(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
31 December 2008 (31.12.2008)

PCT

(10) International Publication Number
WO 2009/002452 A1

(51) International Patent Classification:
A61B 5/05 (2006.01)

(21) International Application Number:
PCT/US2008/007715

(22) International Filing Date: 21 June 2008 (21.06.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/936,782 22 June 2007 (22.06.2007) US
61/124,169 15 April 2008 (15.04.2008) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(54) Title: ORTHOGONAL REFERENCE ANALYSIS SYSTEM WITH ENHANCED SNR

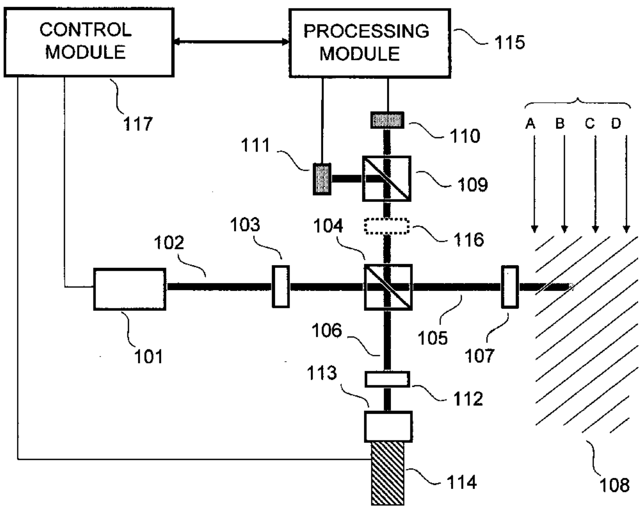

Figure 1

(57) Abstract: A method, apparatus and system for non-invasive imagining and analysis involves generating probe radiation and reference radiation that have orthogonal polarization characteristics and controlling the polarization characteristics such that substantially all the back scattered probe radiation co-propagates with controlled amounts of components of the reference radiation, thereby improving signal to noise ratios and hence performance of imaging and analysis systems. A preferred embodiment of the invention includes a rotational sensitive mirror that systematically rotates the polarization vector of higher order components of the reference radiation.

WO 2009/002452 A1

Title: **Orthogonal Reference Analysis System with Enhanced SNR**

CROSS REFERENCES TO RELATED APPLICATIONS

[0001] This patent application, docket number JH080620PT, claims priority from provisional patent application number 60/936,782 entitled "Orthogonal Reference OCT System" filed on 22nd. June 2007 and also claims priority from provisional patent application number 61/124,169 entitled "An Analysis System with Enhanced SNR" filed on 15th. April 2008.

FIELD OF THE INVENTION

[0002] The invention relates to non-invasive imaging and analysis techniques such as Optical Coherence Tomography (OCT). In particular it relates to optical imaging and analysis of defects or malignant aspects of targets, such as cancer in skin or human tissue; or monitoring for possible malignancies in organs, such as the eye.

[0003] This invention also relates to non-invasive analysis of concentrations of specific components or analytes in a target, such as the concentration of glucose in blood, tissue fluids, tissue, or components of an eye or other biological entities. This invention also relates to analysis or monitoring for manufacturing defects in components for improved quality control.

BACKGROUND OF THE INVENTION

[0004] Non-invasive analysis of targets is a valuable technique for acquiring information about systems or targets without undesirable side effects, such as damaging the target or system being analyzed. In the case of analyzing living entities, such as human tissue, undesirable side effects of invasive analysis include the risk of infection along with pain and discomfort associated with the invasive process. In the case of quality control, it enables non-destructive imaging and analysis on a routine basis, for example, for quality control purposes.

[0005] Optical coherence tomography (OCT), is a technology for non-invasive imaging and analysis. OCT typically uses a broadband optical source, such as a super-luminescent diode (SLD), to probe and analyze or image a target. It does so by applying probe radiation from the optical source to the target and interferometrically combining back scattered probe radiation from the target with reference radiation also derived from the optical source.

[0006] The typical OCT optical output beam has a broad bandwidth and short coherence length. The OCT technique involves splitting the output beam into a probe and reference beam, typically by means of a beam splitter, such as a pellicle, a beam splitter cube or a fiber coupler. The probe beam is applied to the system to be analyzed (the target). Light is scattered by the target, some of which is back scattered to form a back scattered probe beam, herein referred to as signal radiation.

[0007] The reference beam is typically reflected back to the beam splitter by a mirror. Light scattered back from the target is combined with the reference beam, also referred to as reference radiation, by the beam splitter to form co-propagating reference radiation and signal radiation. Because of the short coherence length only light that is scattered from a depth within the target whose optical path length is substantially equal to the path length to the reference mirror can generate a meaningful interferometric signal.

[0008] Thus the interferometric signal provides a measurement of scattering properties at a particular depth within the target. By varying the magnitude of the reference path length (by moving the reference mirror) in a conventional time domain OCT system, a measurement of the scattering values at various depths can be determined and thus the scattering value as a function of depth can be determined, i.e. the target can be scanned.

[0009] The reference radiation is typically reflected from a mirror. In addition to generating a useful interferometric signal, the reference radiation also contributes to generating noise in the detector which degrades the signal to noise ratio and hence performance of the system. In order to optimize the signal to noise ratio of typical OCT imaging and analysis systems the magnitude of the reference radiation should be arranged to be compatible with the magnitude of the back scattered optical radiation also referred to herein as the signal radiation.

[0010] This is typically achieved in conventional OCT systems by including a fixed attenuation element in the reference beam path. The magnitude of the fixed attenuator is typically selected to maximize signal to noise performance. This involves a compromise between having a low attenuator value to maximize the amplification of the back scattered radiation (by having a high intensity reference level) and having a high attenuator value to minimize the detector noise associated with a high intensity reference level.

[0011] The attenuation level is typically selected as a compromise between these two competing considerations. This technique is described in the paper titled "A Simple Intensity Noise Reduction Technique for Optical Low-Coherence Reflectometry" by authors W. V. Sorin and D. M. Baney published in IEEE PHOTONICS TECHNOLOGY LETTERS, Vol. 4, No. 12, Pages 1404 -1406, December 1992.

[0012] This compromise is further exacerbated in the multiple reference analysis systems and frequency resolved imaging systems described in patent application 11/025,698 filed on 29th. Dec. 2004 titled "A Multiple Reference Analysis System" and patent application 11/048,694 filed on 31st. Jan. 2005 titled "Frequency Resolved Imaging".

[0013] In such systems there is typically a significant portion of the reference radiation that is unwanted or valueless for signal detection and therefore only contributes to generating detector noise and hence degrades the signal to noise ratio, commonly abbreviated as SNR.

[0014] Various techniques for minimizing the magnitude of the portion of the reference radiation that is unwanted or valueless for signal detection are described in patent application 11/789,278 filed on 23rd. Apr. 2007 titled "Optimized Reference Level Generation". These techniques, however, add additional complexity and cost to such systems.

[0015] Furthermore, typical OCT systems use a non-polarized beam splitter to generate probe and reference radiation. A disadvantage of this approach is that because the beam splitter is non-polarized typically only fifty percent of the back-scattered probe radiation is directed towards the detector, thus reducing the achievable signal to noise ratio of the analysis system.

[0016] Other OCT systems, such as Fourier domain OCT using either a wavelength scanning swept source or a diffraction grating (spectrometer) for wavelength separation, similarly have components of the reference radiation that are not useful for signal detection and therefore only contribute to generating detector noise. In the case of Fourier domain OCT using a diffraction grating, this further exacerbates a problematic "DC component" in the interference signal.

[0017] With all of the above approaches, there is a compromise between combining a maximum amount of the scattered probe radiation with an optimum intensity reference radiation so as to optimize signal to noise aspects of the analysis system. These approaches suffer from either additional complexity or introduce problematic noise generating aspects associated with unwanted or valueless co-propagating reference radiation components.

[0018] There is therefore an unmet need for a method, apparatus and system for combining a maximum amount of the scattered probe radiation with an optimized amount of reference radiation or reference radiation components while minimizing the problematic noise generating aspects of unwanted or valueless co-propagating reference radiation components at one or more detectors, such a method, apparatus and system providing enhanced signal to noise ratios and thereby improved non-invasive analysis system.

SUMMARY OF THE INVENTION

[0019] The invention taught herein meets at least all of the aforementioned unmet needs. The invention provides a method, apparatus and system for non-invasive imagining and analysis wherein generated probe radiation and reference radiation have orthogonal polarization characteristics. In the embodiments taught herein scattered probe radiation forms signal radiation.

[0020] Polarization characteristics are controlled such that substantially all the signal radiation co-propagates with controlled or modified amounts of components of the reference radiation, thereby improving signal to noise ratios. Improved signal to noise ratios enhance the imaging and analysis capability of the inventive system.

