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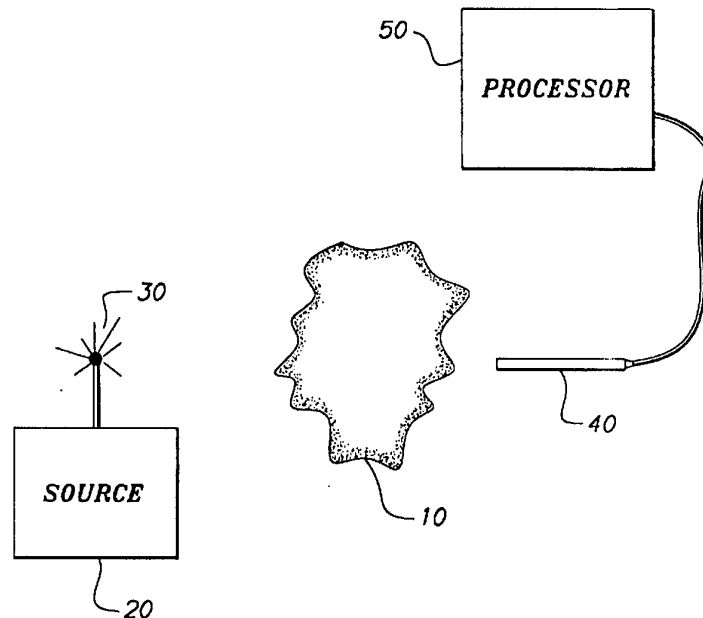
(57) Abstract

     Methods of imaging objects with diffused light. The method preferably can comprise the steps of illuminating the object with a source of light (20) which can be scattered by the object (10), collecting the scattered light with a detector (40) from multiple positions surrounding the object (10), measuring a means free path of photons scattered from the object (10) from the collected scattered light, and determining a diffusion constant for the photons scattered from the object (10) as a function of the measured mean free path, and determining in the transmission of the photons between the source (20) and the detector (40) as a function of the diffusion constant, thereby imaging the object (10), taking into account source-detector orientation and boundary effects.

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METHODS AND APPARATUS FOR IMAGING WITH DIFFUSE LIGHT

Field of the Invention

This invention relates generally to imaging of objects. More specifically, this invention relates to methods
5 and apparatus for imaging objects using diffuse light.

Background of the Invention

Techniques for imaging objects have been used for nearly a century in the medical arts for diagnosing and understanding the myriad diseases and maladies that afflict
10 the human body. Imaging techniques have also found use in such diverse fields as radio astronomy, sonar, radar and other fields which require information about an object which is not readily visible to the naked eye and therefore not easily examined. Medical imaging techniques include, for example, X-
15 ray imaging, positron emission tomography (PET), ultrasound imaging and the well known magnetic resonance imaging (MRI).

In all of the imaging techniques mentioned above, narrow band frequency radiation illuminates the object of interest to produce reflected or emitted radiation which is
20 then gathered from the object by a detector. The reflected or

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emitted radiation is then processed by an imaging algorithm to obtain useful information about the object.

In medical applications, the use of ionizing radiation in imaging, for example with X-rays, involves
5   significant health risks to a patient when the patient is exposed to the radiation for prolonged periods of time or in multiple imaging schemes. Furthermore, certain of these imaging techniques undesirably involve the use of invasive procedures which are both costly and painful. Yet other
10 techniques such as MRI do not yield consistently useful clinical results.

There has thus arisen in the medical imaging art an interest in developing non-invasive, safe imaging techniques which can take advantage of the natural scattering of visible
15 and infrared light through media containing objects to be imaged. Techniques using diffuse light could be used in conjunction with other imaging schemes such as X-ray imaging or MRI to produce highly useful clinical images for diagnostic purposes.

20   Much of the progress in imaging with diffusive light has focused on ballistic techniques using lasers. With these methods, an intense pulsed laser illuminates a sample. Time gating the earliest photons -- those photons that have been scattered only a few times, while rejecting all other
25 photons -- permits mapping of optical absorption. This technique works best when the allowed time window is short and photons deviate the least from their "ballistic" trajectory. Unfortunately, the transmitted intensity of unscattered photons diminishes exponentially with increasing sample
30 thickness.

Because of these limitations on ballistic imaging, it is difficult to obtain high quality images of relatively thick objects with low power lasers. Examples of ballistic imaging techniques are disclosed in K. M. Yoo, F. Lie and R.
35 R. Alfano, *Optics Letters*, Vol. 16, p. 1068 (1991), and in D. A. Benaron and D. K. Stevenson, *Science*, Vol. 259, p. 1463 (1993).

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A second technique in the prior art is optical phase
modulation. This technique can locate single absorbers using
low power, continuous wavelength lasers by creating photon
density waves. Anomalous phase shifts due to a single
5 absorber are readily interpreted; however for a more
complicated object a general analysis is required.

One such example of obtaining a characteristic of an
object with diffuse light is disclosed in U.S. Patent No.
5,119,815, Chance. The Chance patent reports a solution of
10 the diffusion equation for a homogeneous medium to obtain the
mean optical absorption of the entire object. This is
possible for the homogeneous medium because the long time
limit of the logarithmic derivative of the detected intensity
yields the absorption characteristics directly. Thus the
15 absorption characteristics for uniform structures may be
obtained with the methods and apparatus disclosed in the
Chance patent. However, in reality objects are heterogeneous
and the long time limit of the intensity does not reveal the
structure of the object.

20 Still other attempts to image with diffuse light are
disclosed in U.S. Patent No. 5,070,455, Singer et al. In the
Singer et al. system, light intensities are measured at many
sensor positions (pixels), initial values of absorption or
scattering coefficients are assigned at each pixel, and then a
25 new set of intensities at each pixel is calculated. The
calculated intensities are compared to the real intensities,
and the intensity differences are used to generate a
subsequent interaction of absorption or scattering values for
each pixel.

30 The methods described in Singer et al. usually
require many iterations since the absorption or scattering
values may not converge rapidly. The methods described in
Singer et al. utilize cumbersome Monte-Carlo statistical
techniques which consume large amounts of processing time
35 without guaranteeing computational success. Singer et al.'s
methods may also produce false local minima providing
misleading results for the absorption characteristics.

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Thus prior techniques using diffuse light for scattering fail to solve a long-felt need in the art for robust imaging techniques which can produce reliable images in biological systems. Solution of the aforementioned problems
5 has heretofore eluded the medical imaging art. The inventor of the subject matter herein claimed and disclosed has recognized that solution of the diffusion equation to obtain images would solve these problems and fulfill the long-felt need in the art for an effective clinical tool in medical
10 imaging.

Summary of the Invention

The above described needs are met with methods, systems and apparatus provided in accordance with the present invention. In a preferred embodiment, methods of imaging an
15 object with diffuse light are provided. The methods preferably comprise the steps of illuminating the object with a source of light which can be scattered by the object, collecting the scattered light with a detector from multiple positions surrounding the object, determining a diffusion
20 constant for the photons scattered from the object as a function of from the object as a function of the measured mean free path, and determining a net transmission of the photons between the source and the detector as a function of source-detector locations, thereby imaging the object.

25   Systems for imaging objects with diffuse light are also provided in accordance with the present invention. The systems preferably comprise a source which produces light to be scattered by the object, a detector for measuring light emitted from the source and scattered by the object, and
30 processing means interfaced with the detector for determining net transmission of photons scattered from the object and detected by the detector, the processing means adapted to determine the net transmission as a function of a probability of photons hitting the detector after being scattered by the
35 body.

