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(54) **METHOD AND APPARATUS FOR THREE-DIMENSIONAL IMAGING IN THE FOURIER DOMAIN**

(75) Inventors: **J. Richard Rahn**, Sammamish, WA (US); **Alan C. Nelson**, Gig Harbor, WA (US)

(73) Assignee: **Visiongate, Inc.**, Gig Harbor, WA (US)

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(51) **Int. Cl.**^{7} **G06K 9/00**
(52) **U.S. Cl.** **382/131**
(58) **Field of Search** 382/131, 333, 382/280; 250/455.11, 461.2, 339.08; 353/28; 378/8, 11, 23; 377/10; 359/559, 564

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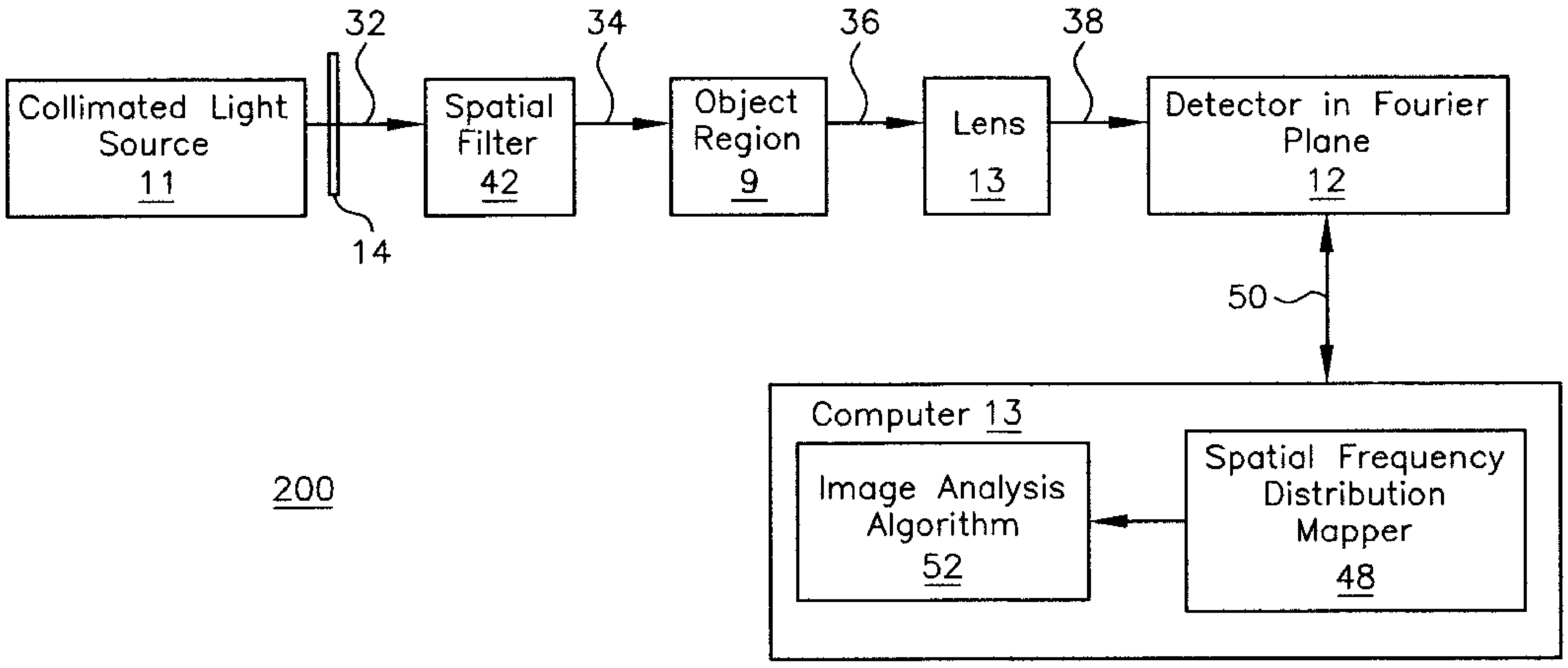
Primary Examiner—Andrew W. Johns
Assistant Examiner—Shervin Nakhjavan
(74) *Attorney, Agent, or Firm*—George A. Leone

(57) **ABSTRACT**

Two or more two-dimensional Fourier transforms are acquired from different perspectives of a three-dimensional object region. A three-dimensional Fourier transform is then constructed using tomographic methods, permitting the application of image analysis algorithms analogous to those used for two-dimensional images.