[0021] The preferred embodiment of the invention includes a rotational sensitive mirror that systematically rotates the polarization vector of higher order components of the reference radiation. The inventive method for analyzing a target of interest includes the steps generating probe radiation and reference radiation that have orthogonal polarization characteristics; modifying the polarization characteristics; capturing at least part of the probe radiation scattered from within the target to form signal radiation; combining the signal radiation and at least some of the reference radiation to form co-propagating radiation, wherein said co-propagating radiation is composed of maximized signal radiation and optimized amounts of reference radiation components; detecting at least one interferometric signal generated by at least part of the co-propagating radiation to form an electronic signal; and processing the electronic signal to achieve non-invasive analysis of the target.

[0022] In the preferred embodiment of the invention polarization characteristics are modified to maximize signal radiation by rotating the polarization vector of the signal radiation.

Polarization characteristics are also modified by rotating at least some of the polarization vectors of components of the reference radiation by means of a rotational sensitive mirror whereby those co-propagating components corresponding to at least some deeper regions of the target have larger magnitudes than co-propagating components corresponding to less deep regions of the target thereby forming optimized amounts of reference radiation components.

[0023] The magnitude of the "DC component" of reference radiation co-propagating with the signal radiation and other components of the reference radiation is minimized thereby further optimizing the reference radiation co-propagating with the signal radiation to one or more detectors.

[0024] An alternate embodiment of the invention includes a polarized beam splitter with a finite extinction ratio that allows an attenuated portion of the reference radiation to co-propagate with the signal radiation to a detector. In this embodiment the co-propagating radiation that reaches the detector is composed of maximized signal radiation and optimized amounts of reference radiation components or reference radiation components.

[0025] The preferred system includes a broadband optical source, such as an SLD which, generates broadband collimated output radiation which is applied to a polarization optic which may be either a half wave plate or a quarter wave plate. The resulting radiation is applied to a first polarized beam-splitter to generate probe radiation and reference radiation that have orthogonal linear polarization. The probe radiation is passed through a quarter wave plate and applied to the target. Back-scattered radiation from the target again passes through the quarter wave plate and is applied to the first polarized beam-splitter to form signal radiation directed towards a detection system.

[0026] The reference radiation is directed through a partially reflective mirror to a rotational sensitive mirror mounted on a modulating device. Multiple reflections between the partially reflective mirror and the rotational sensitive mirror generate multiple components or orders of reference radiation. The rotational sensitive mirror systematically rotates the plane of polarization with each reflection to generate reference radiation such that larger magnitudes of higher order components pass through the first polarized beam splitter to co-propagate with the signal radiation.

[0027] Substantially all of the radiation reflected from the partially reflective mirror back towards the first polarized beam splitter is directed by the first polarized beam splitter away from the detection system. The co-propagating radiation comprised of signal and reference radiation is applied to a second polarized beam splitter, oriented at 45 degrees to generate true and complementary or balanced interference signals in a pair of detectors.

[0028] The alternate embodiment of the system is in many respects similar to the preferred system, however the alternate embodiment uses a conventional high reflective mirror in place of the rotational sensitive mirror of the preferred embodiment. Leakage through a polarized beam splitter with a finite extinction ratio enables reference radiation or reference radiation components to co-propagate with the signal radiation and generate an interference signal in a detector.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig 1 is an illustration of a preferred embodiment of the analysis system according to the invention.

Fig 2 is an illustration of the sequential systematic rotation of linearly polarized radiation by a rotational sensitive mirror.

Fig 3 is an illustration of an alternative embodiment of the analysis system according to the invention.

Fig 4 is an illustration of yet another embodiment of the inventive system.

Fig 5 is an illustration of the inventive system in a conventional time domain OCT application.

Fig 6 is an illustration of the inventive system in a Fourier domain OCT system.

DETAILED DESCRIPTION OF THE INVENTION

[0029] A preferred embodiment of this invention is illustrated in and described with reference to Figure 1. The preferred embodiment includes a broadband optical source 101, such as an SLD which, generates broadband collimated output radiation 102 which is applied a polarization optic 103. The polarization optic 103 may be either a half wave plate or a quarter wave plate. In the case of a half wave plate, the half wave plate rotates the polarization of the output radiation 102 such that when the output radiation 102 is applied to a polarized beam-splitter 104, the radiation 102 is split into probe radiation 105 and reference radiation 106.

[0030] In the case that the polarization optic 103 is a quarter wave plate, the quarter wave plate transforms linearly polarized radiation onto circularly polarized radiation such that when the output radiation 102 is applied to a polarized beam-splitter 104, the radiation 102 is split into probe radiation 105 and reference radiation 106.

[0031] The probe radiation 105 and reference radiation 106 have orthogonal polarization characteristics: they are both linearly polarized and are orthogonally linearly polarized with respect to each other. The electric field vector of one is orthogonal to the electric field vector of the other and the magnetic field vector of one is orthogonal to the magnetic field vector of the other thus constituting two orthogonal polarization characteristics. A consequence of being orthogonally linearly polarized is that, if they are combined, for example by a beam-splitter, they may not generate an interference signal. For purposes of this invention "interference signal" and "interferometric signal" are equivalent and interchangeable and can refer to a composite signal which can include multiple interference signals, typically each in a different frequency range.

[0032] The probe radiation 105 is passed through a quarter wave plate 107 and applied to the target 108. Back-scattered radiation from the target again passes through the quarter wave plate 107 and is applied to the polarized beam-splitter 104. This back-scattered radiation applied to or "captured" by the beam-splitter 104 is herein referred to as signal radiation.

[0033] The double pass of radiation through the quarter wave-plate 107 rotates the polarization of this signal radiation by ninety degrees such that it is now directed by the polarized beam-splitter 104 towards a second polarized beam-splitter 109 and a detector 110.

The second polarized beam-splitter 109, can also direct the signal radiation towards an optional second detector 111.

[0034] The reference radiation 106 is directed to a partial reflective element 112 and a second reflective element 113 mounted on a modulating device 114. The modulating device may be a Piezo device or voice coil that translates the reflective element 113 along the line of propagation of the reference radiation. The reference radiation undergoes multiple reflections between the partial reflective element 112 and the second reflective element 113 to form composite or multiple reference radiation.

[0035] Further description of generation of composite or multiple reference radiation can be found in patent applications 11/025,698 filed on 29th. Dec. 2004 titled "A Multiple Reference Analysis System" and 11/048,694 filed on 31st. Jan. 2005 titled "Frequency Resolved Imaging".

[0036] In the preferred embodiment the second reflective element 113 is highly reflective for linear polarization radiation at a first rotational orientation of the mirror about the axis normal to the mirror and its equivalent orientation 180 degrees from the first rotational orientation. The reflectivity of this rotational sensitive mirror decreases as it is rotated about the normal axis, reaching a minimum when it is substantially 90 degrees rotated from the first rotational orientation.

[0037] The rotational sensitive mirror 113 is aligned such that it has maximum reflectivity for linear polarized radiation whose polarization vector is orientated at an angle that is rotated 45 degrees from the polarization vector of the linearly polarized incident reference radiation. The direction of the polarization vector of the linearly polarized incident reference radiation is referred to herein as the direction of the original reference radiation polarization.

[0038] The effect of the rotational sensitive mirror 113 on radiation undergoing multiple reflections between reflective elements 112 and 113 is illustrated in Figure 2. The direction of linear polarization of the reference radiation initially incident on the rotational sensitive mirror 113 is indicated by the vector 201 of Figure 2(a) (and is referred to as the direction of the original reference radiation polarization).

[0039] This vector 201 can be considered as being comprised of the two orthogonal components 202 and 203. In the illustration of Figure 2 the highly reflective orientation of the rotational sensitive mirror 113 is aligned with the component 202.

[0040] With successive reflections between the reflective surfaces 112 and 113 the component 203 that is aligned with the less reflective polarization direction is reduced in magnitude with each reflection. The lower reflectivity causes the reflective magnitude of the 203 component to be systematically reduced, as indicated by diminishing magnitude of components 203, 204, 205, 206, 207 and 208 of Figures 2(a), 2(b), 2(c), 2(d), 2(e) and 2(f).

[0041] A consequence of the systematic reduction of the 203 component is the systematic rotation of the total or resultant polarization vector as indicated by the rotating vectors 201, 209, 210, 211, 212, 213 and 214 of Figures 2(a), 2(b), 2(c), 2(d), 2(e), 2(f) and 2(g). The illustration of vector 214 in Figure 2(g) indicates a resulting polarization vector aligned with the highly reflective orientation. In the preferred embodiment the polarization direction of further or higher order reflections will remain substantially at this orientation.

