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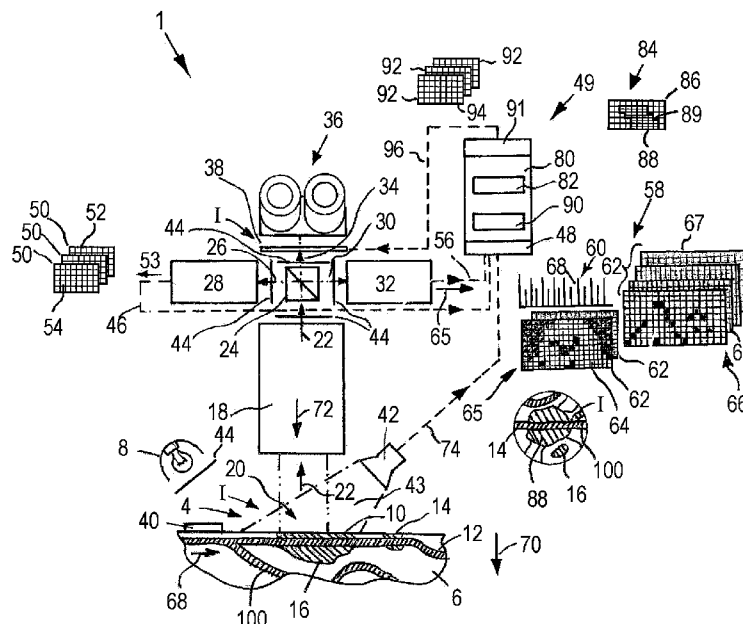
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(54) Title: MEDICAL OBSERVATION DEVICE, SUCH AS A MICROSCOPE OR AN ENDOSCOPE, AND METHOD USING A PSEUDO-COLOR PATTERN HAVING TEMPORAL AND/OR SPATIAL MODULATION

Fig. 1



(57) **Abstract:** The invention relates to a medical observation device (1) such as a microscope or endoscope. Further, the invention relates to a method for processing medical images. Input image data (52) are generated by a visible-light camera (28) and overlaid with auxiliary input data (58) such as fluorescent-light image data (65) generated from auxiliary input data (58) e.g. a fluorescence camera (32) or an ultrasound sensor (40, 42). From the auxiliary input data (58), subsequent sets (84) of pseudo-color image data (86) are generated by an image processor (80). The pseudo-color images (84) are merged with the input image data (52) to obtain output image data (94). A pseudo-color pattern field (88) comprising at least one of a temporally and/or spatially modulated pattern (87) is generated depending on the content of at least one of the image input data (52) and the auxiliary input data (58).



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Medical observation device, such as a microscope or an endoscope, and method using a pseudo-color pattern having temporal and/or spatial modulation

The invention relates to a medical observation device and method. A typical medical observation device for realization of the invention is a microscope or an endoscope.

5 It is known in the prior art to inject a fluorophore into tissue that is observed by an optical imaging device such as a microscope or an endoscope. The fluorophore is configured to mark only specific tissue. For example, the fluorophore may be adapted to remain in the blood stream only during the observation time so that only blood vessels are marked by the fluorophore. Another fluorophore may be provided in the form of a precursor material, which reacts only with tumor cells to produce a
10 fluorophore which only marks cancer. Thus, fluorescence imaging can provide useful diagnostic information. However, fluorescence typically does not provide anatomical information, i.e. tissue color appearance. Conversely, visible-light image provides anatomical information but not fluorescence diagnostic information. Pseudocolor is a convenient way to present in a single image the information of those two different image types: visible-light and fluorescence. It is known in the prior art to superpose
15 or merge the visible-light images and the fluorescence images.

The use of such an image superposition device and method greatly facilitates diagnosis and surgery. However, there is a need for further improving the technology thus to further facilitate diagnosis and surgery.

It is therefore the goal of the present invention to provide a device and method, which further improves
20 the existing devices and methods.

For the medical observation device, this goal is achieved according to the invention in that the medical observation device comprises an input interface, an image processor and an output interface, the input interface being configured to receive subsequent sets of input image data and subsequent sets of auxiliary input data, the output interface being configured to output subsequent sets of output image
25 data at an output data rate, the image processor being connected to the input interface for receiving the sets of input image data and auxiliary input data and to the output interface for outputting the output image data, the image processor being further configured to generate subsequent sets of pseudo-color image data depending on a content of at least one of the auxiliary input data and the input image data and to generate at least one synthetic pseudo-color pattern field within the pseudo-color
30 image data depending on the content of at least one of the input image data, the auxiliary input data and the pseudo-color image data, the pseudo-color pattern field comprising at least one of a temporally and a spatially changing pattern, and the image processor being configured to merge the pseudo-color image data and at least one section of the input image data to generate the output image data containing the pseudo-color pattern field.

35 The objective of the invention is also achieved by a method for displaying medical images, comprising the steps of receiving subsequent sets of input image data, receiving subsequent sets of auxiliary input data, generating subsequent sets of pseudo-color image data depending on the content of at least one of the auxiliary input data and the input image data, generating at least one coherent pattern field

within the pseudo-color image data depending on the content of at least one of the input image data, the auxiliary input data and the pseudo-color image data, the pattern field having at least one of a spatial and a temporal modulation, merging the pseudo-color image data with the input image data to obtain output image data, and displaying the output image data with the pseudo-color pattern field.

- 5 The use of the temporally and/or spatially modulated pseudo-color pattern allows the merging of further data in particular representing additional data sources to the output image. Further, the use of a pseudo-color pattern allows visualizing data in the output image data that would be otherwise be imperceptible in the pseudo-color image.

10 As the pattern field is both of pseudo-color and synthetic, it is immediately distinct from the input image, which is preferably used as the background in the output image data and based on visible-light image data.

In the context of this invention, a pattern designates a discernible regularity, in which elements repeat in a predictable manner. The regularity and predictability means that the pattern is not reliant on human cognitive processes. Rather, the pattern can be automatically discerned and discovered using
15 pattern recognition algorithms. A pseudo-color is a color which does not occur naturally in that context, such as a neon color in biological tissues. A color in the context of this disclosure is marked as a particular combination of wavelengths of light and thus independent of human cognitive processes.

In the following, further aspects of the invention are described. Each of the further aspects described herein below, has its own advantage and technical effect and thus can be combined arbitrarily with any
20 other of the aspects.

For example, the pattern field may be filled with a spatial pattern such as a hatching or with a regular repetition in time and/or space of a template. A template may, in a pattern having spatial modulation, consist of geometric forms such as dots, tiles, symbols and/or pictures. In a pattern having temporal modulation, the pattern consists of a regular repetition of a set of different images over time. A typical
25 example of such a pattern is a hatching or a bitmap template of simple geometric forms such as circles, polygons and/or waves.

In a pattern having both temporal and spatial modulation, different patterns having spatial modulation are repeatedly displayed. The subsequent patterns in a temporally modulated pattern may be similar to each other, e.g. spatially displaced relative to each other but otherwise identical, to represent a
30 direction of motion. For example, subsequent hatchings of a temporally modulated pattern within one cycle of the variation rate may all be shifted geometrically with respect to each other by the same amount. This can be used to produce a temporally modulated pattern which indicates a motion direction. A propagating wave pattern may, e.g. be used to indicate the direction of a fluid flow, such as a blood or lymph flow.

35 The pseudo-color pattern preferably extends over at least one coherent or contiguous section of the pseudo-color image data and thus forms a pseudo-color pattern field. Within a pseudo-color pattern field, the content of at least one of the image input data and the auxiliary input data satisfies preferably the same condition. For example, if the content of the auxiliary input data and/or the pseudo-color

image data exceeds an upper threshold, this may represent saturation in the data. These data may then be represented by the pattern field so that they are marked as being unreliable. The same approach can be used in connection with a lower threshold, which may represent data which are below a sensitivity threshold and thus may be considered unreliable. An example of a temporal modulated pattern may be a pseudo-color image or a coherent part thereof, which is filled with a pseudo-color and in which the pseudo-color is switched on and off, or changes at least one of brightness, hue and saturation according to the variation rate.

A temporally modulated pattern may have a variation rate in which a cyclic repetition of alternating patterns occurs. In order to be clearly visible, the variation rate should be smaller than the flicker fusion rate, i.e. in particular be smaller than 25 Hz.

The image processor may be configured to determine the variation rate depending on the content of at least one of the input image data and the auxiliary input data. The variation rate may be automatically varied by the image processor over time. In particular, the variation over time may be dependent on the content of at least one of the input image data, the auxiliary input data and the pseudo-color image data. If, for example, the auxiliary data are ultrasound data, the variation rate may depend on the momentary flow velocity, or on a frequency and/or amplitude of velocity changes, e.g. caused by a pulse in a blood flow.

If the pseudo-color pattern field is a temporal pattern, wherein the image processor is configured to generate the temporal pattern with a variation rate, it is of advantage if the output data rate is larger than the variation rate. Thus, the temporal variation of the pattern can be smoothly displayed. The output data rate usually corresponds to a frame rate, and thus should be higher than the flicker fusion rate in order to produce a smooth sequence of images. In contrast, the variation rate is configured to produce a perceptible motion.

