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**Grosskopf**

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(54) **CONFOCAL COLOR**

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This patent is subject to a terminal disclaimer.

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(52) **U.S. Cl.** ..... **356/613**; 359/397; 359/619; 359/626; 250/234

(58) **Field of Search** ..... 357/368, 385, 357/397; 356/376, 371, 445, 446, 448, 616, 622, 601, 603, 604, 606, 613, 600; 250/201.3, 234

(56) **References Cited**

U.S. PATENT DOCUMENTS

| | | | | |
|---|---|---|---|---|
| 5,239,178 A | | 8/1993 | Derndinger et al. | |
| 5,587,832 A | * | 12/1996 | Krause | 359/385 |
| 5,877,807 A | | 3/1999 | Lenz | |
| 5,978,095 A | * | 11/1999 | Tanaami | 356/445 |
| 6,031,661 A | * | 2/2000 | Tanaami | 359/368 |
| 6,111,690 A | * | 8/2000 | Tanaami | 359/368 |
| 6,226,036 B1 | | 5/2001 | Grosskopf | |
| 6,252,717 B1 | | 6/2001 | Grosskopf | |

FOREIGN PATENT DOCUMENTS

| | | |
|---|---|---|
| DE | 3837063 C1 | 3/1990 |
| DE | 4113279 C2 | 8/1996 |
| DE | 19648316 C1 | 4/1998 |

* cited by examiner

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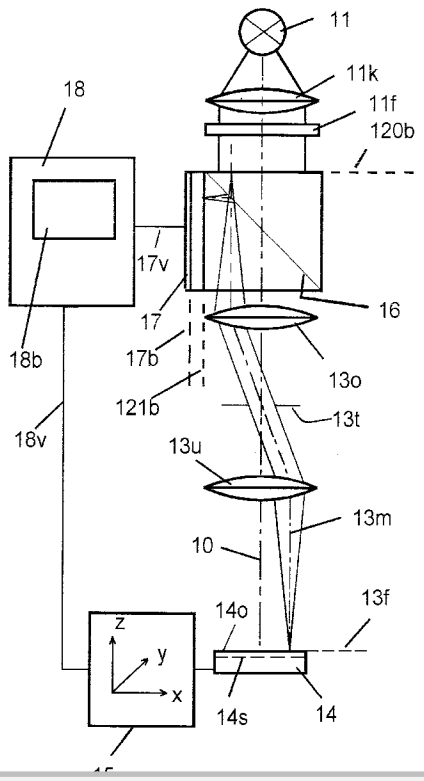
(57) **ABSTRACT**

An apparatus for examining an object in three dimensions including an optical system having an illumination side and an observation side; an illumination grid located in an illumination plane on the illumination side of the optical system and which during use generates an array of illumination points that is projected by the optical system onto a focus plane at a site at which the object is located, the optical system in turn directing light from that site into an observation plane on the observation side of the optical system, the illumination grid being a first aperture plate having a first passive array of pinholes; a detector array of light-sensitive regions located on the observation side of the optical system; and a second aperture plate located between the detector array and the optical system, said second aperture plate having a second passive array of pinholes.