[0042] The illustration in Figure 2 shows a polarization rotation of approximately 7.5 degrees per reflection. This is indicated by angle 217 of Figure 2(b). The systematic rotation results in a total rotation of approximately 45 degrees with six reflections. This magnitude is for illustrative purpose only. The actual magnitude of the rotation depends on the relative reflectivity of the highly reflective and the less reflective properties of the rotational sensitive mirror 113. The relative magnitude of the highly and less reflective property can be selected to achieve a desired rotation per reflection to optimize for specific applications.

[0043] The illustration in Figure 2 also shows the relative magnitude of the components 202, 203 as the 203 component systematically decreases. With each reflection at the partial reflective element 112, the reference radiation reflected back to the second reflective element 113 will be reduced in magnitude because a portion will be transmitted through the partial reflective element 112 to contribute to the reference radiation used in the detection process. In the preferred embodiment the partial reflective element is a partial mirror.

[0044] Because of the reduction in magnitude due to transmission through the partial reflective element 112, both components 202 and 203 of Figure 2(a) and their equivalents in Figure 2(b), 2(c), 2(d), etc. will be systematically reduced in magnitude with each reflection. The component 214 of Figure 2(g) would in practice be reduced with respect to component 202 of Figure 2(a). In Figure 2, component 214 is shown as being of equal magnitude with component 202 for the illustrative purpose of more clearly depicting the polarization rotation with successive reflections. Furthermore, non-linear (trigonometric) variations in polarization rotation of successive reflections are ignored for illustrative clarity.

[0045] The magnitude of the of the reflectivity of the partially reflective element 112 affects the relative magnitude of successive reference radiation reflections. This reflectivity magnitude and the magnitude of rotation per reflection can be selected, to optimize for the relative magnitude of reference radiation components for specific applications.

[0046] The component of the reference radiation reflected back towards the polarized beam-splitter 104 by the partially reflective element 112 is still linearly polarized in the direction of the original reference radiation polarization (as it initially emerged from the beam-splitter 104) and is therefore substantially directed away from the second beam-splitter 109 and detector 110. This component of the reference radiation, referred to herein as the DC component, is typically significantly larger than the other components of the reference radiation and typically would generate undesirable noise if directed towards the detector.

[0047] Because the DC component is problematic, it is desirable to minimize the amount of the DC component that is directed towards the second beam-splitter 109 and detector 110. Minimizing the amount of the DC component directed towards the second beam-splitter 109 can be achieved by maximizing the extinction ratio of the polarized beam-splitter 104. This approach substantially reduces the amount of the problematic DC component of the reference radiation co-propagating with signal radiation and useful reference radiation towards the detector.

[0048] The useful reference radiation generated by successive reflections between the reflective surfaces 112 and 113 of Figure 1 contains components that are linearly polarized in the direction orthogonal to the direction of the original reference radiation polarization. These useful reference radiation components substantially pass through the beam-splitter 104 and co-propagate with the signal radiation towards the second beam-splitter 109 and detector 110.

[0049] The magnitude of these components that pass through the polarized beam-splitter 104 increases for higher order reflections due to the polarization rotation that occurs with successive reflections. For example, the high order radiation with rotated polarization indicated by vector 214 of Figure 2(g) can be considered as composed of the two components 215 and 216. The component 216 is polarized along the direction of the original reference radiation.

[0050] This component 216 is therefore substantially directed by the beam-splitter 104 away from the second beam-splitter 109 and detector 110. The orthogonal component 215, however, substantially passes through the beam-splitter 104 and co-propagates with the signal radiation towards the second beam-splitter 109 and detector 110.

[0051] In the illustrative example of Figure 2, the magnitude of the useful co-propagating component 215 is 50% of the rotated reference radiation represented by 214. Since there is no further rotation for higher order reflections, such higher order reflections would also have a magnitude of the useful co-propagating component of 50% of their rotated reference radiation. In other words half of the higher order reference radiation will pass through the beam splitter to form useful co-propagating reference radiation. This may also be expressed as 50% of the available photons of the higher order reference radiation will pass through the beam splitter to form useful co-propagating reference radiation.

[0052] By comparison with 215 of Figure 2(g), 218 of Figure 2(f) is of lower value. This is true because for lower order reflections the magnitude of the useful co-propagating component is less than 50% of the rotated reference as indicated by the magnitude of component 218 of Figure 2(f) and systematically decreases for lower order reflections. Note, for clarity of depiction, the other lower order components that would co-propagate are not shown. It should also be noted that these are vector quantities are illustrated in Figure 2.

[0053] The relative magnitude of the useful co-propagating components of the rotated reference radiation generated by different order reflections can be optimized for particular applications by (a) selecting the reflectivity of the reflective element 112 and (b) selecting the magnitude of the rotation per reflection which in turn is influenced by the relative reflectivities of orthogonally polarized components.

[0054] At this point components of the reference radiation (related to different order multiple reflections) co-propagating with the signal radiation, have a linear polarization orthogonal to the signal radiation and being orthogonal cannot generate an interference signal. The co-propagating reference and signal radiation is applied to the beam-splitter 109 which in the preferred embodiment is orientated substantially at 45 degrees with respect to the direction of polarization of both the co-propagating reference and the signal radiation.

[0055] The beam-splitter 109 separates the signal radiation into two orthogonal components, substantially equal in magnitude, one of which is directed at detector 110 and the other directed at detector 111. The beam-splitter 109 also separates the co-propagating reference radiation into two orthogonal components, substantially equal in magnitude, one of which is directed at detector 110 and the other directed at detector 111.

[0056] Resulting co-propagating components of the reference and signal radiation generate one interference signal that is detected by detector 110 and an inverted interference signal that is detected by detector 111. The two detected interference signals, also referred to as true and complementary signals can undergo conventional processing in an electronic processing module 115 to achieve balanced or differential detection which can reduce or substantially eliminate common mode noise, such as relative intensity noise of the optical source 101.

[0057] This is typically performed in the processing module by summing the signals in an operational amplifier prior to digitizing the resultant signal. This summing may be done prior to or within a typical pre-amplification stage but could also be performed after the detected electronic signals have been digitized. The detected electronic signals are digitized and further processed in the electronic processing module 115 to achieve non-invasive analysis of the target.

[0058] A control module 117 coordinates modulating the reflective element 113 and other aspects of the imaging and analysis system with processing the interference signals. In a variation of the preferred embodiment, an additional optic element 116, such as a half-wave plate, is used to rotate the polarization orientation of both the co-propagating reference and the signal radiation by 45 degrees. This eliminates the requirement to have the beam-splitter 109 orientated at 45 degrees.

[0059] In the preferred embodiment the quarter-wave plate 107 controls the linear polarization of the probe radiation by circularizing the probe radiation and by re-linearizing the back-scattered probe signal on its return pass through the quarter-wave plate 107. The quarter-wave plate 107 thereby controls orthogonal polarization characteristics to form linearly polarized signal radiation whose polarization vectors are rotated by ninety degrees with respect to the original linearly polarized probe radiation. The beam-splitter 104 directs substantially all of the signal radiation towards the detection system.

[0060] The beam-splitter 104 and reflective element 113 control components of the reference radiation such that the problematic DC component reflected by the reflective element 112 towards the beam-splitter 104 is substantially all directed away from the detection system by the beam-splitter 104. The beam-splitter 104 combines some components of the reference radiation with the signal radiation such that the components of the reference radiation and the signal radiation co-propagate towards the detection system.

[0061] The relative magnitude of the polarization components of higher order components (or multiple reflection orders) of the reference radiation that co-propagate with the signal radiation is determined by the reflective elements 112 and 113. Thus in the preferred embodiment the combination of the quarter-wave plate 107, the beam-splitter 104 and reflective elements 112 and 113 control or modify the relative properties of the orthogonal characteristic of the signal and reference radiation.

[0062] Thus the radiation co-propagating to the detection system is composed of maximized signal radiation and optimized amounts of reference radiation components. The signal radiation is maximized by rotating the polarization vector of the signal radiation. The reference radiation is optimized by rotating at least some of the polarization vectors of components of the reference radiation such that components corresponding to at least some deeper regions of the target have larger magnitudes co-propagating with the signal radiation to the detection system than co-propagating components corresponding to less deep regions of the target and by minimizing the amount of DC component of reference radiation that co-propagates with the signal radiation to the detection system.

[0063] The co-propagating signal radiation and controlled or modified magnitudes of components of reference radiation are thus substantially un-accompanied by problematic DC component of the reference radiation. The co-propagating signal and reference radiation is separated by the polarized beam-splitter 109 into two beams of co-propagating radiation of substantially equal magnitude which generate two substantially complementary interferometric signals that are detected by the opto-electronic detectors 110 and 111.