The pseudo-color image data may also comprise symbols, such as arrows, letters and numerals.

The input interface may, according to another aspect of the invention, comprise an input section configured to receive at least one of ultrasound data and fluorescence image data as auxiliary input data. The ultrasound data may be a one-dimensional data field as generated by the recordings of an ultrasound microphone. The ultrasound data may in addition or alternatively be multi-dimensional such as produced by an ultrasound sensor head or scanner. In particular, the ultrasound data may be two-dimensional or three-dimensional (in spatial dimensions) and contain, at each data point representing a spatial location additional data, such as a velocity and direction of flow or movement.

The image processor may comprise spatial alignment module, which is adapted to spatially align the input image data and any auxiliary input image data so that spatial features in both data are spatially congruent.

If for example the input image data are image data received from a visible-light camera and the auxiliary input data are fluorescent-light image data received from a fluorescence-camera, where both the visible-light camera and the fluorescence camera have overlapping field of views, the spatial alignment module rectifies at least one of the images so that the spatial features are of the same size and

orientation in both image data. This allows exact merging of the various image data in the output image data. The auxiliary input data in such a case may alternatively or additionally comprise data from sensors detecting other physical, preferably non-visible, quantities. These data may be rectified in the same way using the spatial alignment module as the fluorescence image data mentioned above.

- 5 If the fluorescence takes place in the NIR range, the fluorescence camera may be a NIR camera and the fluorescence image data may be NIR image data.

If the auxiliary data are image data from a fluorescence camera, in particular fluorescent-light image data, the temporal and/or spatial pattern may depend on the saturation and/or brightness of the fluorescence image data. The pseudo-color pattern field may further be generated where two different
10 colors or wavelengths in the fluorescence-image data overlap and, as an optional further criterion, each color or wavelength exceeds a minimum intensity.

If the auxiliary input image data comprise a three-dimensional data set, the temporal and/or spatial pattern may depend on the location, in particular depth, at which the pre-determined condition for switching this pattern on is detected. This allows including data in the output image data which
15 represent structural and/or physical features in a plane that is below what is represented in the input image data, such as a blood vessel or a bone beneath a tumor marked by a fluorophore.

According to another aspect, the image processor may be configured to generate subsequent sets of pseudo-color image data according to a temporal modulation scheme. The temporal modulation scheme is preferably stored in the image processor. The modulation scheme may comprise at least one
20 of a time-varying alteration between sets of different pseudo-color image data representing different pseudo-colors, pseudo-color image data of different saturation and/or brightness, different pseudo-color image data representing cyclically changing patterns.

The modulation scheme may further comprise a propagating wave pattern, wherein, in the propagating wave pattern, at least one of speed, direction and wavelength depends on the content of the auxiliary
25 input data.

According to another aspect of the medical observation device, the output image data may comprise three-dimensional image data. The image processor may be configured to generate and/or to process three-dimensional output image data, in which pseudo-color image data are generated at different depths or planes of the three-dimensional image data depending on the content of the auxiliary data.
30 This aspect may be realized independent of the generation of a pseudo-color pattern field.

For example, three-dimensional input image data may be generated by Z-stacking using either a visible-light camera or a fluorescence camera. The pseudo-color image data may thus be used to present three-dimensional features. The three-dimensionality of the image data may, as has already been explained above, also result from a three-dimensional ultrasound image.

35 The output image data may be, according to a further aspect of the invention, two-dimensional image data and at least one of the input image data and auxiliary input data may comprise three-dimensional data. The image processor is adapted to compute the two-dimensional output image data from the

three-dimensional input data using pseudo-colors for features which are not in the plane of the two-dimensional output image data. The pseudo-color image data, in particular a pseudo-color pattern field thereof, may be used to display data content of a part of the three-dimensional input image and/or the three-dimensional auxiliary input data that is not within the plane rendered in the two-dimensional output data.

The use of a pseudo-color image in connection with three-dimensional input image or auxiliary input data is advantageous on its own, i.e. without using pseudo-color pattern fields.

The medical observation device may comprise at least one visible-light camera which is connected to the input interface for providing the input image data. The visible-light camera may provide three-dimensional input image data or two-dimensional input image data. The medical observation device may further comprise at least one sensor device configured to sense a physical quantity which is not electromagnetic radiation in the visible wavelength range, such as at least one fluorescence camera, at least one ultrasound sensor, at least one microradiation camera, at least one gamma ray camera, at least one Roentgen camera and/or at least one thermographic camera. These devices may be connected to the input interface for providing the auxiliary input data. The auxiliary input data may be one-dimensional, two-dimensional, three-dimensional or provide sets of auxiliary input data of different dimensionalities.

The medical observation device is preferably configured to discern, process and display more than one fluorophore, i.e. more than one different fluorescent spectra. For this, at least one of a fluorescence camera, a light source and a visible-light camera may be provided with a filter arrangement for selectively blocking and/or transmitting the fluorescent spectra. The pseudo-color image comprises in such a case preferably at least two different pseudo-colors, wherein each pseudo-color is assigned to a different fluorescence spectrum, i.e. to a different fluorophore.

The image processor and its constituents may be hardware devices or may be, at least partly, represented by software modules executed in a multi-purpose computer or processor.

The invention may employ the merging of the pseudo-color image data with the input image data as described in the parallel application EP 16 155 625.3, which is herewith incorporated in its completeness by reference.

In the following, the invention is described exemplarily with reference to the accompanying figures. In the figures, elements which correspond to each other with respect to at least one of function and design are assigned identical reference numerals.

The combination of features shown in the figures and described below is only an example. Individual features can be added or omitted if the technical effect of that particular feature is described above is needed or not necessary for a particular application.

In the figures,

Figure 1 shows schematically an embodiment of a medical observation device according to the invention;

Figure 2 shows a schematic representation of a method of operation for superposing medical images according to the invention;

5 Figure 3 shows schematically an example of a set of input image data and auxiliary input data being merged to output image data;

Figure 4 shows schematically another example of input image data and auxiliary input data being merged to an output image;

10 Figure 5 shows schematically pseudo-color pattern fields having spatial modulation within pseudo-color image data;

Figure 6A-7C show schematically a time-modulated pattern;

Figure 7A-7I show schematically a time-modulated pattern.

First, the structure of a medical observation device 1 which includes the invention is described with reference to Figure 1.

15 Just by way of example, the medical observation device 1 is shown in Figure 1 to be a microscope. The medical observation device 1 may also be an endoscope.

The medical observation device 1 is used to inspect an object 4, such as live tissue 6, for diagnostic or surgery purposes. In the object 4, one or more fluorophores may be present.

20 Upon excitation by certain wavelengths of a light source 8, the fluorophores emit fluorescence light at different peak emission wavelengths, e.g. in the NIR range. If two or more fluorophores are used, they may emit light of different peak emission wavelengths, or just have different spectra. Different fluorophores may be used to mark different types 10, 12 of live tissue 6, so that these types 10, 12 may be discerned by the different fluorescent wavelengths they emit. The light source 8 may also serve as illumination for observation of the object in the visible-light range.

25 For example, a first fluorophore 14, which is schematically represented in Figure 1 by one type of hatching, may be used for marking specifically one type 12 of live tissue 6, for example blood vessels. A second fluorophore 16, represented in Figure 1 by another type of hatching, may e.g. mark exclusively another type 10 of live tissue 6, for example tumor cells.

30 The medical observation device 1 may comprise an optical system 18, such as a zoom magnifying lens. In the case of an endoscope, the optical system 18 may also comprise fiber optics. The optical system 18 is, in operation of the medical observation device 1 and its medical image superposition device 49, directed onto at least a section of the live tissue 6. The visible section of the object 4 is determined by the field of view 20 of the optical system 18. Light reflected off the live tissue 6 together with any fluorescent light

emitted from the at least one fluorophore 14, 16 is collected by the optical system 8 and directed to one or more beam splitter system 24 which contains at least one beam splitter.

A part 26 of the light 22 is directed to a visible-light camera 28 by the at least one beam splitter system 24. Another part 30 of the light 22 may be directed to a fluorescence camera 32. Another part 34 of the light 22 may be directed to an ocular 36 which may be monocular or binocular.

The ocular 36 may be directed onto a transmissive display 38, which is arranged between the ocular 36 and the at least one beam splitter system 24. The transmissive display 38 allows the part 34 of the light 22 to pass and to superpose a picture, which is currently displayed on the display 38, onto the image provided by the optical system 18.

Alternatively, the display 38 may not be transmissive. In this case, the display 38 may render a live view of the object 4 with additional information or display any other information that an operator of the medical image superposition device 49 or the medical observation device 1 requests. In particular, the background image, which in the case of a transmissive display 38 would be provided directly by the optical system 18, may be instead provided in real time by the visible-light camera 28.

