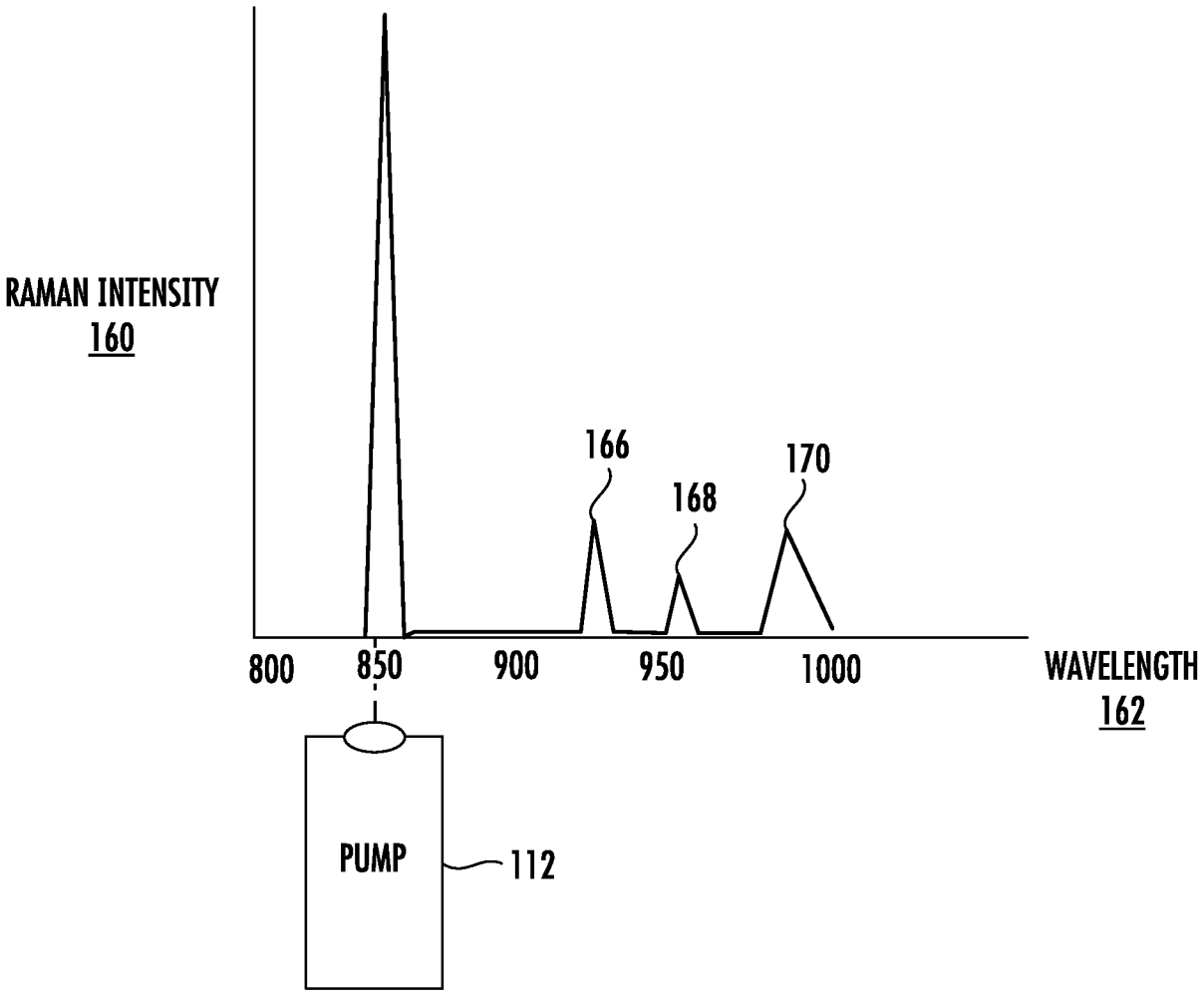

RAMAN INTENSITY
160
166
168
170
800
850
900
950
1000
WAVELENGTH
162
PUMP
112

FIG. 2A

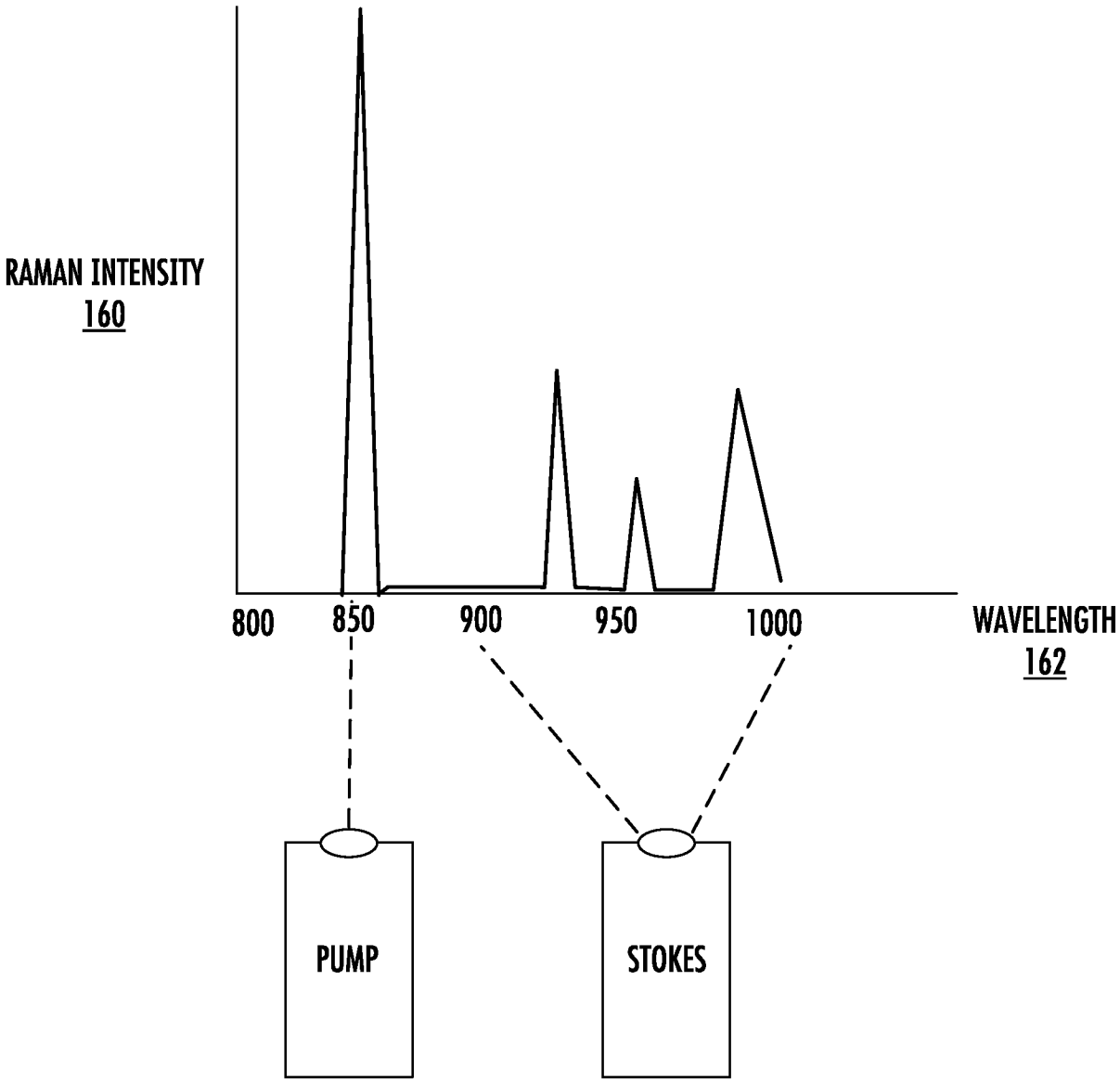

RAMAN INTENSITY
160
800
850
900
950
1000
WAVELENGTH
162
PUMP
STOKES

FIG. 2B

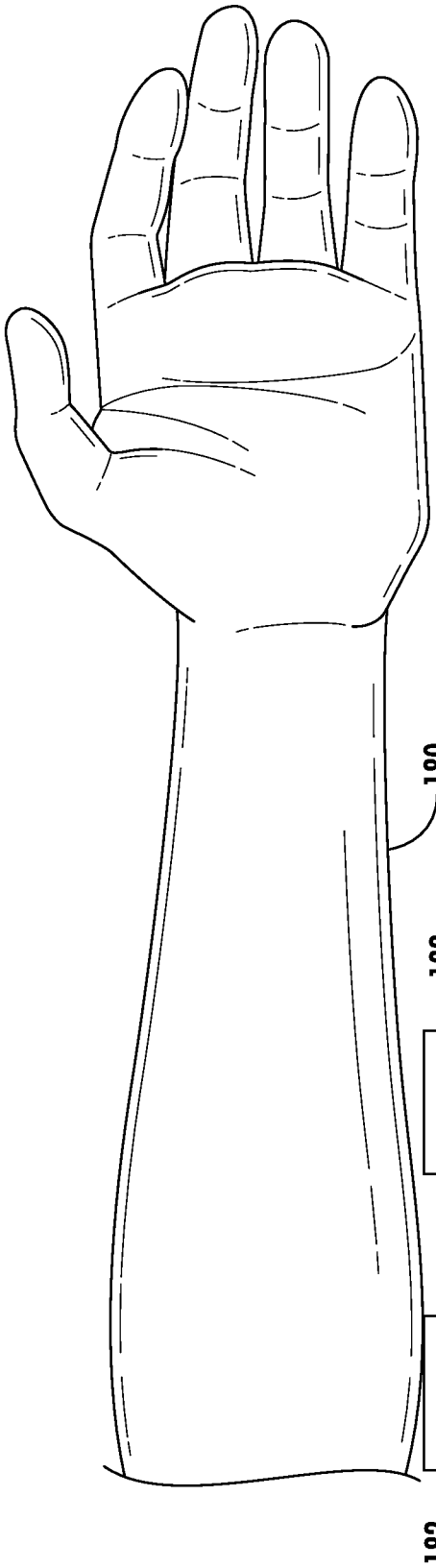


FIG. 2C

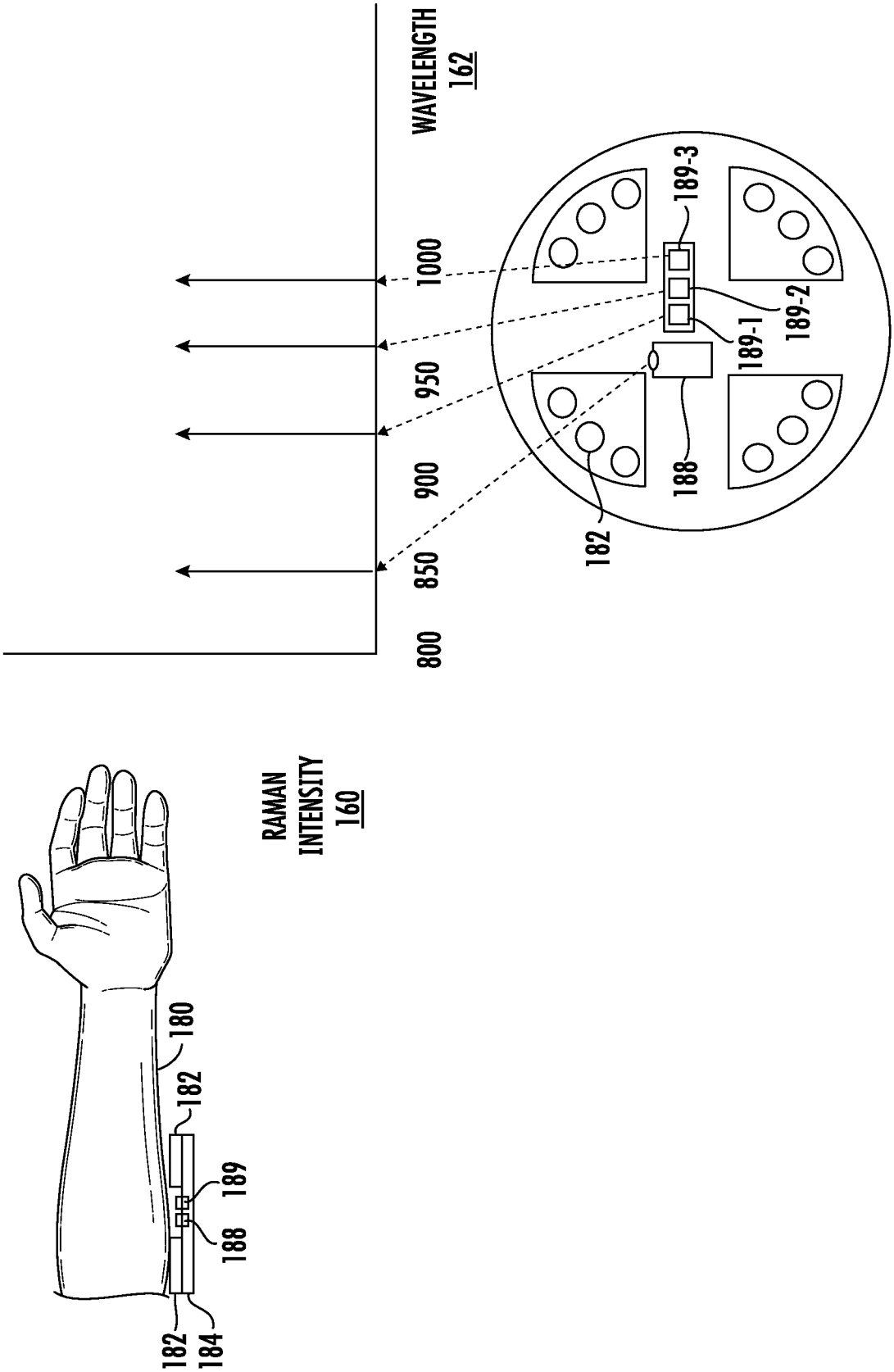

WAVELENGTH
162
1000
950
900
850
800
189-3
189-2
189-1
188
182
RAMAN
INTENSITY
160
180
182
189
188
182
184

FIG. 2D

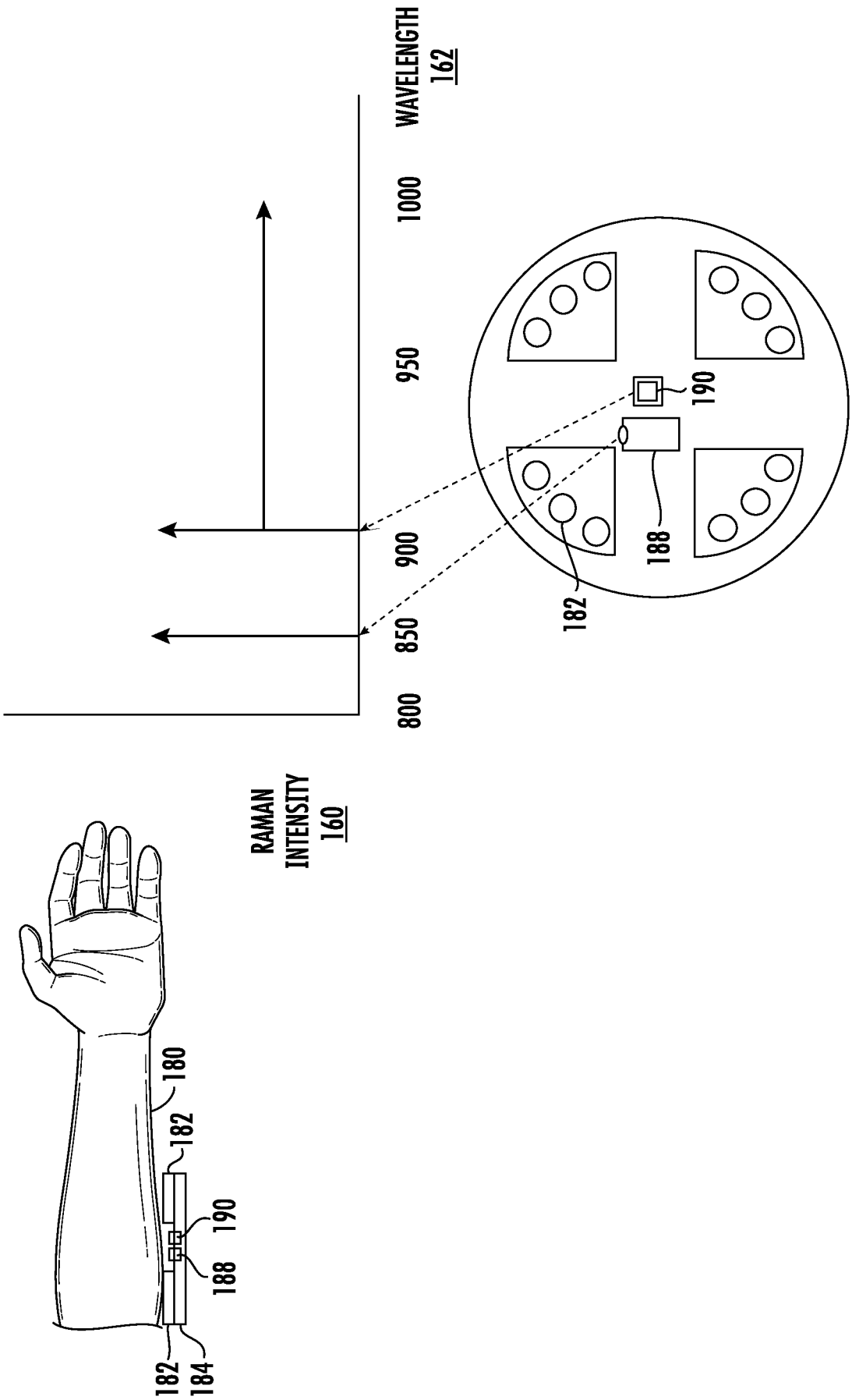

WAVELENGTH
162
1000
950
900
850
800
RAMAN
INTENSITY
160
190
188
182
180
182
190
188
182
184

FIG. 2E

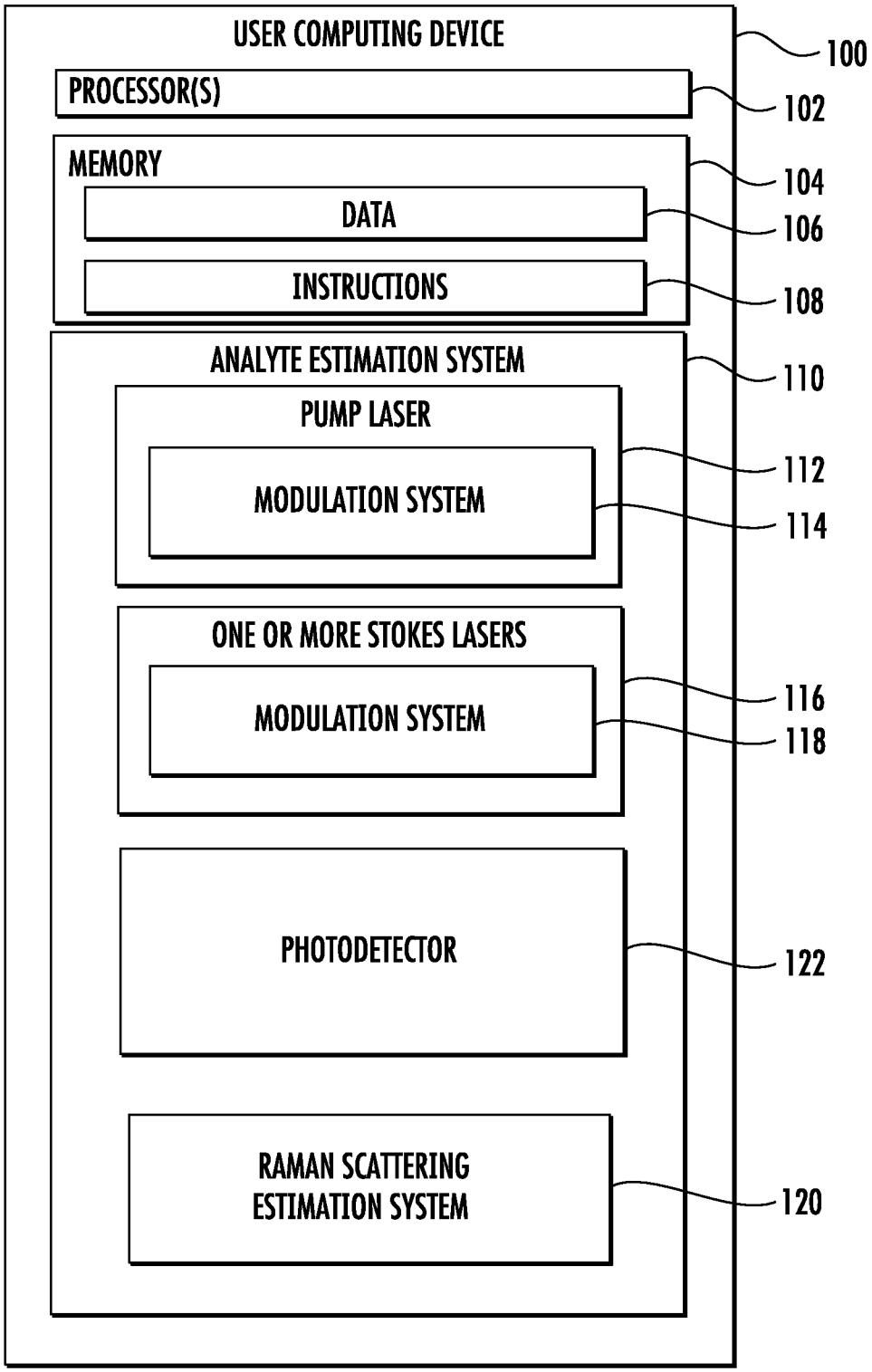

USER COMPUTING DEVICE
100
PROCESSOR(S)
102
MEMORY
104
DATA
106