[0064] The detected interferometric signals form electronic signals that are processed by conventional electronic processing techniques to achieve non-invasive analysis of the target 108. The preferred embodiment of the invention described above enables maximizing the signal to noise performance of the non-invasive analysis system by controlling or modifying the relative magnitude and direction of polarization of the signal radiation and various components of the reference radiation, or in general, the properties of the orthogonal polarization characteristics of the radiation and the properties of at least some components of the same polarization.

[0065] For example, for imaging applications, a small rotation angle 217 of Figure 2(b) can be selected to minimize the magnitude of co-propagating radiation to detectors of lower order reflections and only achieve the maximum magnitude of co-propagating radiation to detectors for sufficiently high order reflections such that adjacent scans overlap and can therefore yield a continuous composite scan suitable for generating an image of the target. The non-overlapping interference signals related to the weaker lower order components of the reference radiation can be used for other purposes such as front surface location or alignment.

[0066] In applications including the non-invasive glucose monitoring, an advantage of minimizing the magnitude of co-propagating radiation of lower order reflections is that it minimizes the interference signal from the skin surface and thus minimizes the digitizing noise of interference signals associated with deeper regions of tissue. It also minimizes or eliminates the requirement for logarithmic amplification.

[0067] In another example, the rotation angle 217 of Figure 2(b) can be selected to achieve maximum magnitude of co-propagating radiation to detectors at a very high order reflection in order to exploit the extended (or amplified) scan capability, without overlapping scans. In this example the separation between the reflective elements 112 and 113 can be large. In such cases the rotational sensitive mirror could be replaced by a wave plate and a conventional highly reflective mirror.

[0068] Many variations of the system described in the preferred embodiment are possible. For example, a simpler single ended (as opposed to a balanced) detection system can be configured by replacing the half-wave plate 116 and beam-splitter 109 of Figure 2 with a linear polarizer orientated at 45 degrees with respect to the direction of polarization of both the co-propagating signal and reference radiation (which are orthogonal or at ninety degrees with respect to each other).

[0069] The resulting signal and reference radiation have aligned directions of polarization and can generate an interferometric signal that can be detected by the detector 109 to form (or output) and electronic interferometric signal also referred to as an electronic signal or composite electronic signal.

[0070] An alternative embodiment is illustrated in and described with reference to Figure 3. In this embodiment a broadband optical source 301, such as an SLD which, again generates broadband collimated output radiation 302 which is applied a polarization optic 303 (such as a half wave plate) that rotates the polarization of the output radiation 302 such that when it is applied to a polarized beam-splitter 304 it splits the radiation 302 into probe radiation 305 and reference radiation 306. The probe radiation 305 and reference radiation 306 are linearly polarized and are orthogonally polarized (each with respect to the other).

[0071] As in the preferred embodiment, the probe radiation 305 is passed through a polarization optic 307 and applied to the target 308. Back-scattered radiation from the target passes through the polarization optic 307 and is applied to the polarized beam-splitter 304. In this embodiment the polarization optic 307 is a quarter wave-plate. The double pass of the radiation through the quarter wave-plate 307 rotates the polarization of this radiation such that it is now directed by the polarized beam-splitter 304 towards the detector 309.

[0072] The captured back-scattered probe radiation referred to as signal radiation 305 also now has the same polarization as the reference radiation 306. The reference radiation is applied to the partial reflective element 309 and a conventional highly reflective or full mirror 310 mounted on the Piezo device 311. The combination of the partial reflective element 309 and the full mirror 310 mounted on the Piezo device 311 generates composite reference radiation as described in patent applications 11/025,698 and 11/048,694.

[0073] As in the preferred embodiment, the reference radiation that does generate useful interference signals, corresponding to the locations such as those indicated be the arrows 313 label "A, B, C and D", does not need to be attenuated but can be the highest intensity compatible with the reflectivity of the partial reflective element 309. The magnitude of this useful reference radiation can be determined by the extinction ratio (or leakage) of the beam-splitter 304.

[0074] The composite radiation that is reflected back to the polarized beam-splitter 304 also includes a large portion of radiation reflected by the partial reflective surface 309. This portion of the radiation typically has relatively high intensity and typically does not generate a useful interference signal (unless the optical system is moving with respect to the target).

[0075] A substantial portion of this high intensity, but typically unused, portion of the reference radiation is directed by the polarized beam-splitter 304 away from the detector 312 (towards the optical source 301 and therefore does not generate noise in the detector. However a portion of what has been referred to herein as the DC component of the reference radiation is directed towards the detector 312. The magnitude of this portion is determined by the extinction ratio of the beam-splitter 304.

[0076] The embodiment depicted in Figure 3 has reduced signal to noise performance, as the DC component is applied to the detector and the higher order reference radiation components systematically decrease in magnitude. However, this embodiment does maximize the magnitude of the signal radiation detected and can use a conventional mirror 310. This embodiment also includes control and processing modules 314 and 315 similar to the preferred embodiment (but without the double balanced processing aspect).

[0077] Another multiple reference embodiment is illustrated in and described with respect to Figure 4. This is similar in many respects to that illustrated in Figure 3, with similar elements 301, 303, 304, 307, 312, 314 and 315. However, the partial reflective surface 309 of Figure 3 is replaced by an additional beam splitter 401 and an additional mirror 402 mounted on an additional Piezo device 403 which generate interference signals related to regions in the target 404 indicated by the arrows 405 labeled "A" and "B".

[0078] Variations of these multiple reference arrangements are described in patent applications 11/025,698 and 11/048,694. The present invention is applicable to these and other variations.

[0079] An embodiment using a conventional time domain scanning reference mirror is illustrated in and described with respect to Figure 5. As in the preferred embodiment a broadband source 501 generates radiation 502 which passes through a polarization wave-plate 503 and is applied to a polarized beam-splitter 504 to generate probe radiation 505 and reference radiation 506. The probe radiation 505 is passed through a polarization optic 507 and applied to the target 508.

[0080] Back-scattered radiation from the target again passes through the polarization optic 507 and is applied to the polarized beam-splitter 504. This polarization optic 507 controls the orthogonal polarization characteristic of the probe radiation such that the back-scattered probe radiation can generate an interference signal if re-combined with the reference radiation. In this embodiment the polarization optic 507 is a quarter wave-plate. The double pass of radiation through the quarter wave-plate 507 rotates the polarization of this radiation by ninety degrees such that it is now substantially all directed by the polarized beam-splitter 504 towards the detector 509.

[0081] The back-scattered probe radiation 505 also now has the same linear polarization as the reference radiation 506 that is reflected back to the polarized beam-splitter 504 by the reference mirror 510. Since the back-scattered probe radiation 505 and the reflected reference radiation 506 have the same polarization they can generate an interference signal.

[0082] As the reference mirror 510 is translated through the scanning range 511 the generated interference signal relates to locations within the target spanning a corresponding region of the target indicated by arrow 512. The magnitude of the reference radiation co-propagating with the signal (or back-scattered probe) radiation is determined by the extinction ratio (or leakage) of the polarized beam-splitter 504.

[0083] In this embodiment signal to noise performance is optimized by using substantially all of the signal (or back-scattered probe) radiation and an optimal amount of the reference radiation by designing an appropriate extinction ratio of the polarized beam-splitter 504 or by a combination of the extinction ratio and a conventional attenuation element.

[0084] As in conventional time domain OCT systems, the reference mirror can be translated by conventional electromechanical or fiber stretcher means, typically controlled by an electronic control module 513. While the reference mirror is translated, the detected interferometric signal is typically acquired and processed by an electronic processing module 514. The processed signal is typically made available for display, further processing or storage.

[0085] Another embodiment, similar in many respects to that illustrated in Figures 5, where the optical source or radiation source 501 is a swept source which emits radiation that changes wavelength (or sweeps through a wavelength change). This is a Fourier domain OCT system in which depth scanning is effectively achieved by wavelength scanning and processing the resulting interference signal. In this embodiment the reference mirror can be stationary.

[0086] Yet another embodiment is illustrated in and described with respect to Figure 6. This is also similar in many respects to that illustrated in figure 5 with similar elements 503, 504, 507, 513 and 514. In this embodiment the optical source (or radiation source) 601 is a broadband source, such as an SLD. However, the interferometric signal 602 is applied to a diffraction grating (or spectrometer) 603 to separate the signal into different wavelength components.

[0087] The different wavelength components are detected by a detector array 604, for example a CCD (Charged Coupled Device) array. This is a Fourier domain OCT system in which depth scanning is effectively achieved by detecting the interferometric signal associated with the individual wavelength components and processing the results. In this embodiment the reference mirror 605 can be stationary or optionally translated by a Piezo device for Fourier domain OCT variations, such as sinusoidal phase-modulating interferometry (as depicted in Figure 6).