The medical observation device 1 may further comprise at least one sensor 40, e.g. an ultrasound or blood-flow sensor, which may be in contact with the object 4.

In addition to the at least one sensor 40 at east one further sensor device 42 may be provided. The sensor device 42 is preferably a non-optical sensing device that is configured to sense non-visible physical quantities such as microradio, gamma, Roentgen, infrared, or sound data. The non-optical sensing device 42 provides two- or three-dimensional data. Examples for the non-optical sensing device 42 are microradiography cameras, ultrasound sensor heads, thermographic cameras, gamma ray cameras and Roentgen cameras.

The non-optical sensing device preferably has a sensor field 43, which overlaps the field of view 20 so that the data captured by the optical system 28 and the non-optical sensing device 42 represent different physical quantities from the same area of the object 4.

In order to separate the light in the visible-light range from the light in the fluorescence wavelengths and in order to avoid reflections, a filter arrangement 44 may be used preferably immediately in front of at least one of the light source 8, the beam splitter system 24, the visible-light camera 28, the fluorescence camera 32, the ocular 36 and the display 38.

The visible-light camera 28 is connected via a data connection 46 to an input interface 48 of a medical image superposition device 49. The medical superposition device may be realized by hardware dedicated to carry out specific functions, such as an ASIC, by software executed by a general-purpose computing device, or a combination of both.

The input interface 48 receives, in operation of the medical image superposition device 49 and the medical observation device 1 subsequent sets 50 of input image data 52. The input image data 52 is two-dimensional and organized to contain pixels 54. In the embodiment of Fig. 1, the subsequent sets

50 of the input image data 52 correspond to the sequence of visible-light image data 53 provided by the camera 28.

The input interface 48 is further configured to receive auxiliary input data 58, which may be one-dimensional auxiliary input data 60, sets 62 of two-dimensional auxiliary input data 64 or three-dimensional auxiliary input data 66 consisting of several planes 67 of two-dimensional data. Of course, the auxiliary input data 58 may also comprise data of a higher dimensionality, e.g. if hyperspectral cameras are used or ultrasound sensor heads, which output three-dimensional pictures which contain additional physical data such as blood flow velocity and direction for each pixel or voxel.

The fluorescence camera 32 may transmit, via the data connection 56, subsequent sets 62 of two-dimensionally auxiliary input data 64 which may in particular represent fluorescence image data 65 from the fluorescence camera 32. The fluorescence image data 65 may have the same format as the input image data 52 but at a different resolution.

The sensor 40 may provide one-dimensional auxiliary input data e.g. in the form of a time sequence blood flow velocity 68 in the blood vessel 12.

The sensing device 42 may provide subsequent sets 62 of two- or three-dimensional auxiliary input data 64 e.g. in planes 67 parallel to the depth direction 70 of the object 4, i.e. to the viewing direction 72 of the medical observation device 1.

The sensing device 42 may be connected to the input interface 48 of the medical superposition device 1 by a data connection 74. Another data connection, not shown for simplicity's sake, may exist between the ultrasound sensor 42 and the input interface 48. All data connections may comprise wired and/or wireless sections.

It is to be understood that auxiliary input data 58 can be received by the medical image superposition device 49 from any one of the described devices, e.g. only from the fluorescence camera 38 or only from the ultrasound sensor 40, as well as any combination of such devices. Moreover, other devices may also be employed to provide auxiliary input data 58, although not shown in Figure 1. For example, a thermographic camera, a microradiography camera, a Roentgen camera and/or a gamma ray camera may be used instead of or in addition to an ultrasound sensor and/or the fluorescence camera.

The medical image superposition device 49 comprises an image processor 80 which is configured to blend the input image data 52 from the visible-light camera 28 with the auxiliary input data 58 and provide output image data 81 which contain both at least parts of the input image data 52 and at least parts of the auxiliary input data 58. The input image data 52 are used as background data whereas the auxiliary input data 58 are assigned at least one pseudo-color and/or a pseudo-color pattern before they are merged with the input image data 52. The pseudo-color is manually or automatically by the image processor 80 selected from a list of colors which is not present in the image input data 58 and which preferably does not exist in tissue 6, such as neon colors. Preferably, each different physical quantity is assigned a different pseudo-color and/or pseudo-color pattern.

For this, the image processor 80 comprises a pseudo-color image generator 82. The pseudo-color image generator 82 assigns a pseudo-color to the auxiliary input data 58 depending on the content and/or source of the auxiliary input image data 58. Preferably for each set 50 of image data 52, the pseudo-color image generator 82 is configured to generate a corresponding set 84 of pseudo-color image data 86 in real time. The pseudo-color image data 86 are then blended with the input image data 52.

The image processor 80, in particular the pseudo-color image generator 82 is further configured to generate at least one pseudo-color pattern 87 within the pseudo-color image data 86. The pattern 87 extends over a coherent section of the pseudo-color image data 86 and thus forms a pseudo-color pattern field 88. The pattern 87 may comprise a temporal modulation and/or a spatial modulation of zones of pseudo-color within the pseudo-color image data 65. A spatially modulated pattern has regularity in space, a temporally modulated pattern has regularity over time. Regularity means that the pattern repeats in a predictable way.

If the pattern 87 has temporal modification, it is generated by the pseudo-color image generator 82 to have a variation rate, which represents the time between successive repetitions of the pattern 87.

The pattern 87 is generated in dependence of the content of the auxiliary input data 58. For example, a pattern 87 may be generated instead of a solid pseudo-color by the pseudo-color image generator 82 in an area of the auxiliary input data 58, in particular the fluorescent-light image data 65, where a threshold, for example a brightness threshold, is not met. Different patterns 87 may be generated depending on how far the content is below the threshold. This is exemplarily described in the following with reference to Figures 5, 6A to 6C and 7A to 7I. Fig. 5 shows a pseudo-color pattern 87' having spatial modulation, Fig. 6A to 6C show a pattern 87'' having temporal modulation, and Fig. 7A to 7I show a pattern 87''' having both temporal and spatial modulation, the temporal modulation being based on a temporal modulation scheme 87''''.

In Fig. 5, a schematic representation of one set of pseudo-color image data 86 is given. The pseudo-color image data 86 contains at least one pseudo-color 89, in this example two different pseudo-colors 89a and 89b, and two different pseudo-color pattern fields 88 containing different pseudo-color patterns 87, having in this example only spatial modulation. One pseudo-color pattern field 88a for examples is built up of a repeating wave-form template and can be used to designate an area in the auxiliary input data 58, e.g. from an ultrasound sensor, in which an increased liquid content has been discovered by automatically comparing the auxiliary input data 58 with a data library. Another pseudo-color pattern field 88b can be used to designate an area of the auxiliary input data 58, in which the intensity is below or above a threshold. As the patterns 87 have only spatial modulation, they do not change over time. The extent of the pseudo-color pattern field 88, however may change over time, as it depends on the content of the input image data 52 and/or the auxiliary input data 58.

Fig. 6A to 6C show a pseudo-color pattern 87 with temporal modification. In this example, the temporal modification is a simple blinking operation over time. In Fig. 6A, the pseudo-color pattern field 88 contains a first pseudo-color 89a. In Fig. 6B, the same pseudo-color pattern field 88 is shown to contain a second pseudo-color 89b (or no pseudo-color) at a later point of time, which has replaced the first pseudo-color 89a. At again a later point in time, shown in Fig. 7C, the pseudo-color pattern field 88 is

restored to the state shown in Fig. 6A. Thus, a repetitive pattern is displayed over time. The time-period between successive repetitions is determined by the variation rate of the temporally modulated pseudo-color pattern 87. The variation rate is determined in the pseudo-color image generator 82 depending on the content of the input image data 52 and/or the auxiliary input data 58. In order to have a clearly visible temporal modulation, the variation rate is smaller than the flicker fusion rate, in particular less than half the flicker fusion rate.

The temporal modulation shown in Fig. 6A to 6C may for example be assigned to auxiliary input data, in which the intensity is above a threshold, and which if assigned to a static pseudo-color, would, not be discernible in the pseudo-color image data 86, e.g. because saturation has been reached. In such a case, instead of showing a second pseudo-color 98b, the pseudo-color can be switched of in the pseudo-color image data 86.

Another example, where the temporal modulation shown in Fig. 6A to 6C may be used is an area, where otherwise two static pseudo-colors would have been assigned. Using the temporal modification, it can be clearly indicated that the pseudo-color pattern field 88 results from auxiliary input data of which the content satisfies the criteria for the assignment of more than one pseudo-color 89. Of course, the temporal modulation shown in Fig. 6A to 6C can be extended to contain more than two pseudo-colors 89a, 89b in sequence.

The pseudo-color pattern field 88 may comprise a pseudo-color pattern field 88 which has both temporal and spatial modulation. This is shown in Fig. 7A to 7I, which depict a pattern 87 comprising at least one solid pseudo-color pattern area 87a which assumes a different location in subsequent sets 84 of pseudo-color image data 86 to produce a progressing wave pattern 87b progressing in the direction of the arrow 87c. Each of the Fig. 7A to 7I shows one of the subsequent sets 84 during one variation period. At the end of the variation period, in Fig. 7I, the cycle is repeated by starting with the pattern of Fig. 7A.