**13 Claims, 3 Drawing Sheets**



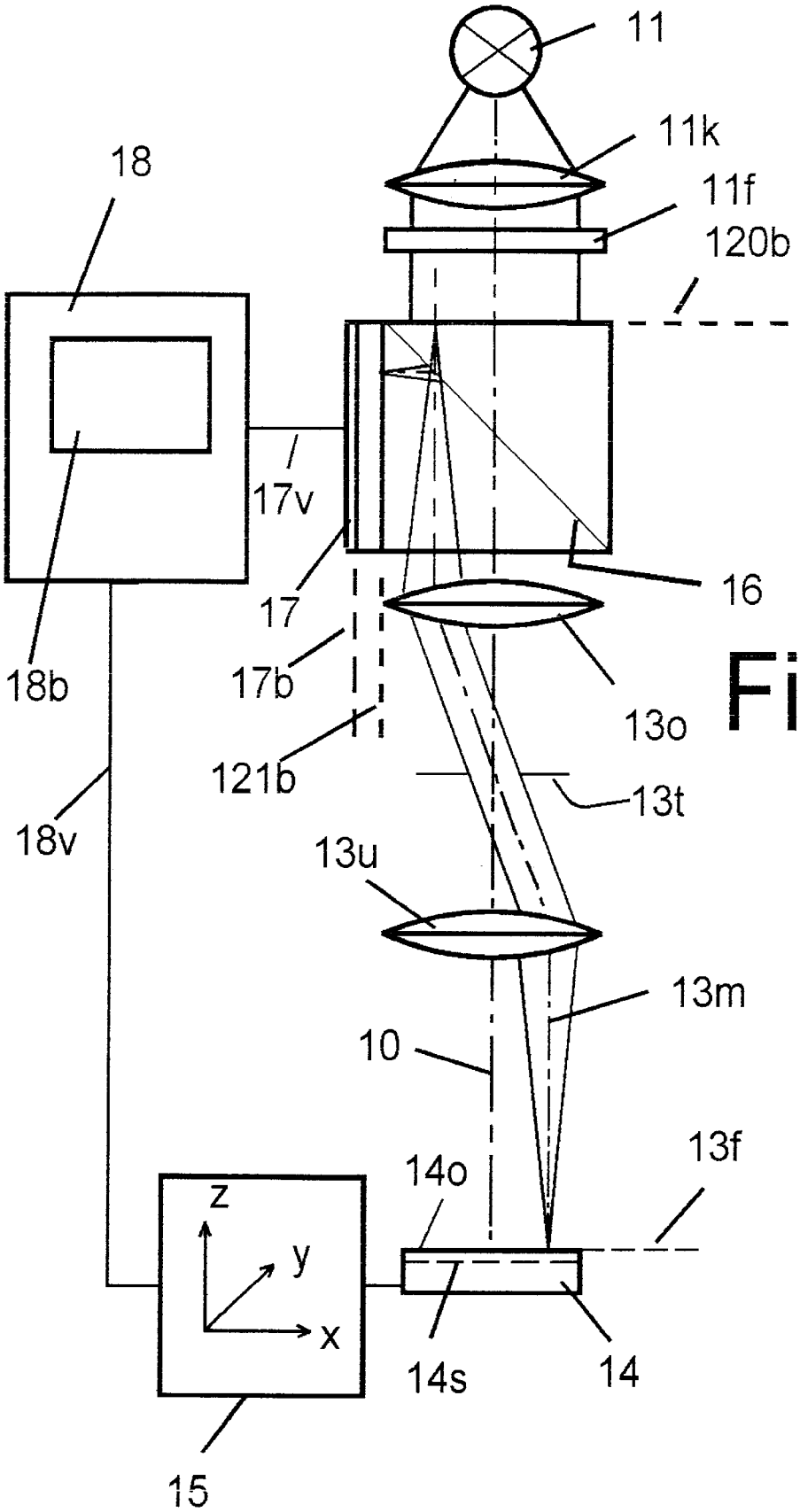



Fig. 1

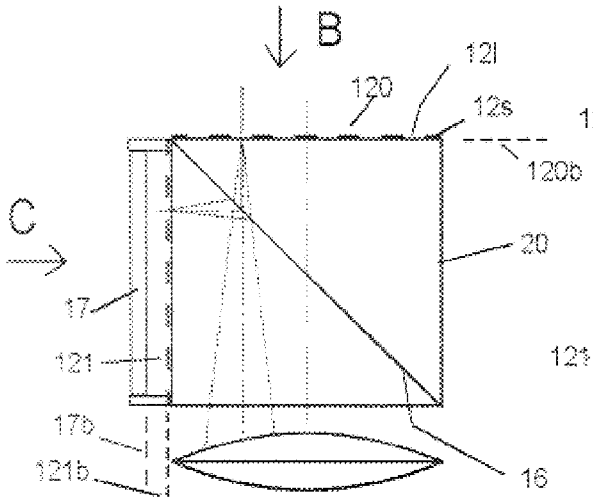



Fig. 2a

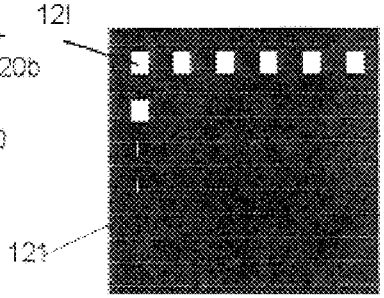



Fig. 2c

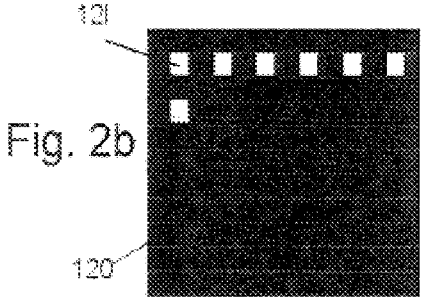



Fig. 2b

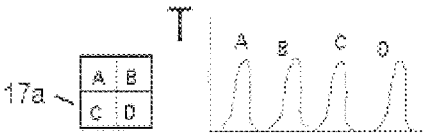



Fig. 4a

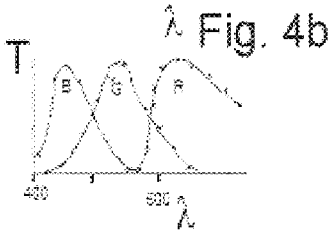



Fig. 4b

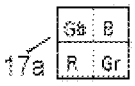



Fig. 5a

Fig. 5b

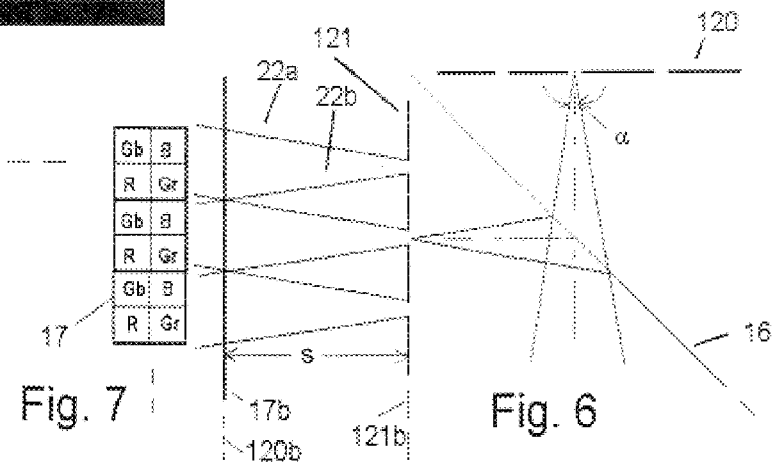



Fig. 7

Fig. 6

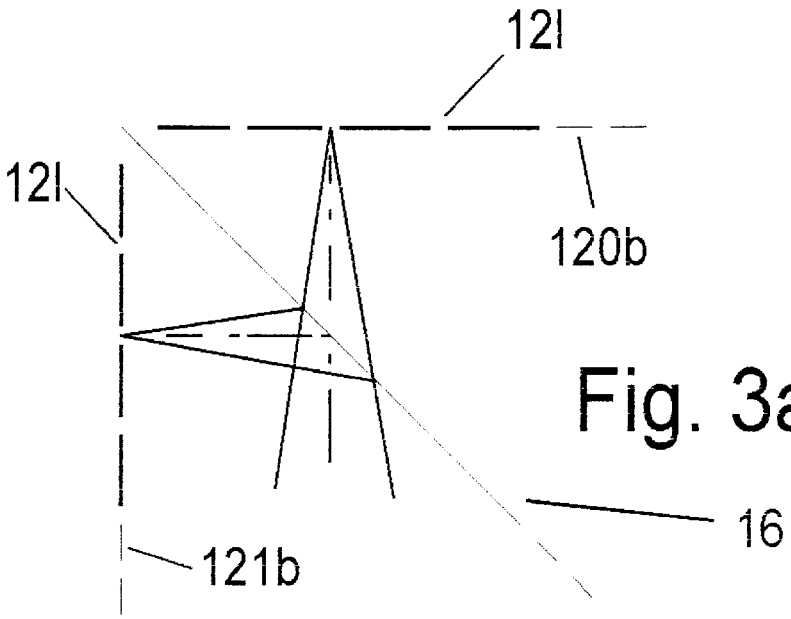



Fig. 3a

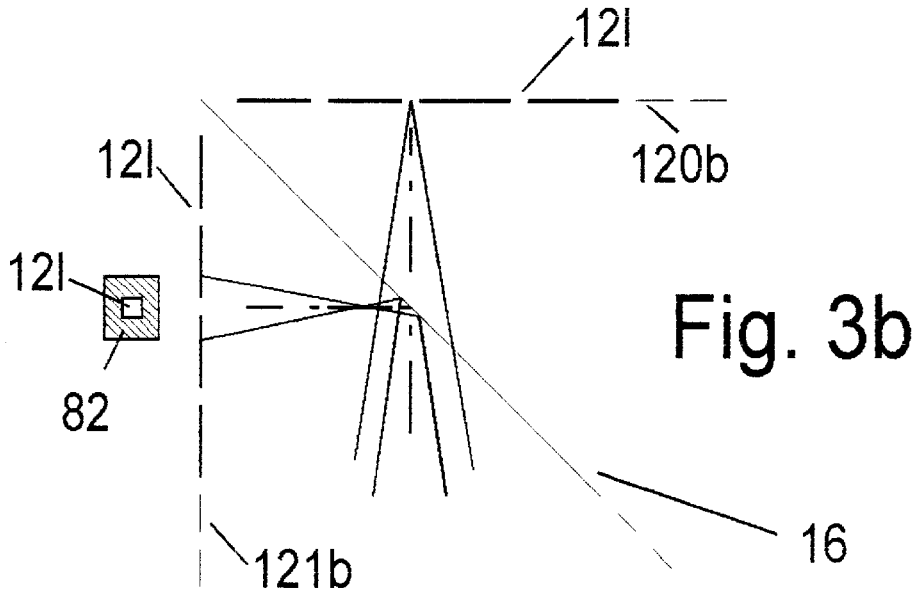



Fig. 3b

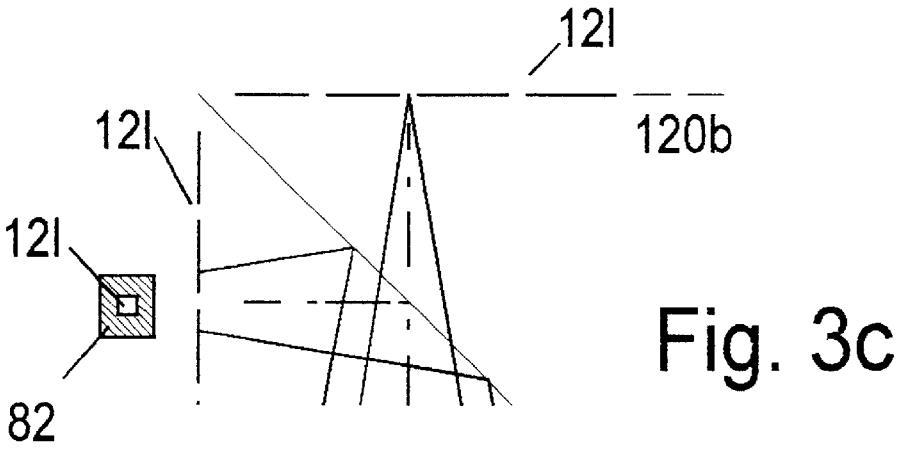



Fig. 3c

# CONFOCAL COLOR

## FIELD OF THE INVENTION

This invention relates to a device for examining an object in three dimensions.

## BACKGROUND

In confocal microscopy, an object is illuminated in known fashion through an aperture diaphragm and the illuminated point is observed by a radiation detector for which the light-sensitive surface is just as small as the illuminated point (Minsky, M., U.S. Pat. No. 3,013,467 and Minsky, M., Memoir on inventing the confocal scanning microscope. Scanning 10, p. 128–138). Compared to conventional microscopy, confocal microscopy has the advantage of delivering resolution in depth (measurement of the z axis) and of creating little scattered light during imaging. Only the plane of the object in focus is brightly illuminated. Object planes above or below the focus plane receive much less light. The image is built up through a scanning process. One or more points may be illuminated and observed simultaneously.

Three scanning methods are well known: mirror scanning, Nipkow disk, and electronic scanning using a matrix detector. Additional details on prior art relating to scanning with a mirror or Nipkow disk may be found in the *Handbook of Biological Confocal Microscopy*, Plenum Press, New York (James D. Pawley, Editor).