[0088] It is understood that the above description is intended to be illustrative and not restrictive. Many variations and combinations of the above embodiments are possible. Many of the features have functional equivalents that are intended to be included in the invention as being taught and many other variations and combinations of the above embodiments are possible, for example, various combinations of modulators can be used, including but not limited to: phase modulators: Piezo-electric modulators: mechanically amplified Piezo-electric actuators (to increase length changes). In some embodiments the relative optical path lengths of reference beams could be systematically varied to vary the relative locations from which information is obtained.

[0089] The preferred embodiments illustrated are free space configurations. Equivalent configurations could be implemented in optical fiber or in combinations of free space and optical fiber. In such designs or configurations beam-splitters could be replaced by fiber couplers. Mirrors could be replaced by fiber reflective elements, such as fiber loops or Bragg gratings. The preferred embodiments describe back-scattered radiation, however, systems involving transmissive scattered radiation could also be configured.

[0090] Embodiments, involving re-arrangements of the preferred embodiment design are included. For example, a quarter wave plate could be inserted in the reference path, rather than the probe (or signal) path. In this case, the DC component of the reference radiation would pass

straight through the beam-splitter 104 of Figure 1 and the useful components of the reference radiation would co-propagate along with substantially all the backscattered probe or signal radiation towards optic 103 (a half-wave plate) of Figure 1.

[0091] In this embodiment, the co-propagating useful components of the reference radiation and the backscattered probe or signal radiation could be separated out by polarization optics. In another embodiment, the radiation passing through the first beam splitter 104 could form the reference radiation and the radiation directed at 90 degrees could form the probe radiation.

[0092] Embodiments, both time domain and Fourier domain, that do not include a rotational sensitive element, could also have a quarter wave plate and attenuator between the first beam splitter and a reference element, i.e. between 504 and 510 of Figure 5; and 504 and 605 of Figure 6 or between elements 304 and 309 of Figure 3; and between elements 304 and 401 of Figure 4. This arrangement would have maximized signal radiation co-propagating with orthogonally polarized reference radiation and would thereby enable balanced detection with an arrangement similar to that of elements 109, 110, 111 and optionally 116 of Figure 1.

[0093] The preferred embodiments are described and illustrated in terms of an optical processing system generating optical probe and reference beams (or radiation), however the invention is not limited to optical radiation. The invention applies to all regions of the electro-magnetic spectrum, including but not limited to, micro-wave or X-ray, and is not restricted to the region conventionally referred to as optical and can include other forms of radiation.

[0094] Optical sources, include but are not limited to, light emitting diodes (LED); superluminescent diodes (SLD); laser sources; laser diodes; fiber lasers; wavelength tunable laser diodes; swept source lasers; mode-locked lasers; and continuum generating sources.

[0095] Many of the features have functional equivalents that are intended to be included in the invention as taught. For example, the optical source could include multiple SLDs with either over-lapping or non-overlapping wavelength ranges, or, in the case of a mode-locked laser source could be an optically pumped mode-locked laser, it could be a solid state laser, such as a Cr:LiSAF laser optically pumped by a diode laser.

[0096] The element rotating the polarization vectors of components of the reference radiation could be a rotational sensitive mirror based on technologies that include but are not limited to: anisotropic thin film; bi-axial materials; multi-layer dielectric stacks; obliquely deposited thin; photonic crystal structures; a reflective element with aligned magnetic properties.

[0097] The element rotating the polarization vectors of components of the reference radiation could be a reflective element combined with a magnetic field, such as a Faraday mirror or it could be a reflective element combined with wave plate or optical retarder. Such combinations are herein referred to as a rotational sensitive reflective unit.

[0098] The quarter wave plate through which probe radiation passes to the target could be replaced by a Faraday rotator or equivalent to apply linear polarized radiation to the target and yet still have the back scattered radiation rotated by 90 degrees so that substantially all the signal radiation is still directed towards the detection system.

[0099] The optical source could be an actively mode-locked laser diode or a passively mode locked by a Kerr lens or a semiconductor saturable absorber mirror. Gain switched optical sources, with optical feedback to lock modes may also be used. For purposes of this invention, mode-locked lasers will include gain switched optical sources. The optical source could be a VCSEL (vertical cavity surface emitting laser), or an LED (light emitting diode) or an incandescent or fluorescent light source or could be arrays of the above sources.

[0100] The preferred embodiments include collimated optical sources, however, they could also various combinations of lenses or lens arrays could be employed to collimate the source radiation or to focus the probe radiation into the target or to have converging or diverging beams at the beam splitter. Other examples will be apparent to persons skilled in the art. The scope of this invention should be determined with reference to the specification, the drawings, the appended claims, along with the full scope of equivalents as applied thereto.

What is claimed is :

1. A method of non-invasive analysis of a target, said method comprising:
   generating probe radiation and reference radiation that have orthogonal polarization characteristics;
   modifying at least some of said polarization characteristics;
   capturing at least part of said probe radiation scattered from within said target to form signal radiation;
   combining said signal radiation and at least some of said reference radiation to form co-propagating radiation, wherein said co-propagating radiation is composed of maximized signal radiation and optimized amounts of reference radiation components;
   detecting at least one interferometric signal generated by at least part of said co-propagating radiation to form an electronic signal; and
   processing said electronic signal to achieve non-invasive analysis of said target.

2. The method of claim 1, wherein said polarization characteristics are modified to maximize signal radiation by rotating the polarization vector of the signal radiation.
3. The method of claim 1, wherein said polarization characteristics are modified by rotating at least some of the polarization vectors of components of the reference radiation.
4. The method of claim 3, where components of the reference radiation corresponding to at least some deeper regions of the target have larger magnitudes than components of the reference radiation corresponding to less deep regions of the target thereby forming optimized amounts of reference radiation components.
5. The method of claim 3, wherein at least some of the polarization vectors of components of the reference radiation are rotated by means of a rotational sensitive mirror.
6. The method of claim 3, wherein at least some of the polarization vectors of components of the reference radiation are rotated by means of a rotational sensitive reflective unit.
7. The method of claim 1, wherein said signal radiation and said reference radiation are combined to form co-propagating radiation by a polarized beam-splitter.

8. The method of claim 1, wherein the co-propagating radiation contains a minimized amount of DC component of reference radiation, said DC component of reference radiation thereby forming an optimized amount of a reference radiation component.
9. The method of claim 1, wherein radiation is generated by at least one optical source.

10. The method of claim 9, wherein said optical source is selected from the following: a light emitting diode (LED), a superluminescent diode (SLD), a solid state laser, a laser diode, a fiber laser, a tunable laser diode, a swept source laser, a mode-locked laser, a continuum generating source.
11. The method of claim 1, wherein analysis of a target is analysis to generate an image of at least some aspects of the target.
12. The method of claim 1, wherein analysis of a target is analysis to determine the concentration of a metabolite.
13. The method of claim 12, wherein the metabolite is glucose.

14. An apparatus for non-invasive analysis of a target, said apparatus comprising:

means for generating probe radiation and reference radiation that have orthogonal polarization characteristics;

means for modifying at least some of said orthogonal characteristics;

means for capturing at least part of said probe radiation scattered from within said target to form signal radiation;

means for combining said signal radiation and at least some of said reference radiation to form co-propagating radiation, wherein said co-propagating radiation is composed of maximized signal radiation and optimized amounts of reference radiation components;

means for detecting at least one interferometric signal generated by at least part of said co-propagating radiation to form an electronic signal;

and

means for processing said electronic signal to achieve non-invasive analysis of said target.

15. The apparatus of claim 14, wherein said polarization characteristics are modified to maximize signal radiation by rotating the polarization vector of the signal radiation.

16. The apparatus of claim 14, wherein said polarization characteristics are modified by rotating the polarization vectors of at least some components of the reference radiation.
17. The apparatus of claim 16, where components of the reference radiation corresponding to at least some deeper regions of the target have larger magnitudes than components of the reference radiation corresponding to less deep regions of the target thereby forming optimized amounts of reference radiation components.
18. The apparatus of claim 16, wherein at least some of the polarization vectors of components of the reference radiation are rotated by means of a rotational sensitive mirror.
19. The apparatus of claim 16, wherein at least some of the polarization vectors of components of the reference radiation are rotated by means of a rotational sensitive reflective unit.
20. The apparatus of claim 14, wherein said signal radiation and said reference radiation are combined to form co-propagating radiation by a polarized beam-splitter.
21. The apparatus of claim 14, wherein the co-propagating radiation contains a minimized amount of DC component of reference radiation, said DC component of reference radiation thereby forming an optimized amount of a reference radiation component.
22. The apparatus of claim 14, wherein radiation is generated by at least one optical source.
23. The apparatus of claim 22, wherein said optical source is selected from the following: a light emitting diode (LED), a superluminescent diode (SLD), a solid state laser, a laser diode, a fiber laser, a tunable laser diode, a swept source laser, a mode-locked laser, a continuum generating source.
24. The apparatus of claim 14, wherein analysis of a target is analysis to generate an image of at least some aspects of the target.
25. The apparatus of claim 14, wherein analysis of a target is analysis to determine the concentration of a metabolite.
26. The apparatus of claim 25, wherein the metabolite is glucose.
27. The apparatus of claim 14, further comprising a second polarized beam splitter for splitting an interference signal into true and complementary signals for balanced detection.