The pseudo-color pattern field 88 shows regularity in its change both over time and space in that the at least one solid pseudo-color pattern area 87a alternates regularly in space with a transparent area or an area filled with another pseudo-color, and in that the same spatial pattern is contained in the pseudo-color pattern field 88 after each passing of the variation rate. It is to note, that the variation rate itself may change over time depending on the content of the auxiliary input data 58.

The pseudo-color pattern 87 shown in Fig. 7A to 7I may e.g. used for auxiliary input data 58 which represent a velocity, flow rate and/or direction, such as blood flow data. The velocity represented in the auxiliary input data 59 may be represented by the variation rate, the flow rate by the spatial variation rate or the intensity of the pseudo-color 89 in the pattern 87. The extent of the pseudo-color pattern field 88 is determined automatically from the auxiliary input data 58 for each set 52.

The image processor 80 may further comprise a spatial alignment module 90. The spatial alignment module 90 is configured to rectify the input image data 52 and the auxiliary input data 58 spatially so that each set 52, 62 is spatially congruent to each other. This can for example be done by algorithmically correlating spatial features which are present both in the input image data 52 and the auxiliary input

image data 58. The spatial alignment module 90 is configured to rectify at least one of the image input data 52 and the spatial input data 58 by morphing the image so that correlating structures are aligned. The morphing operation may comprise stretching, rotating, adjusting resolution, and/or warping of at least one of the input image data and the auxiliary input data.

5 For example, fluorescence image data from the fluorescence camera 32 may be slightly rotated, warped and displaced relative to the visible-light image data from the visible-light camera 82. Further, two-dimensional data 64 from the ultrasound sensor 40 may have a different scale and resolution, and be warped and rotated with respect to the input image data 50 and/or the fluorescent-light image data 65 from the fluorescence camera. In order to correctly superpose these data, the spatial alignment module
10 90 is configured to execute a correlation algorithm to identify common structures in the respective data 52, 58 and compute their respective orientation and scale. The spatial rectification is performed depending on the result of this algorithm for each synchronized set of input image data and auxiliary input data.

Further, the spatial alignment module 90 may comprise transfer functions of the devices which generate
15 the auxiliary input data 58, which transfer functions have been obtained by initial calibration processes. The transfer functions may be used to correct errors in the optical system such as vignetting, distortion and/or aberration.

The medical image superposition device 49 further comprises an output interface 91, which is configured to output subsequent sets 92 of output image data 94. The output image data 94 result from
20 the merger of the pseudo-color image data 86 and the input image data 50.

An example for such a merger is given in applicant's application EP 16 15 5625.3, which is herewith incorporated by reference in its entirety. Although the merging is described in this reference in relation to fluorescent-light image data only, the merging can be used for any other type of two-dimensional auxiliary input data 58, 64, 67 without any further change. S

25 The output image data 94 are output at an output data rate which is preferably larger than the highest variation rate of a temporarily modulated pattern 87 in the output image data 94 by an order of magnitude. In particular, the output data rate is higher than the flicker fusion rate, in particular higher than 25 Hz. The variation rate in contrast is smaller than the flicker fusion rate, so that the regular variation of the pseudo-color pattern 87 is clearly visible.

30 It is to be understood, that recognition of the pattern 87 does not depend on cognitive processes of the human mind but that the pattern 87 can be recognized by any automated pattern recognition process due to its regularity in at least one of the spatial and temporal domain.

The display 38 is connected via a data connection 96 to the output interface 91. In the display 38, the output image data 94 are displayed. If the display 38 is transmittive, the input image data 52 may be
35 omitted from the output image data 92, and only the pseudo-color image data 86 may be displayed. The input image data 50 in this case are used only for aligning the pseudo-color image data 86 and the pattern 87 with the input image data 52. As the input image data 50 give an accurate rendition of what

is seen through the display 38, the effect is the same as using a non-transmissive display and displaying the merged input image data 52 and the pseudo-color image 86.

A schematic example of what is seen through the ocular 36 is presented in detail I of Figure 1.

The fluorophores 14, 16 are each assigned a different pseudo-color by the pseudo-color image generator 82. The output image data 94 comprise at least one pseudo-color pattern field 88, which is generated in real time by the pseudo-color image generator 82 and which has a temporal and/or spatial modulation. The pattern field 88 comprises the pseudo-color pattern 87 and is generated depending on the content of the input image data 52 and/or the auxiliary input data 58.

For example if, in the fluorescent-light image data 65 of the fluorescence camera 32, there are areas within the fluorescent-light image data 65 having a fluorescence intensity below a predetermined but preferably adjustable threshold, they may be marked with a pseudo-color pattern 87 in which the pseudo-color 89 may have at least half of their full brightness, so that in spite of the low intensity in the fluorescent-light image data 65, this area is still visible to an observer. Alternatively, or additionally, a different pattern 87 may be used in an area where the fluorescent-light image data have an intensity which exceeds a predetermined but preferably adjustable threshold. This may indicate to an observer that these data are unreliable or that he has to adjust the camera sensitivity.

The medical image superposition device 49 and the medical observation device 1 may provide two- and/or three-dimensional images in the display 38 and, accordingly, the display 38 may be a 2D- or 3D-display.

If auxiliary input data 58 are used which comprise data from locations which are situated in the depth direction 70 beneath the plane of the field of view 20 of the optical system 18 and thus are not contained in the visible-light image data 53 from the visible-light camera 28 or in the fluorescent-light image data 65 from the fluorescence camera 32, they may be added to the pseudo-color image data 86 using a pseudo-color pattern 87. For example, if the ultrasound sensor 40 or 42 has detected a coherent structure 100 in the object 4, such as a large blood vessel or a nerve beneath the field of view 20, the structure 100 may be rendered by using a pseudo-color pattern field 88 in the pseudo-color image data and ultimately in the output image data.

Various auxiliary input data 58 from different devices may be simultaneously displayed by using different pseudo-colors and different patterns 87.

Next, the process of generating output image data from the input image data and auxiliary input data via pseudo-color image data is explained with reference to Figure 2. In Fig. 2 optional steps are indicated by dashed lines.

Figure 2 shows that the input image data 52 are pre-processed, in a first step 110, which may be carried out by the medical image superposing device 1. The pre-processing step 110 may include any one or any combination of histogram equalization, automatic adjustment of contrasts, compensation of aberration, vignetting and distortion errors caused by the optical system 18 as well as noise reduction, but may not be limited to these.

The auxiliary input data 58, such as the fluorescent-light image data 65 or other and further auxiliary input data 58, such as ultrasound data, microradiography image data, thermographic image data and/or Roentgen image data may also undergo a pre-processing step 112 to compensate at least one error, noise and distortions. The pre-processing algorithms carried out in step 112 may in general be the same as for the input image data 52 in step 110, using however, different parameters to account for the different physical parameters and systems. For example, the compensation of errors introduced by the optical system 18 may be different for the fluorescent-light image data 63 than for the visible-light image data 53.

In particular for the auxiliary input data 58, the pre-processing 112 may also comprise a threshold comparison, in which those auxiliary input data with a content below a certain sensitivity threshold are for example blanked or deleted so that they will not be contained in the output image data. For example, pixels may be blanked or set to zero or set to transparent in auxiliary input data 58, if the intensity of that pixel is below a sensitivity threshold. The sensitivity threshold may be determined by a user of the medical image superposing device 1 or medical observation device 1. Thus, pixels which represent only a very low signal strength, i.e. fluorescence level or ultrasound reflectivity, may thus not be considered in the pseudo-color image generation.

The next step 114 comprises spatial adjustment of at least one of the input image data 52 and the auxiliary input data 58, in particular of two-dimensional and/or three-dimensional auxiliary input data so that spatial features are located at the same location and in the same size and orientation in both the input image data 52 and the auxiliary input data 58. At the end of spatial adjustment 114, the input image data and the auxiliary input data are at least substantially spatially congruent. Preferably, the input image data 52 are used for reference in the spatial alignment step 114. The auxiliary input data 58 are thus modified in the spatial alignment step 114, whereas the input image data 53 are left unchanged. This is of particular advantage if the auxiliary input data 58 contain less data than the input image data, e.g. because pixels have been blanked and/or because the resolution measured in pixel of the fluorescence camera 32 and/or a microradiographic, thermographic or gamma-ray camera and/or ultrasound sensor is smaller than the resolution of the visible-light camera 28. However, leaving the input image data unchanged will maintain the field of view 20 of the optical system 18 and the visible-light camera 28 and thus will render faithfully the field of view 20 on the display 38.

In the spatial alignment step 114 the auxiliary input data 58 of a set 62 or a plane 67 may be distorted, rotated and changed in its resolution to spatially correlate it to the input image data 52. The input image data 52 and the auxiliary input data 58 may be time-stamped so that a set of input image data 52 is processed together with a set of auxiliary input data 58 that has been sampled at the same time as the input image data.

