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(54) Title: BIO-PHOTONIC-SCANNING CALIBRATION METHOD

(57) Abstract: Methods (188), apparatus (10), and compositions (30) calibrate a bio-photonic scanner detecting selected molecular structures of tissues, nondestructively, in vivo. The apparatus (10) may include a processor, memory, and scanner. The scanner directs light nondestructively onto tissue in vivo, then receives back a radiant response through a system of mirrors and lenses back into the detector. Software for controlling the scanner and processing its output may be calibrated using a synthetic material (30) to mimic the radiant response of tissue. Calibration may account for background fluorescence and elastic scattering, mimicking skin tissue materials having substantially no Raman scattering response of interest. Dopants (125c) may be added to the matrix (125b) of white scan material to mimic selected molecular structures in tissue. Matrix materials (125b) include a dilatant compound, and dopants (125c) include biological materials as well as K-type polarizing film and other materials.
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BIO-PHOTONIC-SCANNING CALIBRATION METHOD

BACKGROUND

1. The Field of the Invention

This invention relates to optical measurement of intensity of light and, more particularly, to novel systems and methods for calibrating detectors of Raman scattering.

2. The Background Art

Optical and electronic mechanisms have been developed to generate, detect, observe, track, characterize, process, manipulate, present, and otherwise manage characteristic signals representative of materials, properties, systems, and the like. In the world of engineering, many principles of physics operate predictably, repeatably, and in accordance with the plans and schemes of those harnessing those laws of physics and engineering. Accordingly, over time, the mathematics of analysis or prediction of the performance and behavior of physical systems has been developed to a fine art and a reliable science.

The application of mechanical and electronic apparatus, as well as optical systems, radiation (e.g. radar, light, etc.), and sound (e.g. ultrasonic scanning, sonar, etc.) have proven useful in monitoring many types of systems. Many systems that are tested or monitored, and other systems that are designed and controlled rely, upon the technologies that combine physical phenomena with mathematical representations of those phenomena and the processing power of computers. Add to this mix various systems for detecting physical behaviors, converting those behaviors into signals, and submitting those signals for processing to computers, and much of the technical world in which people operate can be designed, analyzed, constructed, observed, and otherwise rendered more understandable and useful.

In the biological sciences, instrumentation has proven extremely helpful in both diagnostics and treatments. Electrocardiograms, electroencephalographs, and the like record weak electromagnetic signals characterizing the operation of the heart, nervous system, and so forth. Similarly, ultrasonic images, x-rays, and the like provide insight and literal vision into certain biological processes. The CT scan, or computed tomography technology has likewise provided greatly enhanced abilities to image biological systems and processes.

Likewise, the field of chemistry has benefitted from technology including much instrumentation, including such devices as chromatographs, spectral analysis, and the like. In all this knowledge being gained and applied to the understanding and control of biological
organisms, processes, and the like, a continuing need is the reliable calibration of
instrumentation used for such tasks.

For example, systems for measurement of selected chemical compositions in
biological tissue have been developed in recent years. Useful examples of such apparatus
are disclosed in United State Patent No. 5,873,831 issued February 23, 1999 to Bernstein et
al. and directed to a method and system for measurement of macular carotenoid levels,
incorporated herein by reference. Likewise, a patent was issued for non-invasive
measurement of other tissues as well. This work is documented in United States Patent No.
6,205,354 B1 issued March 20, 2001 to Gellermann et al. and directed to a method and
apparatus for non-invasive measurement of carotenoids and related chemical substances in
biological tissue, also incorporated herein by reference. Follow on work by substantially the
same team of scientists resulted in a United States Patent Application No. 10/040,883
method and apparatus for Raman imaging of macular pigments, and incorporated herein by
reference. This work or this entire body of work provides among other things for
determination of levels of carotenoids of similar chemical compounds in tissues such as
living skin. Certain methods and apparatus are disclosed for non-invasive, rapid, accurate,
and safe determination of carotenoid levels. These determinations may be used as diagnostic
information regarding cancer risk or as markers for conditions where carotenoids or other
antioxidant compounds may provide diagnostic information. Thus, much of this work is
directed to early diagnostic information and possible prevention or intervention.

In general, these processes rely on a technique of resonance Raman spectroscopy to
measure levels of carotenoids in similar substances and tissue. In certain embodiments, a
laser light is directed onto an area of tissue of interest. A small fraction of this scattered light
is scattered inelastically by a process of Raman scattering in which energy is absorbed by
selected molecules of interest, and is re-radiated at a different frequency from that of the
incident laser light. The Raman signal may be collected, filtered, and measured. The
resulting signal may then be analyzed in order to remove elastic scattering (e.g. reflectance)
of the illuminating source light, as well as background fluorescence in order to highlight the
characteristic peak identified as the Raman scattering signal.

In certain embodiments, a laser light source is passed into a probe system containing
various lenses, beam splitters, and the like. Accordingly, coherent light from a laser source
may be passed through this series of lenses and beam splitters to a mirrored surface through
which the beam may pass on it way to impinging upon a subject (e.g. skin, macula, etc.) in order to generate a response. The responsive radiation passes back into the probe, is typically reflected off the beam splitter or partially silvered mirror to be redirected into a detector.

In one example, a spectrally selective system, such as a charge coupled device detects radiation (e.g. light waves, photons, etc.) according to intensity and frequency (reciprocally wavelength). Thus, the wavelengths and intensities may be processed in order to quantify the amount of irradiance occurring along a spectrum of frequencies or wavelengths.

The response to impinging, coherent light on tissues may thus be characterized by the amount of energy, the number photons, or the like arriving at a detector in response to a particular illumination source. One can imagine that such a device, if sufficiently precise might conceivably measure even down to an individual photon level of quantum variation in radiant energy response.

In order to implement such devices, a method and apparatus are needed that can reliably calibrate scanners (e.g. systems for illumination of subjects and retrieval of radiant responses thereto for processing) and for processors or computers to manipulate and otherwise process the data received therefrom. Several needs arise in attempting to project a laboratory device or laboratory curiosity into a medical and diagnostic field or into a marketplace for such instruments. For example, tissues vary by their nature and by the difference in organisms.

For example, tissues of plants may behave characteristically, and some particular average or normal value or range of values may be established for a particular variety of plant under certain conditions. Similarly, tissues of animals or people may be analyzed invasively or non-invasively in order to correlate certain characteristics thereof with the radiant responses of such tissues to illumination and Raman scattering. Averages are an interesting characteristic of a property of a population.

Nevertheless, the variation between electronic components is not negligible. Accordingly, any combination of electrical and optical components will have certain inherent characteristics. In operating a scanner, the electrical and electronic artifacts (e.g. errors, characteristics, anomalies, bias, and so forth) of the device in question need to be characterized in order to be factored out of measurements or calculations. Typically, the variations between any two devices produced need to be some how calibrated (e.g. measured, compensated, scaled, normalized, etc.) in order that an output by a particular device be repeatable between devices. That is, two or a hundred devices of a same design need to be
able to produce the same or substantially the same value of a detected parameter when evaluating the same subject. That is, the skin of an individual scanned by two or a hundred different machines of the same design should provide substantially the same output value, within some reasonable repeatability (precision) and accuracy (reflection of true reality).

Thus, what is needed is an apparatus and method to calibrate individual scanners in order that the machine-to-machine variation can be factored out, resulting in an output from each machine that will be identical within some acceptable degree of variation, for a scan conducted on the same sample. Moreover, inasmuch as conditions change, such as temperature, humidity, chemistry, physical properties, and the like, over short times and long times in some expected, unexpected, predictable, or unpredictable manner, a machine needs to be calibrated to remove its own temporal (time wise) variations in operation.

That is, a scanning device operated on one day needs to be able to produce substantially the same output on another day or at some other time when exposed to the same identical condition in substantially the same subject. That is, the day-to-day variations or the time-to-time variability in outputs obtained from a particular device need to be calibrated out. That is, a method and apparatus are needed to calibrate a scanner in such a way as to factor out the vagaries of physics, chemistry, temperature, external conditions, and the like that may otherwise affect the output of a device. Thus, a method and apparatus for field calibration for a scanner would be an advance in the art.

To the extent possible, it would be an advance in the art to establish a process for processing signals received from a scanning device, in order that the hardware not be required to be adjusted. That is, for example, to the extent that various conditions can be monitored, or detected in a calibration process, then the output signals from such a device can simply be processed in order to correct the values of those signals, rather than actually correcting or altering any performance parameter, physical characteristic, or other control parameter associated with a scanning device. Thus, it would be an advance in the art to develop signal processing or computational processing of signal data obtained from a scanner in order to provide all the foregoing calibration benefits.

Biological materials are inherently highly variable. That is, a statistically significant sample over a properly identified population may have utility. Nevertheless, the portability of a sample may be problematic. For example, how does one normalize or calibrate two different machines on two different continents scanning two different populations in order that those devices read the same. Calibration samples taken from biological materials are
inherently problematic. Biological tissues are either in vivo or not. In either event, the 
amount of a sample, the repeatability of a sample, the control and observable characteristics 
of a sample are nearly impossible to maintain when dealing with biological materials. 
Moreover, the replication of biological materials, organisms, tissues, or other substances is 
extremely difficult. Moreover, the variation in conditions cannot be precisely controlled in 
many circumstances. Providing identical conditions, genetics, and the like in an organism 
is not a practical mechanism for generating calibration samples.

On the one hand, generating complex sets of physical data, electron counts, currents, 
voltages, photon counts, and the like may be possible. On the other hand, collection of such 
detailed data may be impossible. As a practical matter, such collection and analysis can be 
extremely complex and prohibitively expensive.

Thus, what is needed is a synthetic material that can be generated, manufactured, or 
otherwise produced by a predictable set of standards, with some processing that can be 
repeatably controlled, in order to provide a sample for calibrating a scanner. That is, what 
is needed is a synthetic material or a system of synthetic materials that can be relied upon to 
produce and maintain over an extended period of time a consistent radiant response when 
iluminated by a scanner. Accordingly, such synthetic materials may then be used to 
establish calibration standards that can be transported and verified worldwide.

Moreover, even within the context of a factory, having a stable, repeatable, 
reproducible, easily manufactured synthetic sample that can be used to calibrate machine-to- 
machine variations out of the performance of those machines would be extremely valuable.
Moreover, some type of field calibration apparatus and method, particularly if including a 
reliable synthetic material as a sample, would be a substantial advance in the art in calibrating 
out the day-to-day or time-to-time variations in the output of an individual scanning 
apparatus and associated processor.

**BRIEF SUMMARY AND OBJECTS OF THE INVENTION**

In accordance with the foregoing needs, a system of various apparatus and methods 
is disclosed herein for calibrating bio-photonic scanning systems. Moreover, synthetic 
materials have been discovered, formulated, evaluated, and otherwise made available to 
perform the various calibration functions required of a bio-photonic scanner. For example, 
mechanisms have been developed for presenting to a scanner certain calibration materials in 
repeatable structures and positions in order to obtain reliable radiant responses therefrom.
Likewise, various compositions for factory and field calibration operations have been developed. For example, a dark cap for returning substantially no radiant response to a scanner, in response to laser illumination, provides for a mechanism to factor out the electrical and electronic artifacts of the machine. Similarly, a white scan sample has been developed that replicates the shape and values of the spectral response of biological tissues, while being reproducible as a simple non-biological chemical composition.

Moreover, materials have been discovered and developed for doping a matrix of material in order to present synthetic mimics of certain molecular structures of interest. For example, carotenoids and other chemical compositions existing in biological tissue appear to contain certain characteristic carbon bond structures. Synthetic materials have been discovered that contain similar bond structures, responsive to illumination by providing a radiant response (e.g. Raman scattering, etc.) similar to that of biological molecular constituents.

Accordingly, a system and method have been developed to implement synthetic materials as calibration samples in order to calibrate scanning systems repeatably. Moreover, the various compositions and apparatus developed and discovered have been implemented successfully in a series of calculations and mathematical manipulations of data in order to process the output of a scanner, normalizing and otherwise neutralizing undesirable or uninteresting characteristics of spectral curves of radiant intensity. Thus, machine-to-machine variations as well as time-to-time variations within a single machine can be factored out, yielding much better signal to noise ratios and much more evident Raman responses. Accordingly, proper calibration apparatus and methods provide for accurate and repeatable utility of bio-photonic scanner.