28. A system for non-invasive analysis of a target, said system comprising:

a source operable to generate probe radiation and reference radiation that have orthogonal polarization characteristics;

at least one polarization optic operable to modify at least some of said polarization characteristics of said probe and said reference radiation;

a polarized beam-splitter operable to combine scattered probe radiation and at least some of said reference radiation to form co-propagating radiation, wherein said co-propagating radiation is composed of maximized signal radiation and optimized amounts of reference radiation components;

a detector operable to detect at least one interferometric signal generated by at least part said co-propagating radiation to form an electronic signal;

and

a processing module operable to process said electronic signal to achieve non-invasive analysis of said target.

29. The system of claim 28, wherein a polarization optic operable to modify polarization characteristics of at least some components of said reference radiation is a rotational sensitive mirror.

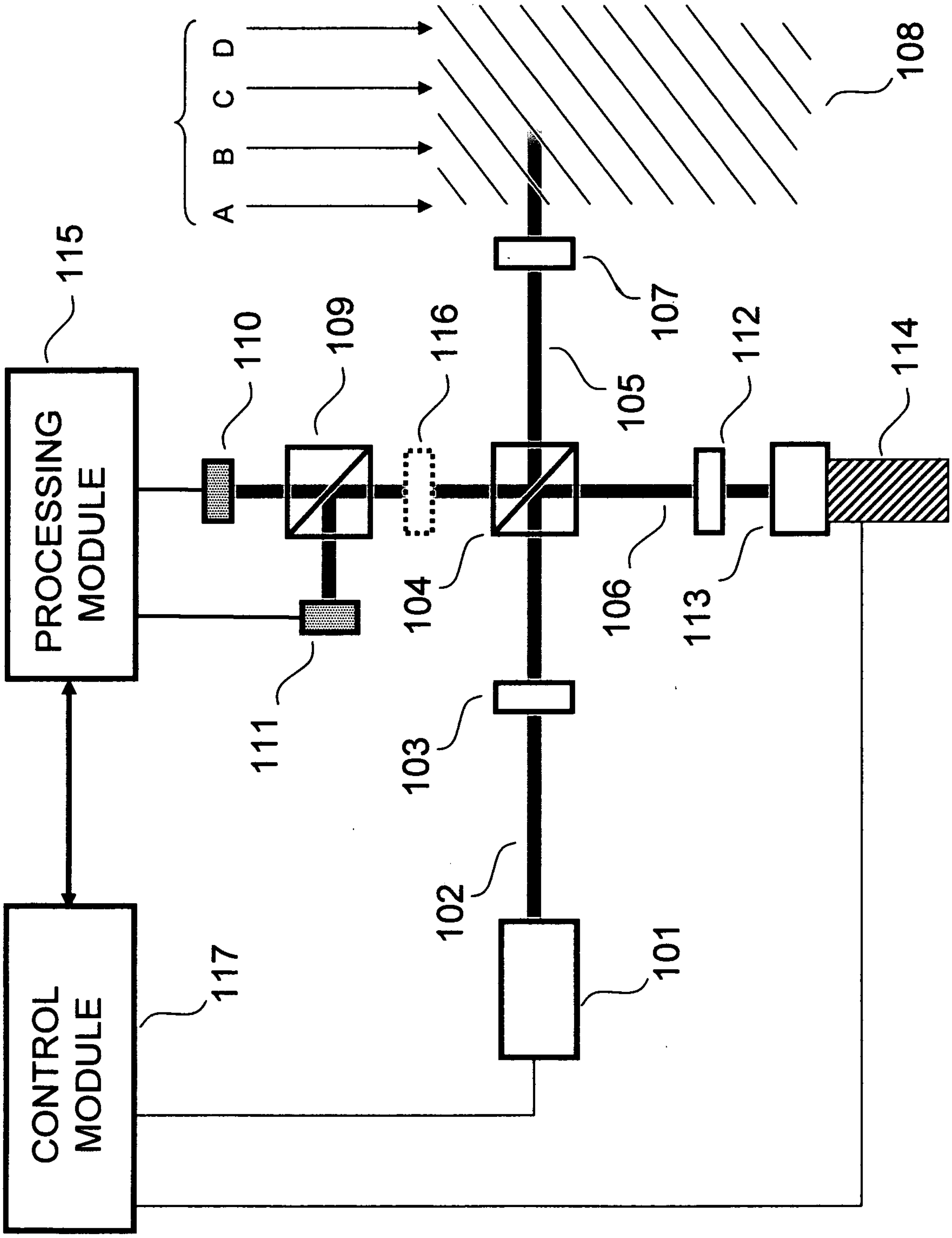
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Figure 1 of 6

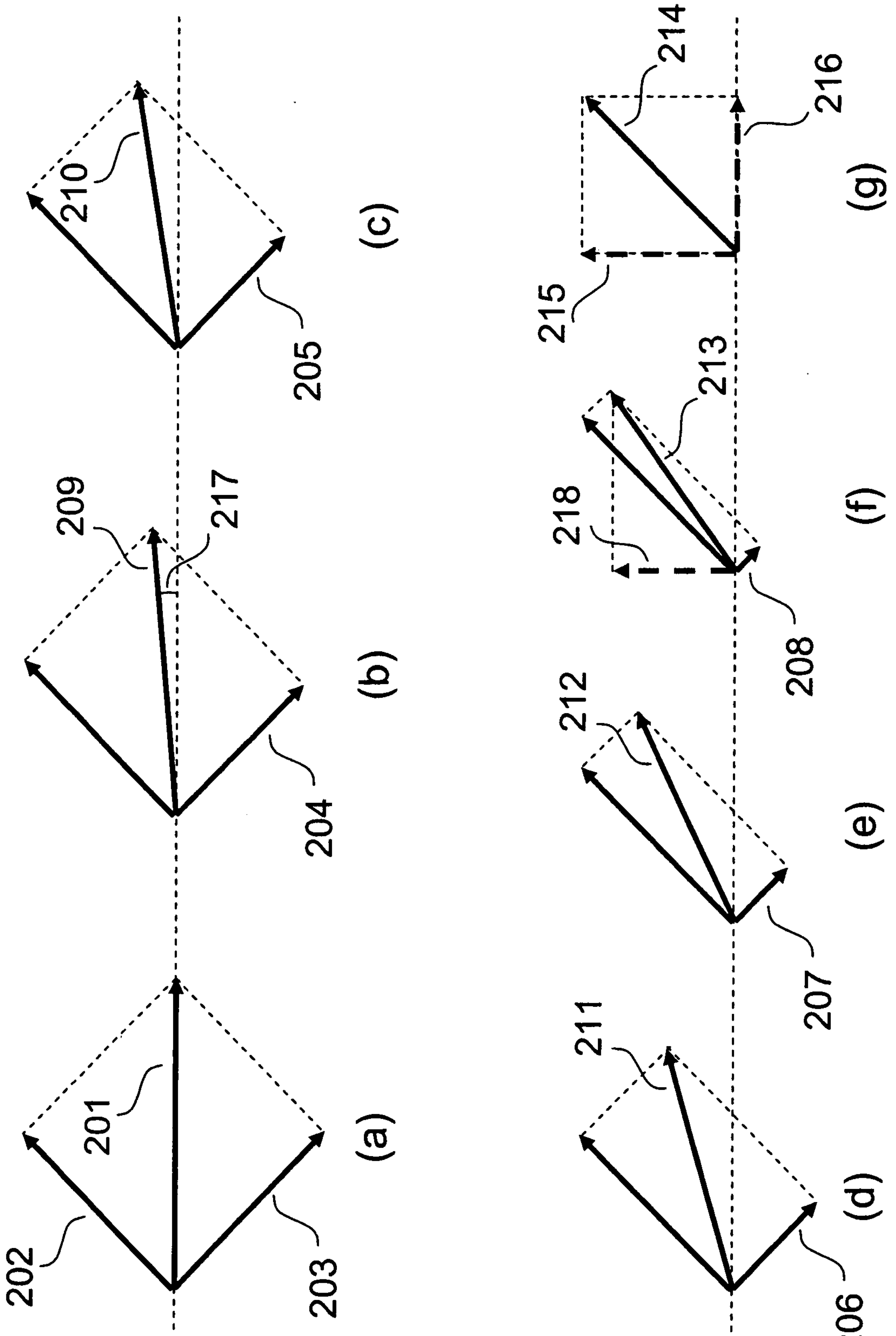
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Figure 2 of 6