INSTRUCTIONS
108
ANALYTE ESTIMATION SYSTEM
110
PUMP LASER
112
MODULATION SYSTEM
114
ONE OR MORE STOKES LASERS
116
MODULATION SYSTEM
118
PHOTODETECTOR
122
RAMAN SCATTERING ESTIMATION SYSTEM
120

FIG. 3

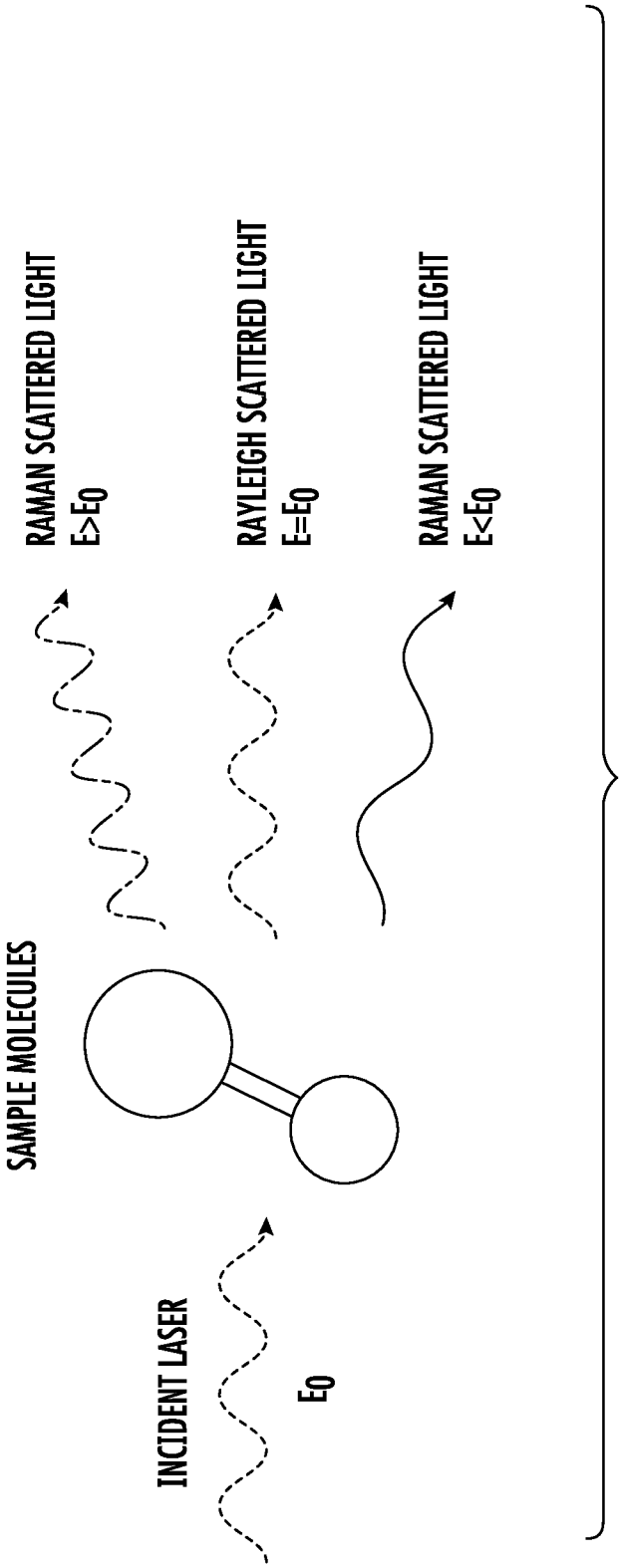

RAMAN SCATTERED LIGHT
E>E0
RAYLEIGH SCATTERED LIGHT
E=E0
RAMAN SCATTERED LIGHT
E<E0
SAMPLE MOLECULES
INCIDENT LASER
E0

FIG. 4A

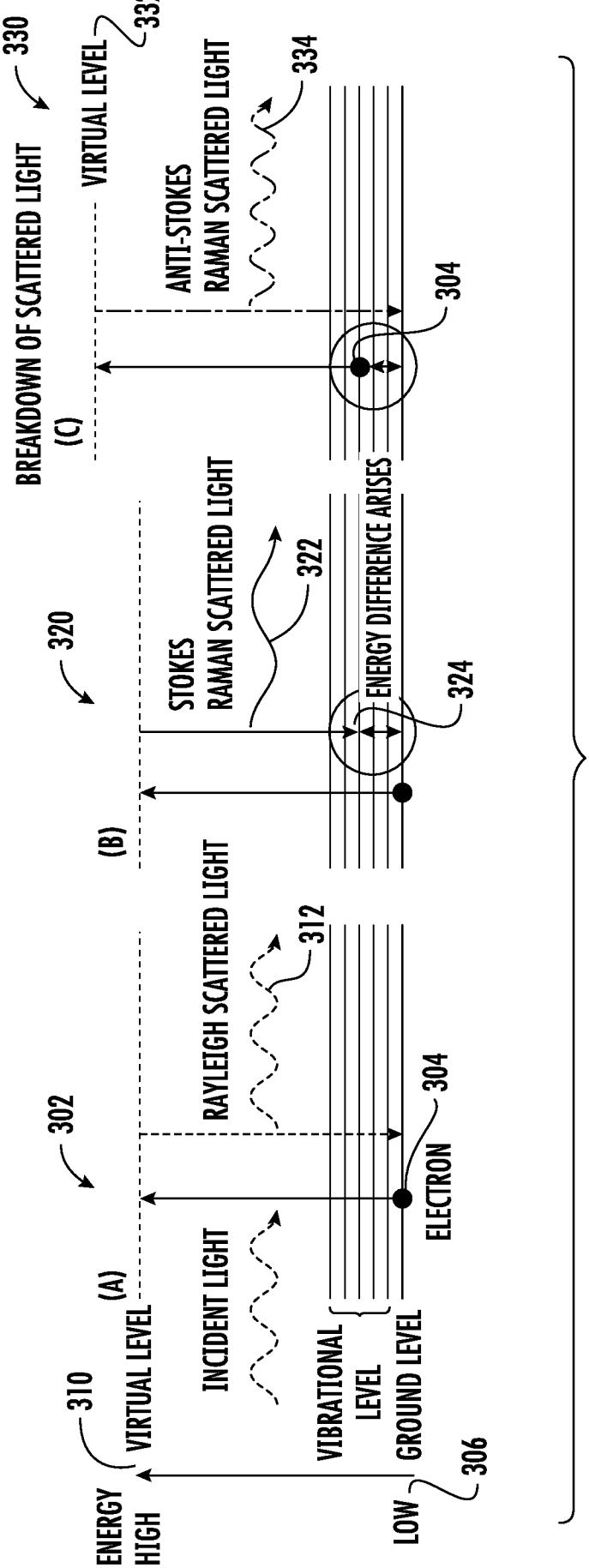

ENERGY
HIGH
LOW
310
VIRTUAL LEVEL
(A)
INCIDENT LIGHT
VIBRATIONAL
LEVEL
GROUND LEVEL
306
302
RAYLEIGH SCATTERED LIGHT
312
304
ELECTRON
(B)
320
STOKES
RAMAN SCATTERED LIGHT
322
ENERGY DIFFERENCE ARISES
324
(C)
BREAKDOWN OF SCATTERED LIGHT
330
VIRTUAL LEVEL
332
ANTI-STOKES
RAMAN SCATTERED LIGHT
334
304