**BRIEF DESCRIPTION OF THE DRAWINGS**

The foregoing and other objects and features of the present invention will become more fully apparent from the following description and appended claims, taken in conjunction with the accompanying drawings. Understanding that these drawings depict only typical embodiments of the invention and are, therefore, not to be considered limiting of its scope, the invention will be described with additional specificity and detail through use of the accompanying drawings in which:
Figure 1 is a perspective view of one embodiment of an apparatus in accordance with the invention including several mechanisms for presenting scanning samples during calibration processes;

Figure 2A is a perspective view of the convex side of a dark cap used in calibration in accordance with the invention;

Figure 2B is a perspective view of the convex side of the dark cap of Figure 2A;

Figure 2C is a perspective view of one embodiment of a shield for identifying an "on" condition of a laser and for diffusing laser energy to preclude specular transmission or reflection of coherent light;

Figure 3A is a perspective view of one embodiment of a precision cap containing multiple samples of synthetic calibration materials for use in an apparatus and method in accordance with the invention;

Figure 3B is a right side elevation view of a precision cap positioned for calibration of a scanner in accordance with the invention;

Figure 3C is a side elevation cross-sectional view of an alternative embodiment of a precision cap illustrating the use of an offset in order to provide a low-valued sample using a high-valued material in accordance with the invention;

Figure 3D is a side, elevation, cutaway view of a dark cap installed on the barrel and window of an apparatus for calibration in accordance with the invention;

Figure 4 is a perspective view a spring-loaded calibration apparatus in a closed position;

Figure 5 is a perspective view of the calibration apparatus of Figure 4 showing the open attachment bracket, corresponding detent, and the use of a spacer to obtain a reduced-value reading for calibration from a single sample;

Figure 6 is a rear perspective view of the calibration apparatus of Figure 4 showing the plunger in the drawn position retracting the sleeve and sample away from the barrel of a scanner as appropriate during installation of the calibration mechanism;

Figure 7 is a rear perspective view of the apparatus of Figures 4-6 showing the plunger and handle in the deployed position placing the sleeve and sample toward the window and barrel of a scanner in accordance with the invention;

Figure 8 is a perspective view of one embodiment of a double-ended sample system for calibration of a scanner in accordance with the invention;
Figure 9 is a partially cutaway perspective view of a double-ended, double-sample calibration apparatus in accordance with the invention illustrating the sliding mechanisms and retraction handles for positioning the apparatus in a scanner for use during calibration operations;

Figure 10 is a perspective view of a window and barrel portion of the probe of a scanner, together with the master sample system and installation thereof during calibration of a scanner using a synthetic mimic material to replicate the radiant response of tissues;

Figure 11A is a perspective view of a vertically oriented film material illustrating the operation oriented light waves with respect thereto;

Figure 11B is a perspective view of a horizontally oriented film material illustrating the operation oriented light waves with respect thereto;

Figure 11C is a schematic diagram of one embodiment of a lay up of oriented polymeric film typical of those useful in a calibration apparatus in accordance with the invention, typical of a low-valued calibration sample;

Figure 11D is a schematic diagram of an alternative embodiment of an oriented, polarizing-type, polymeric film of particular utility as a high-valued sample for use in a calibration apparatus and method in accordance with the invention;

Figure 12 is a schematic diagram illustrating the relationships between synthetic and other non-tissue materials useful in operation of an apparatus and method for calibration in accordance with the invention, including undoped synthetic matrix materials, dopants, with the resulting master samples and selected radiant response characteristics of the foregoing;

Figure 13 is a chart illustrating schematically the form of an intensity curve of radiant response as a function of wavelength as a result of elastic, fluorescent, and Raman radiant response effects of a subject;

Figure 14 is a chart illustrating schematically the Raman scattering effects after normalization for reduction of elastic scattering and fluorescence, as well as dark-scanned electronic artifacts of an apparatus and method in accordance with the invention;

Figure 15A is a chart illustrating schematically a method for selecting a baseline curve fit to match underlying data above which a Raman scattering peak may project in accordance with the invention;

Figure 15B is a chart illustrating actual normalized and processed scan data from a synthetic master sample, including the fitting of a baseline curve for determination of the characteristic peak desired for calibration processes;
Figure 15C is a chart illustrating actual data after processing and normalization, fitted with a baseline curve in order to ascertain the value of the characteristic peak for an actual scan of tissue by an apparatus and method in accordance with the invention;

Figure 15D is a chart illustrating actual data after processing and normalization, and fitted with a baseline polynomial curve, based on a scan of a calibrating sample of the film type in accordance with the invention;

Figure 16 is a schematic diagram illustrating various material compositions and formats that can be scanned or otherwise evaluated to obtain raw data, radiant responses, or calibration curves, along with a schematic chart for scaling the calibration of an individual scanned result to the scale of a particular standard for scanning results;

Figure 17 is a schematic block diagram of one embodiment of a process for calibration relying on synthetic or other master samples to obtain unit-to-unit uniformity, as well as condition-to-condition uniformity over time for a scanner and calibration system in accordance with the invention;

Figure 18 is a schematic block diagram of a process for formulation and use of a master sample for calibration of a scanner in accordance with the invention, applicable to naturally occurring materials dopants as well as fully synthetic matrix and dopant materials; and

Figure 19 is a schematic block diagram of a method for field operation and calibration of a scanner and calibration apparatus and method in accordance with the invention.

**DETAILED DESCRIPTION OF THE ILLUSTRATED EMBODIMENTS**

It will be readily understood that the components of the present invention, as generally described and illustrated in the Figures herein, could be arranged and designed in a wide variety of different configurations. Thus, the following more detailed description of the embodiments of the system and method of the present invention, as represented in Figures 1 through 19, is not intended to limit the scope of the invention, as claimed, but is merely representative of certain presently illustrated embodiments of the invention.

The various embodiments in accordance with the invention will be best understood by reference to the drawings, wherein like parts are designated by like numerals throughout.

Referring to Figure 1, an apparatus 10 in accordance with the invention may include a scanning mechanism including a power supply, a light source, such as a laser light source, and a detector. The detector may receive signals including background fluorescence,
elastically scattered light (reflections of source light), as well as Raman-scattering light returning to the detector at a wavelength different from that of the incoming illumination beam.

In general, the scanning mechanism will be enclosed within a housing 12, having a barrel 13 penetrating therethrough in order to deliver both illumination and returning detectable beams therethrough. Typically, a barrel 13 may be provided a certain amount of relief or clearance radially between the barrel 13 and the housing 12.

A window 14 mounted in the barrel 13 passes an illuminating beam outward to a subject, and a return "radiant response" back through the window 14 to be received by a detector. For example, a charge-coupled device (CCD) or charge-injection device (CID) may constitute an array of sensors capable of detecting light of various frequencies (e.g. and corresponding wavelengths). Accordingly, a histogram or spectrum of intensities may be displayed over a domain of frequencies or a domain of corresponding wavelengths.

In one embodiment of an apparatus 10 in accordance with the invention, a rest 16 is positioned below and outwardly or in front of the window 14. Supports 18 may extend from the apparatus 10 within the housing 12 to support the rest 16. Accordingly, a hand, arm, or other member of a subject may be positioned on the rest 16 in front of the window 14.

In one presently contemplated embodiment of an apparatus 10 and method in accordance with the invention, a hand of a user is positioned on the rest 16, placing the skin of the palm of the hand against the window 14. In this way, distance effects, as governed by Bier's law are repeatably controlled by the position of the window 14.

A shield 20 may provide several functional features. For example, in one embodiment, the shield 20 is formed of a translucent material shining in response to a beam of light output through the window 14 from the apparatus 10. Light passing through empty space has no mechanism to render it visible outside of the beam itself. Accordingly, as a matter of safety, laser light may be intercepted and scattered by the shield 20. By the same token, a user may be notified that the apparatus 10 is powered up and operating by the visibility of a spot of light illuminating the shield 20.

In various embodiments, the shield 20 may be clear, translucent, textured, or simply otherwise formed to diffuse light randomly. In certain embodiments, the shield 20 may be opaque. In such an embodiment, a user or operator may only see the evidence of a spot of light on the shield 20 between the window 14 and the shield 20. In one presently
contemplated embodiment, a diffusion surface is formed on the shield 20 regardless of whether opaque, translucent, or transparent.

In yet another embodiment, a diffusion layer of a material, such as, for example, linen or the like, may be embedded within layers of transparent or translucent polycarbonate in order to provide substantial diffusion. In another embodiment, a simple plastic such as an acrylic or other transmissive polymer may be provided with a dappled or roughened surface on one or both sides in order that the shield 20 provide no specular transmission or reflection of light from the window 14.

Various functional features of the apparatus 10 may be served by a series of accessories such as a dark cap 22 or a dark sample 22. A dark sample 22 returns no significant beam to the apparatus 10 in response to illumination received from the window 14. Accordingly, a response or radiant response detected by the apparatus 10 after illumination of the dark cap 22 through the window 14 will correspond to substantially no radiation (e.g. light) of interest.

As a result, illumination of the dark cap 22 through the window 14 results in a signal in the apparatus 10 representing background anomalies, (e.g. electrical or electronic artifacts) of the apparatus 10. In other words, a signal received back into the apparatus 10 in response to a beam illuminating the dark cap 22 provides a signal representing spurious contributions to the apparatus 10 as a direct result of the electrical or electronic artifacts (e.g. errors, background noise, etc.) of the apparatus 10 itself.

Precision samples 24 may be embodied in a film cap 24, sometimes referred to as a field calibration cap 24. The cap 24 may be placed over the window 14 in either a low value or a high value position. That is, the precision samples 24 represent a comparatively high value of a return signal into the apparatus 10 and a comparatively low value of a return signal into the apparatus 10. Each may result directly from material samples in the precision cap 24.

That is, the precision cap 24 may be placed in either of two orientations, one hundred eighty degrees apart, in order to expose to the signal (e.g. beam) a material yielding a high or a low radiant response. Both illuminating beam and radiant response propagate through the window 14 from the apparatus 10 and into ti, respectively.

As a direct result, either a high or low value of a radiant response will be transmitted back through the window 14 into the apparatus 10 from the particular materials in the precision samples 24. The high and low values may be a result of the radiant response of materials, the result of distance from the window 14, or both.
A loaded cap 26 provides a mechanism that can be repeatably and stably mounted to the supports 18 in order to provide spring-loaded positioning of a test sample against the window 14. Similarly, a double cap 28 or a test block 28 having spring-loaded caps on both ends, each with a sample, producing a high or low value, is shaped and sized to be positioned between the window 14 and the shield 20. The double cap system 28 provides spring loading in which the sample of interest is urged against the window 14 to provide repeatable registration thereagainst.

Master samples 30 are used primarily in factory calibration. In certain embodiments, master samples 30 may be used for field calibration. The master samples 30 comprise moldable materials that may be temporarily adhered to the window 14 to replicate synthetically the scanning of a bodily member such as a hand. For example, the master samples 30 are structured to be positioned as a putty-like material adhered to the window 14 to produce or appear as neutral background (white scan) results, comparatively low concentrations of molecular compositions of interest and comparatively high concentrations of molecular compositions of interest. The molecular composition of interest is distributed within the putty of the master samples 30 in accordance with the comparative value of the concentration of the molecular constituent of interest desired.

Referring to Figures 2A-2C, while continuing to refer generally to Figure 1, a cap 22, 24 may include, in general, an alignment mark 32. With the dark cap 22, alignment is not particularly significant. However, with respect to the precision samples 24, at least certain embodiments thereof, alignment may be a significant variable and the witness mark 32 or alignment mark 32 may assist in providing precise alignment of the precision samples 24.

Nevertheless, in the dark cap 22, a sleeve 34 fits snugly over the barrel 13, registering a shoulder 36 against the window 14 thereof. That is, the shoulder 36 provides a registration surface 36 that fits against the face 15 of the barrel 13. Typically, the face 15 and the window 14 may be substantially flush with one another.

Shims 38 or spacers 38 provide grip or a snug fit between the barrel 13 and the sleeve 34. As a practical matter, the sleeve 34 may distort to a certain extent as a result of the shims 38 contacting the barrel 13. Accordingly, deflection of the barrel 34, the shims 38, or both elastically provides the force to keep the dark cap 22 snugly fitted against the face 15, and comparatively immovable with respect to the barrel 13.