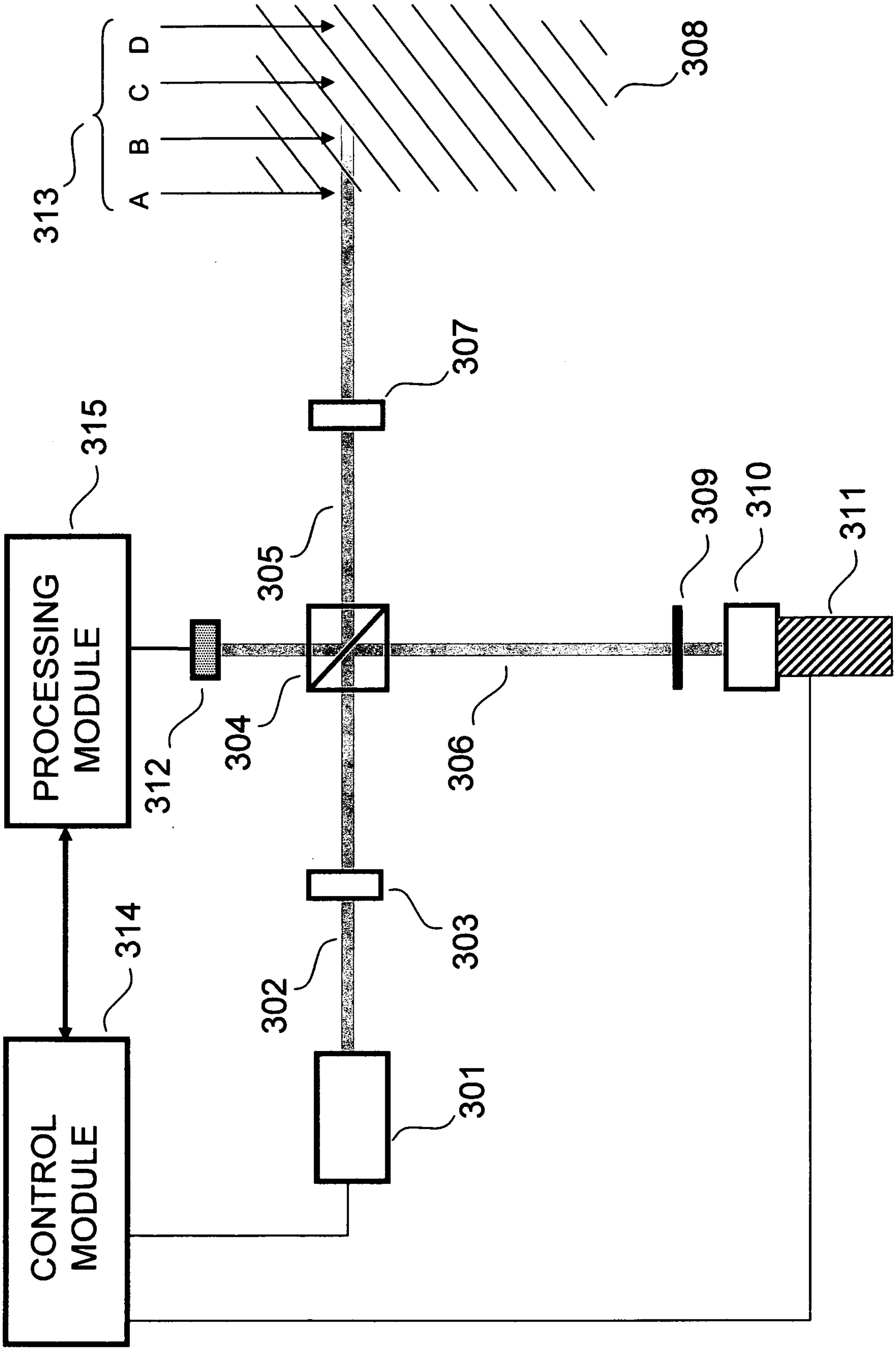
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Figure 3 of 6

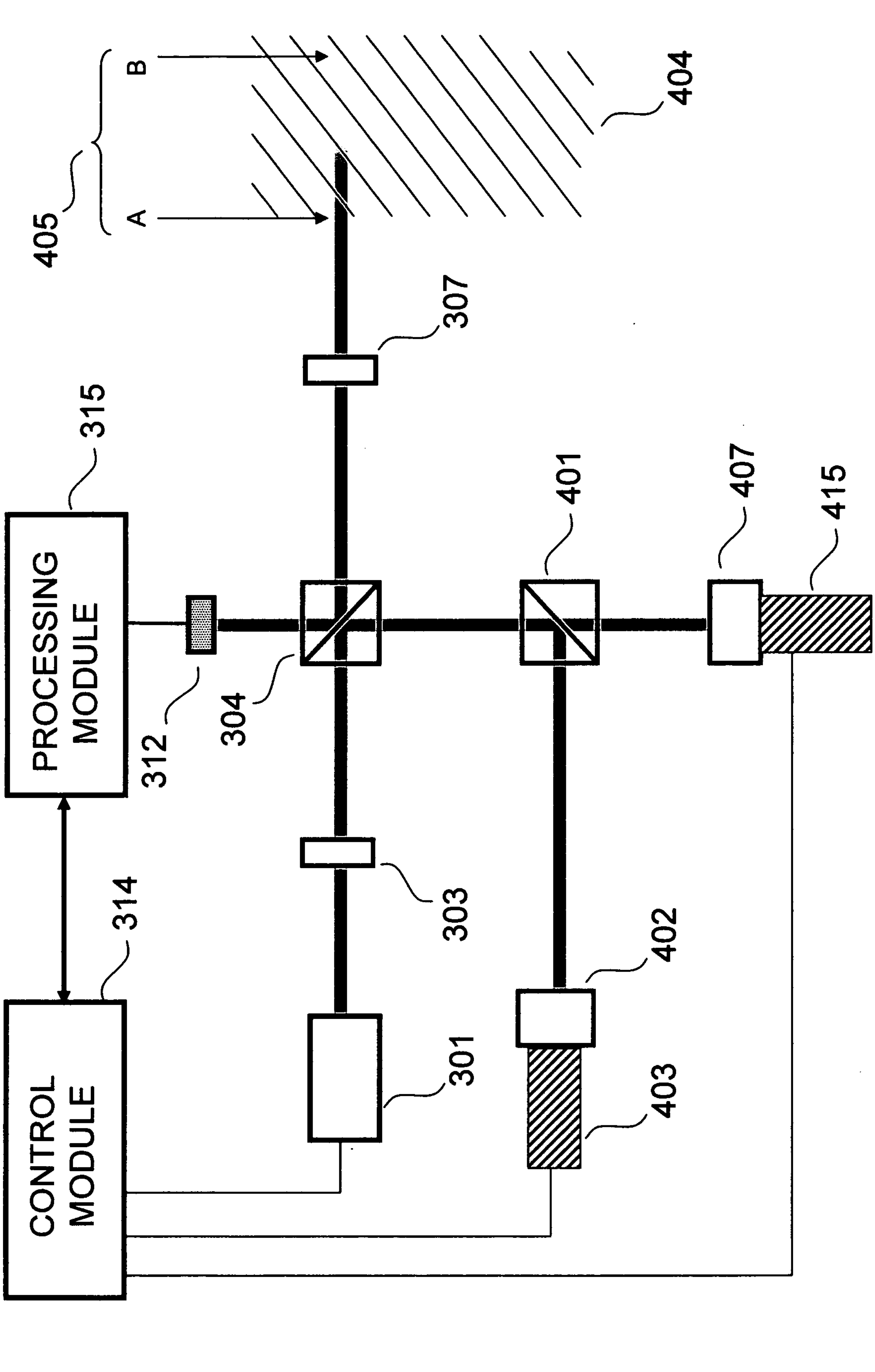
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Figure 4 of 6