23 Claims, 4 Drawing Sheets



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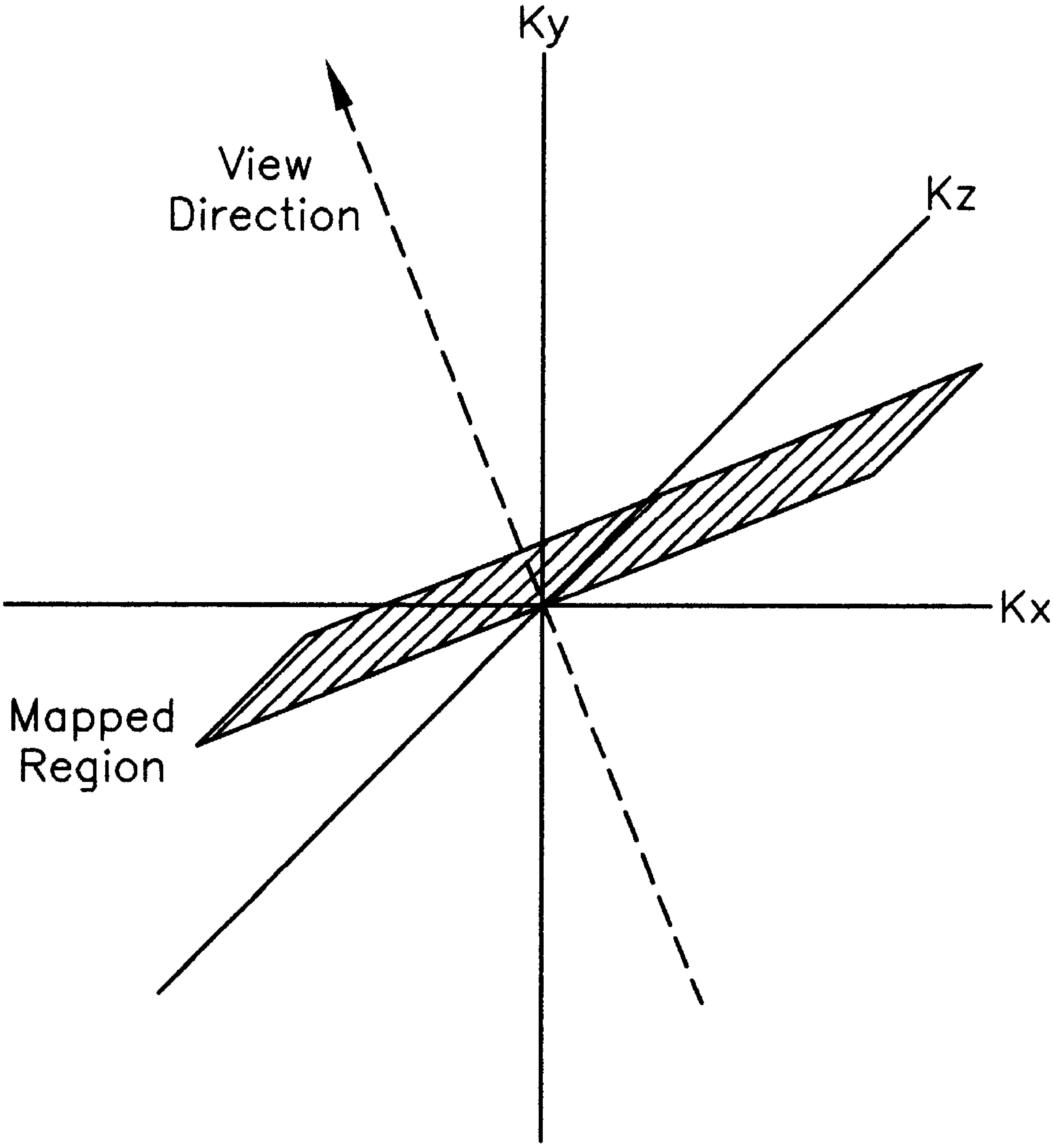
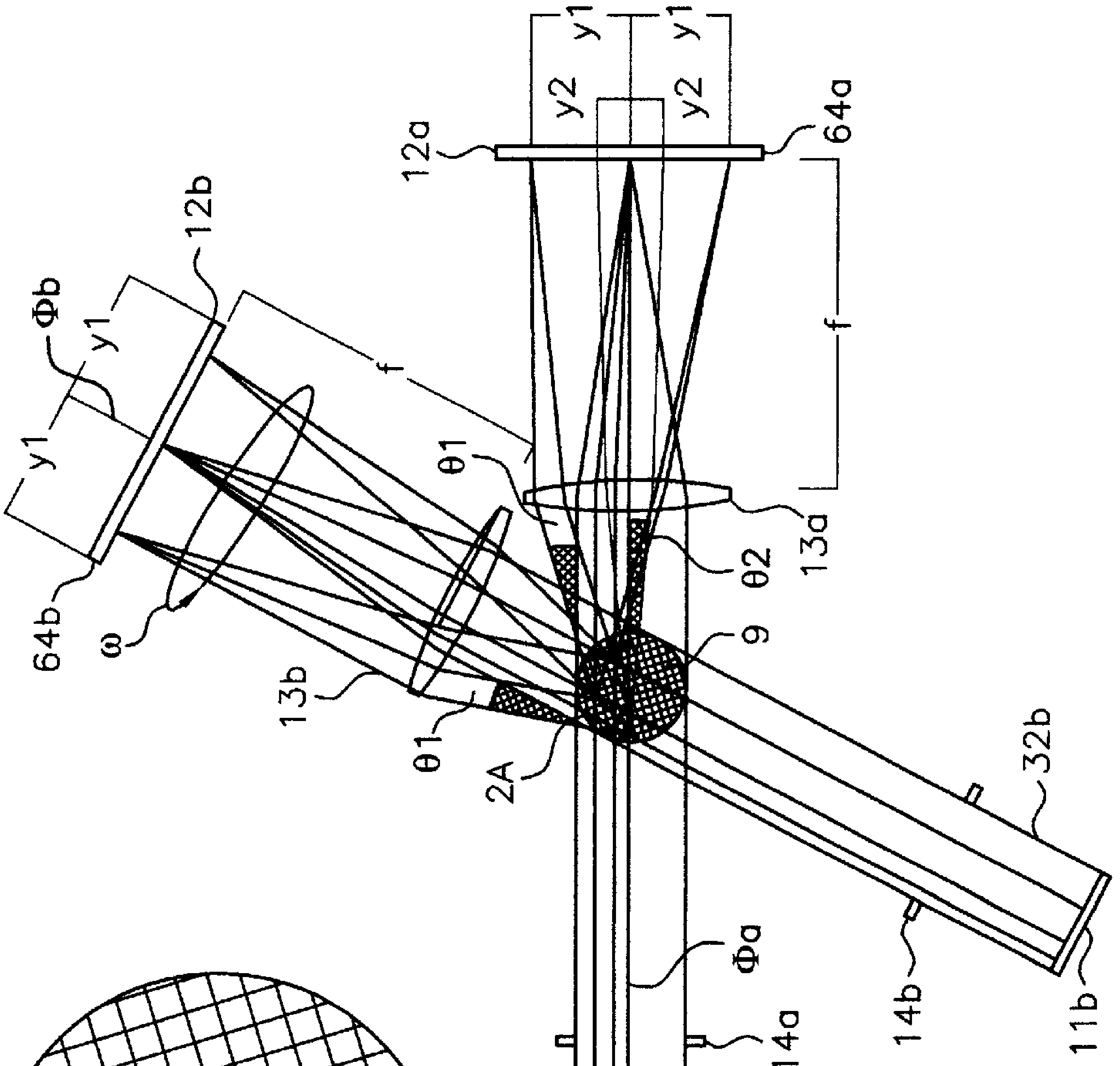