In operation, the dark cap 22 includes a black sample 40. In the illustrated embodiment, the black sample 40 is simply a concave, dark, surface 40. In certain
embodiments, a light trap, collimated, black, light trap, a black fabric, or the like may serve as the black sample 40. The angled surface and the black material of the black sample 40 disperse away from the window 14 the illumination proceeding out of the window 14, in order that substantially no radiant response be returned back through the window 14 into the apparatus 10.

Accordingly, the dark cap 22 absorbs, deflects, and otherwise disperses the signal proceeding from the window 14 in order to provide to the apparatus 10 a "dark" reading reflecting nothing more than the electrical and electronic artifacts of the apparatus 10. The reading or any signal detected or recorded by the apparatus 10 in response to the illumination of the dark cap 22 is actually only an artifact of background and error effects endemic to the apparatus 10. Accordingly, the dark cap 22 may be used to provide a background signal to be deducted from scanning readings in order to factor out the electrical and electronic artifacts of the apparatus 10.

Opposite the concave surface 40 constituting the black sample 40, a convex surface 41 proceeds to a vertex 42. The convex surface 41 may serve as a dark sample 41. Nevertheless, since manufacturing processes typically provide easily for a sharp vertex 42 on the interior (concave) surface 40, but do not provide a precision point of a convex surface 41, the vertex 41 typically interferes with proper operation of the dark cap 22 if used as the dark surface 41.

Referring to Figure 2C, the shield 20 may be illuminated by a beam of light through the window 14 resulting in a light spot 43. The light spot 43 or light region 43 may be seen from either major surface of the shield 20. If the shield 20 is translucent or transparent, the light spot 43 may be viewed from substantially any significant angle with respect to the apparatus 10. However, if the shield 20 is opaque, then the light spot 43 will typically only be seen from a position viewing the surface of the shield 20 directed toward the apparatus 10.

Nevertheless, in one embodiment of an apparatus and method in accordance with the invention, the shield 20 may be formed of multiple layers 44. In one embodiment, a single layer 44a of a translucent material, such as acrylic, polycarbonate, polystyrene, or the like may serve as the bulk material of the shield 20. The surfaces 44d, 44e of the shield 20 may themselves be textures on an otherwise transparent material in order to provide diffusion dispelling any specular reflection or transmission of a beam from the light spot 43.

In one presently contemplated embodiment, a layer 44a, together with a layer 44c, may sandwich a diffusion material 44b therebetween. For example, polycarbonates are
virtually unbreakable. Accordingly, two layers 44a, 44c of polycarbonate may be molded as a unit embedding a layer 44b, or laminated together with a layer 44b of linen therebetween. In the illustrated embodiment, the layer 44b intermediate the layers 44a, 44c may provide a substantial scattering effect precluding the passage of any substantial specular light.

As a practical matter, laser powers within the apparatus 10 may be selected to be sufficiently low as to cause no tissue damage, particularly ocular damage, even accidently. Nevertheless, the shield 20 serves as both a warning that the apparatus 10 is powered up and operating, as well as a protection against any over exposure of eyes to its modest intensity. The highly diffusive shield 20 may substantially inhibit any specular transmission or reflection of light impinging at the light spot 43 from the window 14. With or without the intermediate diffusion layer 44b, the surfaces 44d, 44e may still be provided with roughening or texturing as a scattering mechanism.

Referring to Figures 3A-3D, while continuing to refer generally to Figures 1-3, a precision cap 24 may include a witness mark 32 or alignment mark 32 in order to orient the cap 24 circumferentially with respect to the barrel 13. The precision cap 24, or more properly the sample materials 50 incorporated therein, may be orientation sensitive. Rotation of the precision cap 24 with respect to the barrel 13 may alter the radiant response reading detected by the apparatus 10 in response to illumination of the sample material 50 by a light beam.

Typically, two sleeves 34 on opposite sides of the precision cap 24 are provided, each with shims 38 for a snug fit against the barrel 13. The shoulder 36 serves to register the cap 24 against the face 15 of the barrel 13.

In the illustrated embodiment, dust covers 46 fit within and against the sleeves 34 to protect against scratching, accumulation of debris, and the like. In certain embodiments, the dust covers 46 may be connected to the precision cap 24 by an arm 48, which arm 48 may be integrally molded with the basic structure of the precision cap 24.

The foot 52 or feet 52 formed as part of the precision cap 24 are configured to fit snugly against the rest 16. Accordingly, the foot 52 assists in maintaining alignment of the sample material 50 with respect to the window 14. The feet 52 tend to urge the cap 24 into the proper orientation. Meanwhile, the witness mark 32 may assure that alignment of the cap 24 comports with the desired position with respect to the barrel 13.
In one presently contemplated embodiment, an aperture 54 receives a tether 55 anchored to the apparatus 10. For example, the tether 55 may tie to the supports 18 in order that the precision sample 24 may not be removed from nor substituted away from the apparatus 10.

The sample materials 50 may be configured to provide high and low respective values of a radiant response in consequence of illumination by a light beam from the window 14. Opposite sides of the sample 24 provide sleeves 34 surrounding samples 50. One sample 50 provides a comparatively lower reading, and the other sample 50 provides a comparatively higher reading.

In one embodiment, one corner is truncated from the sample 50 and a corresponding relief is formed in the shoulder 36. Accordingly, the sample 50 may only be positioned in one single orientation framed by the shoulder 36. Thus, the sample 50 is precisely aligned with the structure of the precision cap 24, and the precision cap is oriented by the feet 52 against the rest 16 in order to provide precise orientation with respect to the window 14.

It is known that carotenoids return light according Raman scattering principles as a radiant response to illumination by certain light. For example, light on the order of 473 nanometers in wavelength excites certain carbon bonds within carotenoids. It has been discovered that similar carbon bonds, and particularly a double carbon bond exists in certain oriented polymeric films. Accordingly, when the samples 50 are formed of particular types of polymeric films, an excitation of carbon bonds by light of suitable frequencies, such as laser light of approximately a 473 nanometer wavelength, Raman scattering at 510 nanometers wavelength results.

Accordingly, the samples 50 may be formed of a comparatively stable, nonperishable, synthetic material, rather than a naturally occurring or biological tissue material. For example, prior art apparatus such as those developed by Gellermann et al. (see United States Patent No. 6,205,354 B1, issued March 20, 2001 to Gellermann et al., incorporated herein by reference) could rely on actual biological tissue destructively obtained. Comminuted tissue samples from cadavers can provide materials for testing. By contrast, the samples 50, formed of a synthetic material providing a suitable response will provide much better repeatability, much more uniformity, as well as a substantially unlimited supply of uniform samples 50.

Referring to Figure 3B, a precision sample 24 or precision sample cap 24 may fit snugly against the barrel 13 of an apparatus 10. The housing 12 may be relieved in order to
receive the sleeve 34 around the barrel 13. In one presently contemplated embodiment, the sample 50 is adjusted snugly against the window 14 of the apparatus 10. The foot 52 fits against the rest 16 or plate 16, orienting the cap device 24. The cap 24 may be reversed to exchange a high valued sample 50 for a low valued sample 50 over the window 14.

Referring to Figure 3C, in one variation of an embodiment of a precision cap 24 in accordance with the invention, a low valued sample 50a may be set into the structure of the cap 24, providing an offset distance 55. That is, the materials for films forming the samples 50a, 50b are not only sensitive to rotation or orientation of their oriented polymeric fibers, but are governed to some extent by Bier's law. The distance 55 or offset 55 of a sample 50a away from a window 14 will affect the radiant response of the sample 50a to a beam of light from the window 14.

Accordingly, the offset 55 may be selected and calculated to provide a particular decrease in the radiant response of the sample 50a. By the same token, a high valued sample 50b may remain flush with the window 14, or positioned with a different offset 55. Thus, a single actual material with its single value for a radiant response may actually serve to provide different radiant responses by simply positioning a low value sample 50a at a deeper or more distant offset 55 with respect to a higher valued sample 50b.

Referring to Figure 3D, positioning a dark cap 22 against a window 14 exposes an angled and concave surface 40 exposed to the beam from a window 14. Accordingly, the beam is dispersed rather than returning back through the window 14 as a radiant response. Accordingly, the radiant response of a dark cap 22 is substantially a null response, resulting in data corresponding to the background value corresponding to electrical and electronic artifacts (e.g. errors, noise, etc.) of the apparatus 10.

Referring to Figures 4-7, one embodiment of a loaded cap 26 or self-loading cap 26 may include a mount 56 sized to fit over the supports 18. A matching bracket 58 closes against the mount 56. An operator, moving the handle 59 toward the mount 56 engages a detent 57 snugly holding closed the bracket 58 against the mount 56.

The self-loading cap 26 includes a sleeve 34 that can slide with respect to the mount 56 toward the face 15 of the barrel 13. Thus, the shoulder 36 registers a sample 50 with respect to the window 14 in order to achieve the proper and repeatable radiant response. Typically, the supports 18 are received into apertures 60 formed between the mount 56 and the bracket 58. The mount 56 may thus be adjusted to position a receiver 62 sufficiently
close to the window 14 to properly place the sleeve 34 and shoulder 36 with respect to the window 14 and face 15 of the barrel 13.

In one presently contemplated embodiment, the receiver 62 receives a plunger 64 penetrating therethrough and positionable by a handle 66. The handle 66 may be drawn back, compressing a spring 68 between the sleeve 34 and the receiver 62. The plunger 64 is detained by a detent (not shown) operating between the receiver 62, and the plunger 64. Accordingly, the sleeve 34 and shoulder 36, along with their supported sample 50 are effectively retracted away from the window 14. In such a position, as illustrated in Figure 6, the supports 18 of the apparatus 10 may be positioned within the aperture 60 to place the sleeve 34 proximate the barrel 13.

Upon urging the handle 66 toward the barrel 13 and included window 14, the detent is overcome, the spring 68 urges the sleeve 34, shoulder 36, and included sample 50 forward toward the window 14. The shoulder 36 registers against the face 15. Registration of the shoulder 36 against the face 15 positions the sample 50 with respect to the window 14.

In one currently contemplated embodiment, a spacer 72 extends laterally or radially through the sleeve 34 extending out at an end 74. The spacer 72 is perforated to expose to view the sample 50. However, as illustrated in Figure 5, the thickness 76 or standoff distance 76 provided by the spacer 72 spaces a sample 50 a distance 76 away from the window 14 of the barrel 13. The offset 76 is calculated and tested to provide a sufficient decrease in the radiant response of the sample 50 to illumination from the window 14 to provide a "low value" of radiant response.

The entry aperture 78 for the spacer 72 may be larger than the exit aperture 79. Thus, the end 74 may be smaller in cross section than the bulk of the spacer 72. Accordingly, the spacer can be registered within the sleeve 34 in order to provide a stable positioning of the perforation exposing the sample 50. The plunger 64 is advanced through the receiver 62 by pressing the handle 66 toward the barrel 13 and enclosed window 14. The plunger 64 advances the sleeve 34, shoulder 36, and sample 50 toward the window 14. Likewise, the spacer 72 positions the shoulder 36 further from the window 14, acting as the shoulder 36 itself 72.

In such a circumstance, the spring 68 urges the sleeve 34 and shoulder 36 with the included sample 50 forward toward the face 13 and window 14 to the extent possible. Thus, a repeatable registration of the sample 50 with respect to the window 14 results. Meanwhile,
the spacer 72 provides a second and lower radiant response from the sample 50 by virtue of the distance differential in positioning of the sample 50 with respect to the window 14.

Referring to Figures 8-9, a double cap 28 or a double-ended cap 28 may include a frame 80 fitted with opposing slides 82a, 82b from the ends thereof. The slides 82a, 82b may each carry thereon a respective sleeve 34a, 34b. Each sleeve 34a, 34b may present a respective sample 50a, 50b offset by an appropriate spacer 72 as needed. In operation, the spring 68 urges the slides 82 apart.

Handles 84 operating in slots 86 through the wall of the frame 80 secure to the slides 82 in order to retract the slides 82. That is, for example, the handles 84, or the handles 84 provided with plates 88 or thumb plates 88 can be drawn together by a user in order to retract the slides 82a, 82b with their respective sleeves 34a, 34b. In this way, the effective length 89 of the apparatus 28 or cap system 28 may be reduced in order to fit easily between the window 14 or face 15 and the shield 20.

