(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 May 2009 (22.05.2009)

PCT

(10) International Publication Number
WO 2009/063379 A1

(51) International Patent Classification:
G01N 33/558 (2006.01) *B01J 19/00* (2006.01)

(21) International Application Number:
PCT/IB2008/054686

(22) International Filing Date:
10 November 2008 (10.11.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
07120486.1 12 November 2007 (12.11.2007) EP

(71) Applicant *(for all designated States except US)*: **KONINKLIJKE PHILIPS ELECTRONICS N. V.** [NL/NL]; Groenewoudseweg 1, NL-5621 BA Eindhoven (NL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **SCHLEIPEN, Johannes, J., H., B.** [NL/NL]; c/o High Tech Campus 44, NL-5656 AE Eindhoven (NL). **BRULS, Dominique, M.** [NL/NL]; c/o High Tech Campus 44, NL-5656 AE Eindhoven (NL).

(74) Agent: **VAN VELZEN, Maaike**; High Tech Campus 44, NL-5656 AE Eindhoven, (NL).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(54) **Title:** OPTICAL BIO-SENSOR CARTRIDGE IDENTIFIER

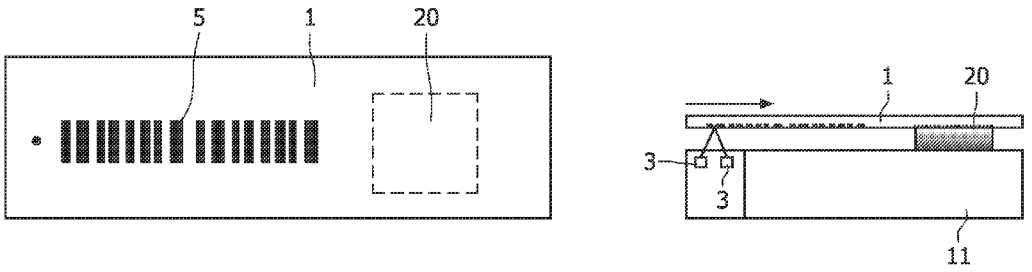


FIG. 1

(57) **Abstract:** The invention provides a method for manufacturing a bio-sensor cartridge with an optical identifier. A bio-marker is printed on a test zone of the cartridge, the bio- marker being for detecting the presence of an analyte in a biological assay applied to the cartridge. Furthermore, an optical identifier, such as a barcode, identifying the cartridge- related formation is printed on the cartridge. According to the invention, the same printing technique is used for both printing steps.

WO 2009/063379 A1

OPTICAL CARTRIDGE IDENTIFIER

FIELD OF THE INVENTION

The invention relates to bio-sensor cartridges, such as test strips, and in particular a method for applying an identifier on a bio-sensor cartridge.

BACKGROUND OF THE INVENTION

Bio-sensors for analyzing a biological assay are used in a wide variety of applications, for example to analyze whether a specific agent is present in the assay or to measure the concentration of a specific agent in the assay. Generally, the assay is filled in a cartridge which is designed to receive the assay and includes a test area. A reagent for detecting the presence of the agent is arranged in the test area. When the assay to be analyzed reaches the test area, the presence or the amount or concentration of the agent to be analyzed may be indicated, e.g., by a color change in the test area.

In bio-sensors, magnetic beads for actuation and detection of bio-markers may be used. The read-out of the bio-markers may be performed with an optical technique using frustrated total internal reflection (FTIR) or other detection methods. Specifically, magnetic actuated beads, these are magnetic particles, are detected using the total internal reflection principle, thus eliminating any background from the biological assay under investigation. By binding or non-binding of the magnetic beads to the surface in the biological assay, the presence of various substances, for example drugs-of-abuse can be detected in the assay, e.g. in saliva.

In US 2003/0124738 A1, a barcode readable diagnostic strip test is disclosed. In order to include the strip information about the lot number, calibration constants, date of expiry and the like, which information is important in clinical applications of strip tests, a barcode encoding this information is printed onto the front or back of the test strip.

SUMMARY OF THE INVENTION

It is desirable to provide an improved method for manufacturing a bio-sensor cartridge which, in order to facilitate and secure read-out automation of the biological assays to be tested and to enable tracing back of possible causes in case of cartridge-failure, is equipped with a sample-to-sample or batch-to-batch unique identifier. The method should allow for a reduction of the production costs of the cartridge.