FIG. 1
(Prior Art)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14b
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32a
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FIG. 2

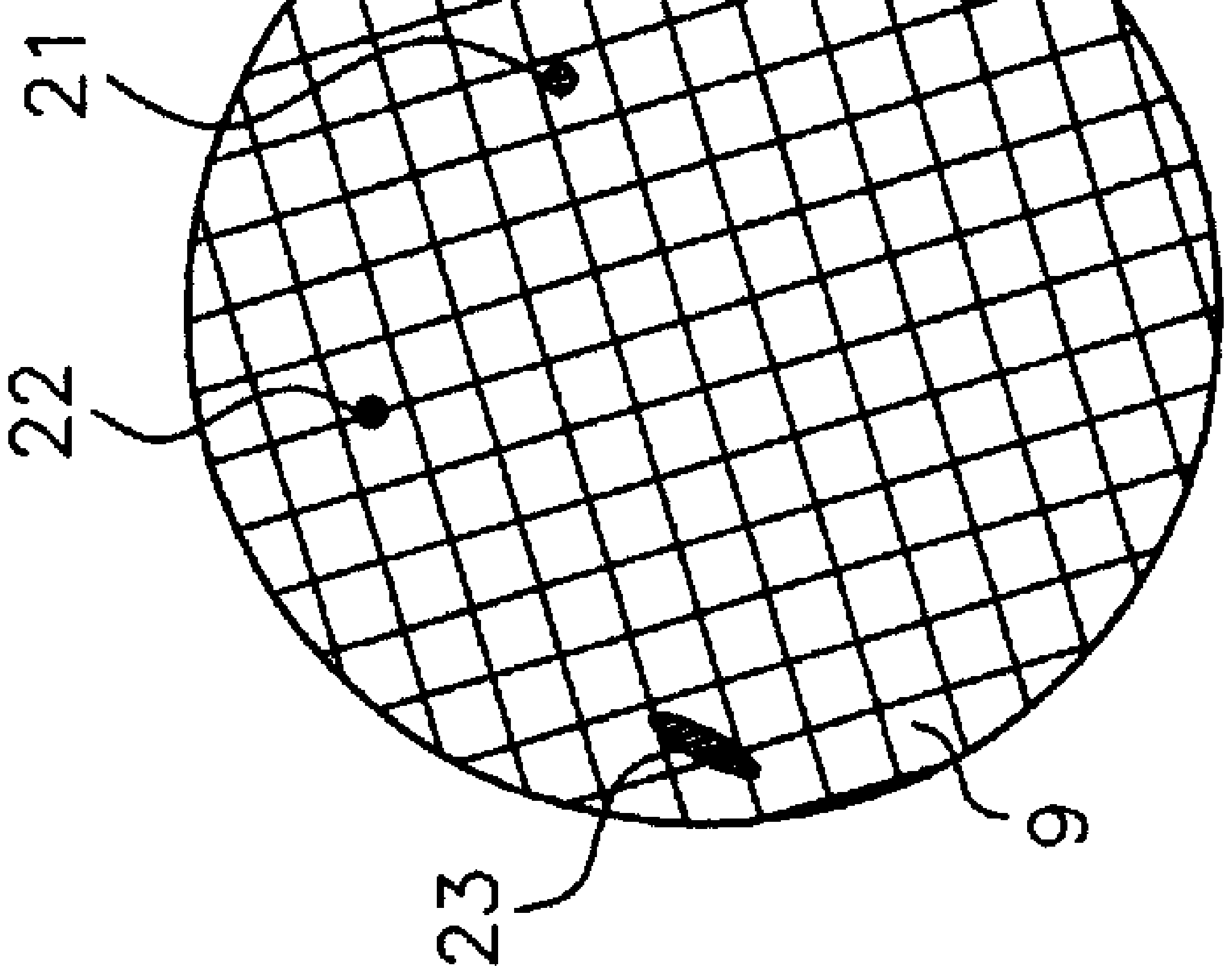
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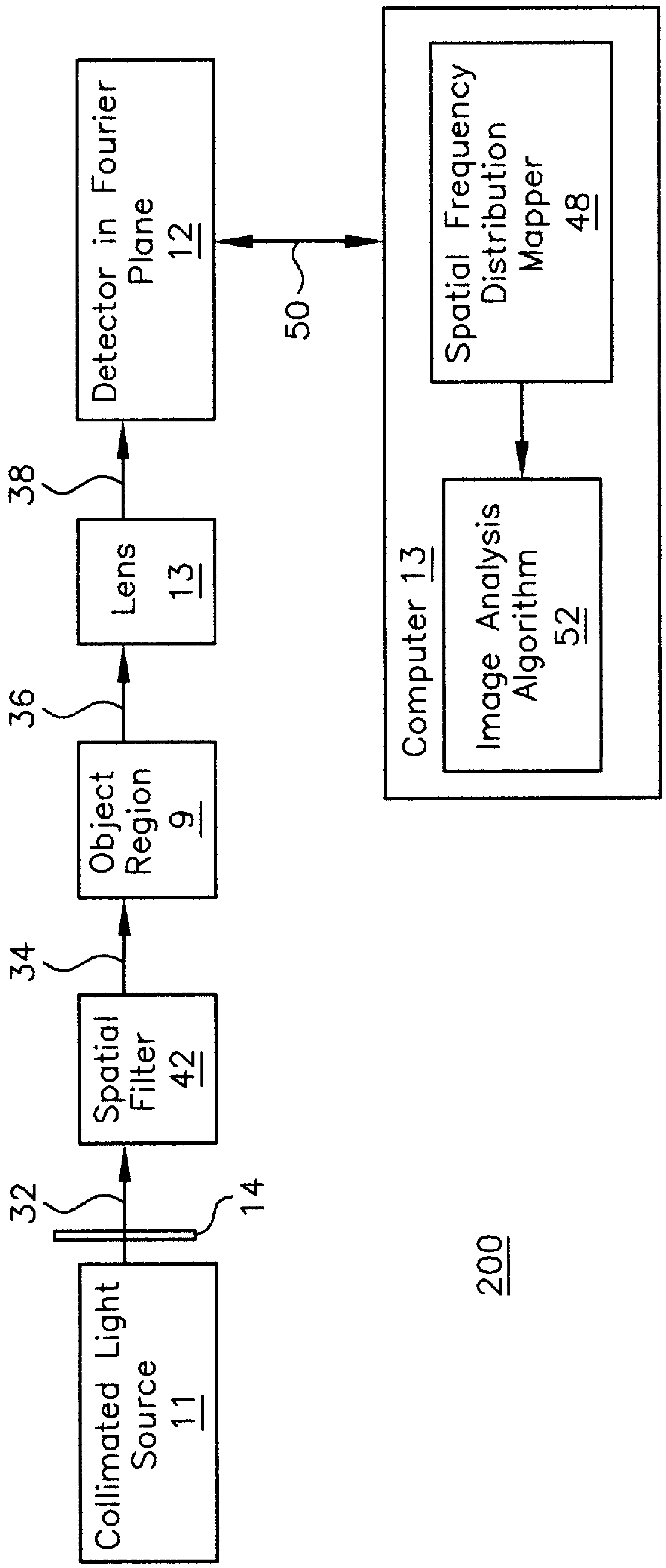
FIG. 2A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32
Spatial Filter 42
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Object Region 9
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Lens 13
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Detector in Fourier Plane 12
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Computer 13
Spatial Frequency Distribution Mapper 48
Image Analysis Algorithm 52
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FIG. 3