Accordingly, the frame 80 is positioned conveniently on the rest 16 or deck 16 under the window 14. Upon release of the handles 84 by a user, the spring 68 urges the respective slides 82 and associated sleeves 34 apart. One sleeve 34a, 34b will contact the shield 20, while the opposite sleeve 34b, 34a will surround the barrel 13 and position the respective shoulder 36 against the face 15 and included window 14. Thus, a snug fit of a shoulder 36 with respect to a window 14 will position a sample 50 properly for returning the designated, calibrating, radiant response through the window 14 in response to illumination received from the apparatus 10 through the window 14.

Referring to Figure 10, a master sample 30 may actually include a neutral sample 90, a low-valued sample 92, and a high-valued sample 94. Having these three samples 90, 92, 94 in a properly labeled case 96 provides a set of standards by which a factory calibration can substantially neutralize machine-to-machine variations in performance. That is, the master sample 30 or sample set 30 provides calibration standards to assure that each apparatus 10 produced will provide a substantially equivalent reading on the same sample material.

A master sample 30 may be adhered to the face 15 and window 14 directly. Typically, the window 14 is secured to or within the barrel 13 by some mechanism, such as a collar 98 or other internal registration mechanism. Accordingly, the window 14, itself, determines the actual positioning of the sample 30.

The thickness of the sample 30 should be sufficient to preclude any transparency or translucence. Likewise, the sample 30 should cover the window completely to preclude
ambient light. By the same token, a hand, arm, or other member of a subject may likewise be placed in direct contact with the window 14 in order to provide a proper preclusion of ambient light as well as distance registration of the subject for testing.

Applicants have discovered that the master sample 30 may be effectively formed of a polymer composition. In one presently contemplated embodiment, a material identified as Dow Corning 3179 dilatant compound has been found highly effective to replicate certain properties of human tissues extremely efficaciously. In general, material comprising silicone oil cross linked by boric acid has been found very effective to provide a similar reflectance or elastic light scattering, as well as similar fluorescence, compared to those detected from human skin.

In one presently contemplated embodiment, the master sample set 30, and in particular the neutral sample 90 or white scan sample 90 may include dimethyl siloxane. These are hydroxy-terminated polymers with boric acid. In addition, silica as crystalline quartz may be added to the composition, as well as a proprietary thickener. The thickener is identified by the manufacturer brand name as thixotrol ST.

Other silicone compositions included include polydimethylsiloxane as well as a trace of decamethyl cyclopentasiloxane. A similar amount of glycerine and titanium dioxide may be added to the composition.

In one presently contemplated embodiment, the master sample 30, and particularly the matrix that forms the neutral sample 90 contains approximately 65 percent dimethyl siloxane, 17 percent silica, nine percent thickener, four percent polydimethylsiloxane, one percent decamethylcyclopentasiloxane, one percent glycerin, and one percent titanium dioxide. The matrix material that forms the neutral sample 90 may be characterized as a viscoelastic material. That is, the material 90 responds elastically in response to high rates of strain (e.g. impact), and responds as a liquid in response to comparatively very low rates of stress and strain (e.g. its own weight).

In order to provide the low-valued sample material 92 and the high-valued sample material 94, a doping agent or dopant may be mixed into the neutral sample 90. Naturally occurring or “organic” materials from biological sources have been found effective. For example, foodstuffs containing high values of carotenoids may be comminuted (e.g. pulverized, ground, etc.) and mixed into the matrix material 90. Tomatoes, carrots, vegetables, fruits, and the like containing suitable values of carotenoids can be substantially mixed or dissolved within the matrix 90 in order to produce the samples 92, 94.
Applicants have also discovered that synthetic materials exhibiting the carbon bonding behaviors of carotenoids may also be ground, milled, or otherwise comminuted and dispersed into the matrix material 90 in order to produce the low valued sample 92 and high valued sample 94. For example, after a factory calibration using the master sample 30 comprising a white scan sample 90, a low-valued sample 92, and a high-valued sample 94 can calibrate out the machine-to-machine variations of the apparatus 10.

That is, different concentrations of a micropulverized or comminuted synthetic material having a radiant response characteristic to mimic carotenoids may serve as a highly stable, repeatable, reproducible sample for the high valued material 94 and the low valued material 92. The concentrations of such synthetic dopants within the matrix 90 may be adjusted in order to provide a suitably low value for the low valued or “low” material 92, and a suitably high value for the high valued or “high” material 94.

It has been found that certain materials made from polyvinyl alcohol operate to perform this doping function. For example, K-type polarizer film materials are formed of long polymers called oligomers. Such materials are used as polarizing filters. They may be formed on substrates as polarizing films. These materials are formed of a molecularly oriented polyvinyl alcohol containing oriented block segments of polyvinylene and polyvinylalcohol. In particular, sheets of such K-type polymeric materials include polyvinylalcohol/polyvinylene block copolymer materials where the polyvinylene blocks are formed by molecular dehydration of a sheet of polyvinylalcohol.

This sheet then forms a uniform distribution of light-polarizing molecules of polyvinylalcohol/polyvinylene block copolymer material varying in length. The length is typically a varied value of a length and is characterized by a large number, n, of conjugated repeating vinylene units of the polyvinylene block of the copolymer, in ranges from two to twenty-four.

The concentration of each polyvinylene block tends to absorb wavelengths ranging from two hundred to seven hundred nanometers, and remain substantially relatively constant. The film is identified by its spectral dichroic ratio or R(D). The dichroic ratio increases with the increasing length n of the polyvinylene blocks. Thus the polyvinylene block concentration and the degree of orientation of the molecules result in a photo-optic dichroic ratio on the order of at least about forty-five. Such materials are produced by various manufacturers, and are disclosed in United States Patent No. 5,666,223 incorporated herein by reference.
Applicants have discovered that grinding such materials into a very finely pulverized size results in a dopant that can be satisfactorily distributed within a matrix 90 of dilatant compound in order to provide suitable low value materials 92 and high value materials 94. Dopant may be ground from the treated face of a CAB/K-type material. K-type material by itself may be milled, sanded, or otherwise comminuted to serve as a dopant. In one presently contemplated embodiment, a four hundred grit emery paper having a closed face in order to prevent impurities has been used to grind the dopant material from integrated solid sheet form into a powder. The powder appears to form as elongated crystals. The powder serves adequately when segregated to pass through a number 200 sieve as known in the chemical arts. Particles in larger sizes such as a number 100 sieve, or even 50 are possible, but uniformity of size and dispersion seem to enhance uniformity of results.

The value of a low value and a high value sample 92, 94 may be ascertained by testing a wide range of samples of human subjects. Thereafter, a suitable amount of dopant may be added to the matrix 90 in order to provide a suitable low value material 92 and a suitable high value material 94 representing comparatively high and comparatively low ranges of radiant response corresponding to those of human tissues in vivo.

The master samples 30 provide great utility inasmuch as they can be repeatably compounded from synthetic materials to provide very stable results. To the extent that radiation (e.g. light) may affect the molecular bonds in a material relied upon for testing and calibration, the matrix 90 may be molded to expose different particles. That is, the matrix 90 being a moldable plastic or viscoelastic material may be molded or kneaded in order to thoroughly and evenly disperse the selected amount of dopant.

By the same token, to the extent that a dopant material may alter its chemical structure as a result of continued or prolonged radiation, the master samples 30 may be kneaded in order to redistribute dopant and provide a continuing, substantially constant value of the radiant response therefrom in response to illumination from the window 14 of the apparatus 10.

Referring to Figures 11A-11D, such a film material may serve directly as a day-to-day calibration material in the precision cap 24. Applicants have discovered that scanning individual human beings or tissue samples presents too many issues of safety, scaling, and the like, and too broad and uncontrollable variations in the performance of the apparatus 10. A day-to-day calibration with synthetic materials is still appropriate in order to work out various conditional variations. For example, temperatures, humidity, electronic drift, and the
like may alter the operation of the components of an apparatus 10. Accordingly, with each startup of a scanning session, or even after an extended period within a single scanning session, calibration of the apparatus 10 may be appropriate.

Tethered to each apparatus 10 is a precision cap 24 used to calibrate with respect thereto the apparatus 10. Thereafter, as the machine ages, conditions change, and so forth, the apparatus 10 may be recalibrated such that it can output numerical values resulting from scans in a predictable, consistent, repeatable manner.

In one embodiment, the samples 50 embodied in the precision cap 24 may actually operate as circular polarizers. Circular polarizers combine linear polarizers with quarter-wave retarders. Unpolarized light passes through a linear polarizer and is oriented in one direction. It then passes through a quarter-wave retarder and becomes circularly polarized. That is, it tends to "spin" in a helical fashion. Upon contacting a surface, it may be reflected, returning from the reflecting surface in a reverse helical direction. Return light is limited in its ability to pass back through the initial polarizer. After being linearly polarized with a new orientation at ninety degrees to the transmission axis of the polarizer, the beam has effectively met a barrier similar to two linear polarizers oriented at right angles.

In order to protect the material that provides the radiant response to incoming light, protective coatings may be applied. In certain embodiments, the film of the samples 50 may include a thin sheet of polyvinylalcohol (PVA) aligned and stretched in a sandwich configuration between supporting sheets of cellulose acetate butyrate (CAB).

Referring to Figure 11A, light may impinge along an incoming axis 102 (for example, axes 102a, 102b) as a vertically oriented wave 104. As a result of impinging upon an oriented film 110 with the orientation as illustrated, the vertical wave may pass through along an outgoing axis 106. Thus, the passed wave 108 passes through a sheet 110 oriented in the same direction as the incoming wave 104. One may note that the orientation of the wave 104 that will be passed through the film 110 is actually orthogonal to the orientation of the actual strands of polymer or oligomer that form the film 110.

By the same token, the vertically oriented film 110, when approached by a wave 112 horizontally disposed along an incoming axis 102b will be absorbed or reflected from the film 110, resulting in a reflective wave 114 traveling along the axis 116b. A beam 101 of nonoriented light will include light 101 in possibly all orientations. Upon impingement of the beam 101 upon a vertically oriented film 110, vertical components 104 pass through as
the passed wave 108, whereas horizontal components 112 are absorbed or reflected back as reflected waves 114.

Referring to Figure 11B, an impinging horizontal wave 112 along an axis 102b will result in a passed-through wave 118 along a retracting axis 106b after impinging on the horizontally oriented film 120. However, just as the beam 101 is effectively “split” by a vertical polarizing film 110, the horizontal polarizing film 120, when impinged upon by a beam 101 or the vertical components 104 thereof along an incoming path 102a, will absorb or return vertical components as a reflected wave 122 along a path 116a and may provide other radiant responses thereto. As a practical matter, the paths 102a and 116a may be identical if a film 120 is oriented precisely normal to an incoming ray 101 of coherent light. Other rules of reflection apply otherwise.

Referring to Figure 11C, in one presently contemplated embodiment, a film identified as a KNCP35 circular polarizing filter available from 3M Company, provides a polyvinylalcohol (PVA) layer 124a that is partially oriented, thus operating as a quarter-wave polarizer. Thereafter, a layer 124b of an optically clear cellulose acetate butyrate (CAB) and substrate may be followed by another layer 124c of polyvinylalcohol and polyvinylene cross linked with boric acid stretched by an order of magnitude in order to provide orientation.

Plastics stretched in a first direction will pass light oriented in a direction orthogonal to the direction of linear orientation of the long molecules. As the light beam 101 from the scanning apparatus 10 passes through a dichroic filter, the light is not polarization controlled. Nevertheless, the films 110, 120 that serve as the samples 50 will be polarity-sensitive.

Accordingly, the precision cap 24 will behave differently on each apparatus 10. The polarization or whatever the polarity might be of a light beam 101 emanating from the window 14 of the apparatus 10, will simply be tolerated in one presently contemplated embodiment. Nevertheless, the orientation of the sample film 50 in the precision sample 24 used in day-to-day calibrations processes must be repeatable.