Next, in step 116, pseudo-color image data are generated from the auxiliary input data 58.

For example, the different fluorescence colors in a fluorescent-light image data 63, which are in the NIR range and thus invisible to humans, may be assigned different pseudo-colors in the visible range. Further, auxiliary input data 58 representing invisible physical quantities, i.e. physical quantities not being electromagnetic waves in the visible light range, such as ultrasound, microradiation, gamma-ray or

thermographic sensing, may also be assigned pseudo-colors. Preferably, each sensing modality is assigned a different pseudo-color and/or a different pattern.

Using many different types of auxiliary input data 58 in a single set of output image data may result in the use of too many pseudo-colors. Thus, a pattern using the same pseudo-color may be used to keep the numbers of different pseudo-colors small. Further, use of a pattern 87 such as a hatching only obscures part of the underlying input image data, and allows having a better view of the underlying input image data.

Further, if the content of the auxiliary input data 58 designates a low intensity of the recorded signal in the auxiliary input data 58, they would be visualized with only subtle pseudo-coloring. Such a subtle pseudo-coloring may be insufficiently set apart from non-pseudo-colored areas. Thus, these areas should be not filled with a solid pseudo-color but with a pattern in which the pseudo-color has a high brightness, e.g. of at least 50 % of the maximum brightness value.

The different patterns and pseudo-colors are preferably selected automatically from a storage 120 maintained in the medical image superposing device 2. The user may be able to preset certain assignments, i.e. to assign e.g. a particular pseudo-color and/or pattern to specific data sources, to specific content of data from a data source, such as to specific fluorophores, to pixel intensities, or to alteration patterns of data, such as rates of change.

In step 116, subsequent sets 84 of pseudo-color image data 86 are obtained, in which at least one pseudo-color pattern field 88 is filled with a pattern 87 depending on the content of at least one of the input image data 52 and the auxiliary input data 58.

In the next step 124, the pseudo-color image and the input image are merged. It is to be understood that this merging occurs for each data set in the subsequent sets of input image data 52 and auxiliary input data 58 to allow a real-time processing.

The merging process is described in detail in the parallel application EP 16 155 625.3 which is incorporated by reference. As a result of the image merging step 124, the output image data 94 are obtained and finally displayed on the display 38.

In Figure 3, the process depicted in Figure 2 is further explained.

Image input data 52 represent visible-light image data 53 from the visible-light camera 28. Fluorescent-light image data 63 are obtained as auxiliary input data 58 from an fluorescence camera 32 and contain the emission spectra of at least two fluorophores 14, 16 which are assigned different pseudo-colors designated FL800 and FL400 in Figure 3.

At least one pseudo-color pattern field 88 has been generated in the pseudo-color image data 86 depending on the content of the fluorescence image data 63. The pseudo-color pattern field 88a designates an area in which the two fluorophores 14, 16 overlap. The pseudo-color pattern field 88a may contain one of or both the pseudo-colors which have been assigned to the respective fluorophores 14, 16 or the corresponding emission spectra, or a different pseudo-color. Another synthetically

generated pseudo-color pattern field 88c designates an area in which one of the pseudo-colors has a very low intensity. This pseudo-color pattern field 98 may use the same pseudo-color assigned to the respective fluorophore or fluorescence emission spectrum.

Two-dimensional auxiliary input data 58 from the ultrasound sensor 42 are also transformed to pseudo-color image data 86. A pattern field 88 is synthetically generated in areas where the pixel intensity in the auxiliary input data 58 from the ultrasound is above a threshold. The pseudo-color images are then merged with the image input data 52 to obtain output image data 94 containing at least one pseudo-color pattern field 88.

In Figure 4, a set 92 of output image data 94 has been generated by merging fluorescent-light image data 65 containing a fluorescent light from a tumor-marking fluorophore 16 with ultrasound image data and visible-light image data 53.

The at least one pseudo-color pattern field 88 in the output image data 94 may have a temporal modulation as indicated by arrow 134. The area occupied by the pseudo-color pattern field 88 corresponds to areas which were automatically recognized as blood vessels having a blood flow velocity and direction in each subsequent set. The pseudo-color pattern field 88 is a wave pattern which is modified in subsequent sets of output image data 94 to produce a wave pattern 87b which propagates in the direction of arrow 134.

The speed and direction of the wave propagation 34 depends on the blood flow direction and the blood flow speed as contained in the auxiliary input data 58 from the ultrasound sensor 40 or 42. The wave length may be selected to be dependent on the distance of the blood vessel from the surface. Information on the location and extent of the blood vessel and the speed and direction of blood flow can be extracted from the ultrasound data by algorithms executed by the image processor 80.

Reference Numerals

	1	medical observation device
	4	object
	6	live tissue
5	8	light source
	10	type of tissue, timorous tissue
	12	type of tissue, blood vessel
	14	first fluorophore
	16	second fluorophore
10	18	optical system
	20	field of view
	22	light collected by optical system
	24	beam splitter system
	26	light branched off to visible-light camera
15	28	visible-light camera
	30	light branched-off to fluorescence camera
	32	fluorescence camera
	34	light branched-off to ocular or binocular
	36	ocular
20	38	display
	40	ultrasound sensor
	42	non-optical sensing device
	43	field of view of non-optical sensing device
	44	optical filter arrangement
25	46	data connection
	48	input interface

- 49 medical image superposition device
- 50 sets of input image data
- 52 input image data
- 53 visible-light image data
- 5 54 pixel
- 56 data connection
- 58 auxiliary input data
- 60 one-dimensional auxiliary input data
- 62 set of two-dimensional auxiliary input data
- 10 64 two-dimensional auxiliary input data
- 65 fluorescent-light image data
- 66 three-dimensional auxiliary input data
- 67 plane of three-dimensional input data
- 68 blood flow velocity / direction
- 15 70 depth direction
- 72 viewing direction
- 74 data connection
- 80 image processor
- 82 pseudo-color image generator
- 20 81 output image data
- 84 set of pseudo-color image data
- 86 pseudo-color image data
- 87 pseudo-color pattern
- 87' pseudo-color pattern having spatial modulation
- 25 87'' pseudo-color pattern having temporal modulation
- 87''' pseudo-color pattern having temporal and spatial modulation

87''' temporal modulation scheme

87a solid pseudo-color area within pseudo-color pattern

87b progressive-wave pattern

87c direction of progression

5 88 pseudo-color pattern field

88a pseudo-color pattern field indicating data overlap

88b pseudo-color pattern field indicating low intensity

89 pseudo-color

89a one pseudo-color

10 89b different pseudo-color

90 spatial image alignment module

91 output interface

92 set of output image data,

94 output image data

15 96 data connection

98 pseudo-color pattern field

100 large blood vessel

110 step of pre-processing input image data

112 step of pre-processing auxiliary input data

20 114 spatial image alignment

116 pseudo-color image generation

120 pseudo-color and/or pseudo-color pattern storage

124 image merging

134 arrow

CLAIMS

1. Medical observation device (1) such as a microscope (2) or endoscope comprising
an input interface (48), an image processor (80) and an output interface (90),
the input interface (48) being configured to receive subsequent sets (50) of input image data (52)
5 and auxiliary input data (58),
the output interface (90) being configured to output subsequent sets (92) of output image data
(94) at an output data rate,
the image processor (80) being connected to the input interface (48) for receiving the sets of
input image data and the auxiliary input data, and to the output interface for outputting the
10 output image data, the image processor further being configured to generate subsequent sets
(84) of pseudo-color image data (86) depending on a content of at least one of the auxiliary input
data (58) and the input image data (52), and to generate at least one synthetic pseudo-color
pattern field (88) within the pseudo-color image data (86) depending on the content of at least
15 one of the input image data (52), the auxiliary input data (58) and the pseudo-color image data
(86),
the pseudo-color pattern field (88) comprising at least one of a temporally and/or spatially
changing pseudo-color pattern (87, 87', 87'', 87'''), and the image processor being configured to
merge the pseudo-color image data (86) and at least one section of the input image data (52) to
generate the output image data (94) containing the pseudo-color pattern field (88).
- 20 2. Medical observation device (1) according to claim 1, wherein the pseudo-color pattern field (88)
comprises a temporally modulated pattern (87'', 87''') having a variation rate, wherein the output
data rate is larger than the variation rate.
3. Medical observation device (1) according to claim 1 or 2, wherein the image processor is
25 configured to compute a variation rate of the temporally modulated pattern (87) depending on
the content of at least one of the input image data (52) and the auxiliary input data (58).
4. Medical observation device (1) according to any one of claims 1 to 3, wherein the input interface
(48) is configured to receive at least one of ultrasound microphone data, ultrasound image data,
microradiography image data, gamma-ray image data, thermographic image data, multispectral
imaging data, and fluorescence image data as the auxiliary input data (58).
- 30 5. Medical observation device (1) according to any one of claim 1 to 4, wherein the output image
data (52) contains at least one pseudo-color pattern field (88) in an area where the contents of
the auxiliary input data (58) are at least one of below and above a threshold.
6. Medical observation device (1) according to any one of claims 1 to 5, wherein subsequent sets
(50) of the output image data (52) comprise a pseudo-color pattern field (88) having a temporally

modulated pattern (87'', 87'''), the temporally modulated pattern comprising a propagating wave pattern (87b) of which at least one of a speed, direction and wavelength depends on the content of the auxiliary input data (58).