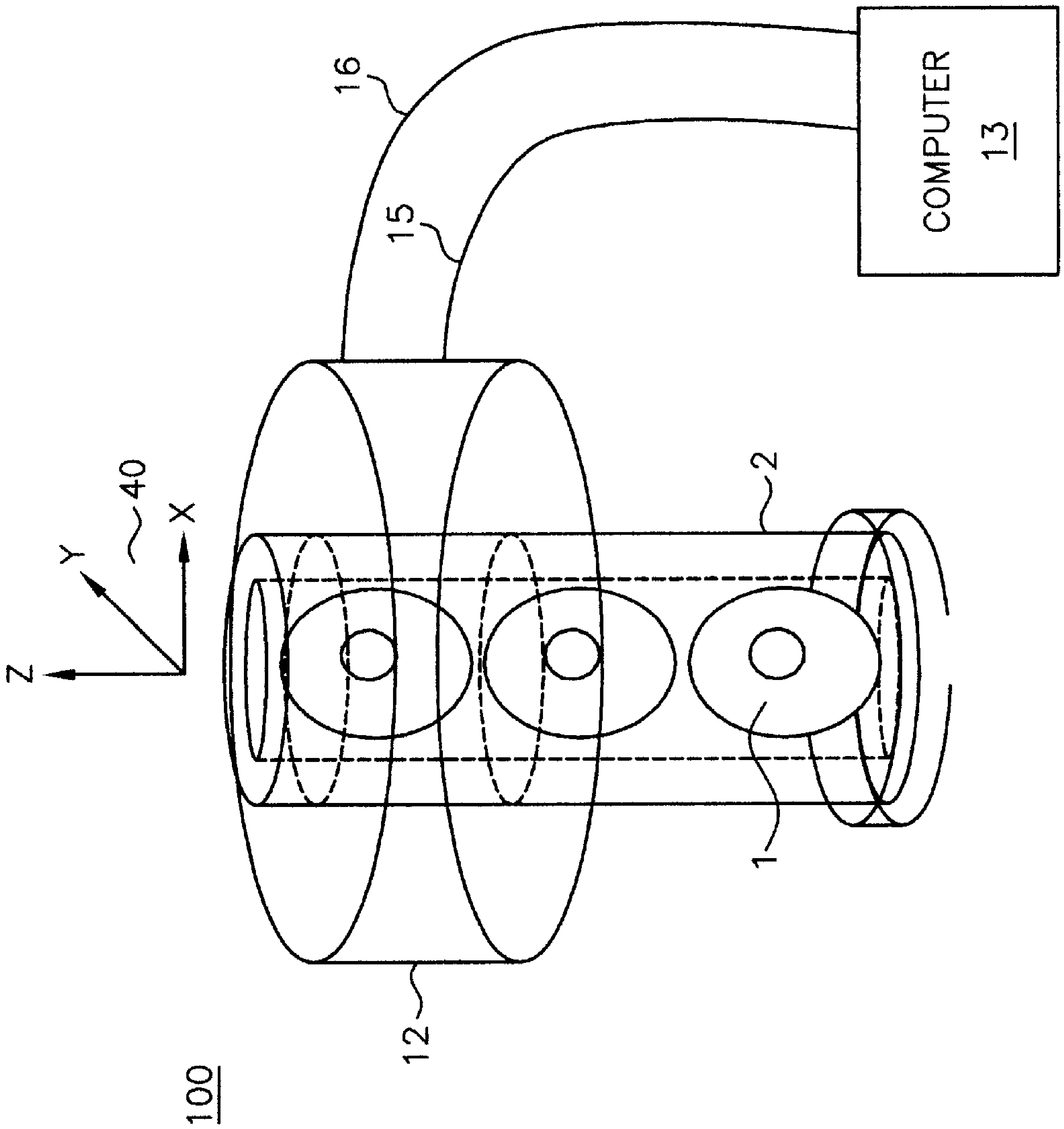

FIG. 4

METHOD AND APPARATUS FOR THREE-DIMENSIONAL IMAGING IN THE FOURIER DOMAIN

This is a continuation in part (CIP) of U.S. patent application Ser. No. 09/927,151, filed Aug. 10, 2001, entitled "Apparatus and Method for Imaging Small Objects in a Flow Stream Using Optical Tomography," issued on Feb. 18, 2003 as U.S. Pat. No. 6,522,775 to Nelson which is incorporated herein by this reference.

FIELD OF THE INVENTION

The present invention relates to a three-dimensional imaging system in general, and, more particularly, to high-resolution optical tomography where the features of interest are of a size comparable to the wavelength of the light used to illuminate the objects of interest.

BACKGROUND OF THE INVENTION

A tomography device is intended to produce three-dimensional reconstructions of objects by providing a measure of light or x-ray attenuation along a set of ray paths through the object. Thus the existence of a focal plane within the object region is forbidden, i.e., the depth of field is infinite, and all the photons reaching an individual detector pixel element have, ideally, traveled along the same geometric path. For x-ray tomography, scattering from inhomogeneities within the object region is not an issue, because the size of such features is typically much larger than the wavelength of the incident radiation. In optical tomography, however, the wavelengths are much longer than they are in the case of x-ray tomography. Therefore, scattering from features within the object region can introduce noise into the system by causing several light rays to reach the same individual detector element after traveling along several different paths between the source and that detector element. The present invention exploits such scattering effects to acquire information about a three-dimensional object region, and re-arranges that information by mapping the spatial-frequency domain (k-space) into real space.

A. C. Kak and M. Slaney, in their book entitled *Principles of Computerized Tomographic Imaging* (IEEE Press, 1988), describe the use of the Fourier Slice Theorem to map transmitted or reflected light from the spatial domain into the frequency domain, as depicted in FIG. **1**. By obtaining projection images from multiple viewpoints and applying a two-dimensional Fourier transform to each one, a set of planar surfaces through the frequency domain (k-space) can be generated. The sum of these planar surfaces can then be operated upon by a three-dimensional inverse Fourier transform to yield a three-dimensional reconstruction of the object region. In the presence of weak scattering within the object region, the planar surfaces become spherical surfaces, and the Fourier Diffraction Theorem should be substituted for the Fourier Slice Theorem. However, both of these approaches break down when strong scattering is present. The Fourier transform of a single projection maps a set of spherical surfaces through k-space, resulting in ambiguous values when the surfaces from different viewpoints are summed.