Therefore, the material 50 may be oriented, and that orientation will be fixed with respect to the cap system 24, and oriented in accordance therewith. Similarly, the cap 24 will be oriented by the feet 52 on the deck 16 or rest 16 under the window 14. In some embodiments, the film of Figure 11C may actually be laminated onto a substrate. For example, a base 124d may actually be formed of glass or the like. In alternative embodiments, no base 124d is present. Rather, the CAB material of the intervening optically clear layer 124b may serve as the structural substrate therefor.
In certain embodiments, a high and low film samples 50 may simply be made of a single film composition, and positioned at different locations in order to provide comparatively higher and lower radiant responses (e.g. readings). In other embodiments, different films may be used for the high and low valued samples. For example, a film known as HR-type may actually provide a comparatively low value of radiant response. Such a film is a polyvinylalcohol/polyvinylene having a particular set of double bonds of carbon atoms. This material is also doped with iodine and is often used in infrared spectroscopy.

By contrast, a film known as KNCP35 and other similarly constituted “K-based” films available from 3M Company provide comparatively high radiant response values when exposed to illumination by a beam 101 from the window 14 of the apparatus 10. The KNCP35-type of film operates as a circular polarizing, sandwich type of film as described hereinabove.

Low values of scanner outputs (e.g. intensity, score, etc.) for calibration may be obtained with HR-type films 110, 120. Such films include layers of PVA 124a, CAB 124b, and K-type film 124c as shown in Figure 11C, with or without the base 124d. On the other hand, high value of scanner output for calibration will result from films 110, 120 such as that of Figure 11D wherein K-type film is bonded to a shielding layer of optically clear CAB.

Referring to Figure 12, applicants have observed that non-tissue materials 125a when exposed to a beam 101 from a window 14 of an apparatus 10 may result in comparatively clearer and well-defined shapes 126a. An area 127a of intersection may place either region 127b, 127c inside the other 127c, 127b or offset as illustrated. The intersection 127a may be substantially less than the area or size of a source envelope 127b representing the area of illumination from the beam 101 proceeding from the window 14. Likewise, the area 127a of intersection may be substantially less than, and misaligned with the area 127c of the detector envelope 127c.

That is, the center of the region illuminated by the source, the source envelope 127b, and the region that is “read” by the detector in the apparatus 10, the detector envelope 127c may be misaligned. The area 127a may therefore be insufficient to be representative of the real radiant response of a sample, calibration material 30, or the like.

By contrast, human skin and the undoped matrix 125b (the neutral material 90 from the master sample set 30) provide a blooming response 127b. Rather than the clearly defined envelopes 127b, 127c that occur in many other materials, human skin as well as the undoped matrix material 125b of the neutral sample 90 or white scan sample 90 of the master sample
30 provide a blooming shape 126b. This blooming shape 126b may be thought of as an enlarged area of radiant response, reflection, scattering, and the like in a highly spread shape 126b. The blooming shape 126b or effect 126b results in a much better intersection 127a between the source envelope 127b and the detector envelope 127c.

Thus, the undoped matrix 125b (e.g. material 90) represents comparatively accurately the behavior of human skin, absent the Raman scattering effect due to carotenoids or other materials containing similar carbon bonds. A curve 126e reflecting the elastic scattering portion and the fluorescence of skin, may be achieved by using the undoped matrix 125b as a calibration sample.

In contrast, dopant materials 125c, such as naturally occurring materials or synthetic materials having the proper carbon bond structures to mimic the behavior of carotenoids or other molecular structures of interest provide a curve 126c identified as a Raman response. Thus, the peaks, and particularly the highest peak typically found at 510 nanometers wavelength, result from illumination of a dopant 125c by the light illuminating test samples 30, 50 from the window 14 of the apparatus 10.

Applicants have discovered that compounding a dopant 125c into the matrix 125b provides the master samples 30 capable of substantially replicating the behavior of human skin reliably and repeatably. The curve 140 of intensity as a function of wavelength obtained by illuminating and reading (e.g. scanning) the master sample 30 provides the full spectral profile 140 expected from the skin of a subject. The neutral sample 90 comprised of the undoped matrix 125b provides a curve 126e capable of identifying, and therefore neutralizing out, the effects of elastic scattering of illuminating light, as well as the skin's natural fluorescence. Meanwhile, different concentrations of doping in the low value sample 92 and the high value sample 94 of the master sample 30 provide comparatively different curves 140 and particularly the Raman response curves 126c contributing thereto.

Referring to Figures 13-15, while continuing to refer generally to Figures 1-12, a chart illustrating a wavelength axis 132 as a domain, with an intensity axis 134 as a range, shows schematically the 473 nanometer wavelength 136 and the 510 nanometer wavelength 138. The 473 nanometer wavelength 136 is characteristic of a unique artifact in the curve 140 of radiant response, namely the elastic scattering peak 142, substantially centered thereon. Meanwhile, a large dome 144 representing the fluorescence response 144 of the curve 140 extends on either side of the characteristic 510 nanometer wavelength 138.
In general, elastic scattering as illustrated in the elastic curve 142 may be thought of as reflected light at the incoming frequency of a beam 101 projected from the window 14. Recall that frequency and wavelength are reciprocal and thus interchangeable, and both may be discussed as the domain over which data is taken. The fluorescence portion 144 of the curve 140 may be thought of as the re-radiation of light at a frequency different from that absorbed, typical of the surfaces of certain materials, including some rocks, and human skin.

Comparatively smaller preliminary peaks 146, 148 represent Raman scattering at wavelengths below the characteristic 510 nanometer wavelength 138. A substantial and recognizable peak 150 represents the Raman response surrounding the 510 nanometer wavelength 138.

Referring to Figure 14, a schematic of the Raman scattering portions 146, 148, 150 of the curve 140 may be subject to some degree of background noise 152. Nevertheless, by correction of the original radiant response curve 140 to remove the elastic scattering portion 142 and the fluorescence portion 144, the signal-to-noise ratio of the Raman scattering curve 146, 148, 150 is substantially improved. Typically, the region of interest extends around the 510 nanometer wavelength region from about 450 nanometers establishing a lower boundary 154 to about 550 nanometers establishing an upper boundary 156 of interest.

To obtain the curve 140 of Figure 14, one may conduct a white field normalization. This may be accomplished by scaling the white scan curve 140 (based on scanning an undoped neutral sample 90) to the active scan curve 140 (based on scanning a doped or active material sample). The white scan may then be used to eliminate the effects of elastic scattering portion 142 and the fluorescent portion 144. The white scan curve 140 may be subtracted from or divided into the active scan curve. Subtraction may be problematic since small differences of large numbers are involved. Dividing the white scan into the active scan results in normalizing the common effects in the two curves 140, putting the peaks 146, 148, 150 in relief as shown in Figure 14.

Although the overall curve 151 of Figure 14 illustrates a nearly level or constant baseline curve 158, this is not necessarily so. That is, a baseline curve may actually have a slope that is non-zero. Nevertheless, in a schematic illustration, proportion may be necessarily exaggerated or minimized.

A white field normalization scan or a white scan may serve to adjust (e.g. calibrate) the control parameters of an apparatus 10 in order to assure that all such devices 10 provide the same output for a scan on a given calibration subject 30. Having the undoped matrix
125b of a neutral sample 90 or white scan sample 90 provides an ability to create a white scan in order to normalize the substantive data from active materials (e.g. doped, active, etc.). White scans may be used much as a dark scan is made using the dark cap 22. The white scan may be used to extract out the effects of optical artifacts of the optical system on the apparatus 10, as well as the elastic scattering 142 and fluorescent 144 responses (radiant responses) of a subject. This corresponds to the dark scan result used to extract our or normalize the artifacts (e.g. errors, anomalies, background, noise, etc.) due to electrical and electronic effects of the scanner 10.

Applicants have discovered that the dilatant compound serves as a neutral sample 90 (e.g. undoped matrix 125b), doing for optical artifacts and background radiant responses a comparative neutralizing or normalizing function similar to that which a dark cap (e.g. dark scan) does for electrical artifacts. Removing these effects from the curve 140 can enhance the signal-to-noise ratio of the resulting Raman scattering curve 151. In this respect, a white scan may be considered as a "filtering" mechanism.

For example, the elastic response portion 142 and fluorescence portion 144 of the curve 140 represent part of the total radiant response of a subject (person, sample, etc.) to a light beam 101 from the window 14. The white scan sample 90 or neutral sample 90 that forms the undoped matrix 125b provides the two portions 142, 144 to be normalized out. Accordingly the curve 140 from a white scan may be scaled (sized, adjusted in range value in the chart) to match the curve 140 resulting from an active scan (using doped samples 92, 94, etc.) and divided into it.

The two curves 140 may be divided point by point (or by any other suitable means) into one another. The two curves could be subtracted, but small differences between comparatively large numbers may cause significant limitations on signal-to-noise ratios. White field normalization or flat field normalization typically relies on an initial scaling of the two curves to fit the same range, followed by division to provide a new normalized curve in which the relative orders of magnitude of points (range values at any location in the domain) are about equal. The division yields a result reasonably near unity. This typically enhances signal-to-noise ratios substantially, and highlights differences between active materials (e.g. samples 92, 94) and white samples 90.

Thus, a white field normalization or white scan using the neutral sample 90 is effective to provide a curve 126e to calculate out the effects of background, electronics, other wavelengths, intensities, optical aberrations, noise, and the like not already removed by the
dark scan data. Together with dark scan reduction of electrical and electronic artifacts in the
curve 140, scans of natural subjects can be relied upon.

Biological variations, perishable decay, and the like do not occur in the synthetic
samples 90, 92, 94 of the master sample 30. Nevertheless, the dilatant compound has
substantially the same fluorescence and reflectance as skin, notwithstanding the fact that the
silicones themselves might have otherwise be optically clear.

The undoped matrix 125b that forms the neutral material 90 of the master sample 30
is actually effective to absorb solidus organic materials (e.g. foodstuffs, crystals of nutrients,
etc.), and may also absorb liquid materials. In some embodiments, the dilatant compound
forming the neutral sample 90 actually contains a small amount of water. Alcohol, acetone,
or other solvents, such as carbon tetrachloride and the like, may be used in order to introduce
materials into the dilatant compound.

The base material 90 or neutral sample 90 becomes a skin mimic, yet has
substantially no “carotenoid mimic” absent proper dopant 125c. Applicants have found
satisfactory a solid particle size that will pass 100 percent thereof through a number 200
mesh sieve. Substantially uniform particles blended uniformly throughout the matrix 125b
(neutral material 90) seem to provide uniform results from the low value samples 92 and high
value samples 94.

It is significant likewise that absent white field correction or “white scan” correction,
excessive nonuniformity occurs in samples. Solid crystals were found to be somewhat
unreliable, and provided no blooming effect 126b. Liquids were typically found to be absent
sufficient uniformity or opacity to provide reasonable results. A hand may be used to
calibrate several machines based on the uniformity of that hand. The ability to adjust
multiple machines to that hand is limited by availability and uniformity. A single sample of
a suspended material in a liquid has not typically provided reliability either. Using a dopant
125c along with an opaque material may provide a suitable liquid suspension.

Nevertheless, the viscoelastic material of the dilatant compound has shown proper
opacity, radiant response, elasticity, adhesive qualities, and ability to suspend and distribute
evenly a dopant 125c. It has shown an uncanny ability to mimic the reflectance portion 142
and fluorescence portion 144 of a radiant response 140 substantially equivalent to that of
skin.

One caveat in scanning dilatant compound as a neutral sample 90 or as a doped
sample 92, 94 relates to the Raman scattering peak 150 in the curve 140. The principal peak
150 appears to relate to a double carbon bond. The peak 148 appears to result from the Raman scattering from a single carbon bond. Likewise, the peak 146 appears to result from a single carbon bond attached to a methyl group. All peaks 146, 148, 150 are unlikely to be exactly matched at once. The value is also relative, regardless.

Calibrations can be done in any suitable scaling. For example, the base value of a curve 140 absent the elastic response 142 and fluorescent response 144 may be set at a value of zero. Meanwhile, a maximum value of a Raman scattering peak 150 may be set at a value of one. Similarly, a baseline could be set at zero, with a maximum value of one hundred. In one presently contemplated embodiment, a maximum value of the Raman scattering peak 150 may be set at a value or contribution value over sixty thousand, for example, sixty-seven thousand. Similarly, a low value may be set at the appropriate value in accordance with the maximum on a scale.