A confocal imaging system with confocal illumination through an aperture plate and electronic scanning by a matrix detector was first proposed in DE 40 35 799. A matrix detector is employed here in which the pixels are light sensitive only one a portion (30%) of the surface assigned to the pixel, and on the illumination side, an aperture plate is typically used which has the same number of holes as the imaging sensor has light-sensitive pixels. The information in depth is gained by recording multiple images from different focus planes and individually evaluating the brightness maximum for the different pixels in a computer.

Document DE 196 48 316 describes an arrangement which is typically provided with one illumination hole on the aperture plate for every four detector pixels assigned to it, and with a prism array immediately in front of the matrix detector. The prism array acts as a beam-forming element which splits the light of each illumination point such that two crescent images are formed outside the focus. Document DE 196 51 667 A1 describes an arrangement in which likewise typically one illumination hole on the aperture plate is assigned to four detector pixels each and which contains an array of anamorphote lenses immediately in front of the detector array. One lens is assigned to each illumination hole. Here the anamorphote lenses also act as beam-forming elements producing an image of the illumination point, the image being circular in focus and oval outside of focus. In these last two arrangements, the information in depth is gained by evaluating the difference between light signals of adjacent pixels.

Arrangements DE 40 35 799, DE 196 48 316 and DE 196 51 667 A1 have the advantage, among others, that many measurement points in depth may be recorded simultaneously, yet have the disadvantage that color images cannot be recorded. The object of the present invention is therefore to disclose an approach by which images may be recorded confocally using available color-capable matrix detectors. This requirement is found for example, in genetic



technology, cancer research and cancer screening where there is a need within a short period to scan many tissue cells for small (e.g. 200 nm) fluorescing or dyed sites in three dimensions.

## SUMMARY

The invention provides for arranging one aperture plate each, both on the illumination side and on the observation side, in those planes which are optically conjugate with the focus plane of the object and arranging at a suitable distance a color-capable matrix detector behind the aperture plate on the observation side, i.e. outside of focus.

The diagrams show examples of possible practical embodiments of the invention.

## BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** shows a complete arrangement of an imaging device according to the invention.

FIGS. **2**, **2***b* and **2***c* show a compact assembly with two aperture plates, beam splitter cube and color-capable matrix radiation detector which are employed according to the invention.

FIGS. **3***a*, **3***b* and **3***c* show the beam path within the beam splitter cube at various focus positions.

FIGS. **4***a* and **5***a* show two color cell embodiments for the matrix detector.

FIGS. **4***b* and **5***b* show the spectral light transmission curves assigned to the color cells for the light filter elements arranged in front of the pixels.

FIG. **6** shows an example of an arrangement for a matrix detector **(17)** at a suitable distance from the plane of the confocal observation diaphragms.

FIG. **7** shows a top view of the three sensor cells of the matrix detector in FIG. **6**.

## DESCRIPTION

In FIG. **1**, **(11)** indicates a light source, e.g. a halogen lamp which with the aid of condenser **(11***k***)** illuminates holes in a layer. This layer may be fabricated in the familiar fashion, e.g. from chromium on a glass plate **(12***g***)**. The holes are arranged in the layer in a grid pattern. For example, the layer contains 256×256 holes spaced 22 $\mu$m apart with the holes measuring, e.g., 4 $\mu$m×4 $\mu$m. The holes are, in other words, considerably smaller than their spacing. The spacing of the holes or the distances from center to center are designated as the grid dimension.

The illumination grid generated through the illuminated holes in the layer lies in observation plane **(120***b***)**. Said plane is projected through lenses **(13***o*, **13***u***)** onto focus plane **(13***f***)** such that within this plane, object **(14)** is illuminated with light points arranged in a grid pattern. In the case of nontransparent objects, only surface **(14***o***)** can be illuminated, whereas with transparent objects, internal layers **(14***s***)** may be illuminated by light points. The light beams reflected from the object in focus plane **(13***f***)** are focused by lenses **(13***u*, **13***o***)** via a beam splitter **(16)** in diaphragm plane **(121***b***)**.

The above-mentioned beam splitter **(16)** is designed as a semitransparent mirror and used for incident-light applications. For fluorescence applications, a dichroic mirror is employed in the known fashion.

Object **(14)** may be moved in all **3** spatial axes by adjustment device **(15)** so that different layers **(14***s***)** and different areas of object **(14)** may be scanned. The distance

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