- 5 7. Medical observation device (1) according to any one of claims 1 to 6, wherein the output image data (52) are three-dimensional and wherein the image processor (80) is configured to generate pseudo-color image data (86) at different depth layers of the three-dimensional output image data depending on the content of the auxiliary input data (58).
- 10 8. Medical observation device (1) according to any one of claims 1 to 7, comprising a visible-light camera (28) connected to the input interface (48) for providing the subsequent sets (50) of the input image data (52) and comprising at least one of an fluorescence camera (32) and an ultrasound sensor (40, 42) connected to the input interface (48) for providing the auxiliary input data (58).
- 15 9. Medical observation device (1) according to claim 8, comprising the fluorescence camera (32) and a light source (8), at least one of the fluorescence camera (32), the light source (8) and the visible-light camera (28) being provided with a filter arrangement (44) for at least two different fluorophores (14, 16), each fluorophore (14, 16) having different peak emission wavelengths, the output image data (94) comprising at least two pseudo-colors (89) and the image processor (80) being configured to assign a different pseudo-color (89) being to each of the different fluorescence peak emission wavelengths.
- 20 10. Medical observation device (1) according to any one of claims 8 or 9, further comprising the ultrasound sensor (40, 42), wherein the image processor (80) is configured to generate the pseudo-color pattern field (88) in the output image data (94) depending on the content of the auxiliary input data (58) from the ultrasound sensor (40, 42).
- 25 11. Medical observation device (1) according to any one of claims 1 to 10, wherein the auxiliary input data (58) comprise three-dimensional auxiliary input data (66) and wherein the image processor (80) is adapted to generate a pseudo-color pattern field (88) depending on the content of the three-dimensional auxiliary input data (67)
- 30 12. Method for displaying medical images, comprising the steps of receiving subsequent sets (50) of input image data (52), receiving auxiliary input data (58), generating subsequent sets of pseudo-color image data (86) depending on the content of at least one of the auxiliary input data (58) and the input image data (52), generating at least one pseudo-color pattern field (88) within the pseudo-color image data (86) depending on the content of at least one of the input image data (52) the auxiliary input data (58) and the pseudo-color image data (86), wherein the pseudo-color pattern field (88) has at least one of a spatial and a temporal modulation, merging each set (84) of the pseudo-color image data (86) with each set of the input image data (52) to obtain a set (92) of output image data (94), the output image data (94) containing the pseudo-color pattern field (88), and displaying the output image data (94) at an output data rate.
- 35

13. Method according to claim 12, wherein at least one set of the auxiliary input data are received from an ultrasound sensor, a microradiography camera, a thermographic camera, an fluorescence camera, multispectral camera, and a gamma-ray camera.
14. Method according to claim 12 or 13, wherein subsequent sets (92) of output image data (94) comprise a pseudo-color pattern field (88) having a temporal modulation at a variation rate which is smaller than the output data rate and which depends on the content of the at least one of the input image data (52), the auxiliary input data (58) and the pseudo-color image data (86).
15. Non-transitory computer storage media storing a program causing a computer to execute the method according to any one of claims 12 to 14.