As a practical matter, the actual range of people based on a maximum value of intensity of about 67,000 was in part determined simply by an arbitrary scale approximating a photon count at a particular level of laser power. Actual values for scans of human skin on such a scale may range between a low of around 20,000, and a high on the order of 50,000. Of course, these vary from person-to-person. However, a range of zero to 67,000 is a suitable though arbitrary scale of intensity in one presently contemplated embodiment. It could as easily be scaled or mapped between any suitable interval, as known in the mathematical, signal processing, and other engineering arts.

For example, this range may be scaled from zero to one, minus one to one, from zero to ten, from one to ten, from one to a hundred, or the like. In other words, scale is always somewhat arbitrary. A value can virtually always be scaled.

Dopant 125c may be added to a suitable undoped matrix 125b in order to provide suitable master samples 30 adequate to represent a range within reason as a standardized “synthetic tissue.” Having developed a standard for calibration, applicants have been able to standardize the outputs dependent on the radiant response of a subject to illumination by a beam 101 from the window 14. Until the advent of such calibration materials, structures, and methods, the number output by the apparatus 10 was simply an arbitrary number, having marginal interpretive value.

Referring to Figures 15A-15D, a curve 140 of radiant response, corrected for electronic and electrical artifacts, reflected or elastic light portions 142 and fluorescence 144, may be characterized by a data curve 160 remaining. The data curve 160 may be fit by
suitable numerical methods with a baseline curve 158. The shape and order of both curves 140, 160 may be of a suitable order. A third order baseline curve 158 has provided a suitable fit. Higher and lower orders have been used successfully, but higher orders may produce anomalous peaks as mathematical artifacts. Lower orders may provide too gross a fit for comparison of the peak 150 against the underlying curve 160.

To form a baseline curve 158, the influence of the carotenoid peak 150 or the Raman scattering peak 150 of interest is best not included. Boundary points 162a, 162b may be selected to remove the peak 150 from consideration. That is, the boundary points 162a, 162b may bound the peak 150 in order that points therein not be included in the curve fit for the baseline 158. Similarly, extrema 164a, 164b may be selected. Intermediate points 166a, 166b are typically included at the sampling periodicity between a respective inner bound 162 and their respect outer bounds 164. Typically, approximately twenty points are included between the bounds 162, 164 on each side of the peak 150. A baseline curve is fitted through all the points 162, 164, 166. Thereafter, the intensity at the highest value of the peak 150 may be compared against that of the baseline 158 therebelow.

Referring to Figures 15B-15D, actual curves 160 have been corrected according to dark scans, white scans and appropriate normalization as discussed above to remove unwanted artifacts and effects in the data. The baseline curves 158 fitted, the curves 160 to which they are fitted, represent actual scans on a low value sample 92, an actual hand (in vivo subject), and a high value sample 94.

In calibration, one curve may be a standard to which a machine is to be calibrated. Accordingly, another curve may be the actual data curve. By enforcing a map between the curves, or more particularly, by aligning the peaks of the curves, the curves may be substantially aligned. Moreover, the peak region 150 will be most accurately mapped.

One may think of adjusting the calibration as correcting the slope and intercept of the curve to match the slope and intercept of the data curve. That is, assuming a linear curve fit, a rotation will result from correction of slope, and a translation will result from a correction of intercept. In the actual apparatus 10, parameters may be adjusted in order to adjust the coefficient and signal subtract or the "slope and intercept" for the baseline curve 158 underlying the peak region 150 of most interest.

Calibration accomplishes at least two purposes. Global consistency between machines (inter-machine consistency) is provided by standard reference materials. This takes a baseline 158 for a machine that can be relied upon in the future for field calibrations. The
standardized settings for the apparatus 10 may then be set in order to achieve from a standardized master sample 30 the proper baseline curve 158 for any individual apparatus 10.

An apparatus 10 may have identified with it something on the order of sixty individual parameters identifiable and unique to that machine. Factory calibration accordingly sets parameters so that any two machines may read the same master sample 30 the same. Likewise, the other controlling parameters of the apparatus 10 may be adjusted in order that such an apparatus 10 may be used repeatably in the field. Accordingly, calibration in the factory of an apparatus 10 with its particular dark cap 22 and precision cap 24 assigned thereto will assure that the apparatus 10 may be field calibrated to its original factory specifications as needed.

The dark cap 22 provides a measure of the non-optical noise or background to be subtracted out. Similarly, the white scan material 90 or neutral sample 90 can be scanned to take out the fluorescence background, reflected light, and normalize the pixel-to-pixel variation in output from the detector (e.g. CCD, etc.). The low value sample 92 can be used to establish the low value (e.g. about 21,500 in one embodiment). The high value sample 94 may be used to establish the high level value (e.g. sixty-seven thousand).

In one embodiment of an apparatus and method in accordance with the invention, a computer, such as a laptop, PDA, or other processing connected to the apparatus 10, or embedded therewithin, may provide all of the calibration calculations, such that the hardware is not necessarily reset after the factory, or except at the factory. For example, once an apparatus 10 is calibrated at the factory, then the controls, illumination, and detection of radiant response from a subject can all be processed according to the calibration factors in software associated therewith. Accordingly, a CPU or processor embedded within, or attached externally to, the apparatus 10 may simply conduct all of the processing required in order to operate the apparatus 10. Thus, calibration may be more a matter of processing of parameters than actual operating parameters.

In one embodiment of an apparatus and method in accordance with the invention, many, many scans or illuminations and reading of radiant responses may occur with respect to a subject. For example, in one presently contemplated embodiment, one hundred seventy-five scans of approximately three hundred milliseconds duration (collection time for reading by a detector) may occur.

Within about a minute, something like one hundred seventy-five scans, images, pictures, etc. representing approximately three hundred milliseconds apiece of collection of
data may occur. In general, Applicants have found effective the scanning of three such series. The average between those three processed series of scans, each representing one hundred seventy-five short scans of about three hundred milliseconds duration, have been found effective, repeatable, and reliable.

A scan time period substantially greater than three hundred milliseconds may saturate the sensors of the apparatus 10. A scan time of less than two hundred milliseconds by any substantial amount may tend to aggravate the signal-to-noise ratio of the resulting radiant response curve 140.

Applicants have found effective the use of certain curve smoothing algorithms. For example, a method sometimes referred to as the Savitsky-Golay method provides for smoothing of a curve, without destroying the peaks thereof. Accordingly, skilled operators can observe the peak region 150, and select the bounding points 162a, 162b. As a practical matter, considerable manual skill may be most effective. Nevertheless, numerical methods available may provide certain automated abilities. However, manual review has been found suitable in establishing the bounding points 162a, 162b, on either side of the principal peak 150. Thereafter, the baseline curve 158 may be fit.

The peak 150 may be fit with a polynomial. For example, third and fourth degree polynomials have been found suitable. Thus, the highest value pixel of the highest value reading in the curve portion 150 may then be established as a maximum, from which the baseline value corresponding thereto is subtracted.

An individual machine may then be adjusted individually by multiplying the maximum value of that peak 150 over the corresponding baseline value. For example, the factory precision caps 124 may be accommodated by a suitable adjustment factor in order to scale a reading received from the radiant response of the detector of the apparatus 10 to the cap 24 to match a standard. As an apparatus 10 is used over time, various conditions may occur hour-to-hour or location-to-location. Warming a machine up provides a certain amount of reduction in variability.

Field calibration represents a comparison of the ratio originally established for the reading of the cap 24, compared to the current day-to-day reading achieved for that same cap 24 on the apparatus 10 to which it is tethered.

Referring to Figure 16, an equation 168 representing a mapping of scale. A particular standard may be established against which other apparatus 10 may be calibrated, including being scaled. A laboratory unit or other device may be established as a standard. The
numerical count (range, intensity, output, etc.) provided by the system or apparatus 10 is actually a reflection of intensity, a function of the number of photons impinging on a detector at a particular frequency and wavelength. Early devices bordering on laboratory curiosities were sufficiently sensitive to provide almost a count of photons. Thus a single count on a scale of zero to 67,000 was actually close to a count of photons impinging on a detector as a result of a scan.

The apparatus 10 need not be so sensitive as to accommodate and register arrival of every photon, so long as a measure of intensity is accurate and repeatable. Each apparatus 10 needs to read a given sample (e.g. master samples 30, live subject, etc.) and output a score or number identifying the same value for intensity of light detected. Thus, each apparatus 10 needs to be calibrated at the factory to match a standard. The advent of the synthetic master sample set 30 provides such a standard. This standard or master sample 30 is more reliable than data taken on biological samples, such as people or plant materials, since it is not subject to the vagaries of biological processes and degradation.

In Figure 16, a skin carotenoid score SCS is a score or number corresponding to a reading achieved as an output of an apparatus 10. In calibration, this is the value output from reading the master sample 30. This is represented on the range (vertical) axis. The domain axis represents a value corresponding to the Raman scattering intensity obtained by a machine 10 under calibration to that same standard (e.g. a master sample 30).

A line may be defined by the peak heights 150 corresponding to scans conducted on the low and high samples 92, 94. The high sample 94 must read at the high value selected, (e.g. for example 67,000 in one embodiment) and the low sample 92 must read at the low value selected (e.g. at 21,500 in one embodiment). Other scales of numbers may be used, as discussed above, but these serve as one example.

Any resulting peak height 150 obtained on a machine 10 after calibration may be adjusted by the line of Figure 16, mapping the output range of that calibrated machine to a set of standard values obtained from the same samples on a standardized test (e.g. apparatus). The map is made, resulting in a linear mapping equation during factory calibration. A coefficient (representing a slope M) and a signal subtract (corresponding to an intercept B) may be used to obtain the readout value (corresponding to dependent variable y) for any input readout value (independent variable x) from the calibrated scanner.

Thus any resultant peak height 150 obtained during a scan conducted by the calibrated machine 10 is scaled to the standard. This is accurate with only two points
required for calibration, since Raman scattering is a linear effect. Accordingly, higher order terms are not required in order to map calibration scales of machines.

In practice, a dermal subject 172 is typically the palm of the hand of a person. Meanwhile, the content of molecular structures in serum 174 (e.g. bloodstream) in users can be correlated. The reading on a dermal subject 172 maps or correlates to the values determined by invasive evaluation of nutrient content (molecular structure of interest) within the serum 174 of the same subject.

Previously, laboratory developers of Raman scanning spectroscopy for carotenoid content could rely on comminuted tissues 176 from cadavers. Setting and fixing slides 177 is inherently subject to a lack of sample supply and repeatability for field calibration. Subject to irradiation, a factory sample has sufficient repeatability problems of its own. Irradiation sometimes affects the chemistry of carotenoids. Therefore, factory samples for evaluation of machines 10 may be problematic. Moreover, any hope for a repeatable, stable, sample from such a source is unthinkable.

Accordingly, applicants have used cuvettes filled with a liquid suspension 178 of synthetic materials, organic materials, and the like. The distance of the sample from the window 14 is problematic. Providing an opaque liquid suspension 178 helps solve that problem.

In fact, the dilatant compound matrix 180 (e.g. the neutral sample 90 of the master sample 30, or the undoped matrix 125b) provides the needed opacity, and is technically a liquid. The viscoelastic material flows under small force, albeit slowly.

The use of film 182, such as the films 110, 120 described above, and the layered system of materials 124 providing a response 123 or radiant response 123 to an incoming beam 101 have been found to be stable, predictable, and very useful. Nevertheless, the oriented nature (e.g. polarizing function) of these oligomeric films 182 makes them best suited for field calibrations of systems that have been matched thereto at the factory.

For example, because an apparatus 10 provides a beam 101 of nonoriented light, or of light having uncontrolled orientation, the apparatus 10 could be increased in complexity in order to assure a specific orientation of the light therefrom. However, as a practical matter, the peak 150 of interest in a response curve 140 calculated from the radiant response 123 to light beams 101 impinging on a sample of film 182 is unnecessary. So long as the particular sample 50 of film 182 is matched to a machine 10 and remains matched, the effects of
polarization of the film sample 50 (e.g. 182) are repeatable and can be calibrated or accommodated into calibration.

One may consider why the distribution of a dilatant matrix 180 compounded as the master samples 30 might not be distributed to every operator of an apparatus 10. This is probably possible. Nevertheless, such a distribution constitutes a substantial amount of material, weight, and numerous control and protection issues. For example, manipulation of the master samples 30 may result in contamination, changed readings, and the like. By contrast, the synthetic films 182 represent substantially stable, protected, consistent calibration samples.