FIG. 4B

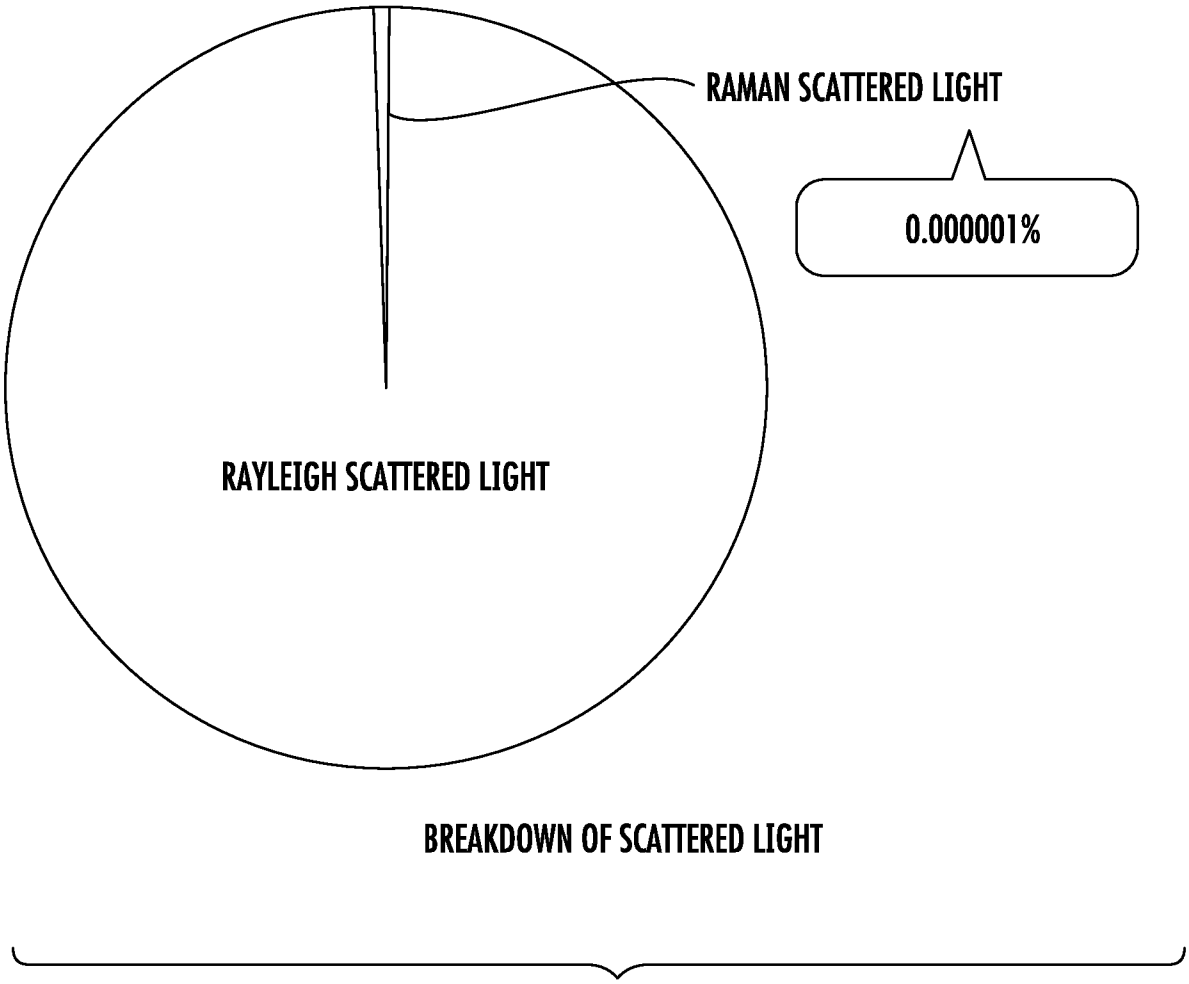
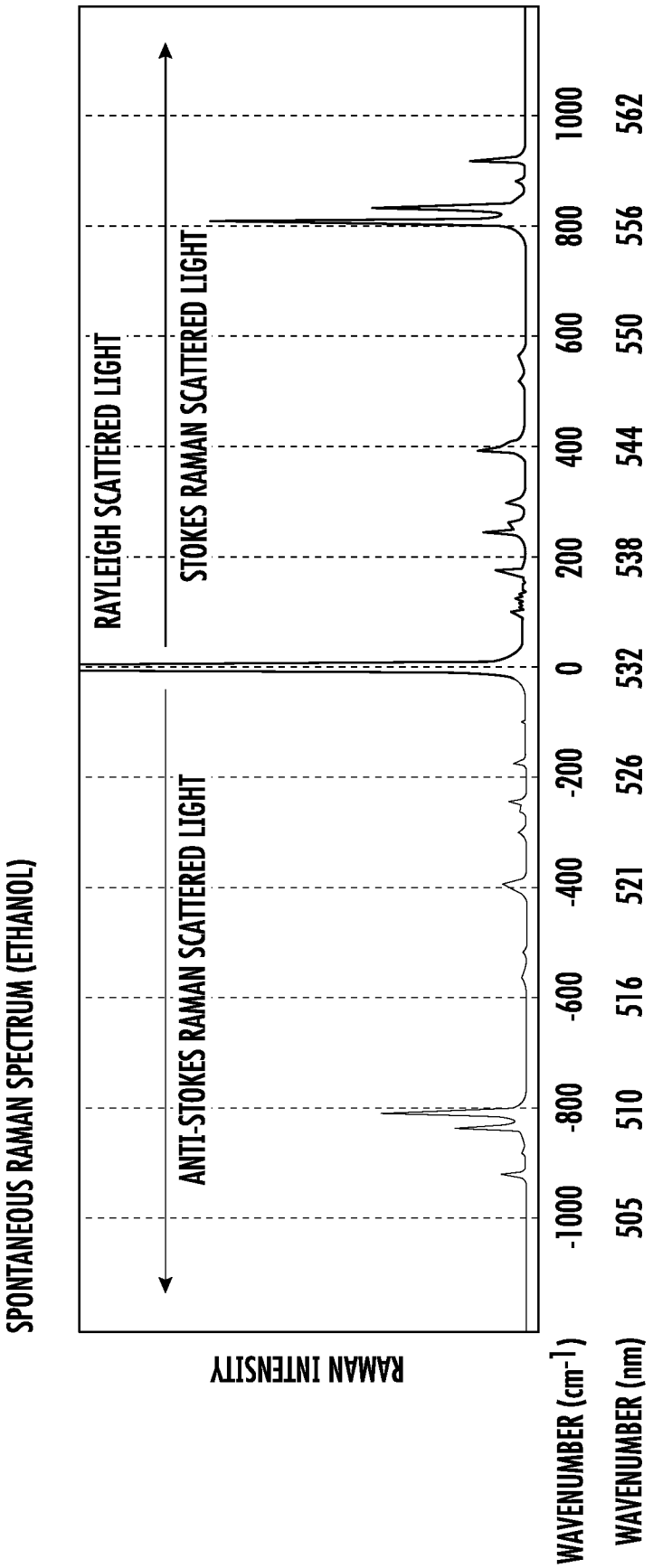

RAMAN SCATTERED LIGHT
0.000001%
RAYLEIGH SCATTERED LIGHT
BREAKDOWN OF SCATTERED LIGHT

FIG. 5



- RAYLEIGH IN CENTER (1,000,000X > STOKES)
- DISCRETE PEAKS PROVIDE MEASUREMENT SPECIFICITY

FIG. 6

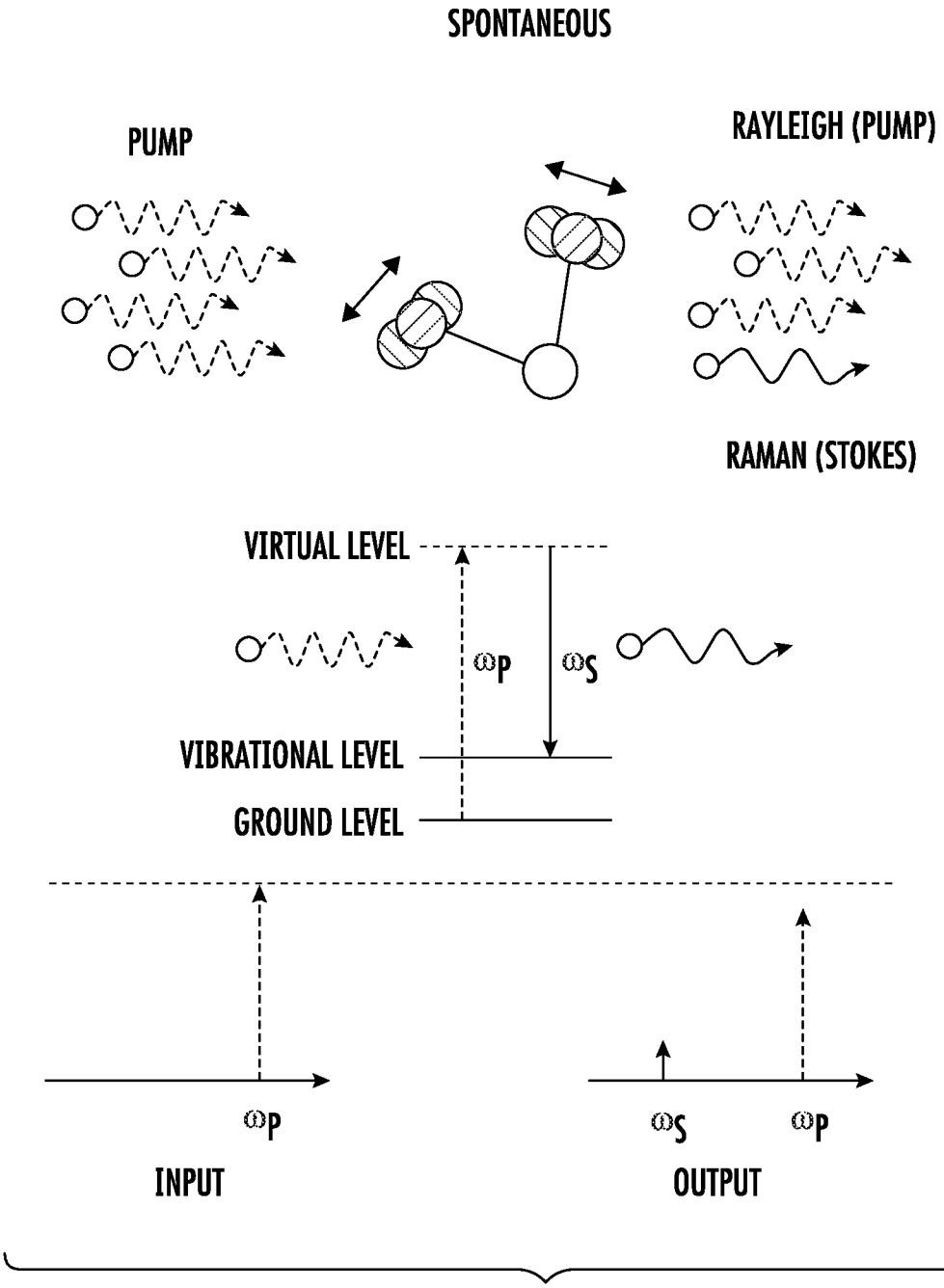

SPONTANEOUS
PUMP
RAYLEIGH (PUMP)
RAMAN (STOKES)
VIRTUAL LEVEL
ωP
ωS
VIBRATIONAL LEVEL
GROUND LEVEL
ωP
ωS
ωP
INPUT
OUTPUT

FIG. 7

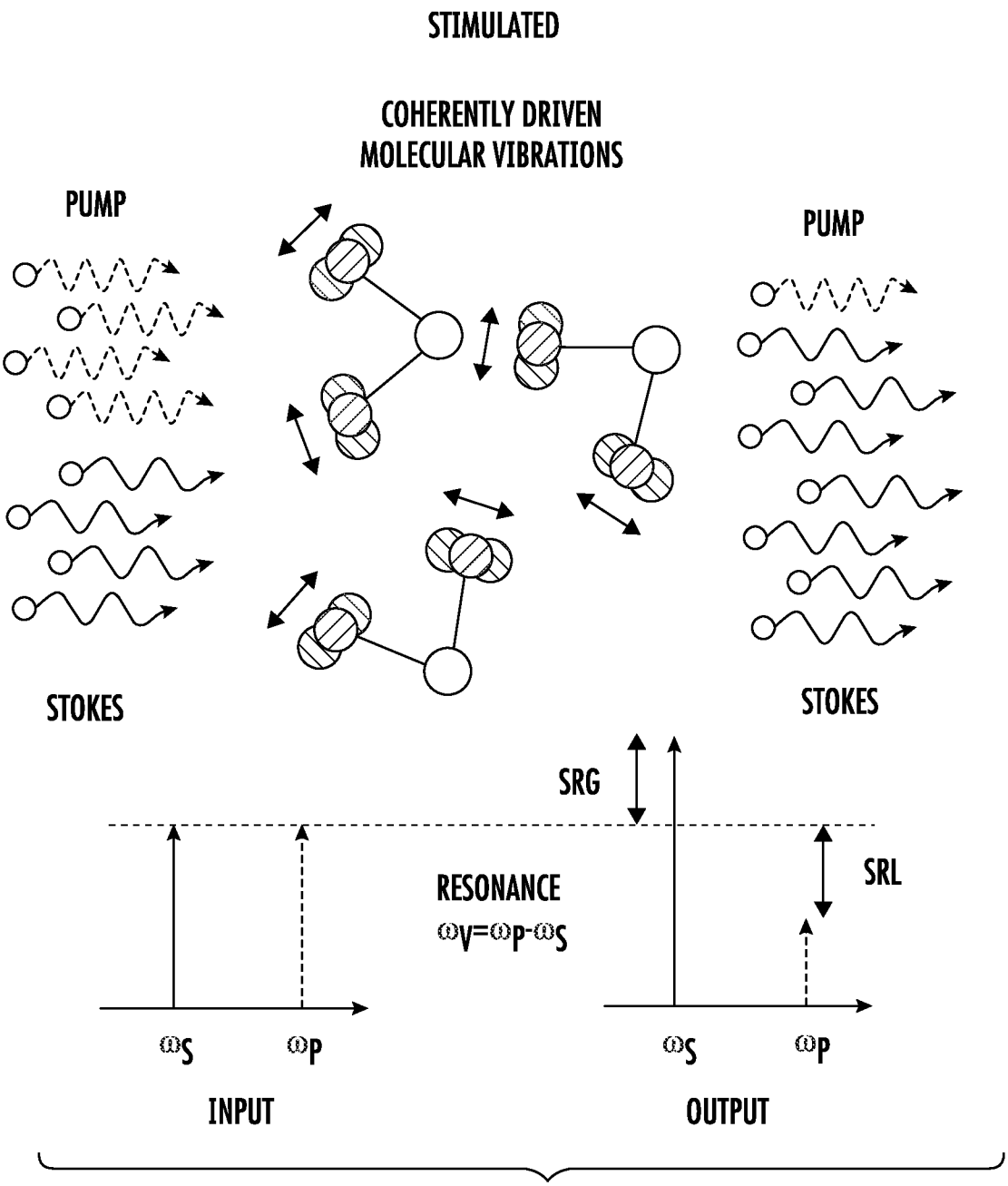

STIMULATED
COHERENTLY DRIVEN
MOLECULAR VIBRATIONS
PUMP
PUMP
STOKES
STOKES
SRG
SRL
RESONANCE
ωV=ωP-ωS
ωS
ωP
ωS
ωP
INPUT
OUTPUT