In the method of the invention, the same printing technique is used for printing a bio-marker on a test zone of the cartridge and for printing an optical identifier, such as a barcode during production of the cartridge. Currently, cartridges are being prepared using ink jet printing of a binding material for binding the bio-marker, for example the magnetic markers. The binding material may be for example BSA (bovine serum albumin). The same ink jet printing technique may be used for printing the optical identifier using a material which is adapted to provide optical contrast. The optical identifier, e.g. the barcode, may comprise information with respect to the manufacturing date, the type and concentration of the bio-markers used, the manufacturer of the cartridge, the processing workflow, and other information relevant to the cartridge used. This information can be used in a control unit of the bio-sensor or reader. Depending on information regarding the manufacturer of the cartridge the control unit of the reader decides whether the cartridge is accepted or not, i.e. whether readout of the test zone is conducted. For instance the information regarding the manufacturing date can be used to determine the durability of the cartridge used and in case of violating the durability to refuse the cartridge to avoid false results. The bio-marker may be adapted for detecting the presence of an analyte such as DNA, RNA, proteins, cells, or drugs-of-abuse in the biological assay applied to the cartridge.

The barcode used as an optical identifier may be a 1-dimensional or 2-dimensional barcode. The optical identifier may be arranged on the surface of the cartridge or in the test area of a cartridge. Depending on the type of optical identifier, and on the position of the optical identifier on the cartridge, different optical readout techniques may be used.

With the invention, a method for manufacturing a bio-sensor cartridge is

provided which allows to reduce the production costs of the cartridge. The invention further provides a bio-sensor cartridge. Since the same printing technique is used for printing the biomarkers in the test area and for printing the optical identifier, providing a separate printing means for printing the optical identifier is avoided.

Printing of the biomarkers and the optical identifier is preferentially with one printer, using a multi-nozzle (multi-outlet) printing head, e.g. using the Fujifilm DIMATIX printing technology. Different ink cartridges contain bio-fluid and identifier-ink, and the required biochemical test pattern and optical identifier pattern can be printed on the cartridge in a single printing step. This increases throughput, reduces costs and guarantees perfect alignment of the optical identifier (that also may contain additional alignment markers) with respect to the biochemical test pattern.

The bio-ink to be printed on the cartridge comprises a buffer fluid containing the relevant biochemical materials to be printed on the cartridge. The biochemical materials to be used depend on the specific bio-assay that is to be performed during the test. The optical identifier ink to be printed on the cartridge has a strong absorption and/or scattering of light (preferentially in the visible range, e.g. at 650 nm), such that the pattern can be read using standard light sources (e.g. visible LEDs or lasers) and detection devices (e.g. CCD or CMOS camera).

These and other aspects of the invention will be apparent from and elucidated with reference to the embodiments described hereafter.

BRIEF DESCRIPTION OF THE DRAWING

Figures 1 to 6 illustrate different types of barcodes in different positions on the cartridge and produced according to different embodiments of the invention, and the corresponding readout techniques.

DETAILED DESCRIPTION OF EMBODIMENTS

The different cartridges 1 shown in the Figures include a test area or test-zone 20 where examplary an FTIR readout is performed in case the cartridge 1 uses a magneto-optical bio-sensor. The term test zone 20 is used for the area at the cartridge 1 at which the detection of the certain analyte by the corresponding certain bio-marker is

done. A bio-sensor is defined by a device for detecting biological, chemical, or bio-chemical analytes or substances. Means for processing and displaying the detected signals of the bio-sensor are not described but common in state of the art. An examplary magneto-optical bio-sensor is defined by a device for detecting biological, chemical, or bio-chemical analytes or substances by a combination of magnetic and optical means. Here, only the optical detection in the bio-sensor is described. For instance the actuation, i.e. mainly the binding of analytes or substances in the bio-sensor, is done by magnetic means exerting forces on the magnetic beads, while the detection of the analytes or substances in the bio-sensor is done optically. The detection of analytes is done at the right side of the reader 11 and the cartridge 1, respectively, characterized at each right side of the Figs by the marked area between the cartridge 1 and the reader 11 at the test zone 20 indicating the light coming from an optical means at the reader 11 to accomplish optical detection. The test zone 20 is also denoted as FTIR area in the description, which means that the optical detection takes place in this area, in this example an optical detection by the optical means using frustrated total internal reflection (FTIR). This optical detection method is described only by way of example, other detection methods are applicable.