Other materials 184 may also be used. Nevertheless, opaque materials tend to be preferable, or at least materials that are sufficiently solid and responsive to fix distance effects. For example, as discussed hereinabove, samples 50 formed of film materials 182 can be used at different distances to represent different radiant responses, as if the distance were instead the molecular structure of interest at a different concentration.

Referring to Figure 17, a calibration process 188 may be thought of as a unit uniformity control process 190 and a condition uniformity control process 192. The unit uniformity control process 190 represents that machine-to-machine uniformity desired and achieved by a proper calibration in the factory. By contrast, the condition uniformity control process 192 represents the day-to-day or the session-to-session uniformity within a single machine.

As described hereinabove, a dark scan 194 may be followed by a background adjustment 195 of the controlling parameters associated with the apparatus 10, and the software processed in the CPU associated therewith, regardless of whether or not the CPU is embedded in or remote from the apparatus 10. Similarly, a white scan 196 results from an illumination of the neutral sample 90 by a beam 101, with collection of the radiant response 123 therefrom. Accordingly, the resulting data curve 140 may be used to make an adjustment 197 to the elastic and fluorescent portions of the data curve 140.

A factory sample scan 198 comprising either the low valued sample 92, or the high valued sample 94 may be conducted, followed by the scan 199 of the opposite high value sample 94 or low value sample 92, respectively. Based on these two data points, or more, if desired, a calibration adjustment 200 may be made. This calibration adjustment then accommodates the parameters and their readings affected thereby in the apparatus 10. The apparatus 10 and data processing are adjusted to provide an output therefrom matching a
standard value of the curve 140, and the characteristic peak 150 off the baseline 158, when compared with other machines using the same master sample 30.

The condition uniformity calibration 192 may be done in the factory, with a precision cap 24 that will be tethered to the apparatus 10 for its operating life. The condition uniformity testing 192 may begin with a dark scan 202, or may rely on the original dark scan 194. Nevertheless, the condition uniformity calibration 192 in the field typically begins with a dark scan 202, in order to accommodate any conditional variation in the apparatus 10 or its environment during the particular time period of the scanning session for which condition uniformity calibration 192 is occurring. Following a dark scan 202, a background adjustment 203 is made to correct out from the data curve 140 the artifacts and other anomalies in the electrical and electronic operation of the apparatus 10.

Thereafter, a field sample scan 204 of a sample 50 embedded in the cap 24 or precision cap 24 is conducted, followed by a scan 205 of the alternate sample. That is, a high value and a low value sample 50 will be scanned 204, 205, in either order, as suitable. As a practical matter, all references herein to the precision cap 24 include the use of an alternative embodiment such as the spring-loaded cap 26, the double-ended cap 28, or the like. In the precision cap 24, or any of the other caps 26, 28, different values of samples 50 may be used on opposite ends or in alternate tries.

Nevertheless, one embodiment of the spring-loaded cap 26 was designed specifically to rely on distance for the variation in response 123 or radiant response 123 to the incoming beam 101. Likewise, either distance may be relied upon or concentration values of the samples may be relied upon to obtain the variations between high and low performance values of samples 50. Following at least two scans 204, 205, a calibration adjustment 206 may be made to adjust the value of the output numbers representing the characteristic peak 150 of interest.

Referring to Figure 18, a process 210 for creating master samples 30 may include selecting materials 212. This may include selection of a suitable material for a matrix 125b, as well as a suitable dopant 125c. By the same token, multiple matrices 125b, or multiple constituents for a single matrix 125b may be selected. Likewise, one or more dopants 125c may be selected for compounding and distribution or suspension in the matrix 125b.

After selection 212 of materials, including suitable testing, and other evaluations, preparation 214 of the matrix 125b may be done to order. This may be done by a supplier capable of delivering repeatable batches of the matrix material 125b.
Preparation 216 of dopants may include, for example, formulation 217a of a proper chemical or molecular structure of interest. Likewise, formation 217b of such a dopant 125c in a suitable format may be required. For example, in one presently contemplated embodiment, a K-type film of the oligomeric, polarizing-type may be ground, cut, or sanded to a fine powder. In one embodiment, a four hundred grit emery paper having a closed face to preclude contamination grinds particles that will substantially pass through a two hundred mesh chemical processing sieve.

Thus, formation of such particulate matter may include mechanical structuring of the particles, sizes, and the like. Ultimately, sizing 217c may be very important in order to provide uniformity. Particle sizes that are too large may provide erratic results. Similarly, particles that are too small may not be cost effective or as controllable.

Ultimately, distribution 218 of the dopant 125 in the matrix 125b results in a full set of master samples. That is, the neutral sample 90 comprises an undoped matrix 125 in one embodiment, but may instead involve a different matrix 125b with some backgrounding dopant of interest. Likewise, the low and high samples 92, 94 will typically involve different concentrations of dopant 125 calculated and tested to provide a particularly suitable and broad range of values near the higher and lower ends of the expected results. For example, a low value registering twenty thousand on a scale of zero to sixty-seven thousand, and a high value composition 94 registering about sixty thousand on a scale of zero to sixty-seven thousand have been found suitable. On such a scale, human subjects have been scanned and found to typically lie between readings of twenty thousand and fifty thousand. Outliers may exist above and below this range, nevertheless.

Referring to Figure 19, an apparatus 10 and method in accordance with the invention may be implemented in a calibration process 224 in the field. The process 224 may initiate with activating 226 the scanner power to a position of "active" or "on." Likewise, selecting 228 the process of scanning will typically be required. That is, somewhat independently from the scanner powering on 226, the activation 232 of a controller connected thereto may occur. Again, the processor (CPU) may be embedded within the apparatus 10, or may be a separate unit. Thus, the powering on 232 or powering up 232 of the controller presents a decision 234 after suitable delay.

After powering up 232, the controller may need to acclimatize for some period of time, such as about one-half hour. Thereafter, the scanner 10 is typically warmed up and prepared to operate. A user may then select between, for example, conducting a scan,
uploading data curves 140 from previous scans, calling for support, reading or outputting reports, or shutting down the operation thereof. Upon evaluation of the options, the test 234 results in a choice of either selecting 228 a scan, or some other operation 236.

Upon selecting 228 to scan, an operator may then load 230 the software for controlling the apparatus 10. Several processes may occur including initiating a scanning session, warming up, calibration processes, retrieving information from previous scans or general information, conducting additional scans without beginning a new scanning session, outputting results, and the like. Accordingly, a user may navigate 238 operations to select a suitable operation.

In the case of conducting of scans, a dark scan 240 may occur first during the calibration process. A reference scan 242 followed by a second reference scan 244 will rely on the precision sample 24 (e.g. cap, spring-loaded cap, double-ended cap, or the like, etc.) in order to support calibration 246 of the specific apparatus 10 under the conditions of this particular scanning session. A quality control check 248 may be conducted on one or more actual subjects in order to verify that readings are operating within the expected ranges.

In one embodiment, control of the apparatus 10 may rely on entering a certificate number 250. The certificate number 250 supports the control of the use of the apparatus 10 in accordance with patents, licenses, and the like, in effect. Beginning either before or during the actual scan, inputting 252 the demographics associated with the subject may include tracking information that will be useful to the scanning operator, the subject, or both. For example, as data is collected anonymously from multiple subjects, additional assistance may be provided for characterizing relationships between intake, serum levels 174 and dermal levels 172 of the subject molecular structures (e.g. carotenoids, antioxidants, nutrients, minerals, amino acids, and other molecules of interest, etc.).

A hand of a subject is positioned 254 in front of the window 14, typically resting on the deck 16, or rest 16. The scanning 256 of the subject may occur as described herein above with hundreds of “scans” over a period of a few minutes in order to obtain a suitable, statistically significant sample. Processing 258 of the data then occurs in order to create the output curves 140 and to identify the value of the peak 150 of a baseline as discussed.

The test 260 determines whether scanning is complete for this session. If not, then entry 250 of another certificate number identifying a new subject permits continued operation. Otherwise, a test 262 determines whether or not a new session will be started. For example, a session may be shut off because the operator is going to change, the group of
subjects is going to change, or calibration may be appropriate after some extended period of operation. If a new session is not to occur, then the apparatus may end 264 operation.

If a new session is to be conducted, then a test 266 may determine whether or not the time, number of scans, or other parameter for controlling use of the apparatus 10 has expired. If the test 266 determines that the time has not expired, then a new session may begin, with a dark scan 240 and other scans 242, 244 in order to complete calibration 246. On the other hand, if the test 266 results in a finding that the timeout or maximum number of scans or other parameter of control has expired, then a test 268 determines whether the currently scanned data will be uploaded to a server. If no upload is to occur, then the system will typically be disabled 270.

If, on the other hand, the data from the curves 140 is to be uploaded, then an upload process 272 occurs. Likewise, at the time of an upload 272, the overall process typically includes a download of authorizations for new scans, more time, or the like. Likewise, an optional step may include downloads 274 of upgrades to operational software. Thus, controller software, calibration schemes, and the like may be updated periodically for an individual operator.

Those of ordinary skill in the art will, of course, appreciate that various modifications to the detailed schematic diagram of Figures 1-19 may easily be made without departing from the essential characteristics of the invention, as described. Thus, the following description of Figures 1-19 is intended only by way of example, and simply illustrates certain presently preferred embodiments of a schematic diagram that is consistent with the invention as claimed herein.

In accordance with the foregoing needs, an apparatus and method are disclosed to calibrate a bio-photonic scanner to detect selected molecular structures of tissues, nondestructively, in vivo. The system may rely on a computer comprising a processor and memory connected to a scanner. The scanner includes an illuminator (e.g. light source, laser, etc.) to direct light nondestructively onto tissue in vivo. Light returns as fluorescence, reflective or elastic scattering, and Raman type scattering to a detector. The detector may be a charge coupled device or other mechanism to detect an intensity of a radiant response of the tissue to the light. A computer interface allows the scanner to communicate with the computer.

In certain embodiments, a calibrator contains a sample comprising a mimic material selected to mimic the radiant response of tissue. Determining a calibration parameter for the
scanner may involve directing light from the illuminator onto the mimic material and detecting a first radiant response thereto. Inputs to the processor corresponding to a state of the light, the first radiant response to the light, and the calibration parameter enable calibration. Inputs are processed to repeatably detect a second radiant response of tissue in vivo as a result of exposure to light from the illuminator.

The method may include determining a calibration parameter, including selecting a curve corresponding to errors attributable to electrical artifacts and optical artifacts of the scanner to be corrected out of the radiant responses. The method may also include selecting a filtering parameter to filter out elastic scattering from radiant responses.

Selecting a curve corresponding to background fluorescence permits correction of this feature out of radiant responses. Points to define a curve corresponding to a radiant response, absent a Raman scattering response of interest therein may isolate a Raman scattering response of interest.

Typically, the light is coherent light from an illuminator such as a laser and the radiant response is an intensity corresponding to a selected molecular structure of the tissue, a constituent of interest, such as carotenoid materials, anti-oxidants, vitamins, minerals, amino acids, or the like. A Raman scattering response corresponding to carotenoids has been found effective. Moreover, calibration scans may be done using “mimic materials” of non-animal-tissue materials, structured to provide distinct readings different from one another. Different intensities can also be achieved for calibration by positioning one type of material at two different and distinct distances from the detector.

Samples found effective include various polymers, synthetic materials such as long chains, and oligomers used in polarizing filters. For example, tests have used K-type film and an HR type film manufactured by 3M company. Other samples include a pliable matrix containing a selected quantity of a dopant in different concentrations. The dopant may be a solid powder or a naturally occurring material, such as plant materials, vegetable derivatives, and the like. A powdered film sized to pass through about a no. 200 sieve has been found to form a good dopant.

A matrix of dilatant compound doped at two concentrations of dopant can receive naturally occurring material or a synthetic material. Effective synthetic materials seem to include a carbon-to-carbon bond corresponding to a similar bond in carotenoids.

Determining calibration parameters may include calculating correction curves to combine with data curves corresponding to the radiant responses of test (calibration)
materials in order to isolate a "carotenoid" type of response therein. The correction curves may include data corresponding to at least one of elastically scattered light, fluorescence, and background artifacts of the scanner.