FIG. 8

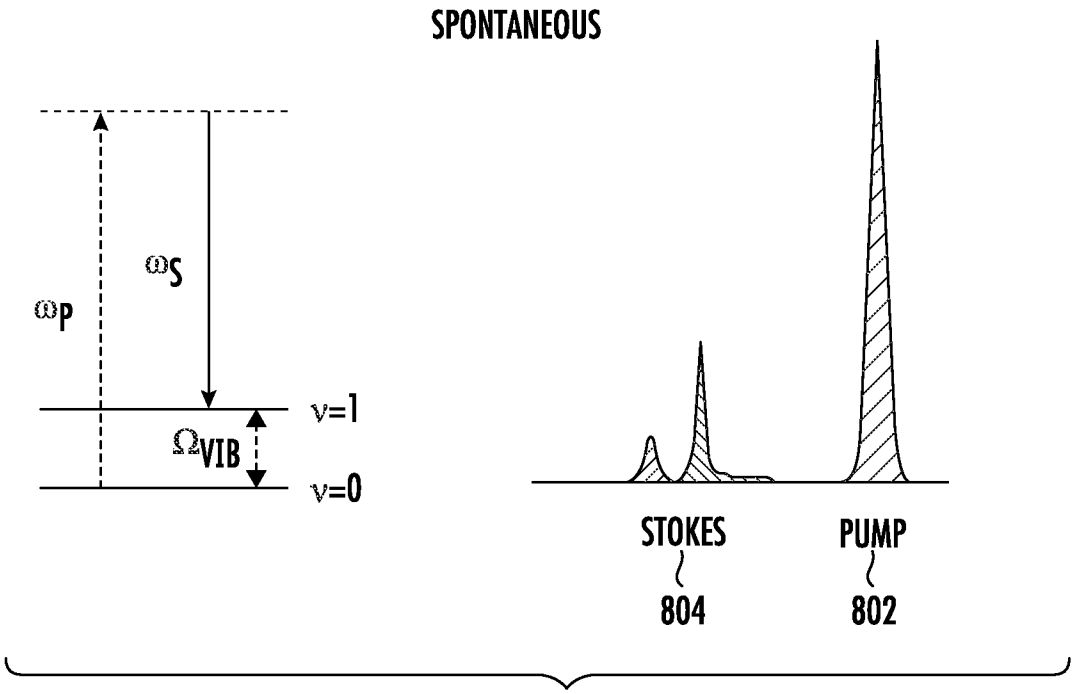

SPONTANEOUS
ωS
ωP
ν=1
ΩVIB
ν=0
STOKES
PUMP
804
802

FIG. 9A

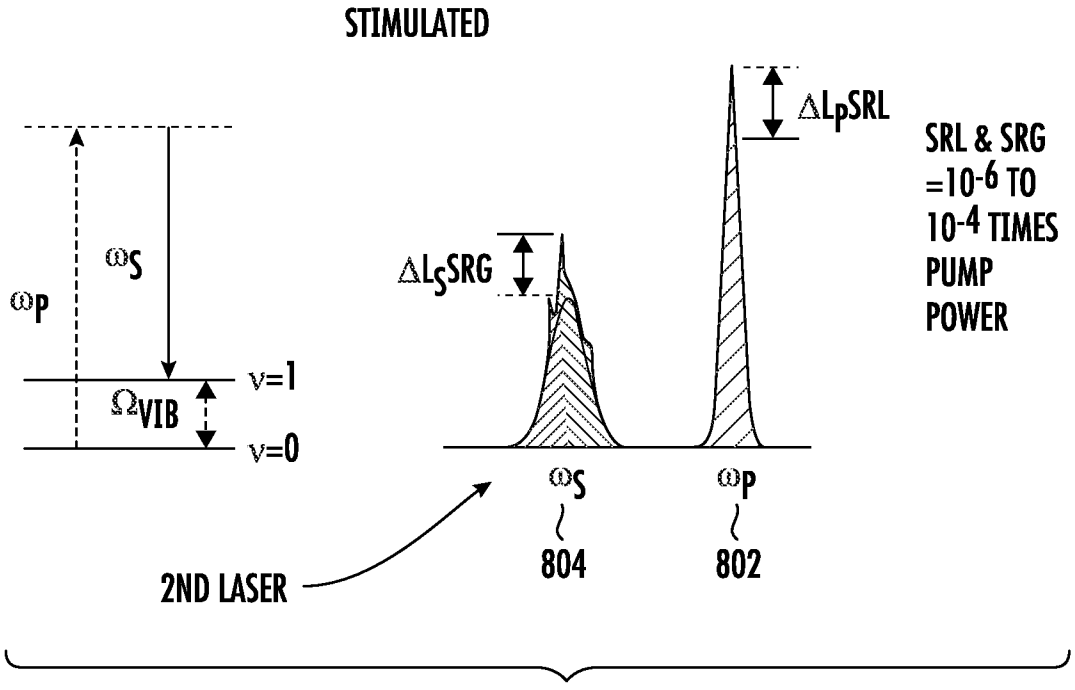

STIMULATED
ωS
ωP
ν=1
ΩVIB
ν=0
2ND LASER
ΔLSSRG
ΔLPSRL
SRL & SRG
=10-6 TO
10-4 TIMES
PUMP
POWER
ωS
ωP
804
802

FIG. 9B

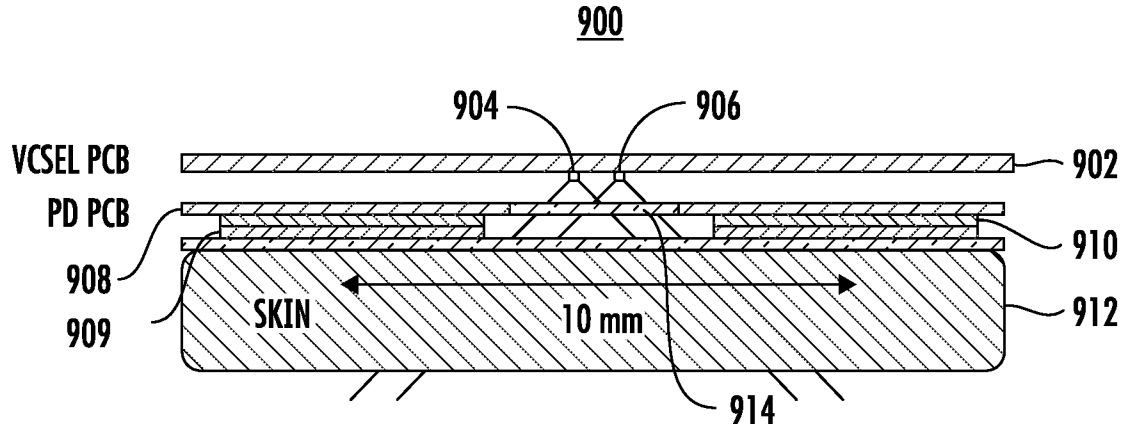


FIG. 10A

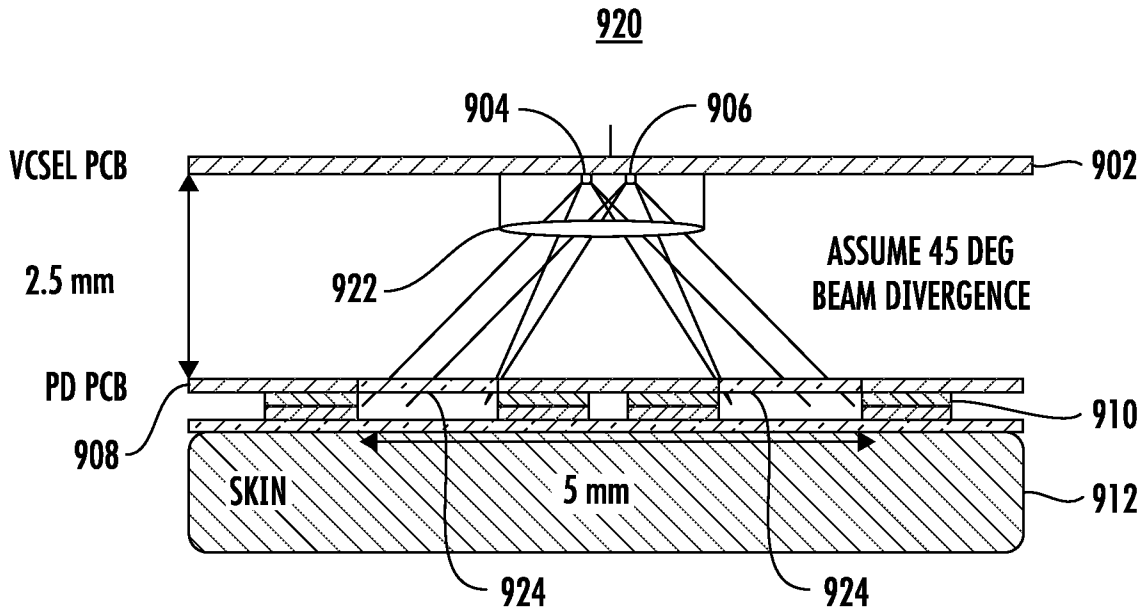


FIG. 10B

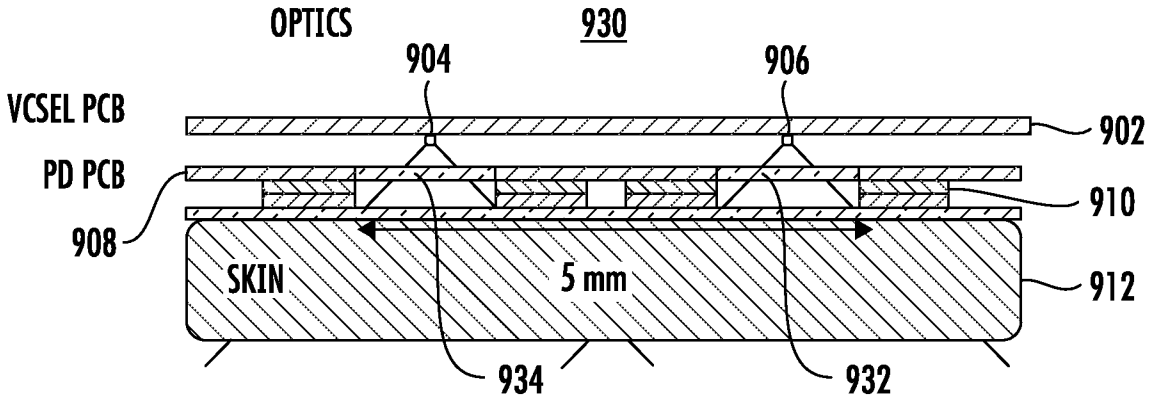


FIG. 10C

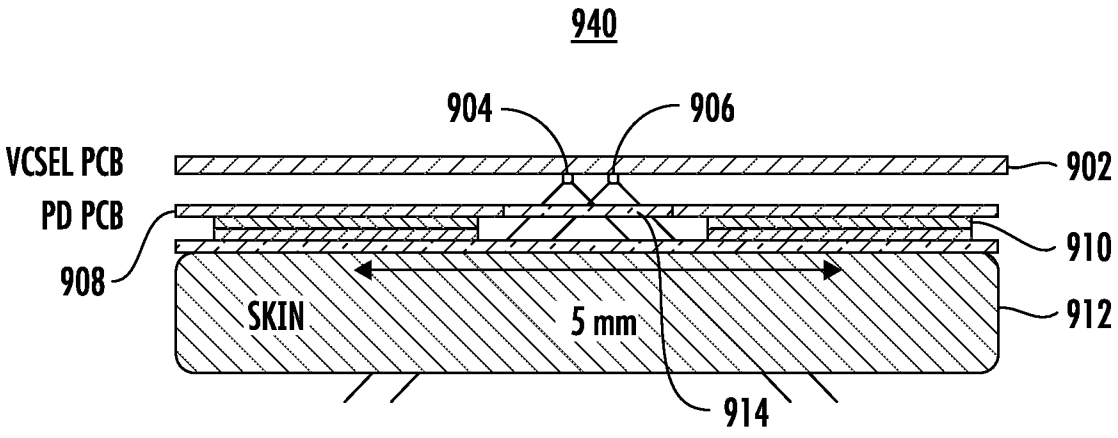


FIG. 10D

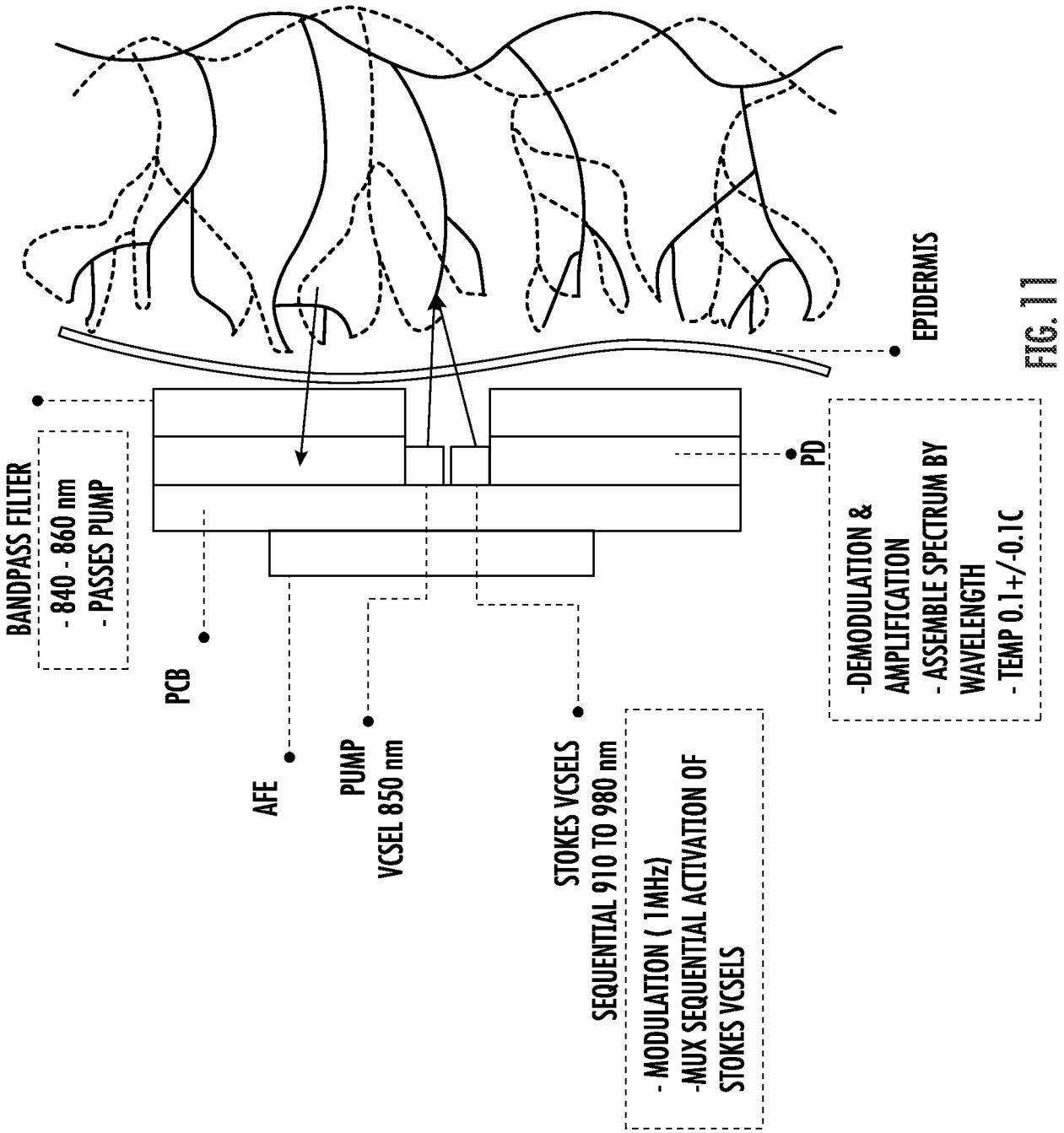

EPIDERMIS
BANDPASS FILTER
- 840 - 860 nm
- PASSES PUMP
PD
-DEMODULATION &
AMPLIFICATION
- ASSEMBLE SPECTRUM BY
WAVELENGTH
- TEMP 0.1+/-0.1C
PCB
AFE
PUMP
VCSEL 850 nm
STOKES VCSELS
SEQUENTIAL 910 TO 980 nm