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The methods, systems and apparatus disclosed and claimed herein solve a long-felt need in the art for imaging objects with diffuse or scattered light. Without intending to be bound by any theories or postulates, the inventor has

5 recognized that comparing the spatial distribution of photons scattered by an object to the flux calculated if the object were homogeneous yields the optical structure of the object being imaged convolved with a computationally tractable probability weight which describes the photon field within the

10 object. By deconvolving the calculated probability weighting function from the data, a tomographic map of the optical absorption of the object can be obtained, thereby imaging the object. Such images have heretofore not been achievable with prior methods of diffusion imaging and evince startling and

15 unexpected results when methods and apparatus provided in accordance with the present invention are employed.

The inventor has also discovered that photon current is anisotropic and therefore the photon flux must be measured paying particular attention to the detector orientation

20 relative to the light source. It was not previously appreciated by those with skill in the art that imaging with diffuse light was sensitive to detector orientation. Comparing the photon flux in the inhomogeneous object with the detector in a given orientation with respect to the source, to

25 the photon flux measured or calculated for a homogeneous object with the detector in the identical orientation is a more preferred mode of operation. This gives results superior to operations where detector orientation is not taken into account.

30 Importantly, methods and apparatus for imaging with diffuse light in accordance with the present invention provide computationally economic solutions for images of large objects with highly diffusive photons. Furthermore, imaging objects found within inhomogeneous media in accordance with the

35 present invention is possible using low power sources such as lasers. This makes imaging techniques described herein

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particularly attractive for biological and medical
applications.

The invention will be better understood with
reference to the following detailed description read in
5 conjunction with the drawings which are first briefly
described below.

Brief Description of the Drawings

Figure 1 is schematic diagram of an imaging system
provided in accordance with the present invention.
10   Figure 2 is a schematic diagram of an experimental
imaging system with which imaging of an object in an Intra-
lipid scatterer was performed using diffuse light.

Figure 3 is a block diagram of a generalized imaging
method provided in accordance with the invention.
15   .   Figures 4A and 4B are block diagrams of an alternate
imaging method which may be more practical with biological
samples.

Figure 5 is a graph of pulses propagating in 0.2%
Intralipid scattering media. The solid line indicates data
20 collected where a normal vector to the detector aperture is
perpendicular to a source-detector axis ($\theta = \pi/2$), while the
dashed line indicates data collected where the detector is
facing the source ($\theta = 0$).

Figure 6 is a graph of the reciprocal of the photon
25 mean free path for different concentrations of scatterers
where squares represent the detector perpendicular to the
source and triangles represent the detector facing the source.

Figure 7 is a graph of the reciprocal of the mean
free path of photons for different concentrations of intra-
30 lipid scatterers wherein squares represent fits to bulk
transmission, stars represent first to surface using pure
absorbing boundary conditions, and triangles represent fits
using mixed boundary conditions. The solid line is the best
fit with respect to bulk transmission data (squares).
35   Figure 8 is a graph of the boundary value parameter,

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h, for different reciprocal values of the photon mean free
path where squares represent the bulk transmission case and
triangles represent the backscattering case.

Detailed Description of Preferred Embodiments

5   Referring now to the drawings wherein like reference
numerals refer to like elements, Figure 1 shows a generalized
imaging system using diffuse light to provide an image of
object 10. Object 10 scatters a directed beam from source 20,
thereby producing diffuse light. Light 30 can be a single
10 wavelength, or multiple wavelengths depending on the applica-
tion in which the imaging system provided in accordance with
the invention is utilized. A detector 40 collects the photons
scattered by object 10, and forwards information concerning
the photons in the form of digital data to a processor 50.
15 The processor 50 constructs an image of object 10 with the
appropriate processing circuitry and software found therein.
          With systems shown generally in Figure 1, light
propagation can be measured through a multiple scattering
medium and the scattering mean free path measured for
20 different geometries of scatterers. The intensity of
scattered light can then be used to determined the composition
of the scattering medium and to further characterize objects
in the scattering medium.
          Generally, scattering media do not have spatially
25 uniform scattering and absorption constants. Thus, a con-
siderable degree of complexity exists in interpreting
scattered light data. Current systems do not have the
ability to provide consistent measurements of the effective
mean free path of scattered photons. Furthermore, prior work
30 in diffusive imaging has not adequately taken into account the
relationship between the orientation of the source of the
light with respect to the detector, nor have prior diffusive
light imaging systems been able to effectively deal with
varying object geometries.
35   The above effects have profound impacts on the
distribution of photon path lengths after the photons have

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been scattered by the object. The inventor of the subject
matter herein claimed and disclosed has discovered that the
orientation of the detector relative to the source affects the
transmitted flux. Furthermore, the appropriate boundary
5 conditions in effect at the interface between a scattering
medium and a medium in which photons propagate freely must be
fully characterized in order to obtain an image of the object.

This has important implications on the desire for
non-invasive techniques in biological imaging, since if a
10 detector is placed outside of the medium, the photons will
naturally cross the interface boundary. Thus, for biological
and medical imaging, boundary conditions should be fully
understood. In accordance with the present invention, imaging
methods and systems efficiently handle boundary conditions or
15 discontinuities at boundary interfaces.

Imaging with diffuse light in accordance with the
present invention begins with an understanding of the
diffusion equation. Photon density within a multiple
scattering medium is described by the diffusion equation in
20 the following form:

$$\frac{\partial u}{\partial t} = D\nabla^2 u - \mu_a c u,$$

where u is the density of photons, μ_a is the absorption
25 coefficient, $D = cl^*/3$, known as the "photon diffusion
constant", and c is the speed of light in the scattering
medium. If the filling fraction of the scatterer is small,
differences in photon phase velocity and energy transport
velocity can be ignored. The effective mean free path l^*
30 describes the length scale over which scattering is isotropic
and is related to the mean free path, l, by the relationship l^*
$= l/(1-g)$ where g is the average cosine of the single particle
scattering angle.

By gathering data from a system such as that shown
35 in Figure 1, solutions to the diffusion equation can be used

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to determine the average light absorption coefficient μ_a and the scattering mean free path Γ.

In order to obtain an image of the object, it is preferred to map the physical absorption and/or scattering 5 constants. According to the present invention, the spatial distribution of photons scattered by an object is compared to the flux calculated if the object were homogeneous. This measured ratio is equivalent to the spatially inhomogeneous optical structure of the object convolved with a probability 10 weight describing the photon field. The data can then be deconvolved using the calculated weighting function to obtain a tomographic map of optical absorption and an image of the object. In order to calculate the weighting function, it is necessary to know the average scattering mean free path Γ.

15   In addition, if sources of illumination are placed outside the scattering medium, it is necessary to determine the photon boundary conditions at the surface of the object. These determine photon propagation through the object.

To obtain the tomographic map, it is necessary to 20 fully characterize the behavior of the scattered photons in the medium. As described above, photon propagation obeys the diffusion equation when the spatial scale, L, of a scattering chamber is many times the size of the photon effective mean free path Γ. The absorption $\mu_a(r)$ of the photons is a function 25 of position, thereby representing the structure of the object. For convenience, define $\mu'_a(r) = \mu_a(r) - \overline{\mu}$, where $\overline{\mu}$ represents the mean absorption in the object. Thus, $\mu'_a(r)$ is the spatially fluctuating component of absorption.