For calibration the machine is provided with a "dark cap" for collecting dark data in which substantially no light of interest returns to the detector, the dark data representing electrical artifacts of the scanner. Adjustments may be made according to the intensity of light from the illuminator, the response of the mimic material used in calibration, and correlation of the radiant responses of samples having different concentrations of dopants. The radiant responses to dopants are correlated between the sample and tissue in vivo.

In one embodiment, an operator may operate the scanner in a feedback control loop to detect in a subject an initial level of carotenoids in tissue. The subject may then ingest nutritional supplements according to some regimen over a subsequent period of time. Later testing with the scanner detects a subsequent level of carotenoids in tissue corresponding to the administration of the nutritional supplements.

Calibration of a scanner connected to a computer having a processor and memory may isolate a Raman response of carotenoids from elastic scattering, fluorescence, and electrical and optical artifacts of the scanner. A first synthetic material may be scanned to provide a "white scan" representing a portion of the radiant response of tissue attributable to optical artifacts of the scanner, reflected light, and re-radiated light at wavelengths not of interest (e.g. fluorescence). A suitable synthetic material is a viscoelastic material originally formulated by Dow Chemical and known as dilatant compound. In addition to serving as a neutral sample for conducting a "white scan" of background radiant effects, the dilatant compound may be doped at various concentrations.

In one embodiment of a system and method in accordance with the invention, a scanner of a bio-photonic type detects selected molecular structures of tissues, nondestructively, in vivo, from radiant responses of tissues to illumination by light from the scanner. The calibration system may include a dark sample returning a dark response corresponding to electrical artifacts of the scanner and comprising substantially no radiant response upon illumination thereof by the light. A white sample includes a first synthetic material returning a white response, upon illumination thereof by the light, substantially corresponding to a radiant response to the light of tissue, absent a characteristic Raman scattering response of interest.
A high valued sample may be formed of the first synthetic material treated with a dopant to return, upon illumination thereof by the light, a high response value corresponding substantially to a comparatively higher value of a radiant response of tissue to the light. A low valued sample may be formed from the first synthetic material treated with the dopant to return, upon illumination thereof by the light, a low response value corresponding substantially to a comparatively lower value of a radiant response of tissue to the light. The dark, white, high, and low samples are each selected, formulated, and formed to provide parameters, which in mathematical combination calibrate the scanner, controlling computer, or both to provide a repeatable value of an output corresponding to molecular content in tissue in vivo in response to the light.

The basic synthetic material (e.g. matrix) is optically opaque, viscoelastic, silicone-based compound. It may include dimethyl siloxane, crystalline silica, a thickener, and polydimethyl siloxane as principle constituents. Decamethyl cyclopentasiloxane, glycerine, and titanium dioxide may be present in comparatively small amounts, and even a little water. The silicone chains are hydroxy-terminated polymers cross-linked by boric acid.

Dopants may be naturally occurring materials (e.g. carotenoids originating in plants, vegetables, foodstuffs, etc.) or a synthetic material. Synthetic materials having a molecular bonding structure corresponding to characteristic molecular bonding found in carotenoids seem to serve the purpose. One dopant is found to contain a chain of carbon bonds, including characteristic carbon-to-carbon double bonds. As a finely comminuted solid, the dopant suspends in the silicone-based matrix to mimic the Raman scattering and other radiant response properties of skin.

An apparatus for calibrating a scanner of a bio-photonic type may include hardware such as a dark scan structure, a factory calibrator of a standardized set of synthetic materials at different levels of doping, a field calibrator of a polarizing film, and a software executable in a computer-readable medium to receive and process data corresponding to scanning the dark scan structure, the factory calibrator, and the field calibrator. A computer programmed to run the executable calibrates the scanner and operates to control the scanner and output a value corresponding to the amount of the selected molecular structure based on data acquired during non-destructive scanning of tissue of a subject.

The present invention may be embodied in other specific forms without departing from its essential characteristics. The described embodiments are to be considered in all respects only as illustrative, and not restrictive. The scope of the invention is, therefore,
indicated by the appended claims, rather than by the foregoing description. All changes within the meaning and range of equivalency of the claims are to be embraced within their scope.

What is claimed and desired to be secured by Patent is:
CLAIMS

1. A method to calibrate a bio-photonic scanner to detect selected molecular structures of tissues, nondestructively, in vivo, the method comprising:
   providing a computer comprising a processor and memory;
   providing a scanner comprising an illuminator to direct light nondestructively onto tissue in vivo, a detector to detect an intensity of a radiant response of the tissue to the light, and a computer interface to communicate with the computer;
   providing a calibrator containing a sample comprising a mimic material selected to mimic the radiant response of the tissue; and
   determining a calibration parameter for the scanner by directing light from the illuminator onto the mimic material and detecting a first radiant response thereto;
   providing inputs to the processor corresponding to a state of the light, the first radiant response to the light, and the calibration parameter; and
   processing the inputs to repeatably detect a second radiant response of tissue in vivo to the illuminator.

2. The method of claim 1, wherein determining a calibration parameter comprises selecting a curve corresponding to errors attributable to at least one of electrical artifacts and optical artifacts of the scanner to be corrected out of at least one of the first and second radiant responses.

3. The method of claim 1, wherein determining a calibration parameter comprises selecting a filtering parameter to filter out elastic scattering from at least one of the first and second radiant responses.

4. The method of claim 1, wherein determining a calibration parameter comprises selecting a curve corresponding to background fluorescence to be corrected out of at least one of the first and second radiant responses.

5. The method of claim 1, wherein determining a calibration parameter comprises selecting points to define a curve corresponding to at least a portion of the radiant response, absent a Raman scattering response of interest therein, to be manipulated with the second radiant response in order to isolate the Raman scattering response of interest.
6. The method of claim 5, wherein the light is coherent and the illuminator comprises a laser and the second radiant response comprises an intensity corresponding to a selected molecular structure of the tissue.

7. The method of claim 6, wherein the first radiant response is a Raman scattering response corresponding to carotenoids.

8. The method of claim 1, wherein the mimic material comprises first and second samples of non-animal-tissue materials, structured to provide distinct readings different from one another.

9. The method of claim 8, wherein the first and second samples comprise substantially the same material, with the first and second samples positioned at two different and distinct distances from the detector.

10. The method of claim 8, wherein the first and second samples comprise a polymer.

11. The method of claim 10, wherein the polymer comprises a synthetic material.

12. The method of claim 11, wherein the synthetic material comprises an oligomer.

13. The method of claim 12, wherein the oligomer is selected from a K-type film and an HR type film.

14. The method of claim 8, wherein the first and second samples each comprise a matrix containing a first selected quantity of a dopant in the first sample and a second selected quantity of the dopant in the second sample.

15. The method of claim 14, wherein the dopant comprises a polymer distinct from the matrix.

16. The method of claim 15, wherein the dopant comprises particles of a polymer.
17. The method of claim 16, wherein the particles are sized to pass through about a no. 100 sieve.

18. The method of claim 17, wherein the particles are sized to pass through about a no. 200 sieve.

19. The method of claim 8 wherein the first and second samples comprise a matrix of dilatant compound doped at first and second values of concentration of dopant, respectively.

20. The method of claim 19, wherein the dopant is a naturally occurring material.

21. The method of claim 20, wherein the dopant is a synthetic material.

22. The method of claim 21, wherein the synthetic material is a polymer containing a carbon-to-carbon bond corresponding to a similar bond in carotenoids.

23. The method of claim 1, wherein determining a calibration parameter comprises calculating correction curves to combine with data curves corresponding to the second radiant response in order to isolate a carotenoid response portion in the second radiant response.

24. The method of claim 23, wherein the correction curves comprise data corresponding to at least one of elastically scattered light, fluorescence, and background artifacts of the scanner.

25. The method of claim 24, wherein:

the method further comprises collecting dark data from a dark scan in which substantially no light of interest returns to the detector, the dark data being incorporated into correcting electrical artifacts of the scanner; and

the correction curves comprise data corresponding to adjustments for at least one of the intensity of light from the illuminator, a variation in first response of the mimic material,
correlation of the first and second radiant responses to the light as received by the detector, and a correlation between the sample and tissue in vivo.

26. The method of claim 24, wherein the correction curves comprise data corresponding to adjustments to remove from the second radiant response and corresponding to at least one of electrical and optical artifacts of the scanner, elastically scattered light, and fluorescence.

27. The method of claim 26, further comprising:

operating the scanner in a feedback control loop to detect in a subject an initial level of carotenoids in tissue;

administering nutritional supplements to the subject over a period of time; and

operating the scanner to detect a subsequent level of carotenoids in tissue corresponding to the administration of nutritional supplements.

28. A method to calibrate a detector of carotenoid content of tissue operating to test subjects in vivo and nondestructively, the method comprising:

providing a scanner comprising an illuminator to direct light nondestructively onto tissue in vivo, a detector to detect an intensity of a radiant response of carotenoids in the tissue to the light, and a computer interface;

providing a computer comprising a processor and memory and operably connected to the computer interface to process data from the scanner to isolate a Raman response of the carotenoids from at least one of elastic scattering, fluorescence, and electrical and optical artifacts of the scanner;

providing a calibrator comprising first, second, and third synthetic materials selected to substantially mimic the radiant response of the tissue;

directing light from the illuminator onto the first synthetic material to provide a white scan representing a portion of the radiant response of the tissue attributable to at least one of electrical artifacts of the scanner, optical artifacts of the scanner, reflected light, and re-radiated light at wavelengths not of interest;

directing light from the illuminator onto the second synthetic material to provide a high value scan corresponding to a comparatively higher number of chemical bonds to mimic a higher value of carotenoids in tissue;
directing light from the illuminator onto the third synthetic material to provide a low value scan corresponding to a comparatively lower number of chemical bonds to mimic a lower value of carotenoids in tissue;

providing inputs to the processor corresponding to the white scan, high value scan, and low value scan; and

processing the inputs to repeatably quantify a second radiant response of tissue in vivo to the light from the illuminator.

29. The method of claim 28, further comprising directing light onto a dark sample selected to provide a dark scan representing a portion of the radiant response of tissue attributable to at least one of uncontrolled variations, erroneous variations, and electrical artifacts of the scanner.

30. The method of claim 28, further comprising conducting a white scan and white field normalization of the radiant response of tissue to remove fluorescent and elastic portions of the radiant response.

31. The method of claim 28, wherein the first synthetic material comprises dilatant compound.

32. The method of claim 31, wherein the second synthetic material comprises dilatant compound doped with a first concentration of a first dopant.

33. The method of claim 32, wherein the third synthetic material comprises dilatant compound doped with a second concentration of a second dopant.

34. The method of claim 33, wherein the first and second dopants are different and distinct.

35. The method of claim 33, wherein at least one of the first and second dopants is a naturally occurring polymer.
36. The method of claim 33, wherein at least one of the first and second polymer is a synthetic polymer.

37. The method of claim 29, further comprising scanning a fourth synthetic material and adjusting the processing of the processor to correct for timewise variations in outputs of an individual scanner corresponding to the second radiant response corresponding to tissues in vivo.

38. A method to calibrate a detector of carotenoid content of tissue in vivo nondestructively, the method comprising:
   providing a scanner comprising an illuminator to direct light nondestructively onto tissue in vivo, a detector to detect an intensity of a radiant response of the tissue to the light, and a computer interface;
   providing a computer comprising a processor and memory and operably connected to the computer interface to process data from the scanner;
   providing a calibrator comprising a synthetic material selected to substantially mimic the radiant response of the tissue; and
   directing light from the illuminator onto the synthetic material and detecting a first radiant response thereeto;
   providing inputs to the processor corresponding to a state of the illuminator and the first radiant response to the light; and
   processing the inputs to repeatably quantify a second radiant response corresponding to tissue in vivo exposed to the light from the illuminator.

39. The method of claim 38, further comprising bleaching the tissue by exposing the tissue to the light for a period selected to reduce the intensity of the second radiant response to within a pre-determined operable range.

40. The method of claim 38, further comprising correlating a serum carotenoid content to the second radiant response of the tissue to the light.
Fig. 13

Filtered Signal

Fig. 14
Select Materials 212

Prepare Matrix 214

Prepare Dopant 216

Formulation 217a  Formation 217b  Sizing 217c

Distribute Dopant 218

Irradiate 220

Redistribute Dopant/Matrix 222

Fig. 18