- MODULATION (1 MHz)
-MUX SEQUENTIAL ACTIVATION OF
STOKES VCSELS

FIG. 11

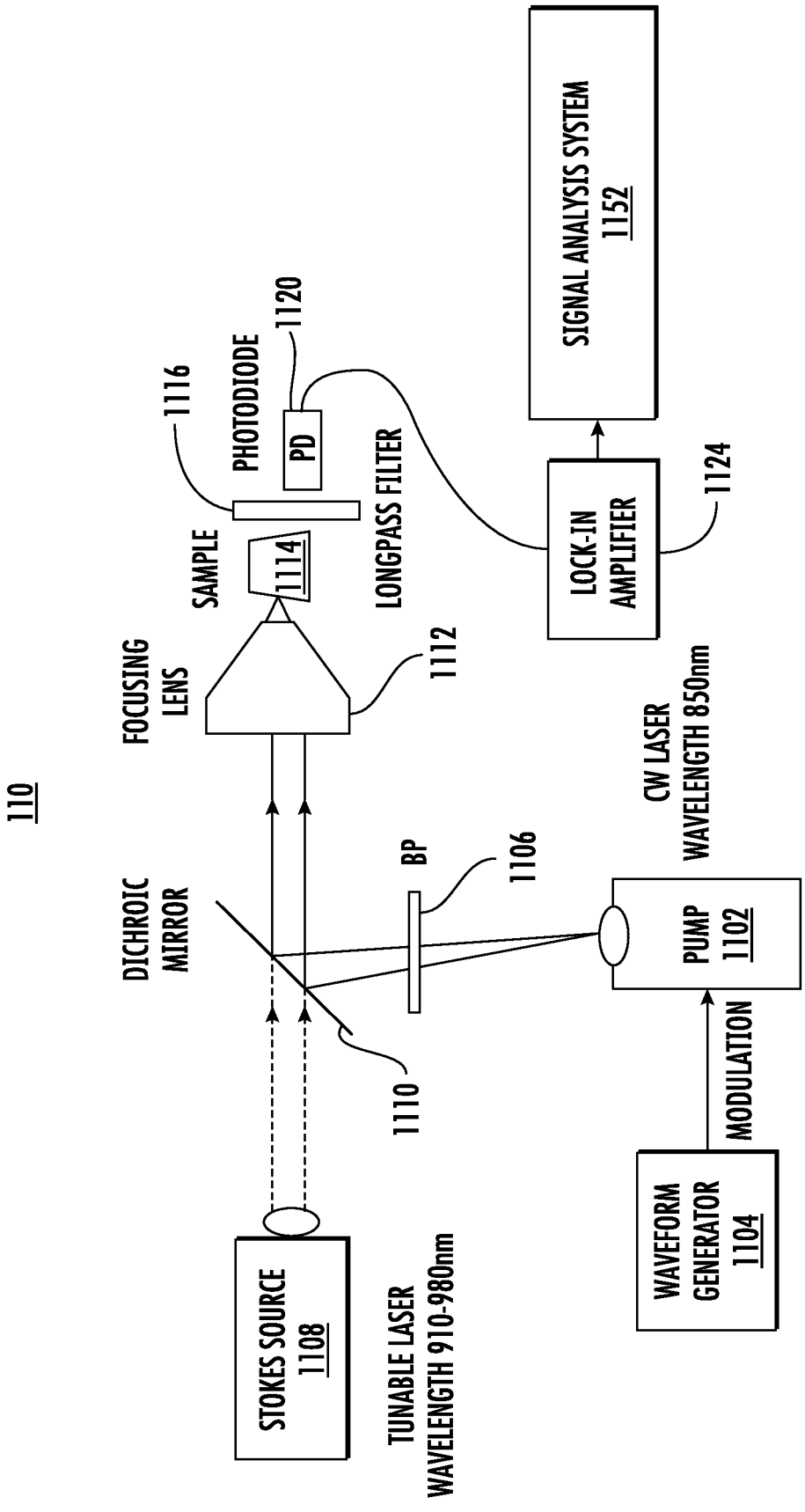

110
STOKES SOURCE 1108
TUNABLE LASER WAVELENGTH 910-980nm
WAVEFORM GENERATOR 1104
MODULATION
PUMP 1102
CW LASER WAVELENGTH 850nm
BP
1106
DICHROIC MIRROR
1110
FOCUSING LENS
1112
SAMPLE
1114
1116
PHOTODIODE
PD
1120
LONGPASS FILTER
LOCK-IN AMPLIFIER
1124
SIGNAL ANALYSIS SYSTEM 1152

FIG. 12A

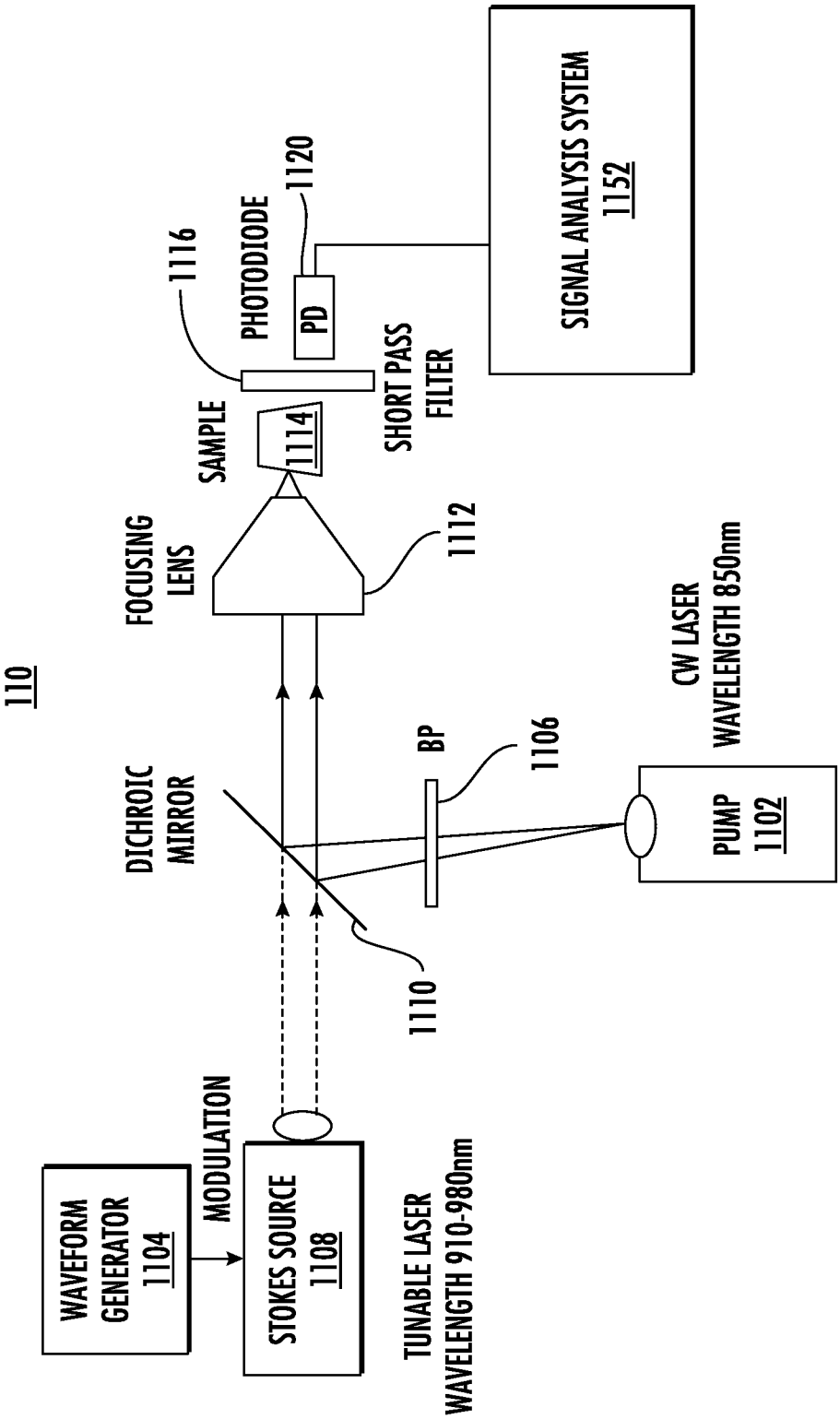

110
WAVEFORM GENERATOR 1104
MODULATION
STOKES SOURCE 1108
TUNABLE LASER WAVELENGTH 910-980nm
1110
DICHROIC MIRROR
BP
1106
CW LASER WAVELENGTH 850nm
PUMP 1102
FOCUSING LENS
1112
SAMPLE 1114
SHORT PASS FILTER
1116
PHOTODIODE
PD
1120
SIGNAL ANALYSIS SYSTEM 1152