A technique to solve the diffusion equation in the 30 presence of a spatially fluctuating absorption, has been partially described in J. Schotland, J. Haselgrove and G. Leigh, *Applied Optics*, Vol. 32, p. 448 (1993) wherein the concept of "hitting density" is introduced. The hitting density, denoted $v(r;r_1,r_2,t)$, is the probability weight at 35 position r for a photon travelling from source position r_1 to

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detector position r_2 in total travel time t. A photon may pass through r at any time between 0 and t. The net transmission, T, of photons at r_2 is then attenuated by the local absorption at r in proportion to the density ν. Taking the natural
5 logarithm of the net transmission, the following is obtained:

$$lnT = - \int \nu(r;r_1,r_2,t)c\mu'_a(r)d^3r,$$

(1)

$T = S/S_0$ where S is the transmitted flux through the scattered object, S_0 is the flux transmitted by a homogeneous object of the
10 same geometry, and ν represents the hitting density in the *absence* of spatially fluctuating absorption. It should be noted that the source-detector orientation can affect substantially the flux. The approximation implicit in the above equation has validity when the limit:

15

$$\int_\gamma \mu'_a(r)dr \ll 1,$$

(2)

where γ denotes a typical path of a photon traversing the absorbing object.

20   To obtain $\mu'_a(r)$ as a function of T the solution to the forward problem stated by Equation (1) must be inverted. In accordance with the present invention, the method for calculating the hitting density is direct. Thus, there is no need for computationally expensive Monte-Carlo simulations or complicated
25 recursive formulae. For the infinite geometry, an analytic form is used to calculate ν:

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$$v(r;r_1,r_2,t) = \frac{1}{4\pi D}\left(\frac{1}{|r-r_1|} + \frac{1}{|r-r_2|}\right)exp\text{-}\left(\frac{1}{4Dt}\left(\left(|r-r_1| + |r-r_2|\right)^2 - \left(|r_1-r_2|^2\right)\right)\right).$$

5   (3)

    In a semi-infinite geometry, v is equivalent to the "banana" shaped photon field which is well known to those with skill in the art.

        A general prescription for v is given by Schotland,

10 Haselgrove and Leigh, who obtain:

$$v = \frac{1}{u(r_1,r_2,t)}\int_0^t u(r_1,r,t')\,u(r,r_2,t\text{-}t')\,dt'$$

15

    where u denotes the 2-point Green's function uniquely determined by the geometry, boundary conditions, and diffusion constant.

        The inversion of Equation (1) is aided greatly by discretization such that:

20

$$\mu'_a(r)_i = \sum_j \frac{v_{ij}^+(r;r_1,r_2,t)}{cdV} \times \left(-lnT_j(r_1,r_x,t)\right).$$

(4)

25 Thus, according to the above equation, the probability weight v can be recast into matrix form and a pseudo-inverse v_{ij}^+ obtained. Using singular value decomposition to obtain v_{ij}^+, the 30 smallest eigenvalues are truncated or dampened. This reduces the propensity of v_{ij}^+ to amplify noise. In this notation, $\mu'_a(r)_i$ is a column vector of absorption coefficients, $T_j(r_1,r_2,t)$ is a column vector consisting of the flux ratios, and the pixel

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volume is denoted by dV. The discrete quantities r_1, r_2, and t
are preferably concatenated to form a single row or column
index.

     In a further preferred embodiment, the imaging system
5 shown in Figure 2 was constructed by the inventor and used to
perform imaging tests in accordance with the present invention.
A chamber 60 was constructed and filled with a 2% intralipid
(IL) solution which in unadulterated form is a white liquid
consisting of 20% soybean oil suspended in 80% water. The light
10 source was a laser 70 which pulsed repeatedly at 5Mhz. The
pulsed 5Mhz signal was injected via an optical fiber 80 into the
chamber 60 through the IL shown generally at 90. The light 100
scattered through the IL was collected by a collector fiber 110
and detected by a detector 120 which in a preferred embodiment
15 was a photomultiplier tube (PMT) manufactured by the Hamamatsu
Company of Japan, Model No. R1517. Detector 120 alternatively
could be a streak camera or microchannel plate detector.
Computer processor 50 processed the data detected by the
photomultiplier 120.

20   The laser pulses were 50 ps wide at 780 nm and the
chamber 60 was a 20 x 20 x 40 cm tank containing the scattering
IL suspension. The chamber was much larger than the largest
separation between source and detector (6 cm). Thus, for
excellent approximation the imaging experiment was performed in
25 a free medium, with vanishing boundary conditions at infinity.
The object 10 was one or more tubes containing IL of the same
concentration as the ambient bath, together with a small
quantity of ink. The scattered light was collected from
multiple positions in the bath by fiber 110 and guided to the
30 PMT 110.

     Generally, it is desired to measure the diffusion
constant D for the object. In accordance with the invention,
and as shown in Figure 3, the generalized block diagram for
performing this function is illustrated. At block 121, D is
35 measured by solving the diffusion equation for the 2-point
Green's function for the infinite geometry of the experiment

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which is given by:

$$u(r,t) = \frac{u_o}{(4\pi Dt)^{3/2}} \, exp(-r^2/4Dt - \mu_a ct) \, .$$

5   (5)

Knowledge of the boundary conditions allow a determination of
the 2-point Green's functions which, together with the geometry
of the system, allow for determination of ν. Furthermore, the
detector orientation affects the observed fluxes J, which are
10 not necessarily equal to the photon densities u. The relation-
ship between the photon density, u, and the observed photon
flux, J, is given by

15      $$J_r = \frac{c}{4} \, (\frac{1 - \hat{s} \cdot \nabla}{h}) \, u$$

where $h \equiv \frac{3}{2l^*}$ and $\hat{s}$ is the unit vector along the source-
detector axis. Alternatively, for the case where the detector
20 is not inside the scattering medium but is placed at its
surface, the photon density is equal to the photon flux, however
the photon density is subject to the boundary condition

25      $$uh + \frac{\partial u}{\partial z} = 0 \, .$$

The inventor has realized a method for measuring the
boundary parameter h, to be described hereafter. In the
presence of a boundary, the photon density u is given by
Equation (11).

30   Thus, by observing the flux for different positions r,
it is possible to fit a single set of diffusion constants D and
absorption constants μ_a for solution to the diffusion equation.
Once this is accomplished at step 122, it is desired to cal-
culate the hitting density ν as defined above. At step 123, if

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light is scattered through the surface, it is then desired to
measure the boundary conditions.

At step 124, it is preferred to then measure the net
transmission function $T(t) = S(t)/S_o(t)$, where $S_o(t)$ is the

5 transmitted flux in the absence of an absorber. Given the
measured flux ratios, and the hitting density, it is then
possible to reconstruct the image at step 125 via deconvolution
of the hitting density from Equation (1).

To calculate ν, it is preferred to first measure Γ and

10 determine D. In principle it is not necessary to measure $S_o(t)$,
given $\Gamma, \bar{\mu}$ and the absolute detector sensitivity.

Figures 4A and 4B are a modified block diagram for
imaging an object in accordance with the invention. As in the
method described with respect to Figure 3, at step 126 in Figure

15 4A, D and $\bar{\mu}_a$ are measured for a typical object. In a preferred
embodiment, using "typical" boundary conditions at step 127
allows absorbing or transmissive boundary conditions to be
utilized to fully characterize the object. For example, to
image a human breast or brain that may contain a tumor, it is

20 not feasible to compare the scattered fluxes through the tissue
to the fluxes through the same tissue with the tumor removed.
It would be greatly desirable to know beforehand what the fluxes
should be through tissue that is known to be free of tumors, or
any other obstructions. Then, at step 128, it is possible to

25 calculate the hitting density and image the object by
deconvolution as discussed above.