Work by Pernick, et al. (1978), Wohlers, et al. (1978), and Backman, et al. (2001) has demonstrated the usefulness of examining biological material in the two-dimensional Fourier domain. (See, for example, B. Pernick et al., "Screening of cervical cytological samples using coherent optical processing. Part 1," *Appl. Optics* 17, 21 (1978), R. Wohlers et al., "Screening of cervical cytological samples using coherent optical processing. Part 2," *Appl. Optics* 17, 35 (1978), B. Pernick et al., "Screening of cervical cytological samples using coherent optical processing. Part 3," *Appl. Optics* 17, 43 (1978), B. J. Pernick et al., Paraxial analysis of light scattering by biological cells in a flow system," *Appl. Optics* 17, 3205 (1978), V. Backman et al., "Measuring Cellular Structure at Submicrometer Scale with Light Scattering Spectroscopy," *IEEE J. Selected Topics Quantum Electron.* 7, 887 (2001)).

Techniques for using light diffraction to examine small features in an object have been described by Kopp, et al. in U.S. Pat. No. 4,150,360, issued Apr. 17, 1979, entitled "Method and Apparatus for Classifying Biological Cells," and U.S. Pat. No. 4,213,036 issued Jul. 15, 1980 entitled "Method for Classifying Biological Cells." Kopp, et al. used Fourier optics to acquire a single two-dimensional Fourier transform of a biological cell. However, three-dimensional object regions were not considered by Kopp, et al. In contrast, the method and apparatus of the present invention acquires multiple two-dimensional Fourier transforms from several different viewpoints. Using the different viewpoints, a three-dimensional Fourier transform is computed using conventional image reconstruction techniques that may be modified according to the specific geometric configuration.

In contrast to known methods, the present invention provides a method that allows real-time, in-situ processing of the light passing through the entire volume of the specimen region. The method of the present invention uses Fourier optics to map the angular distribution of light exiting the object region into real space at the back focal plane of a lens or mirror system. As a result, the three-dimensionality of the object region ceases to pose a problem, since in optical tomography the light rays need not originate within a single plane.