FIG. 12B

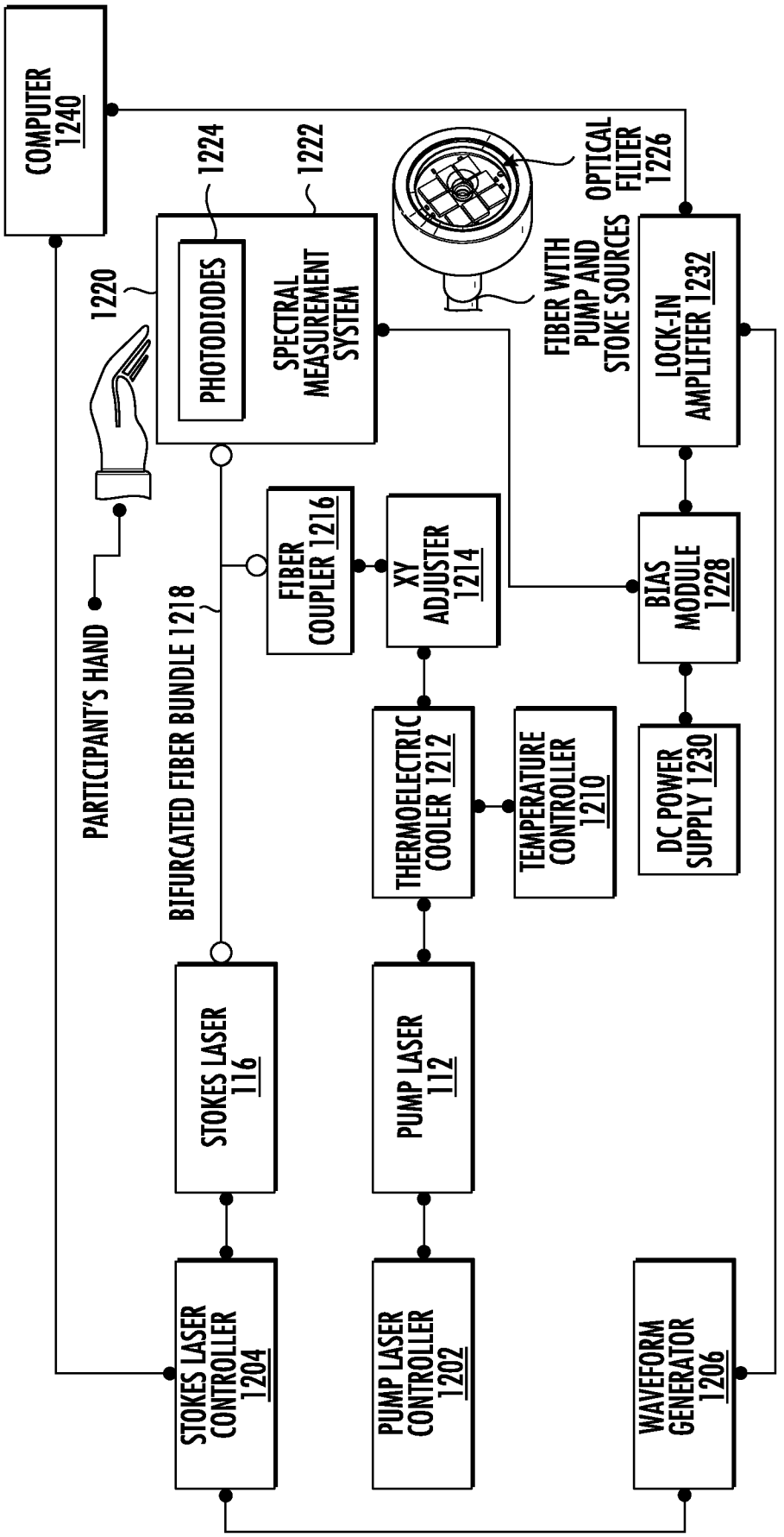

COMPUTER 1240
1224
1222
OPTICAL FILTER 1226
1220
PHOTODIODES
SPECTRAL MEASUREMENT SYSTEM
FIBER WITH PUMP AND STOKE SOURCES
LOCK-IN AMPLIFIER 1232
PARTICIPANT'S HAND
BIFURCATED FIBER BUNDLE 1218
FIBER COUPLER 1216
XY ADJUSTER 1214
BIAS MODULE 1228
THERMOELECTRIC COOLER 1212
TEMPERATURE CONTROLLER 1210
DC POWER SUPPLY 1230
STOKES LASER 116
PUMP LASER 112
STOKES LASER CONTROLLER 1204
PUMP LASER CONTROLLER 1202
WAVEFORM GENERATOR 1206

FIG. 13

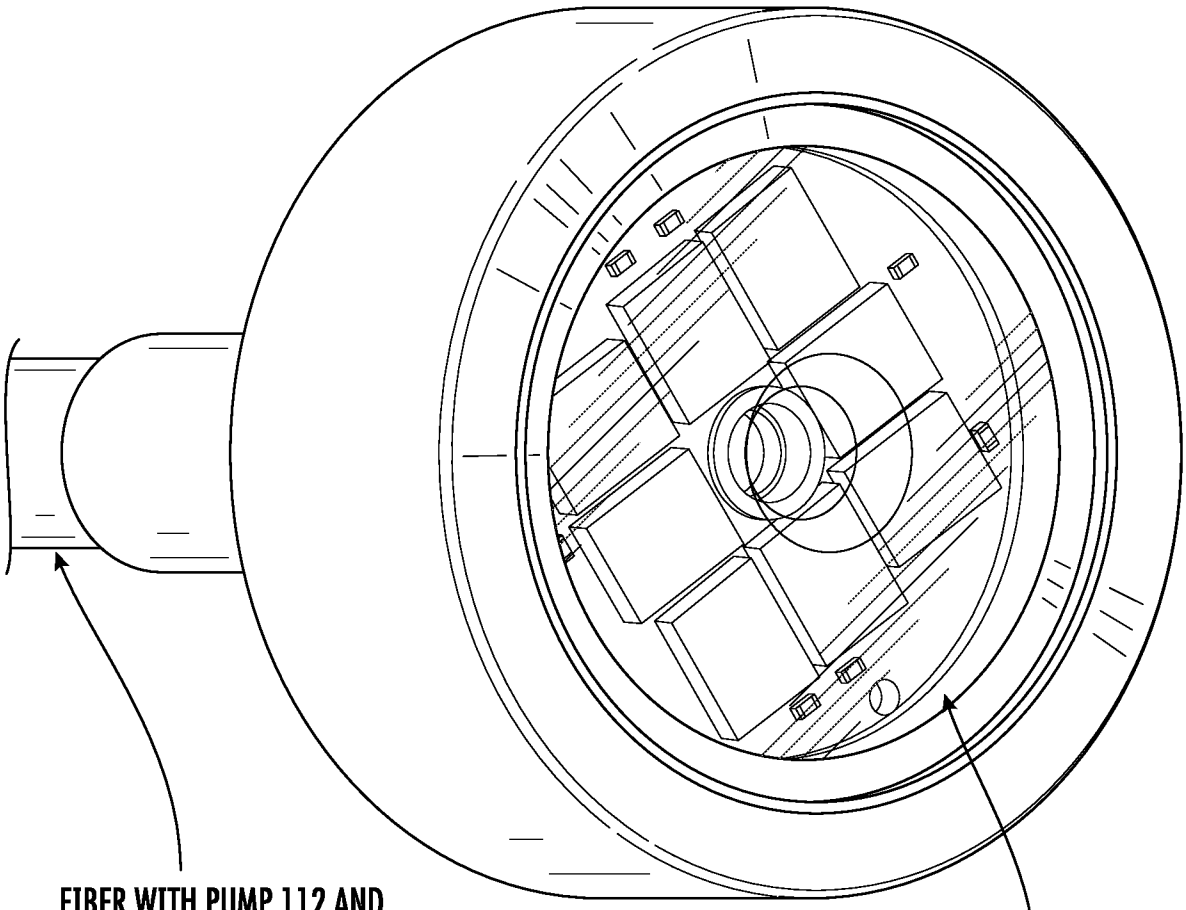

FIBER WITH PUMP 112 AND
STOKES SOURCES 116
OPTICAL FILTER
1304

FIG. 14

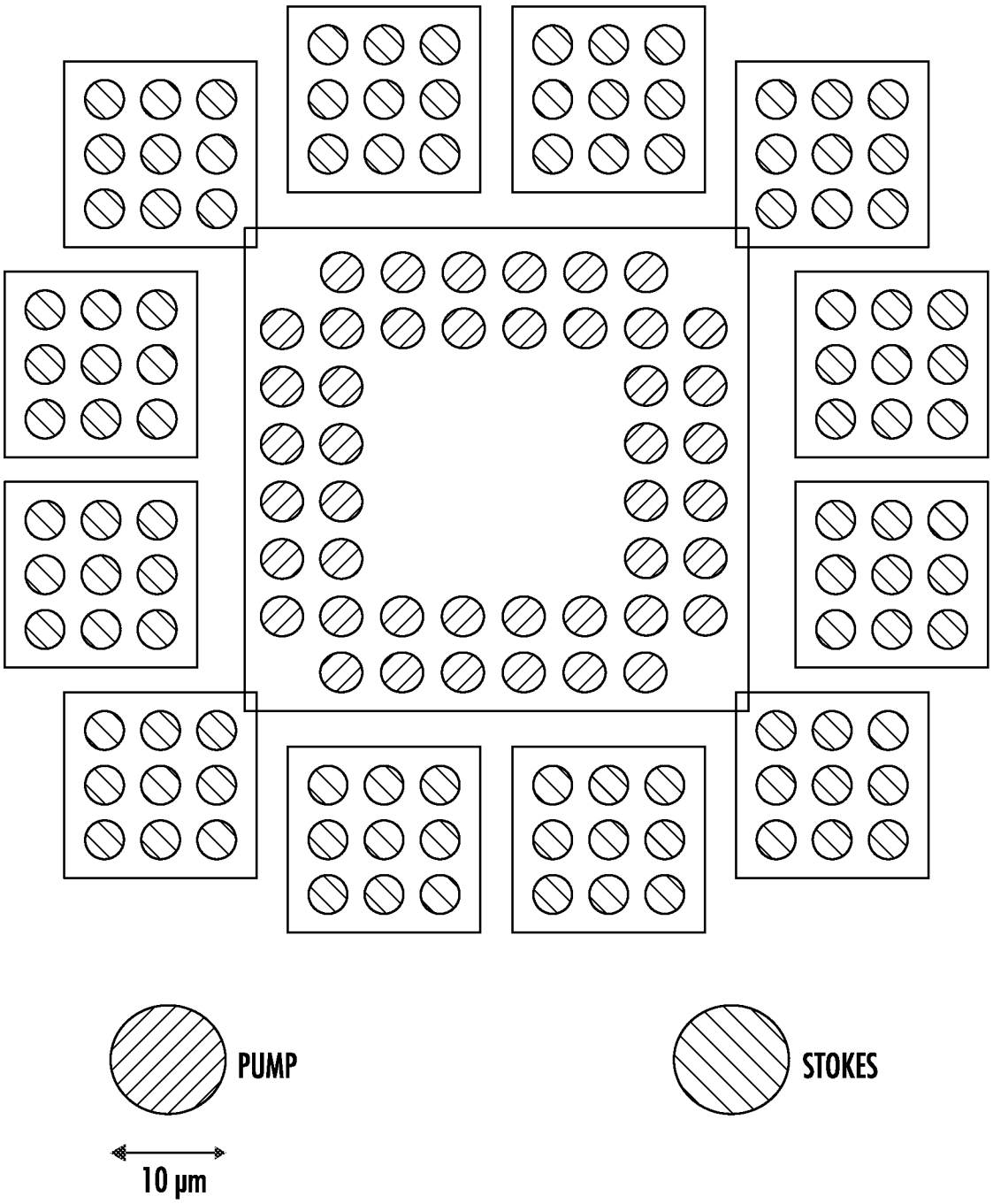


FIG. 15

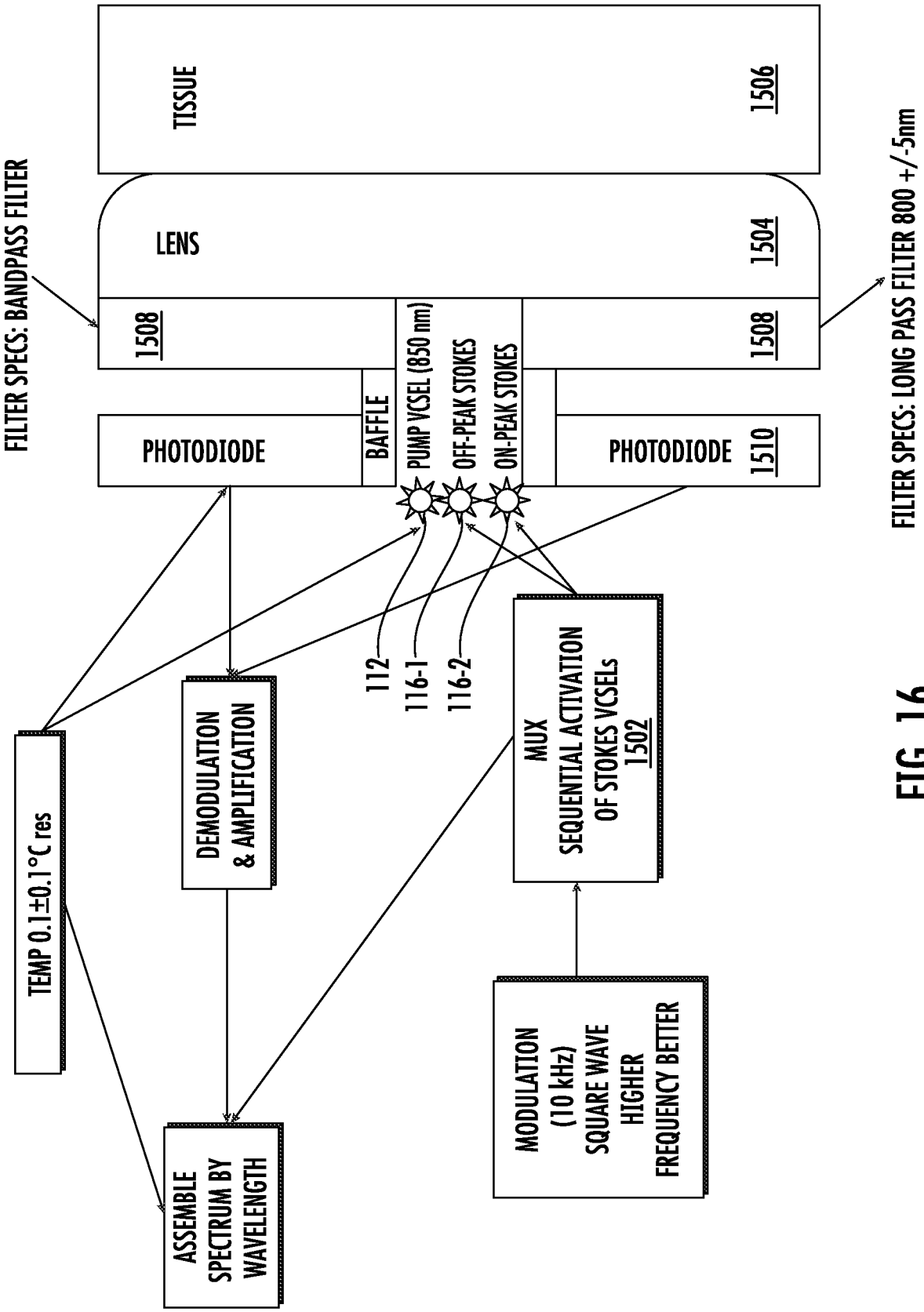

TISSUE
1506
LENS
1504
1508
PUMP VCSEL (850 nm)
OFF-PEAK STOKES
ON-PEAK STOKES
1508
PHOTODIODE
BAFFLE
PHOTODIODE
1510
FILTER SPECS: BANDPASS FILTER
FILTER SPECS: LONG PASS FILTER 800 +/-5nm
112
116-1
116-2
TEMP 0.1±0.1°C res
DEMODULATION & AMPLIFICATION
MUX SEQUENTIAL ACTIVATION OF STOKES VCSELs 1502
ASSEMBLE SPECTRUM BY WAVELENGTH
MODULATION (10 kHz) SQUARE WAVE HIGHER FREQUENCY BETTER