In the second preferred embodiment, Figure 4B
illustrates an alternative imaging scheme wherein measured
fluxes of scattered light through the object of study are first

30 observed at step 129. This is not necessarily the same object
as was discussed with respect to Figure 4A at step 126, since it
may not be practical to accomplish all the measurements required
at step 126 to determine D and $\bar{\mu}_a$ for the object. However, at
step 129 by observing measured fluxes, it is then possible to

35 use previously determined D and μ_a to calculate the flux S_o for

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the fiducial uniform object. It is then possible to calculate
the flux ratios, and at step 131 to reconstruct the image by
deconvolving ν from the flux ratios. In accordance with the
method of Figures 4A, and 4B (and for that matter, the

5   generalized method of Figure 3), accurate determinations can be
made of the object by taking into account the boundary
conditions.

        Using the above analysis, a 1.4 cm diameter tube in an
IL bath was examined wherein l = 0.3 mm. The tube was aligned

10 along the z axis and characterized by an absorption μ_a = 0.64
cm^{-1}. The reconstructed value for the absorption μ_a (for an
object) = 0.34 cm^{-1}.

        For an IL bath where l = 0.5 mm containing three
equally spaced tubes of 5.5 mm diameters, the tubes oriented at

15 the top and right of the chamber were characterized by an
absorption constant μ_a = 0.13 cm^{-1}. The bottom left tube was
characterized by an absorption μ_a = 0.26 cm^{-1}. With imaging
methods provided in accordance with the invention, μ_a = 0.15 cm^{-1}
and μ_a = 0.24 cm^{-1} were measured respectively for the two sets of

20 tubes.

        Generally, the absorption characteristics determined
for this second data set agree quantitatively with actual
absorption. However, with respect to the first dataset, the
size of the object which produced the first dataset and the

25 absorption were both too large for the approximation of
Equations (1) and (2) to hold.

        The methods of optical diffusion imaging described
above extract information from photons scattered many times in
their trajectory from source to detector. Thus, methods in

30 accordance with the present invention open the possibility of
using low power lasers to study thick ($L > 10l$) samples.
Within the limit that the absorption through a finite object is
not too large, absorption coefficients can then be mapped
quantitatively.

35   As discussed above in Equations (1) and (4)
respectively, the effects of detector orientation and boundary

- 16 -

conditions at an interface with a free medium play profound roles in obtaining accurate observed values of μ_a. The inventor has discovered that photon density, $u(r,t)$ can be characterized with respect to these effects so that accurate absorption

5 characteristics can be determined.

The inventor has further recognized that the observed light picked up by the detector is not the photon density *per se*, but is the directional photon current, J_f, into the detector aperture. This current is given by Fick's law, as $J = -D\nabla = J_{+f} -$

10 J_{-f} and represents the net current only, not the directional current. The directional current represents the inward flow component perpendicular to the plane of the detector aperture. By transport theory, the resulting current is expressed as:

15 $$J_f = \frac{c}{4}\ (u - \nabla_f\,u/h)\ = \frac{c}{4}\ (1 - \frac{\hat{s} \cdot \nabla}{h})\,u$$

$$(6)$$

where h is defined as $3/(2\Gamma)$ and $\hat{s}$ is the unit vector along the source-detector axis.

20 The physical interpretation of photon density described by Equation (6) is that the distribution of photons in the diffusion regime is anisotropic. Thus, u is the isotropic part of the photon flux, and the gradient term is the directional component. If there are no directional components,

25 the photon distribution would be isotropic at every position, in which case there would be no tendency for photons to migrate outward from the source.

For a homogeneous infinite medium, the application of Equation (6) is particularly simple, and can be written as:

30 $$J = \frac{u_o c}{4(4\pi Dt)^{3/2}}\ exp(-r^2/4Dt - \mu_a ct)\left(1 + \frac{r\cos\theta}{ct}\right),$$

$$(7)$$

- 17 -

where θ describes the inclination of the detector toward the source-detector axis.

By observing the photon current of Equation (7) with a system such as that of Figure 2, the source-detector orientation
5 can be taken into account and accurate images of an object obtained. Referring to Figure 5, two pulses observed with the same source-detector separation but with the detector orientations corresponding to $\theta = 0$ and $\theta = \pi/2$ are shown. It can be seen that with these two different detector orientations,
10 a different photon current density is observed.

In Figure 6, the scattering mean free path l', determined separately for the detector in the $\theta = 0$ and $\theta = \pi/2$ orientations is shown. The squares represent l' when $\theta = \pi/2$, while the triangles represent l' when $\theta = 0$. The only
15 significant deviation from a straight line fit is for the lowest dilution, in this case, the minimum ratio of source-detector distance to mean free path, that is, L/l' approximately 2.5. In this situation, the diffusion equation is no longer applicable.

As mentioned above, consideration of boundary
20 conditions at the interface with the free medium and the pulse propagation near the surface of the semi-infinite volume is also necessary to obtain accurate μ_a and l^* characteristics. At a surface, $z = 0$ and the scattering medium is divided from a medium in which light travels unhindered. By comparing
25 backscattering data for light that is free to radiate from the surface to light that is absorbed everywhere except at the detector position, accurate μ_a and l^* determinations can be made with systems shown in Figure 2. Boundary conditions were then studied so that absorption constants could be determined and
30 imaging accomplished.

The absorbing condition is preferably treated analytically by an image source with negative intensity at $z = -l'$ together with the source at $z = +l'$. The measured photon current at the surface can then be given by:

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$$J = \frac{u_o r}{(4\pi D)^{3/2} t^{5/2}} \, exp[-(r^2 + r'^2)/4Dt - \mu_a^* ct].$$

(8)

A second preferred approach to photon diffusion across a plane surface is to adopt the boundary conditions inferred from transport theory and which we have been used to interpret directional currents. For the semi-infinite volume containing scatterers for all $z < 0$, the directional current at the surface is $J_z = 0$. That is, no light that leaves the scattering medium returns. However, a finite density of photons is permitted for $z = 0$ at the surface, and the boundary condition for this situation is:

$$uh + \frac{\partial u}{\partial z} = 0.$$

(9)

Interestingly, a subtle distinction exists between this case and the absorbing condition, u at $z=0$ equal to 0. The first statement is concerned with photon flux, while the second statement concerns photon number density. Thus, the second statement is an approximation that describes the photon density at positions sufficiently far from the surface, and is mathematically simpler. However, the first statement is more readily adapted to the case where there is a mismatch in the index of refraction between the scattering medium and the free medium. Such a mismatch may change the boundary conditions which in turn modifies the distribution of photon path lengths. Therefore, if there are internal reflections at the interface, they may be described as an incoming current, J_-, related to the outgoing current, J_+ by $J_- = RJ_+$ where R is an effective reflection coefficient. This in turn is related to the boundary coefficient h by:

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$$h = \frac{3}{2\Gamma} \frac{R-1}{R+1}.$$

<div align="right">(10)</div>

Given the boundary conditions for a semi-infinite volume, the photon density then is:

$$u(r,t) = \frac{u_o exp(-r^2/4Dt - \mu_a ct)}{(4\pi Dt)^{3/2}} \cdot [1 - h\sqrt{\pi Dt} \; erfc(h\sqrt{Dt}) exp(h^2 Dt)].$$

<div align="right">(11)</div>

When the photon current was measured, the source and detector were located at the surface separated by several distinct distances r, and analysis yielded fits for the parameter h, in addition to D and μ_a.