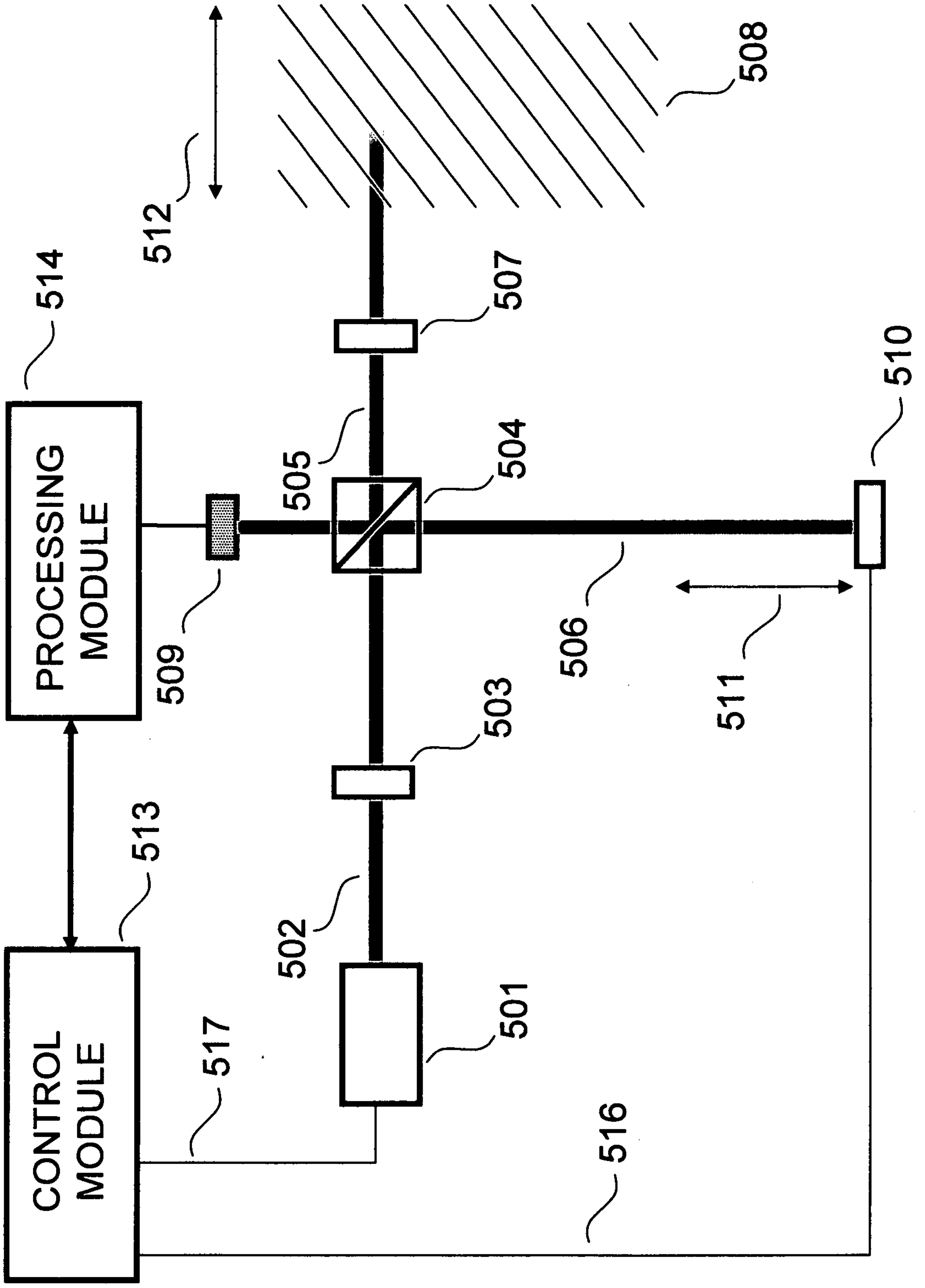
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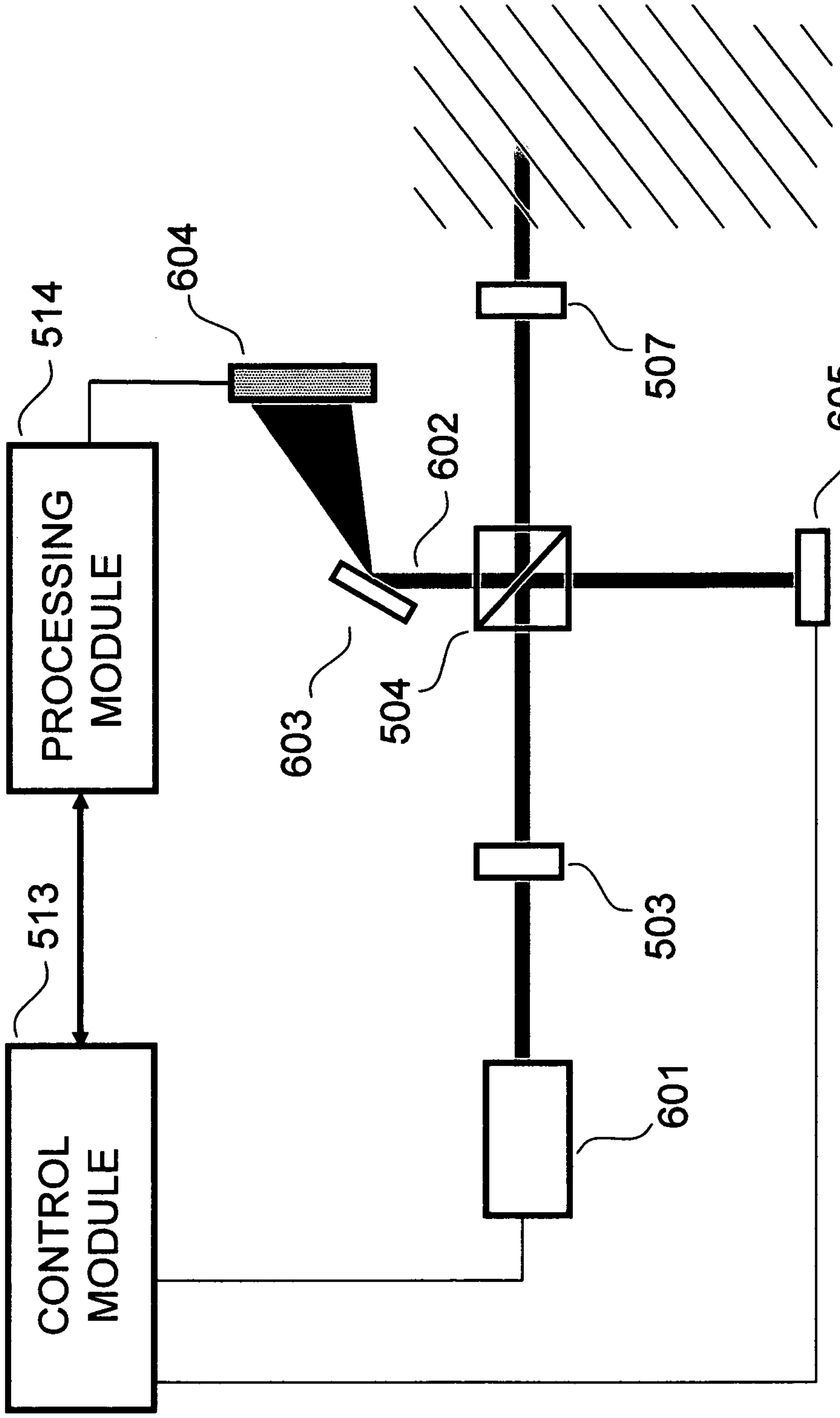
Figure 5 of 6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503
601

Figure 6 of 6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 08/07715

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 5/05 (2008.04)
USPC - 600/425
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)
IPC(8) - A61B 5/05 (2008.04)
USPC - 600/425

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
IPC(8) - A61B 5/05 (2008.04)
USPC - 600/425, 250/336.1; 356/39; 356/319; 356/450

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWest (USPT, PGPB, EPAB, JPAB), Google Scholar, WIPO, PubMed
Search terms - Non-invasive, imaging, analysis, orthogonal polarization, probe radiation, reference radiation, optical coherence tomography, topography, polarization sensitive, polarization, polarization dependent, maximize, maximum, interferometric signal, rotat

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2006/0063985 A1 (Hogan) 23 March 2006 (23.03.2006) (para [0003];[0016];[0031];[0035];[0077];[0078];[0081])	1-29
Y	US 2007/0086017 A1 (Buckland et al.) 19 April 2007 (19.04.2007) (para [0036];[0112];[0114];[0137];[0141];[0147];[0153];[0171];[0174];[0175];[0177];[0193])	1-29
Y	US 2005/0171438 A1 (Chen et al.) 04 August 2005 (04.08.2005) (para [0072])	8, 21

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

* 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
23 September 2008 (23.09.2008)	01 OCT 2008

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774