FIG. 16

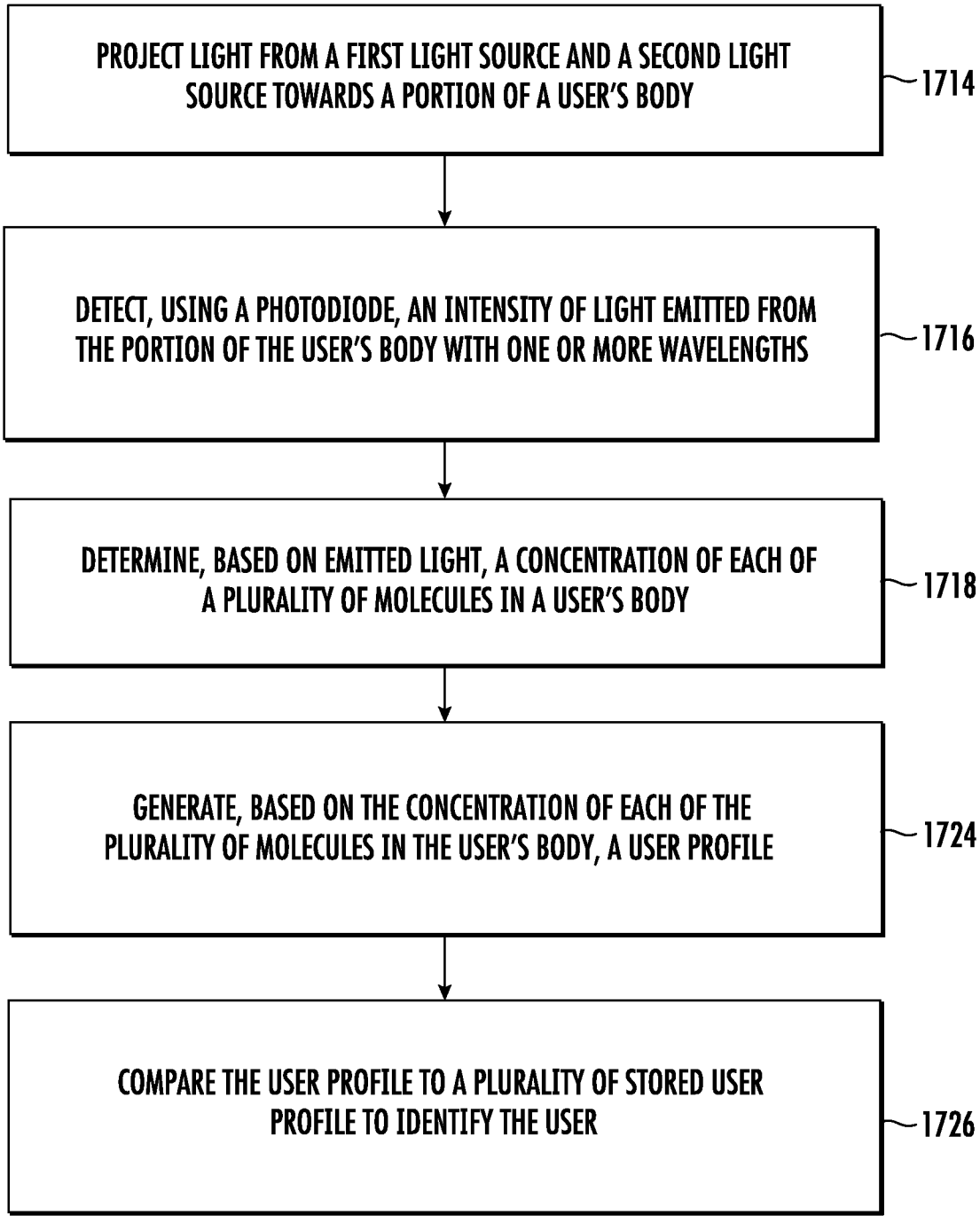

PROJECT LIGHT FROM A FIRST LIGHT SOURCE AND A SECOND LIGHT SOURCE TOWARDS A PORTION OF A USER'S BODY
1714
DETECT, USING A PHOTODIODE, AN INTENSITY OF LIGHT EMITTED FROM THE PORTION OF THE USER'S BODY WITH ONE OR MORE WAVELENGTHS
1716
DETERMINE, BASED ON EMITTED LIGHT, A CONCENTRATION OF EACH OF A PLURALITY OF MOLECULES IN A USER'S BODY
1718
GENERATE, BASED ON THE CONCENTRATION OF EACH OF THE PLURALITY OF MOLECULES IN THE USER'S BODY, A USER PROFILE
1724
COMPARE THE USER PROFILE TO A PLURALITY OF STORED USER PROFILE TO IDENTIFY THE USER
1726

FIG. 17

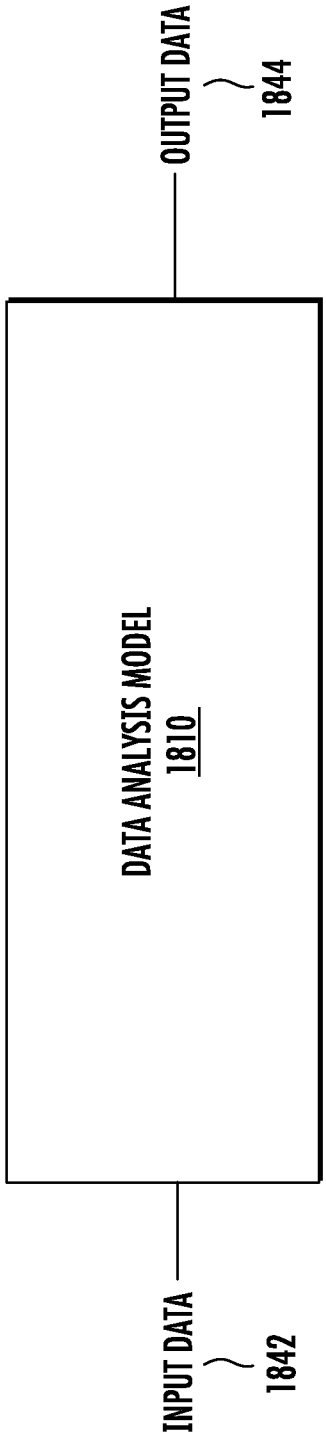


FIG. 18

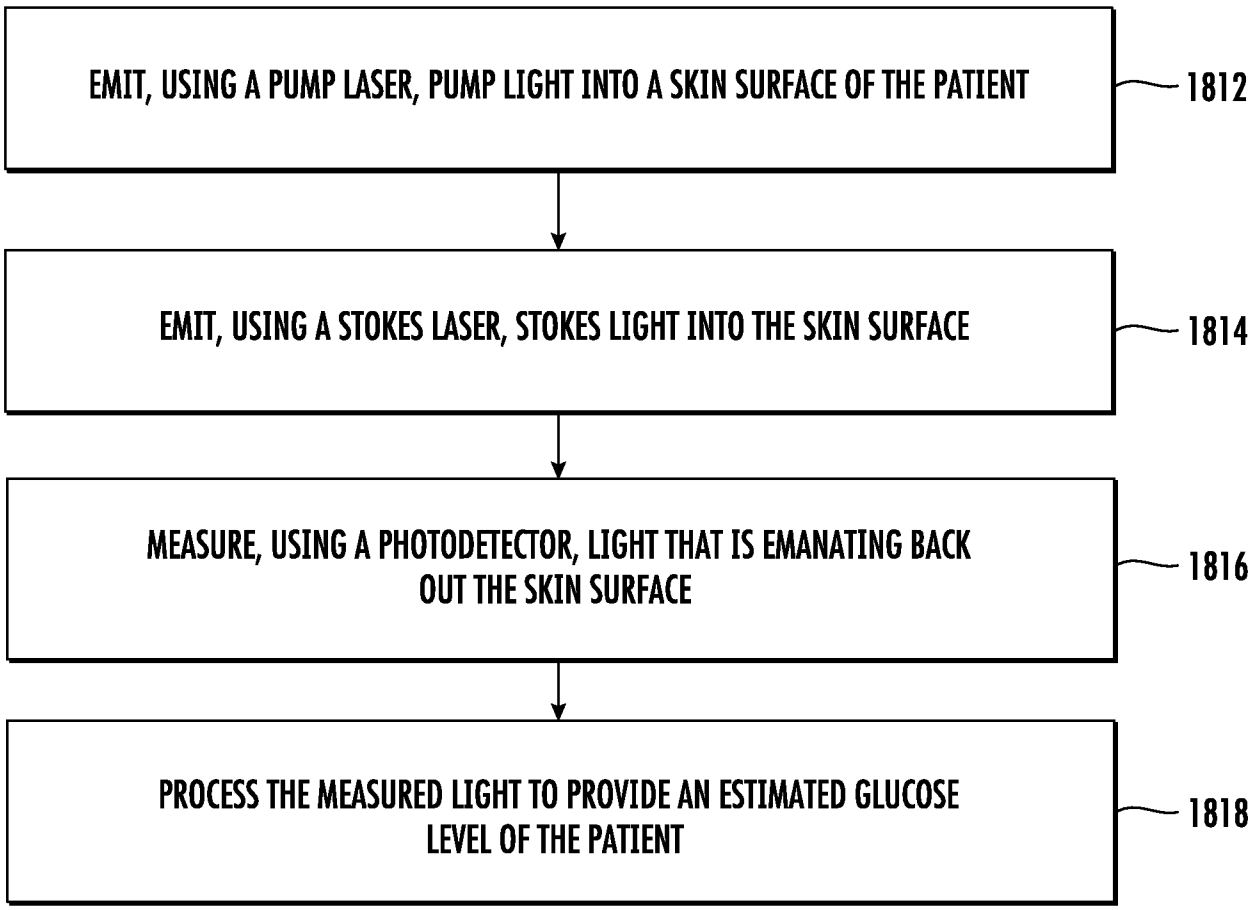

EMIT, USING A PUMP LASER, PUMP LIGHT INTO A SKIN SURFACE OF THE PATIENT
1812
EMIT, USING A STOKES LASER, STOKES LIGHT INTO THE SKIN SURFACE
1814
MEASURE, USING A PHOTODETECTOR, LIGHT THAT IS EMANATING BACK OUT THE SKIN SURFACE
1816
PROCESS THE MEASURED LIGHT TO PROVIDE AN ESTIMATED GLUCOSE LEVEL OF THE PATIENT
1818

FIG. 19

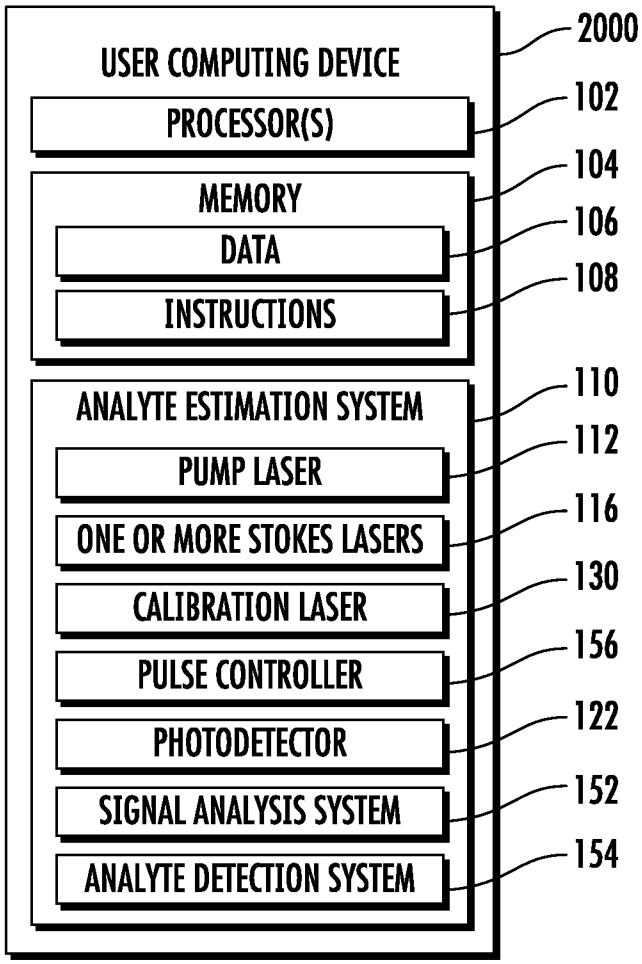

USER COMPUTING DEVICE
2000
PROCESSOR(S)
102
MEMORY
104
DATA
106
INSTRUCTIONS
108
ANALYTE ESTIMATION SYSTEM
110
PUMP LASER
112
ONE OR MORE STOKES LASERS
116
CALIBRATION LASER
130
PULSE CONTROLLER
156
PHOTODETECTOR
122
SIGNAL ANALYSIS SYSTEM
152
ANALYTE DETECTION SYSTEM
154