Referring to Figure 7, the mean free path obtained from a surface backscattering data fit (triangles) was compared to the mean free path obtained in the infinite volume case (squares). The agreement between the two data sets is significantly better than that afforded by the assumption of pure absorption boundary conditions.

Referring now to Figure 8, the value of h measured for different concentrations of scatterers is plotted. The parameter h scales with $1/\Gamma$ as predicted.

It can thus be seen that the diffusion imaging methods, techniques, and apparatus described above produce high quality images of light scattering objects. Systems and methods provided in accordance with the present invention have particularly strong applications in biological and medical imaging where non-invasive approaches are preferred. Furthermore, by taking into account the source-detector orientation as well as boundary conditions and interfaces, objects in inhomogeneous

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media can be clearly and accurately imaged. Such results have
not heretofore been achieved in the art and promise to provide
worthwhile and efficient techniques in medical or biological
imaging for clinical and diagnostic purposes.

There have thus been described certain preferred
embodiments of methods and apparatus for diffusion imaging
provided in accordance with the present invention. While
preferred embodiments have been described and disclosed, it will
be recognized by those with skill in the art that modifications
of the methods and apparatus are within the true spirit and
scope of the invention. The appended claims are intended to
cover all such modifications.

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CLAIMS

What is claimed is:

1.   A method of imaging an object with diffuse light
comprising the steps of:

illuminating the object with a source of light
which can be scattered by the object;

collecting the scattered light with a detector
from multiple positions surrounding the object;

determining a diffusion constant for the photons
scattered from the object as a function of the
measured mean free path; and

determining a net transmission of the photons
between the source and the detector as a function of
source-detector locations as a function of the
orientation of the detector with respect to the
source, thereby imaging the object.

2.   The method recited in claim 1 further comprising
the step of determining boundary conditions for the photons as
the photons traverse a medium between the source and the
detector.

3.   The method recited in claim 2 wherein the step of
determining the net transmission of photons comprises the steps
of:

measuring a mean free path of photons scattered
from the object from the collected scattered light;

calculating a hitting density for the photons
between the source and the detector;

measuring a flux ratio of the photons detected by
the detector; and

reconstructing an image of the object by
deconvolving the hitting density from the measured
flux ratio.

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4.   The method recited in claim 1 further comprising the step of measuring an absorption constant for the photons as they traverse a medium between the source and the detector.

5.   The method recited in claim 4 further comprising the step of measuring boundary conditions for the photons as the photons traverse through the medium.

6.   The method recited in claim 5 further comprising the step of determining an orientation of the detector with respect to the source to determine a photon current detected by the detector.

7.   The method recited in claim 6 further comprising the step of determining a hitting density for the photons between the source and the detector.

8.   A system for imaging an object with diffuse light comprising:

a source which produces light to be scattered by the object;

a detector for measuring light emitted from the source and scattered by the object; and

processing means interfaced with the detector for determining net transmission of photons scattered from the object and detected by the detector as a function of the orientation of the detector with respect to the source, the processing means adapted to determine the net transmission as a function of a probability of photons hitting the detector after being scattered by the body.

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9.   The system recited in claim 8 wherein the
detector is oriented at a known angle with respect to the
source.

10.   The system recited in claim 11 wherein the source
is a laser.

11.   The system recited in claim 10 wherein the
processing means determines the net transmission by calculating
a hitting density for the photons between the source and the
detector, measuring a flux ratio of the photons detected by the
detector, and reconstructing an image of the object by
deconvolving the hitting density from the measured flux ratio.

12.   A method of imaging an object with diffuse light
comprising the steps of:
           illuminating the object with a source of light
       which can be scattered by the object;
           collecting the scattered light from multiple
       positions surrounding the object with a detector that
       is oriented at angle with respect to the source;
           measuring a mean free path of photons scattered
       from the object from the collected scattered light;
           determining a diffusion constant for the photons
       scattered from the object as a function of the
       measured mean free path; and
           determining a net transmission of the photons
       between the source and the detector as a function of
       the diffusion constant and the orientation of the
       detector with respect to the source, thereby imaging
       the object.

13.   The system recited in claim 12 wherein the
detector is oriented at a angle with respect to the source.

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14.   The method recited in claim 13 further comprising
the step of determining boundary conditions for the photons as
the photons traverse a medium between the source and the
detector.

15.   The method recited in claim 14 wherein the step
of determining the net transmission of photons comprises the
steps of:

      calculating a hitting density for the photons
    between the source and the detector;

      measuring a flux ratio of the photons detected by
    the detector; and

      reconstructing an image of the object by
    deconvolving the hitting density and the measured flux
    ratio.

16.   The method recited in claim 13 further comprising
the step of measuring an absorption constant for the photons as
they traverse a medium between the source and the detector.

17.   The method recited in claim 16 further comprising
the step of measuring boundary conditions for the photons as the
photons traverse through the medium.

18.   The method recited in claim 17 further comprising
the step of determining an orientation of the detector with
respect to the source to determine a photon current detected by
the detector.