1/5

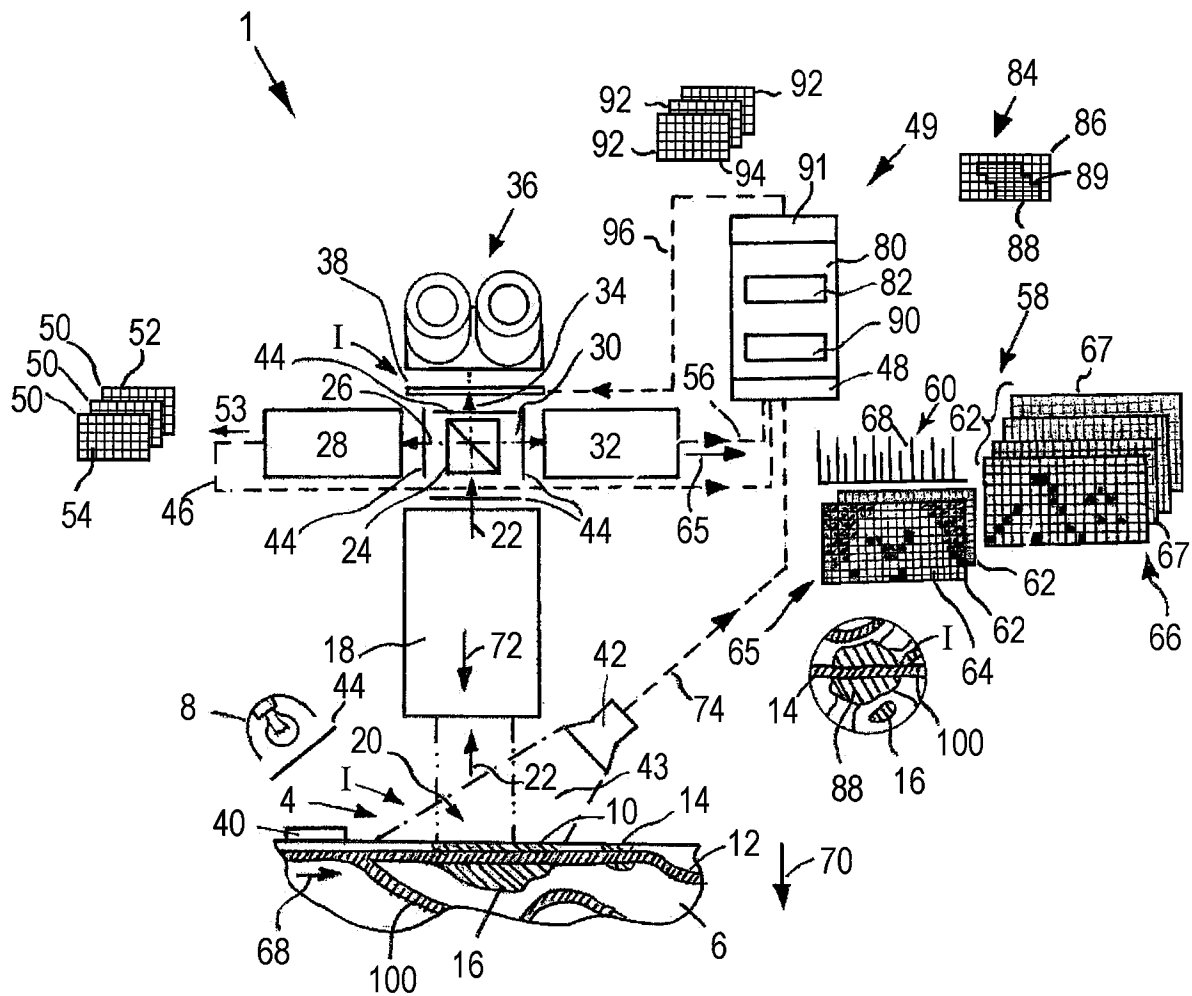


Fig. 1

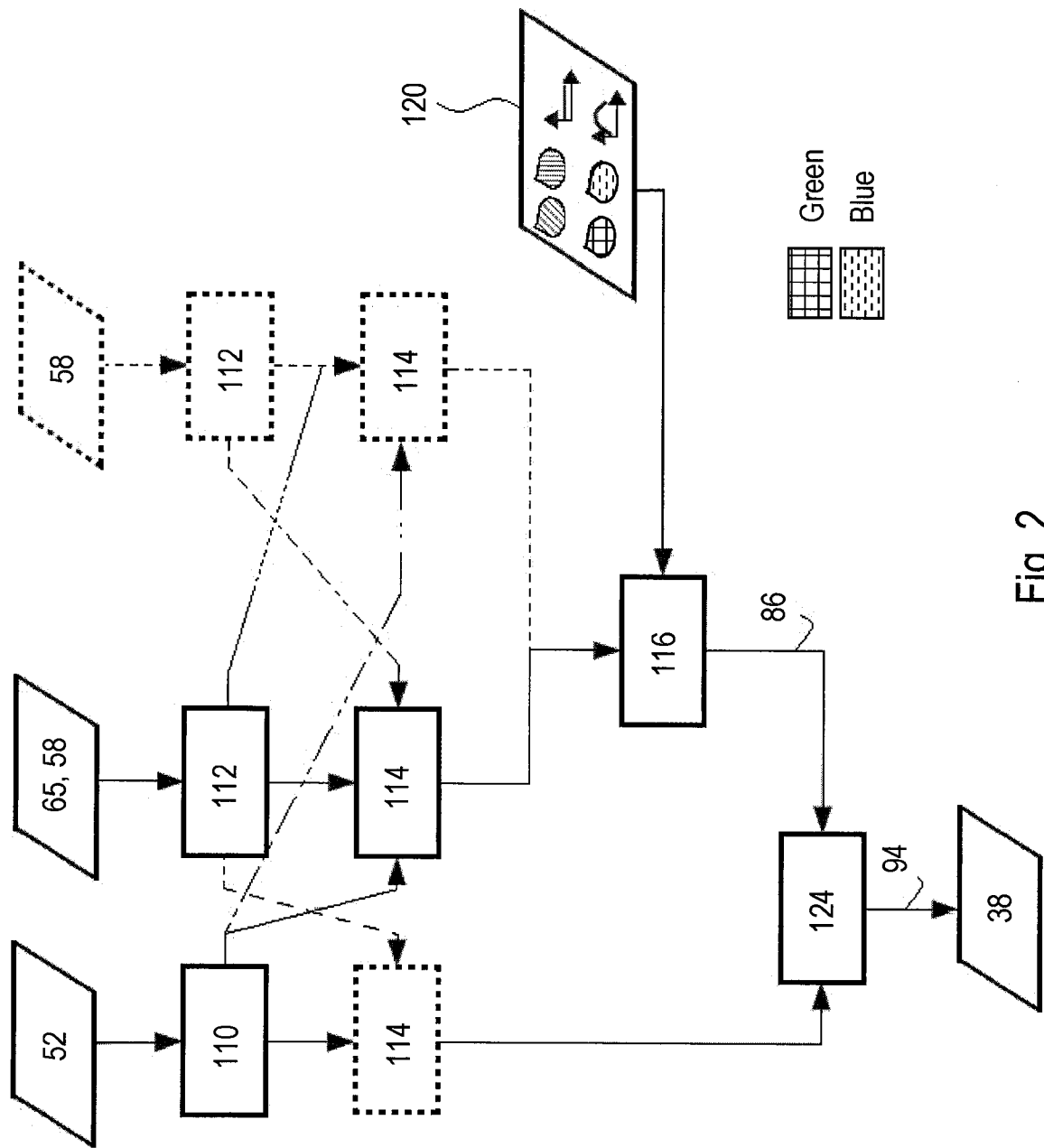


Fig. 2

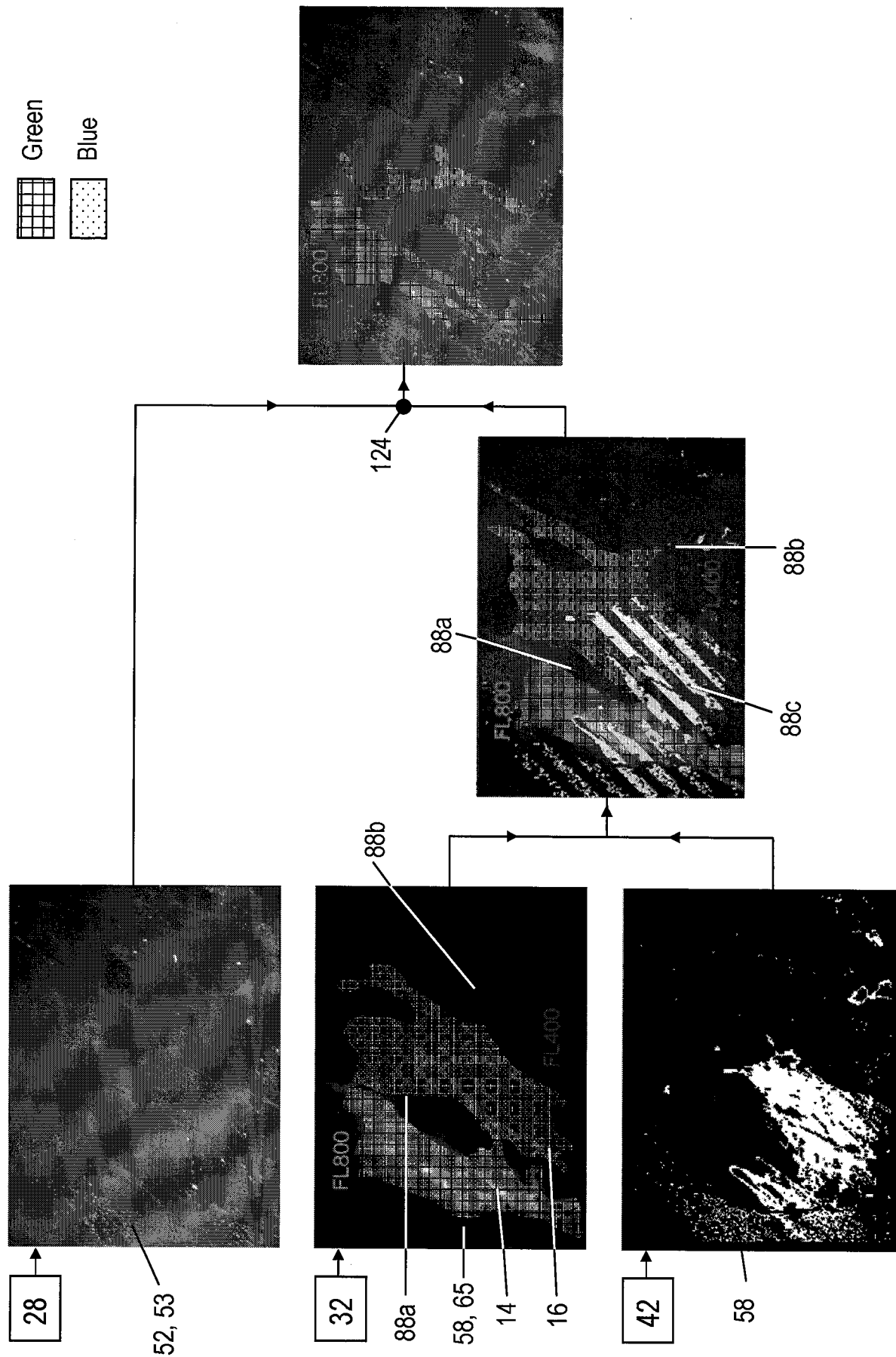


Fig. 3

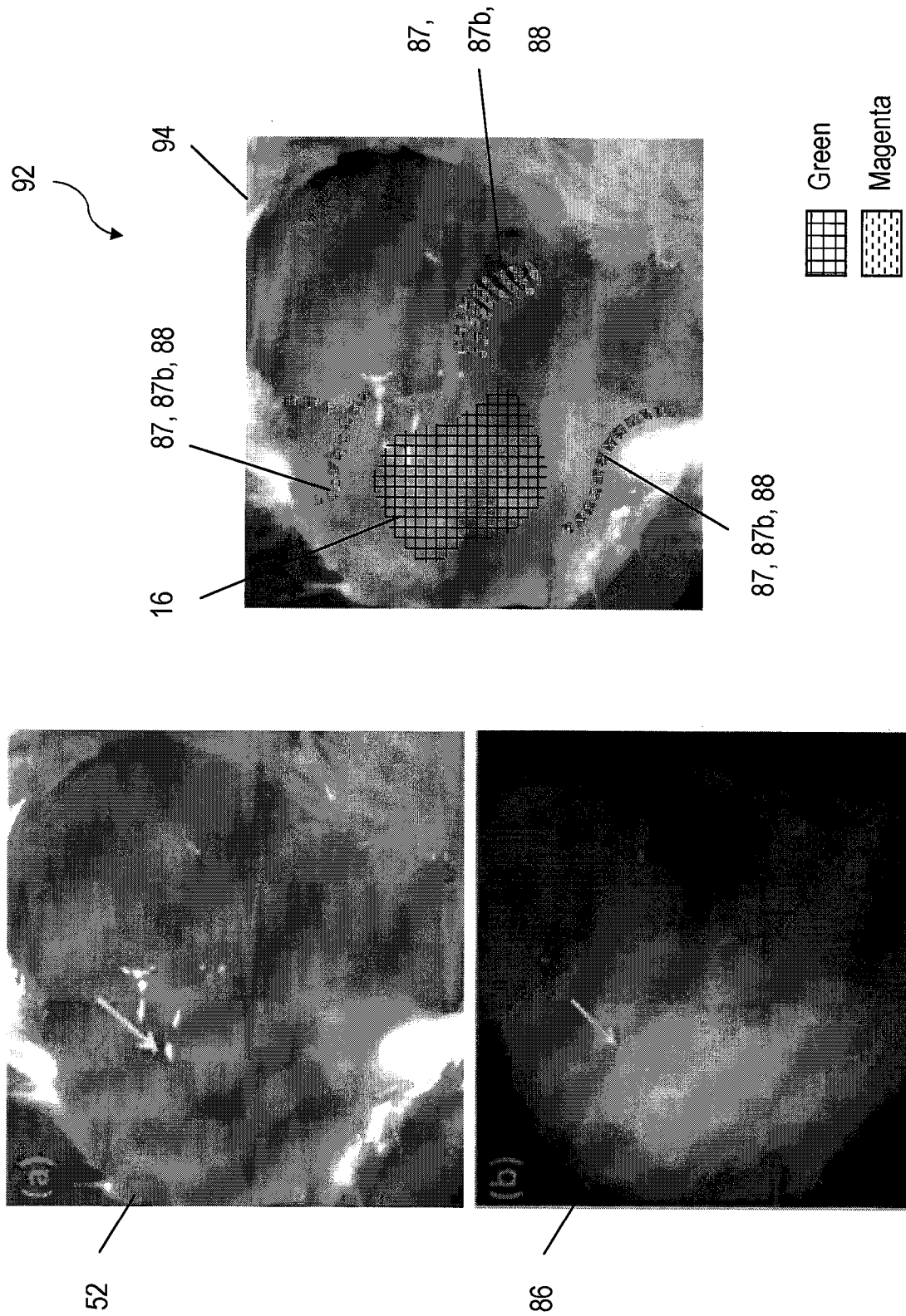
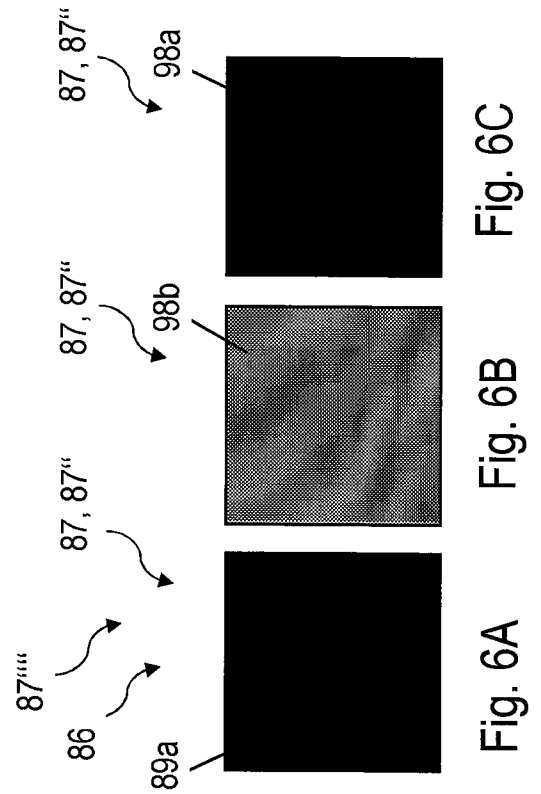
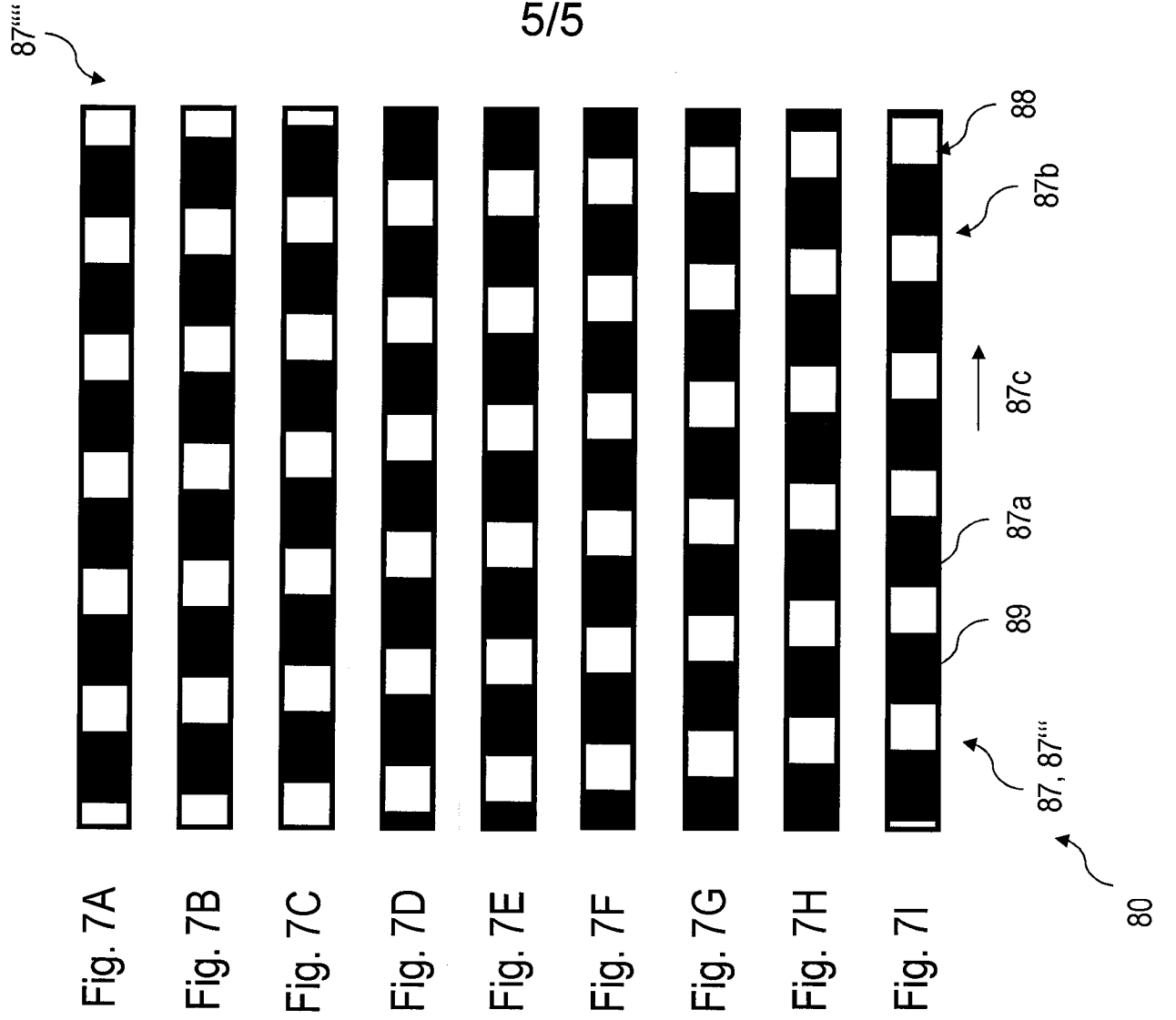
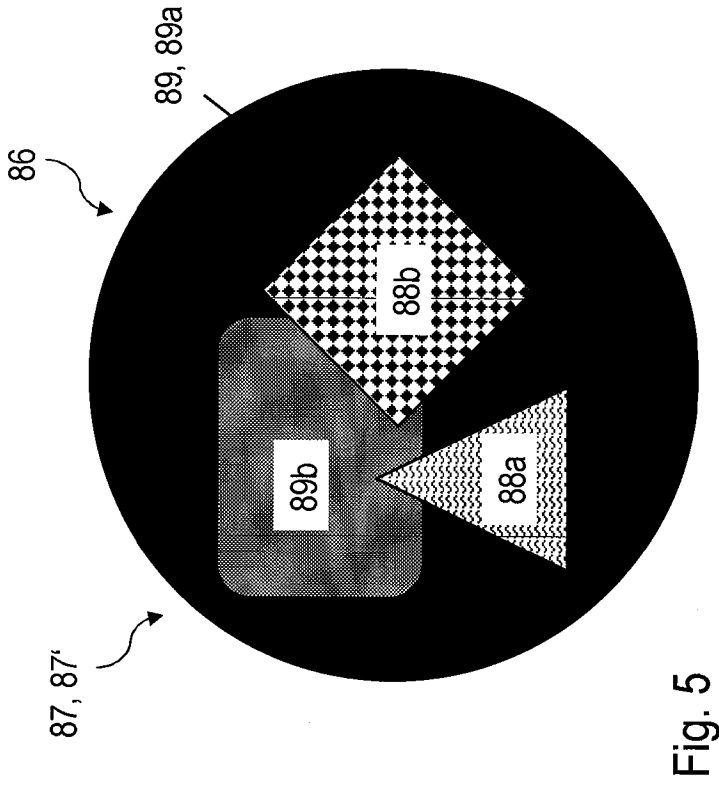


Fig. 4



INTERNATIONAL SEARCH REPORT

International application No
PCT/SG2017/050261

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61B1/00 A61B1/04 A61B1/06 G01N21/64 G02B21/00
G02B23/24 G06T5/50 A61B8/12

ADD.

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)

A61B G01N G02B G06T G06K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

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Y	figures 1,2,5 paragraphs [0018], [0023], [0025] - [0032], [0035] - [0037], [0039] - [0040], [0043] - [0046], [0048] -----	7-11
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Y	US 2001/036304 A1 (YANG MARY M [US] ET AL) 1 November 2001 (2001-11-01) paragraphs [0036], [0040], [0068] ----- -/-	7,9,11



Further documents are listed in the continuation of Box C.



See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

10 July 2017

Date of mailing of the international search report

28/07/2017

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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