FIG. 20

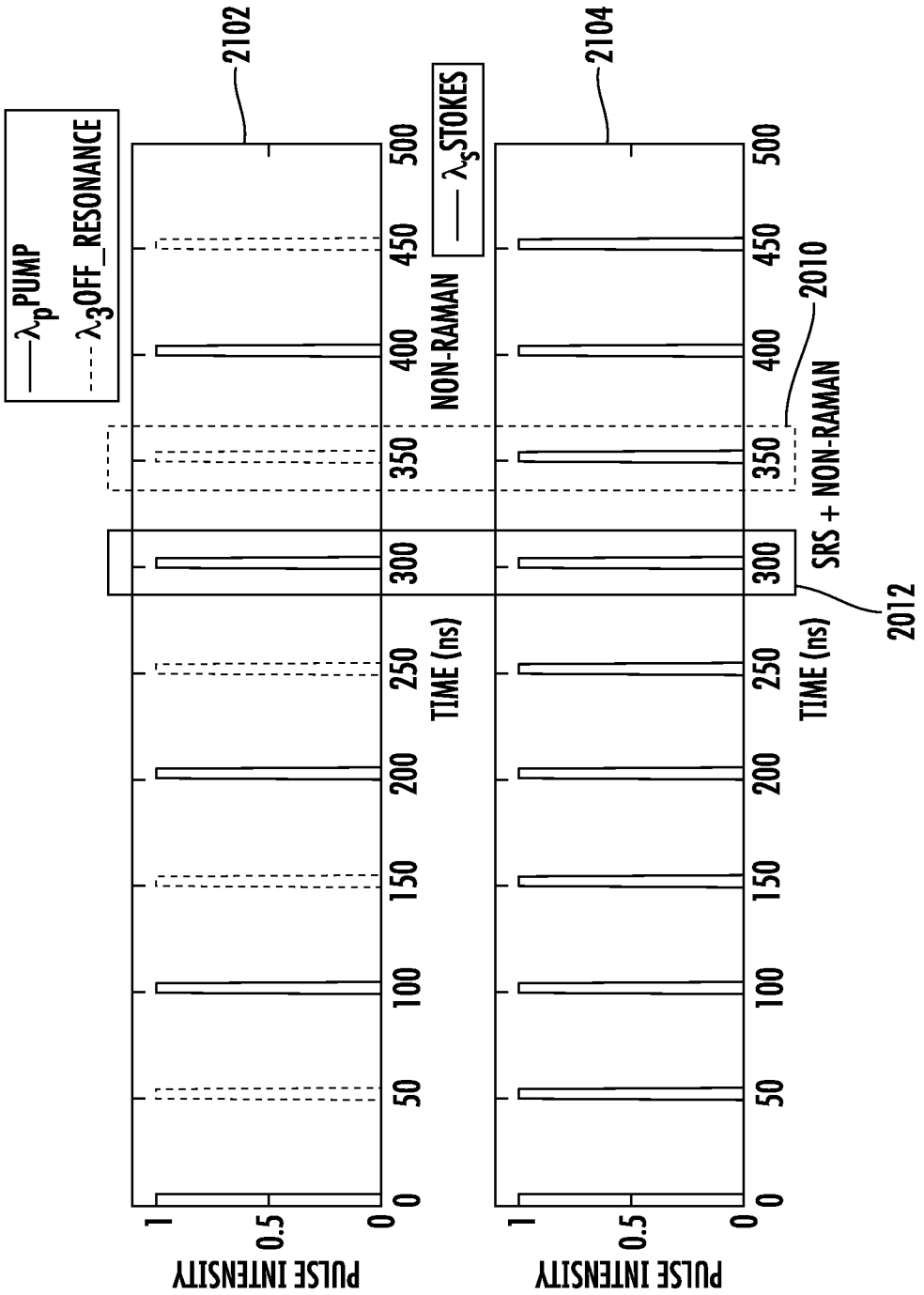

2102
2104
λ_pPUMP
λ_3OFF_RESONANCE
λ_sSTOKES
NON-RAMAN
SRS + NON-RAMAN
2010
2012
TIME (ns)
TIME (ns)
PULSE INTENSITY
PULSE INTENSITY
0
50
100
150
200
250
300
350
400
450
500
0
0.5
1

FIG. 21

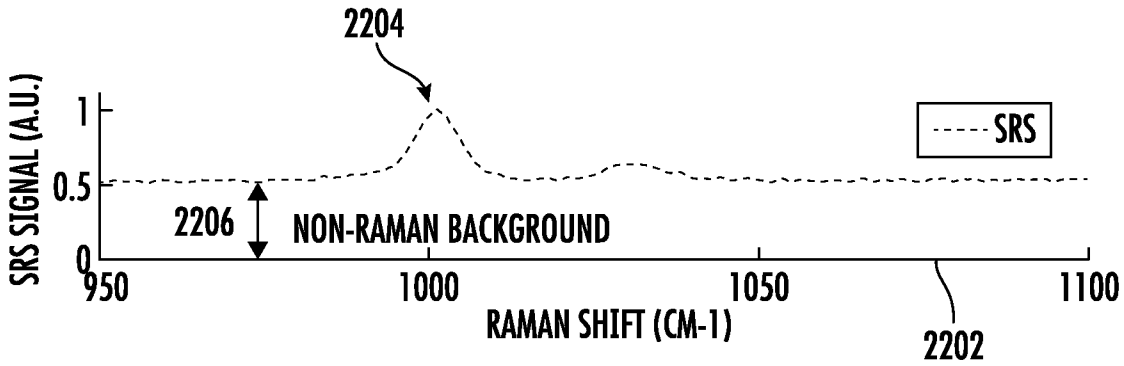


FIG. 22A

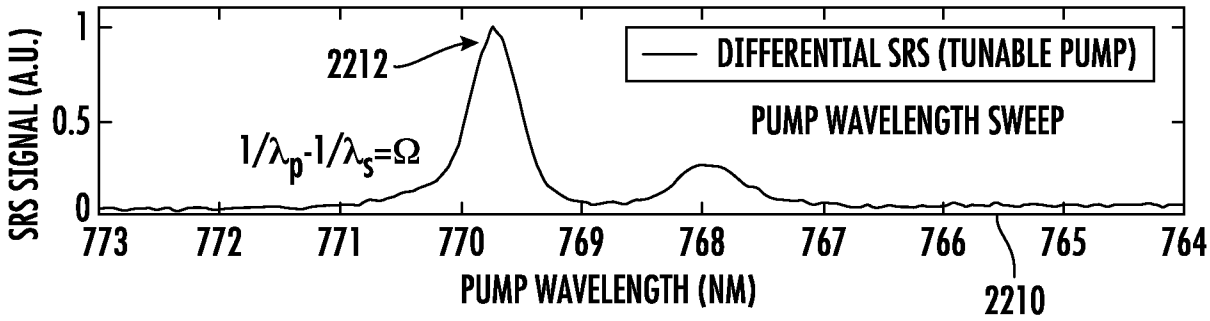


FIG. 22B

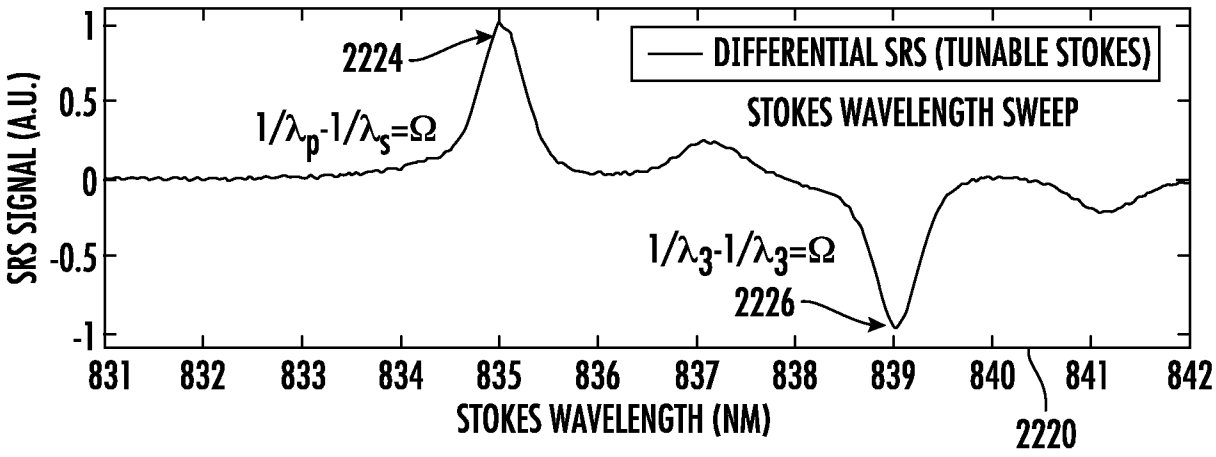

SRS SIGNAL (A.U.)
1
0.5
0
-0.5
-1
2224
$1/\lambda_p - 1/\lambda_s = \Omega$
DIFFERENTIAL SRS (TUNABLE STOKES)
STOKES WAVELENGTH SWEEP
$1/\lambda_3 - 1/\lambda_3 = \Omega$
2226
831
832
833
834
835
836
837
838
839
840
841
842
STOKES WAVELENGTH (NM)
2220

FIG. 22C

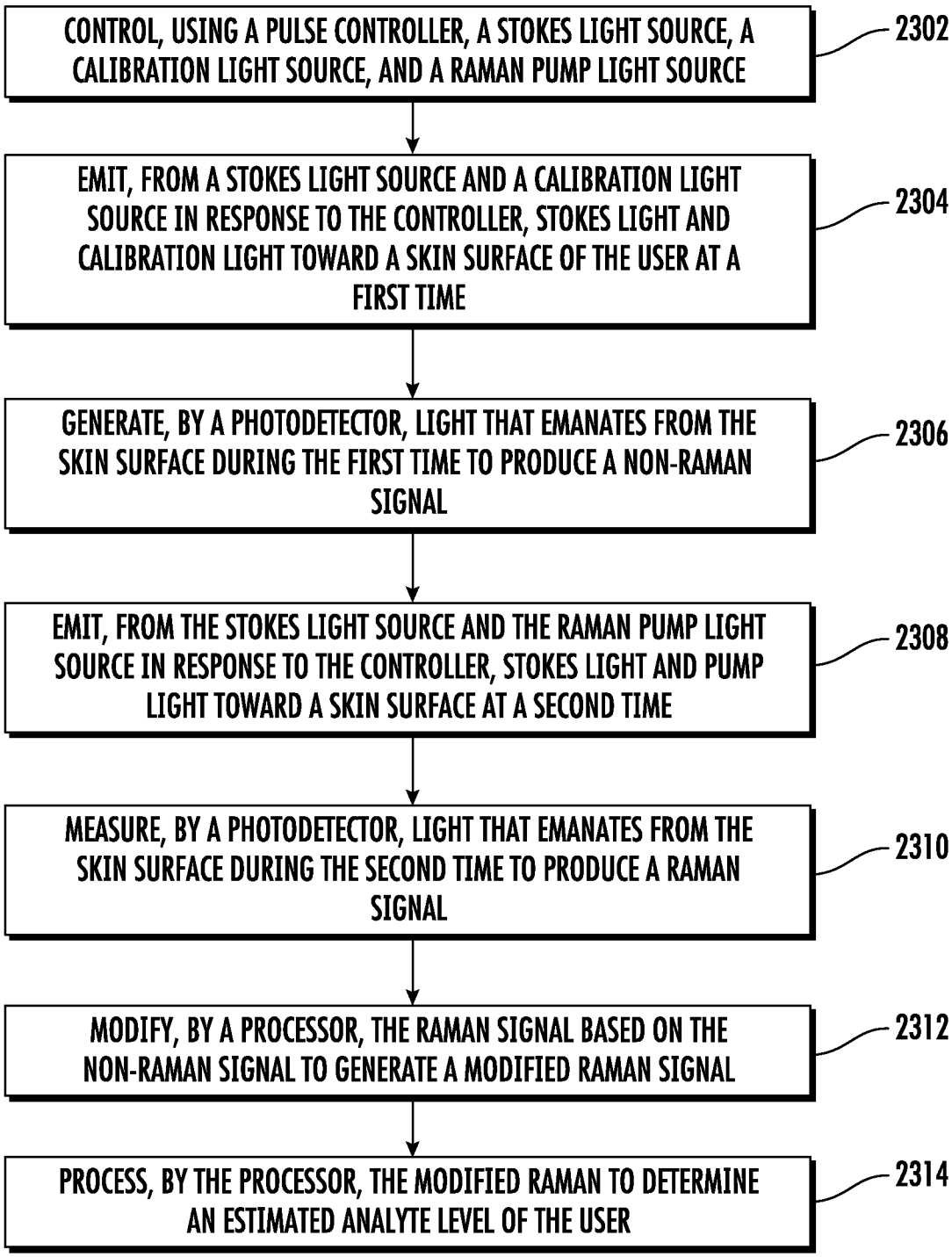

CONTROL, USING A PULSE CONTROLLER, A STOKES LIGHT SOURCE, A CALIBRATION LIGHT SOURCE, AND A RAMAN PUMP LIGHT SOURCE
2302
EMIT, FROM A STOKES LIGHT SOURCE AND A CALIBRATION LIGHT SOURCE IN RESPONSE TO THE CONTROLLER, STOKES LIGHT AND CALIBRATION LIGHT TOWARD A SKIN SURFACE OF THE USER AT A FIRST TIME
2304
GENERATE, BY A PHOTODETECTOR, LIGHT THAT EMANATES FROM THE SKIN SURFACE DURING THE FIRST TIME TO PRODUCE A NON-RAMAN SIGNAL
2306
EMIT, FROM THE STOKES LIGHT SOURCE AND THE RAMAN PUMP LIGHT SOURCE IN RESPONSE TO THE CONTROLLER, STOKES LIGHT AND PUMP LIGHT TOWARD A SKIN SURFACE AT A SECOND TIME
2308
MEASURE, BY A PHOTODETECTOR, LIGHT THAT EMANATES FROM THE SKIN SURFACE DURING THE SECOND TIME TO PRODUCE A RAMAN SIGNAL
2310
MODIFY, BY A PROCESSOR, THE RAMAN SIGNAL BASED ON THE NON-RAMAN SIGNAL TO GENERATE A MODIFIED RAMAN SIGNAL
2312
PROCESS, BY THE PROCESSOR, THE MODIFIED RAMAN TO DETERMINE AN ESTIMATED ANALYTE LEVEL OF THE USER
2314

FIG. 23

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2023/085392

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61B5/00 A61B5/1455 A61B5/1495 G01N21/65
ADD. A61B5/145

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2017/122874 A1 (ALON RAM [IL] ET AL) 4 May 2017 (2017-05-04)	1-3, 7-10,12, 14-20
Y	paragraph [0033] - paragraph [0035] paragraph [0044] - paragraph [0055] paragraph [0082] - paragraph [0154] figures 1-10	11,13

Y	WO 2014/190331 A2 (UNIV CORNELL [US]) 27 November 2014 (2014-11-27)	13
A	paragraph [0015] paragraph [0048] - paragraph [0055]	1-12, 14-20

Y	WO 2023/196388 A2 (GOOGLE LLC [US]) 12 October 2023 (2023-10-12)	11
A	paragraph [0046] - paragraph [0055] paragraph [0082] - paragraph [0090] figures 1A-2	1-10, 12-20

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance;; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance;; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 June 2024	26/06/2024

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Görlach, Tobias

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2023/085392

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2017122874 A1	04-05-2017	EP 3123128 A1	01-02-2017
		US 2017122874 A1	04-05-2017
		WO 2015145429 A1	01-10-2015
WO 2014190331 A2	27-11-2014	NONE	
WO 2023196388 A2	12-10-2023	NONE	