19.   The method recited in claim 18 further comprising
the step of determining a hitting density for the photons
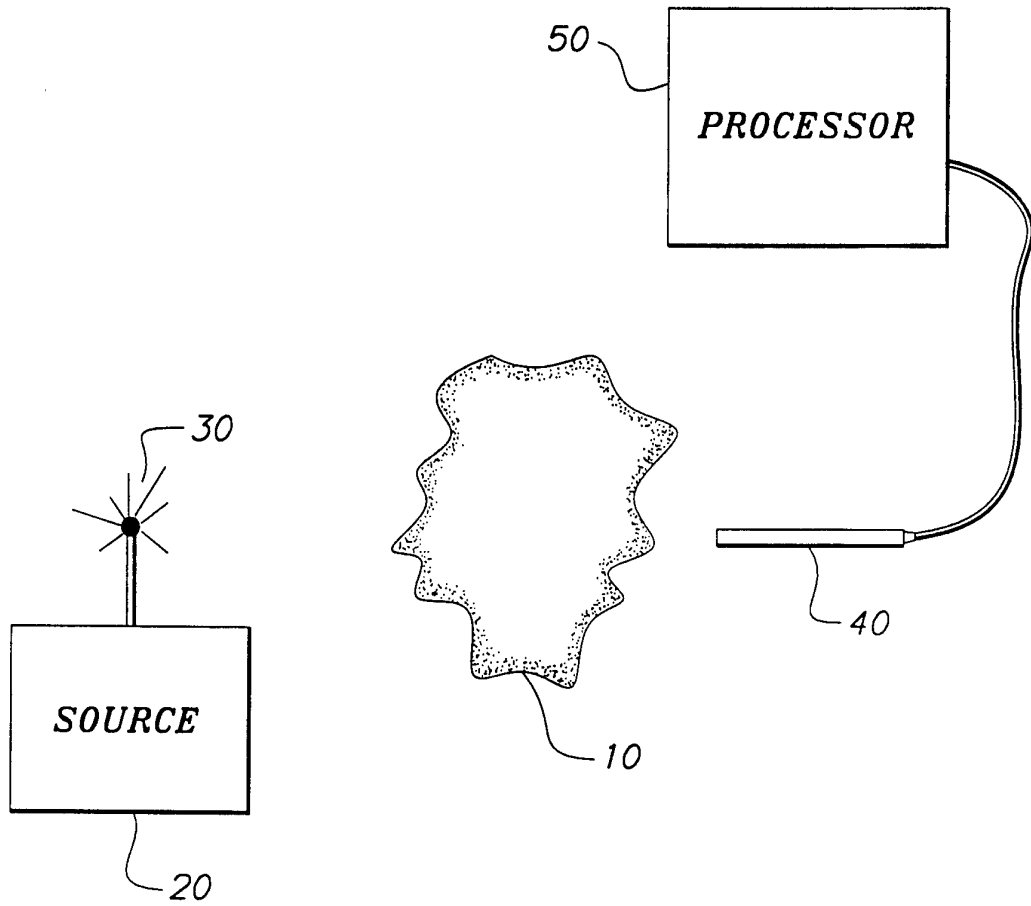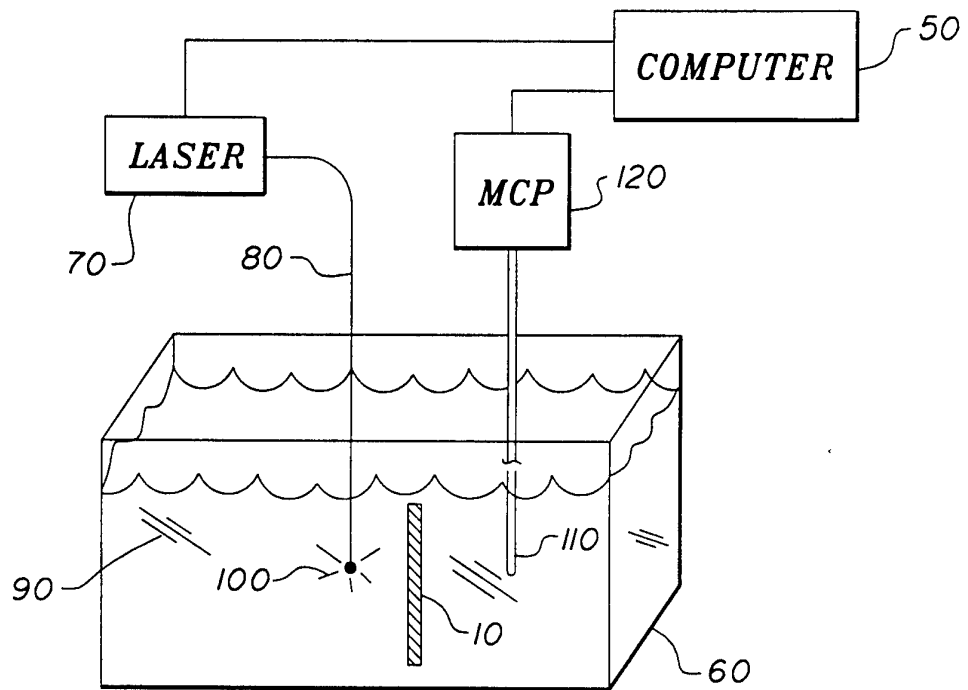between the source and the detector.

50

PROCESSOR

30
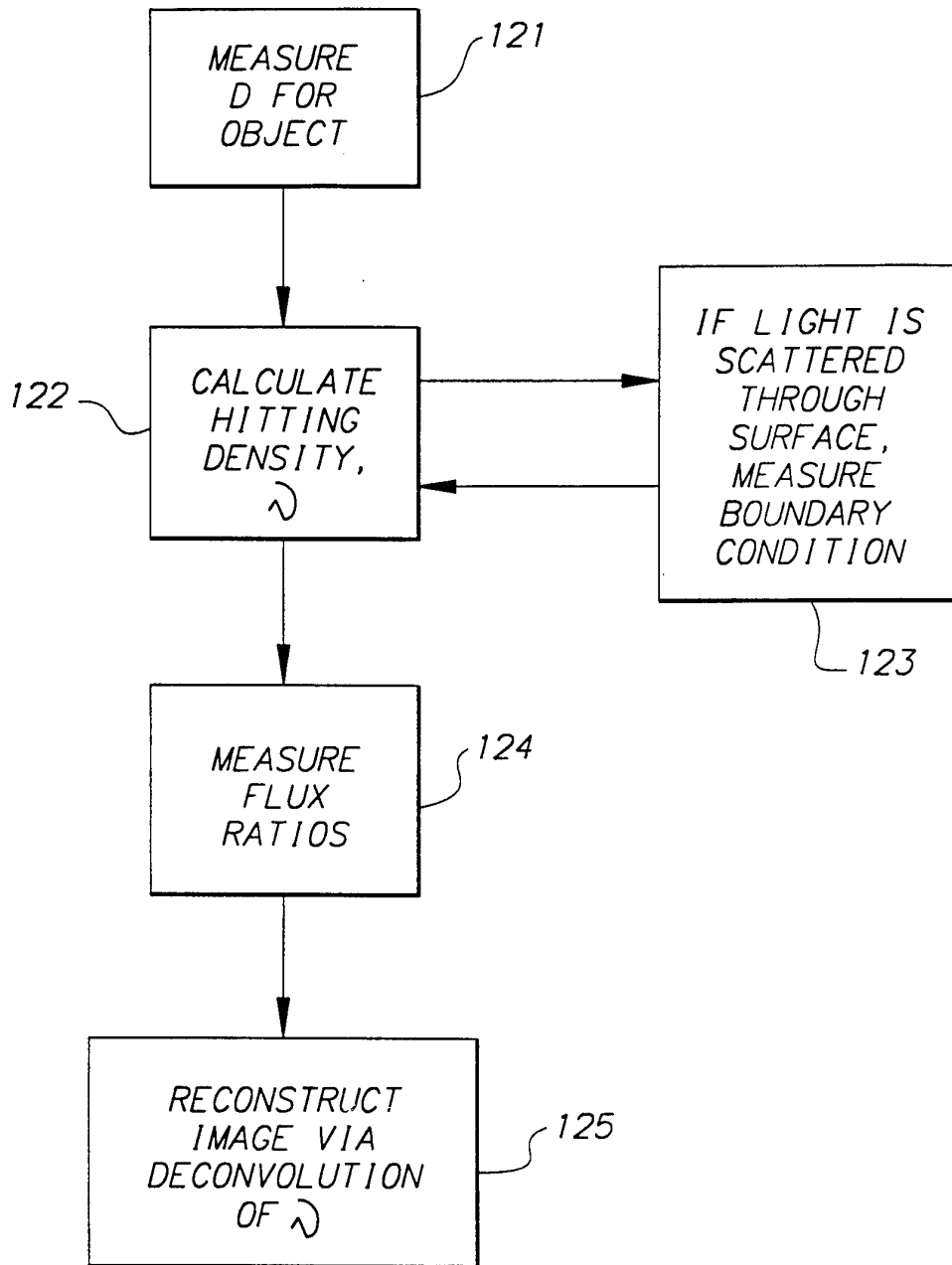
SOURCE

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FIG. 1

FIG. 2

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```
┌─────────────┐
│  MEASURE    │╭─121
│   D FOR     │
│   OBJECT    │
└─────────────┘
       │
       ▼
┌─────────────┐                    ┌──────────────┐
│  CALCULATE  │────────────────────▶│  IF LIGHT IS │
122─│ HITTING     │                    │   SCATTERED  │
│  DENSITY,   │                    │   THROUGH    │
│     ∿       │◀───────────────────│   SURFACE,   │
└─────────────┘                    │   MEASURE    │
       │                           │   BOUNDARY   │
       │                           │  CONDITION   │
       ▼                           └──────────────┘
┌─────────────┐                            └─123
│  MEASURE    │╭─124
│   FLUX      │
│   RATIOS    │
└─────────────┘
       │
       ▼
┌─────────────┐
│ RECONSTRUCT │
│  IMAGE VIA  │╭─125
│DECONVOLUTION│
│   OF  ∿     │
└─────────────┘
```

FIG. 3

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```
┌─────────────┐
│  MEASURE D, │
│  μₐ FOR     │
│  TYPICAL    │──── 126
│  OBJECT     │
└─────────────┘
```

```
┌─────────────┐          ┌─────────────┐
│  MEASURE    │          │             │
│  TYPICAL    │          │  CALCULATE  │──── 128
│  BOUNDARY   │─────────▶│     λ       │
│  CONDITIONS │          │             │
└─────────────┘          └─────────────┘
         └── 127
```