SUMMARY OF THE INVENTION

The present invention provides a method and apparatus for multi-dimensional imaging of an object region. The method includes the step of passing collimated light through an object region to produce transmitted light rays. In another step, the transmitted light rays are captured by at least one optical element, each of said at least one optical element having a back focal plane. At least one detector is used to capture a power distribution of a two-dimensional Fourier transform, where the at least one detector is located in a back focal plane of the least one optical element. For two or more viewpoints, the steps of the method are repeated about an arc at least partially encircling the object region to obtain multiple two-dimensional Fourier transforms.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** illustrates the Fourier Slice Theorem.

FIG. **2** schematically shows an example illustration of light rays as they pass through an object region in a three-dimensional imaging system, entering and exiting from two different viewing angles, as contemplated by an embodiment of the present invention.

FIG. **2A** schematically shows a more detailed view of the object region of FIG. **2** as contemplated by an embodiment of the present invention.

FIG. **3** schematically shows an example illustration of a high level block diagram of a method and apparatus for three-dimensional imaging in the Fourier Domain as contemplated by the present invention.

FIG. **4** schematically shows an example illustration of an optical tomography system employing a system for three-dimensional imaging in the Fourier Domain as contemplated by the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The method and apparatus of the present invention do not require any assumptions about the strength of light scattering. Instead, the present invention takes advantage of the fact that a measurement of the intensity pattern in the back focal plane of a lens yields the magnitude of a Fourier transform of the light rays reaching the lens. A measured intensity pattern from an x-ray projection, on the other hand, can be transformed using Fourier transformation relationships to yield both real and imaginary components of a plane in k-space. In the present invention, the results of the Wiener-Khintchine Theorem can be applied. The Wiener-Khintchine Theorem states that the autocorrelation function, C_{gg}, of an object, g(x,y), is equal to the inverse Fourier transform of the squared magnitude of the Fourier transform of the object:

$$c_{gg}=F^{-1}[|F(g)|^2]$$

where F and F^{-1} represent the Fourier transform and the inverse Fourier transform operators, respectively. In a manner similar to the application of the Fourier Slice Theorem in non-diffracting systems, the intensity in the back focal plane of the lens from each of multiple viewpoints can be measured to find $|F(g)|^2$ for each plane in k-space. An inverse three-dimensional Fourier transform, F^{-1}, can then be applied to the sum to yield the three-dimensional autocorrelation function.

The Wiener-Khintchine Theorem is a special case of Parseval's Theorem, which states that the cross-correlation function, c_{gh}, of two objects g(x,y) and h(x,y), is equal to the inverse Fourier transform of their Fourier transforms:

$$c_{gh}=F^{-1}[F(g)F^*(h)]$$

where F* indicates the complex conjugate of the Fourier transform F.

In addition to using the present invention to generate auto-correlation and cross-correlation information, the measured values can be used directly, enabling image analysis methods to look for specific features in diffraction patterns.

The method and apparatus of the invention uses Fourier optics in an optical tomography device to pass substantially all the light exiting the object region, as limited by the aperture of a lens system. In accordance with one embodiment of the invention, the two-dimensional Fourier transform is mapped at the back focal plane of the lens system. Multiple views provide the ability to construct a three-dimensional Fourier transform and to use the information contained in this Fourier transform to extract information about the object region.

The method and apparatus of the present invention is based, in part, on the following principles. Fine features, such as a small object or a closely spaced grating, are said to have a high spatial frequency. Due to their high spatial frequency, fine features produce large deflections of the light rays that meet them. Conversely, coarse features are said to have a low spatial frequency, and deflect light rays only by a small amount. In conventional imaging, elimination of the high spatial frequencies will cause a loss of resolution in the image due to smoothing out of edges and small features, while eliminating the low spatial frequencies will produce an "outline" of the image, with sharp edges but without filled-in spaces.

Now referring to FIGS. **2** and **2**A, one example embodiment of an optical tomography system for three-dimensional imaging in the Fourier Domain is illustrated. In FIG. **2**, two viewpoints of a three-dimensional object region are shown, along with the distribution of the light in the Fourier planes. It will be understood that the illustrations herein are by way of example only and that the invention is not so limited. For example, while two viewpoints are shown schematically, the two viewpoints may be obtained by a plurality of optical imaging systems located at different viewpoints, by a single optical imaging system that is rotated into the varying views, or by rotating the object region before a single imaging optical system or multiple optical imaging systems, where the optical imaging systems are constructed in accordance with the teachings herein to use Fourier transforms for three-dimensional imaging.

The optical tomography system includes at least one collimated light source **11***a*, **11***b*, an object region **9** including at least one feature of interest **21**, **22**, **23**, the object region being disposed in at least one optical path along optical axis Φ_a or Φ_b to be illuminated by the collimated light source **11***a*, **11***b*. At least one detector **12***a*, **12***b* is located in the at least one optical path along optical axis Φ_a or Φ_b to receive light passing through the object region **9**. At least one lens **13***a*, **13***b* is located in the at least one optical path along optical axis Φ_a or Φ_b between the object region **9** and the at least one detector **12***a*, **12***b* such that a Fourier plane **64***a*, **64***b* is created in the back focal plane of each lens. The at least one detector **12***a*, **12***b* is located in the Fourier plane **64***a*, **64***b* for mapping a spatial frequency distribution of the at least one feature of interest.

In one example embodiment, the collimated light source **11***a*, **11***b* may comprise a monochromatic, collimated source **11** that emits a beam consisting of nearly parallel rays **32**, such as may be produced by a high-quality gas laser. To reduce the signal due to unscattered light passing through the object region **9**, an aperture **14***a*, **14***b* may advantageously be employed in each viewpoint.

FIG. **2** shows an example having a plurality of features **21**, **22**, and **23** within the object region **9**, two being spheres and the third an ellipsoid. In a first viewpoint along the optical path along optical axis Φ_a, each of the plurality of features **21**, **22**, and **23** appear identical, because the size and shape of their projections in the plane of the incident light are identical as registered by the detector **12***a*. Seen from a second viewpoint along the optical path along optical axis Φ_b, however, the anisotropy of the third object **23** produces a diffraction pattern that differs from the diffraction pattern produced by the other two.

As shown in FIG. **2**, placing an optical element, such as lens **13***a* or **13***b* or equivalent optical system, in an optical path along optical axis Φ_a or Φ_b between the object region **9** and the detector **12***a* or **12***b* creates a Fourier plane **64***a*, **64***b* as the case may be in the back focal plane of the lens, i.e., at a distance (f) from a lens of focal length f An image formed in the back focal plane thus comprises a Fourier transform of the light exiting the object region **9** in k-space, where k is a vector that signifies the direction of the light path. The image can be magnified, with the height above the optical axis, y, related to the scattering angle, θ, by:

$$y=f\sin\theta.$$

Note the rotational position, referenced as azimuth angle ω, of the ray about an optical axis, Φ, is the same in both the Fourier plane and the object region. Thus a point in the

Fourier plane can be mapped to a specific direction of the rays in the object region, independent of the positions of those rays. Low spatial frequencies will pass through the Fourier plane close to the optical axis (i.e., near the point that maps into k=0), whereas high spatial frequencies will pass through further from the optical axis. By placing an array of detector elements in this plane, the power distribution of the two-dimensional Fourier transform can be acquired. If the object region or the source-detector pair is then rotated about a central axis, additional two-dimensional Fourier transforms can then be acquired for each new viewpoint.

Having described the apparatus of the invention, further understanding will be promoted by describing its operation. In operation, each of the at least one collimated light source **11***a*, **11***b* emits a beam consisting of nearly parallel rays **32***a*, **32***b*. The nearly parallel rays **32***a*, **32***b* may be subjected to spatial filtering prior to reaching an object region **9**, so as to remove any divergent light. To reduce the signal due to unscattered light passing through the object region **9**, an aperture **14** may advantageously be employed. A lens **13***a* is located in the optical path between the object region **9** and the detector **12***a*, such that a Fourier plane will be created in the back focal plane of the lens. By placing an array of detector elements **12***a* in the Fourier plane, the spatial frequency distribution due to the features **21**, **22**, and **23** can be mapped.

From a second viewpoint, all three features **21**, **22**, and **23** scatter the incoming light from **11***b* into an angle θ_1, such that the detector **12***b* registers the same intensity distribution for all three features, having (for this schematic representation) a central peak and a second peak at a radius y_1 from the center. From viewpoint a, however, the anisotropy of feature **23** is apparent; it scatters into angle Φ_2, producing side peaks at a radius y_2 from the center, while features **21** and **22** continue to produce side peaks at a radius y_1 due to light scattered into angle Φ_1.

Referring to FIG. **3**, there schematically shown is an example illustration of a high level block diagram of a multi-dimensional imaging system **200** using the method and apparatus for three-dimensional imaging in the Fourier Domain as contemplated by the present invention. The multi-dimensional imaging system **200** includes a collimated light source **11**, an optional aperture **14**, an optional spatial filter **42**, an object region **9**, at least one lens or equivalent optics **9**, at least one detector **12**, and a computer **13**. In one example embodiment, the computer **13** may comprise a personal computer or workstation including a conventionally designed computer program serving as a spatial frequency distribution mapper **48** and an image analysis algorithm for producing three-dimensional images or correlation functions from two-dimensional Fourier transforms. The collimated light source **11** generates nearly parallel light rays **32** that are filtered by optional spatial filter **42**. Filtered light **34** illuminates the object region **9**. Transmitted light rays **36** are transmitted through the object region and pass through lens **13**. Lens **13** transmits back plane light rays **38** onto a back focal plane so as to impinge on detector **12** located in the Fourier plane. Information **50** is transmitted between the computer **13** and the detector **12**. The detector **12** may advantageously comprise, for example, image sensors, such as, for example, CCD or CMOS solid state image sensors, detector arrays and the like.

Referring to FIG. **4**, there schematically shown is an example illustration of an optical tomography system employing a system for three-dimensional imaging in the Fourier Domain as contemplated by the present invention. The optical tomography (OT) system **100** includes in one example embodiment a reconstruction cylinder **12**, positioned around object containing tube **2**. The object containing tube **2** may, for example, comprise a cell entrainment tube wherein the cell is held in a gel, or a capillary tube for cell flow, depending on the type of optical tomography system.

The OT system **100** is oriented with reference to a coordinate system **40** having coordinates in the X, Y and Z-directions. In operation, an object of interest **1**, such as, for example a cell, including a human cell, is held, or flows through, an object containing tube **2**. It will be understood that lines **15** and **16** are representative of communication and control lines between the OT system **100** and a computer **13** that communicate data, image information, control signals and other signals between the computer and the OT system **100**. The reconstruction cylinder **12** may advantageously comprise a system for multi-dimensional imaging using Fourier transforms as described hereinabove with reference to FIG. **2**. Signals from the reconstruction cylinder **12** may be analyzed directly or processed using known image processing, image analysis and/or computerized tomographic image reconstruction techniques to provide two-dimensional or three-dimensional information about cells and other objects of interest.