FIG. 4A

```
┌─────────────┐
│  MEASURE    │
│  FLUXES OF  │
│  SCATTERED  │──── 129
│  LIGHT THROUGH│
│  OBJECT OF  │
│  STUDY      │
└─────────────┘
```

```
┌─────────────────┐          ┌─────────────┐
│  USE MEASUREMENTS│─── 130   │  RECONSTRUCT│
│  OF D, μₐ TO    │          │  IMAGE BY   │
│  CALCULATE      │          │  DECONVOLVING│
│  FLUXES FOR     │─────────▶│  λ FROM     │
│  UNIFORM OBJECT │          │  FLUX RATIOS│
│  AND CALCULATE  │          └─────────────┘
│  FLUX RATIOS    │                 └── 131
└─────────────────┘
```

FIG. 4B

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FIG. 5

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FIG. 6

FIG. 7

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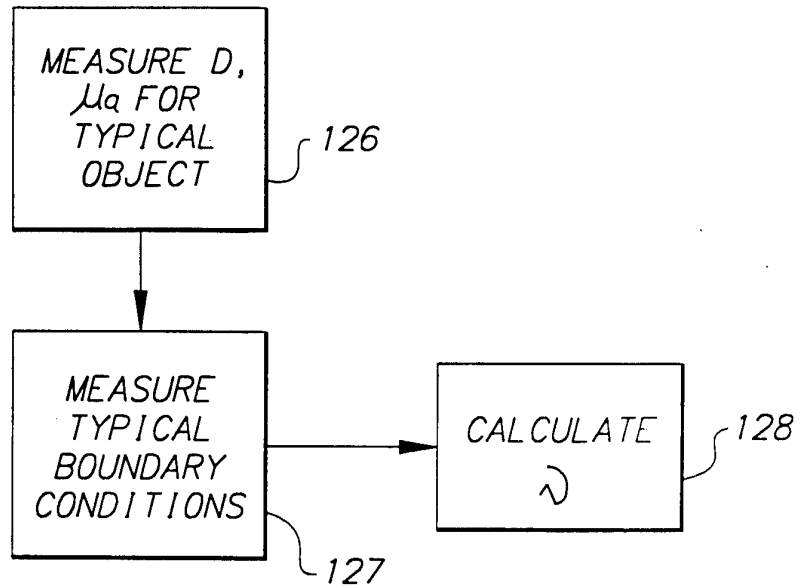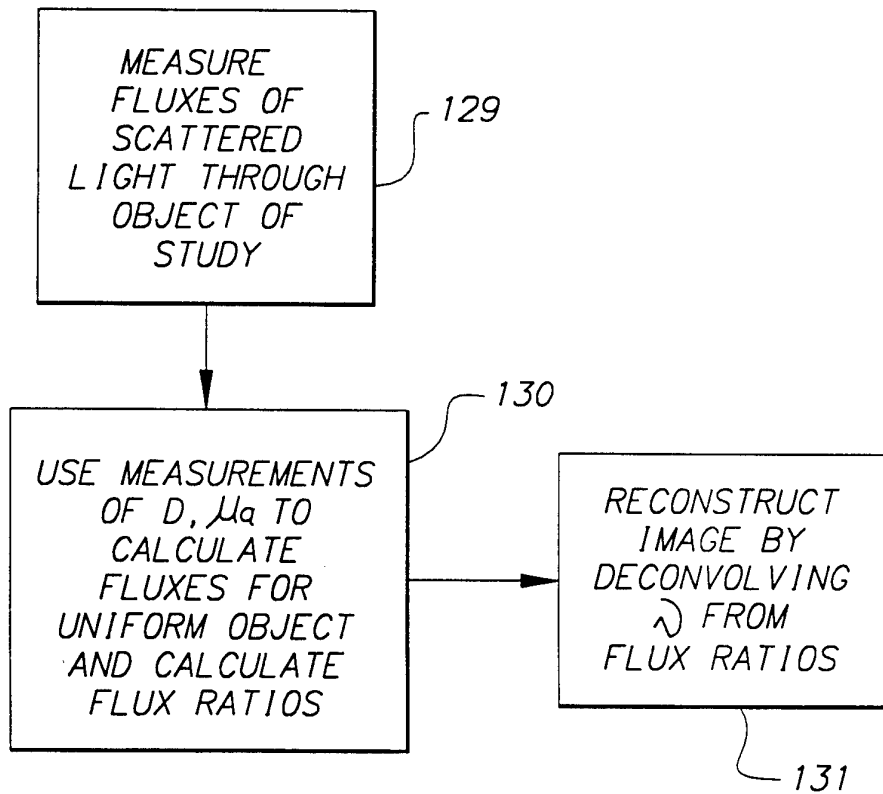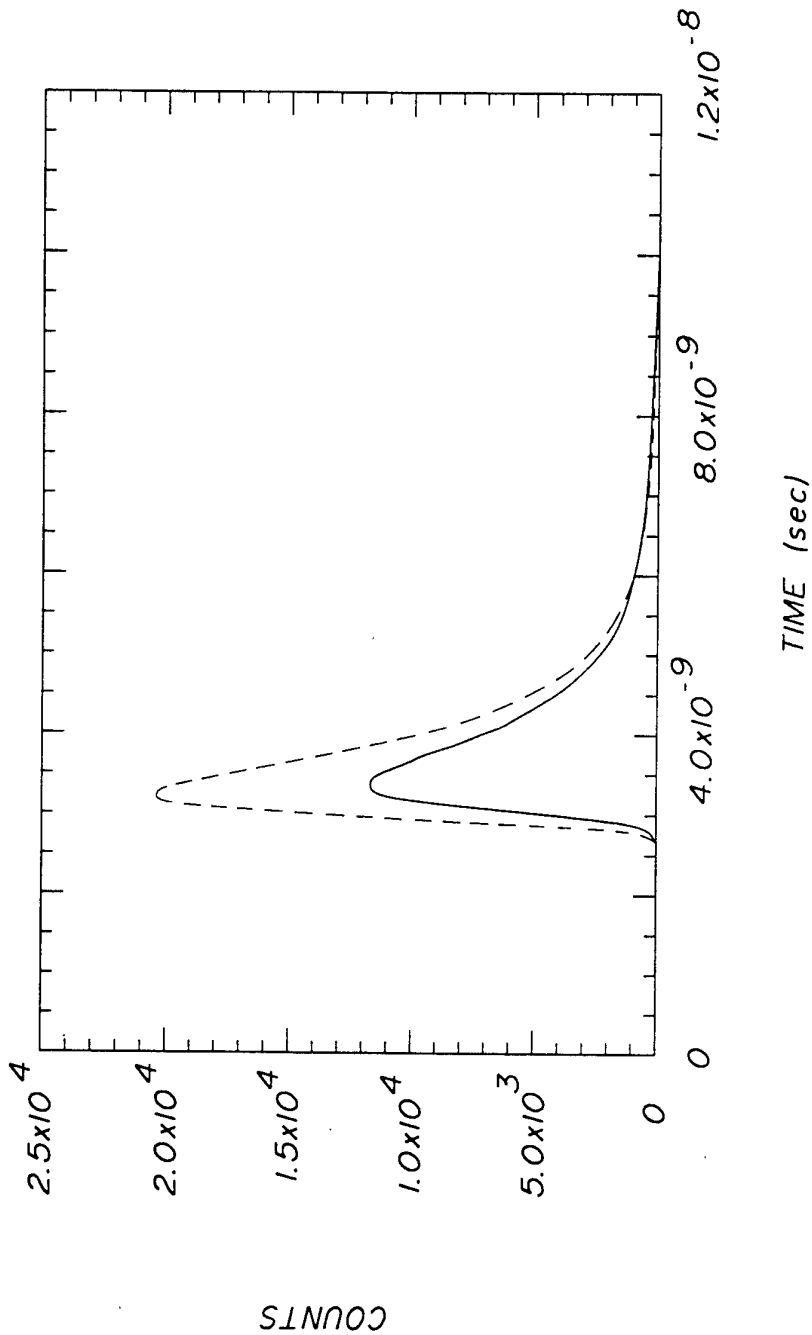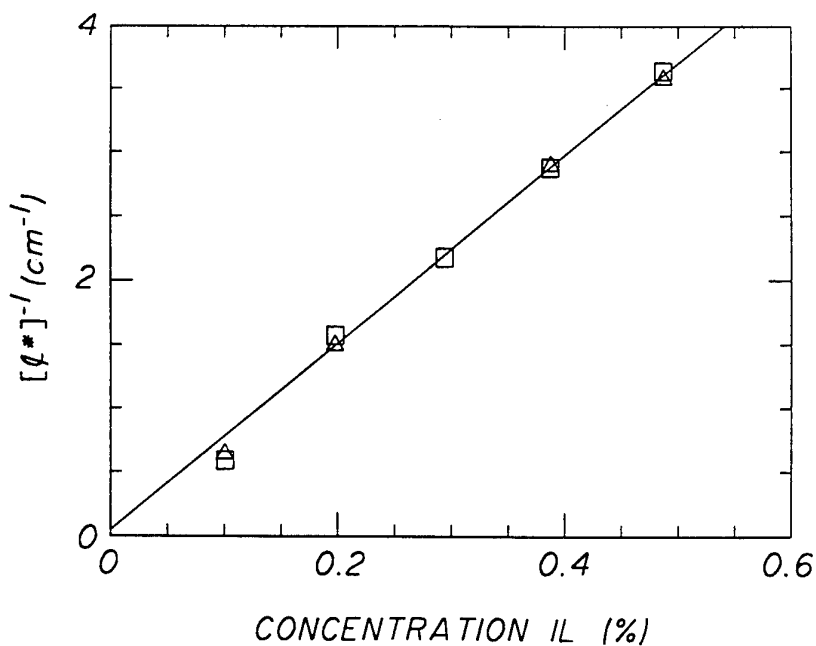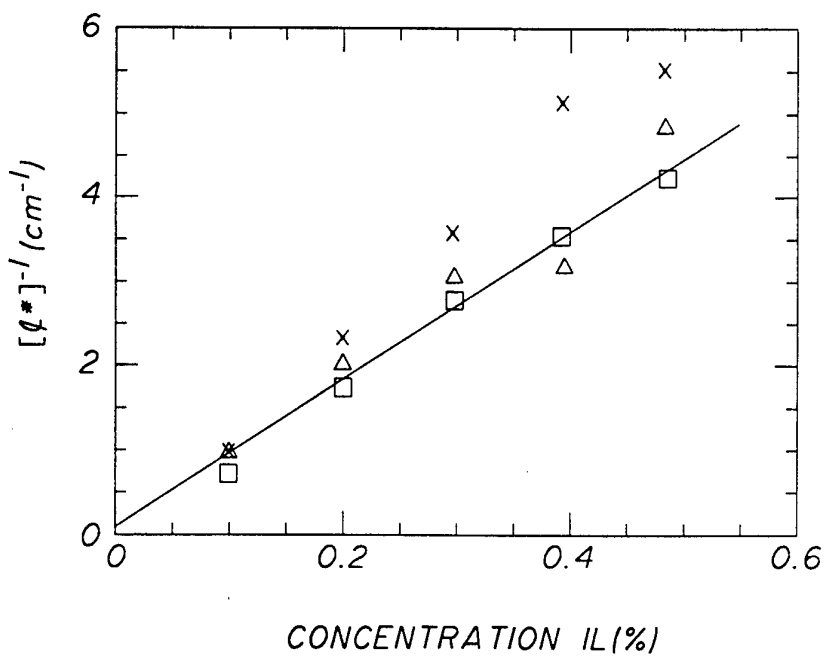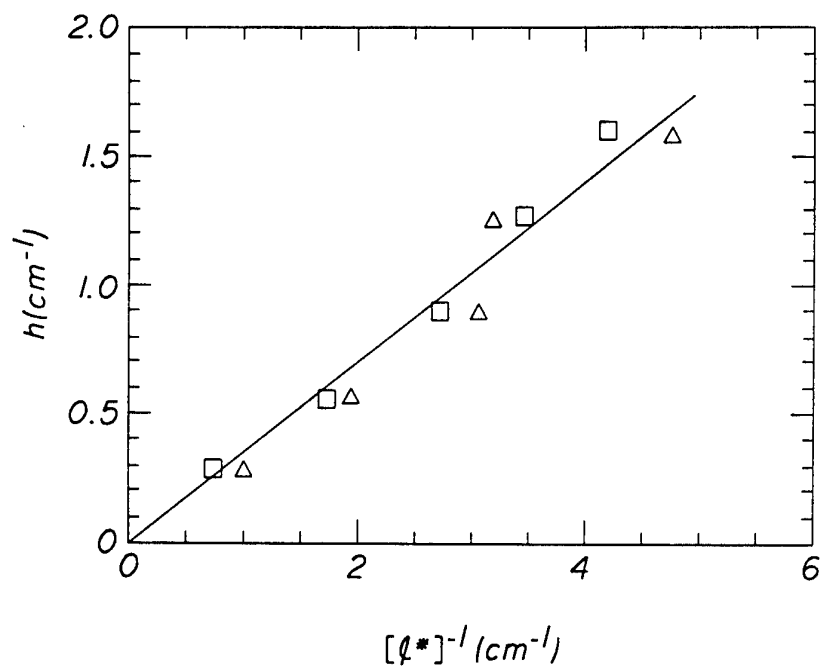
FIG. 8

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) : G01N 21/49
US CL : 356/41
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
U.S. : 356/41

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Applied Optics, Vol 32, No. 4, 01 February 1993, Schotland et al, "Photon Hitting Density", pages 448-453. (Note Figure 5).	1-19
Y	US, A, 5,070,455,(SINGER ET AL) 03 December 1991 (Note abstract)	1-19

☐ Further documents are listed in the continuation of Box C.   ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance		
"E"	earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		
		"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 MAY 1995	0 2 JUN 1995

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer V. MCGRAW
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Form PCT/ISA/210 (second sheet)(July 1992)★