In a further embodiment, the object region can be located between the at least one lens or equivalent optics and its back focal plane, such that an approximation of the Fourier transform of the light exiting the object region is formed in the back focal plane. This approximate Fourier transform can be considered as equivalent to an exact Fourier transform provided that the maximum angle of the convergent light (i.e., the numerical aperture of the optical system), the maximum scattering angle of interest (as measured relative to the incident light ray that is scattered), and the thickness of the object region are small enough to allow all the light scattered at an individual angle (relative to the light ray causing the scattering) to reach a single detector element.

In further embodiments, Parseval's Theorem can be applied to generate auto-correlation and cross-correlation functions of the object region. To generate the autocorrelation function, it is sufficient to measure the intensity, $|F(g)|^2$, of the light in the back focal plane of the at least one optical element. To generate the cross-correlation function, a mask, formed from the diffraction pattern obtained from a different object, can be placed in the back focal plane of the at least one optical element.

The invention has been described herein in considerable detail in order to comply with the Patent Statutes and to provide those skilled in the art with the information needed to apply the novel principles of the present invention, and to construct and use such exemplary and specialized components as are required. However, it is to be understood that the invention may be carried out by specifically different equipment, and devices and reconstruction algorithms, and that various modifications, both as to the equipment details and operating procedures, may be accomplished without departing from the true spirit and scope of the present invention.

What is claimed is:

1. A method for multi-dimensional imaging of an object region, the method comprising the steps of:

a) passing light through an object region to produce transmitted light rays;

b) capturing the light rays by at least one optical element, the at least one optical element having a back focal plane;

c) using at least one detector to capture a power spectrum of a two-dimensional Fourier transform, where the at least one detector is located in a back focal plane of the at least one optical element; and

d) repeating steps a)–c) for two or more viewpoints about an arc at least partially encircling the object region to obtain multiple two-dimensional Fourier transforms.

2. The method of claim **1**, further comprising the step of using an image analysis computer algorithm to extract features of interest from one or more of the multiple two-dimensional Fourier transforms.

3. The method of claim **1** wherein the optical element is selected from the group consisting of a lens and reflective surface.

4. The method of claim **1** further comprising the step of passing the light through a spatial filter placed in an optical path between the light source and the object region.

5. The method of claim **1**, in which the light rays captured by the at least one optical element are transmitted through the object region prior to passing through the at least one optical element.

6. The method of claim **1**, in which the light rays pass through the object region after passing through the at least one optical element.

7. The method of claim **1**, further comprising the step of reconstructing the multiple two-dimensional Fourier transforms to create a three-dimensional Fourier transform.

8. The method of claim **7**, further comprising the step of using an image analysis computer algorithm to extract features of interest from the three-dimensional Fourier transforms.

9. The method of claim **7**, further comprising the step of employing a mask and an image analysis algorithm to construct of a cross-correlation function of the object region with a previously examined object region.

10. The method of claim **9**, in which the previously examined object region is a cell.

11. The method of claim **9**, in which the previously examined object region is an artificially generated phantom.

12. The method of claim **7**, further comprising the step of employing an image analysis algorithm to construct of an autocorrelation function of the object region.

13. A system for multi-dimensional imaging of an object region, the system comprising:

a light source;

an object region including at least one feature of interest the object region being disposed in an optical path to be illuminated by the light source;

at least one detector located in the optical path to receive light passing through the object region;

at least one lens located in the optical path between the object region and the at least one detector such that a Fourier plane is created in the back focal plane of the lens, where the at least one detector is located in the Fourier plane; and

wherein the light source, the at least one detector and the at least one lens are arranged to provide multiple views of the object region for mapping at least one n-dimensional spatial frequency distribution of the at least one feature of interest at each view so as to provide a plurality of spatial frequency distributions used for constructing an (n+1)-dimensional data set, where n is greater than or equal to 1, whereby an n-dimensional Fourier transform may be reconstructed as an (n+1)-dimensional Fourier transform.

14. The system of claim **13** wherein the light source comprises a laser.

15. The system of claim **13** further comprising a spatial filter placed in an optical path between the light source and the object region.

16. The system of claim **13** further comprising an aperture placed in an optical path between the light source and the object region.

17. The system of claim **13** wherein the at least one detector comprises a detector selected from the group consisting of CCD, CMOS, solid state image sensors, and solid state image sensor detector arrays.

18. A parallel-beam optical tomography system for imaging an object of interest having at least one feature of interest, the parallel-beam optical tomography system comprising:

a light source projecting a column of light along an optical path;

an object containing tube located along the optical path, wherein the object of interest is held within the object containing tube;

at least one detector array, where the at least one detector array is located to receive emerging radiation from the object of interest;

at least one lens located in the optical path between the object of interest and the at least one detector array such that a Fourier plane is created in a back focal plane of the lens, where the at least one detector is located in the Fourier plane; and

wherein the light source, the at least one detector and the at least one lens are arranged to provide multiple views of the object region for mapping at least one n-dimensional (n>1) spatial frequency distribution of the at least one feature of interest at each view so as to provide a plurality of spatial frequency distributions used for constructing an (n+1)-dimensional data set, where n is greater than or equal to 1, whereby an n-dimensional Fourier transform maybe reconstructed as an (n+1)-dimensional Fourier transform.

19. The system of claim **18** wherein the at least one detector comprises a detector selected from the group consisting of CCD, CMOS, solid state image sensors, and solid state image sensor detector arrays.

20. The parallel-beam optical tomography system of claim **18** wherein the object of interest comprises a cell.

21. The system of claim **18** wherein the light source comprises a laser.

22. The system of claim **18** further comprising a spatial filter placed in the optical path between the light source and the object region.

23. The system of claim **18** further comprising an aperture placed in the optical path between the collimated light source and the object region.

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