Figs. 1 to 3 show some examples for a single spot FTIR readout where a single light source, which may be a laser or an LED, and a single spot detector are used for reading the bio-marker signal from the test zone 20. The test zone 20 is the area at the cartridge 1 at which the analytes or substances to be detected gather and are bound. Each Fig shows on the left side a surview of the cartridge 1 and on the right side a side view of the cartridge 1 above the detector, also denominated as reader 11, below the cartridge 1, indicating the integration of the cartridge 1 and the reader 11. The direction of insertion of the cartridge 1 to the reader 11 is shown by the arrow with an arrowhead above the cartridge 1 at each right side of the Figs. At the left side of the reader 11 an optical device 3 is attached for scanning the optical identifier 5, 7 or barcode at the cartridge 1, including the light source and detector. This is shown in Fig. 1- 3 schematically by two squares from which a light beam emerges, the light beam is reflected by the cartridge 1 carrying the optical identifier 5, 7, and received by the optical device 3, whereby the light beam in Fig. 1 is depicted by two lines crossing at the edge of the cartridge 1. At the right side of the cartridge 1 the test zone 20 with bio-marker is

detected by an appropriate detection method, as described. The detection of the sample, i.e. the detection of the presence of an analyte in a biological assay, at the right side of the Figs and the detection of the optical identifier 5, 7 at the left side of the Figs can be done at the same time, as is depicted in the Figs. In the case of Fig. 1 there is no 2D imaging present in the reader 11. Therefore, the optical identifier 5, 7 is applied on an area of the cartridge 1 outside the test zone 20 and is read using separate scanning optics, the optical device 3, provided in the reader 11 when the cartridge 1 is inserted into the reader 11, which is schematically shown on each right side of the Figs where the cartridge 1 is adjacent to the reader 11. The scanning optics, the optical device 3, may again include an LED or a laser in combination with a detector. When the cartridge 1 is inserted into the reader 11, as is shown on each right side of the Figs, a varying signal in the time domain is obtained from which the barcode information of the optical identifier 5, 7 can be retrieved. This way of scanning a barcode 5, as example of an optical identifier 5, 7, is known as 0D-imaging or scanning. However, depending on the geometry of the cartridge 1, also the FTIR optics, detecting the analyte in the test zone 20, may be used for reading the optical identifier 5, 7. In this case, the optical identifier 5, 7 and the test zone 20 are scanned one after another with one optical detection means instead of two as described above. According to the examplary structure of the Figs first the test zone 20 is scanned and thereafter the optical identifier 5, 7 is scanned. Also feasible is to scan the optical identifier 5, 7 first and thereafter the test zone 20.

Fig. 1 shows an example of a single optical identifier 5, 7, here a barcode 5, that is being read by a stationary single detector at the reader 11 in combination with a laser or LED, whereby the combination is denoted as optical device 3. This is shown in the Figs schematically by a square representing the light source and a square next representing the detector. In order to obtain stable and reliable readout, the cartridge 1 has to be inserted into the reader 11 by the user at a constant pace for clock extraction.

Fig. 2 shows a similar setup as Fig. 1 with a second scanning optics 4 reading a further barcode 52 with a constant line spacing frequency. The further barcode 52 lies adjacent to the optical identifier 5 at the cartridge 1. The second scanning optics 4 are situated next to the optical device 3 and designed to read the further barcode 52. The signal from this second scanning optics 4 scanning the further barcode 52 may be used for clock retrieval and accurate reproduction of the signal of the optical identifier 5

of the optical device 3. The optical identifier 5 under Fig. 2 and 3 and its detection is similar to the optical identifier 5 described under Fig. 1. Fig. 3 shows that the readout of both optical identifier 5 and further barcode 52, that is the barcode 5 encoding the information and the barcode 52 used for clock retrieval, may be done using a single optical device 3 in combination with a split-detector 6 for detecting both optical identifier 5 and barcode 52 at the same time. The method applied in Figs. 1 to 3 (0D-imaging or 1D-scanning) may only be used for 1D-barcodes, which are in this example optical identifier 5 and further barcode 52.

For the readout of the magneto-optical bio-markers also a CCD/CMOS-2D-sensor for imaging the test zone 20 may be used. The bio-signals may be subsequently read using image processing. In this case the reader 11 is equipped with a 2D sensor that may equally well be used for readout of a 1D or 2D barcode embedded in the cartridge 1 and, in particular, arranged in the test zone 20 of the cartridge 1. Figs. 4 to 6 show three examples where a barcode 5 is being read by 2D imaging using the same 2D sensor as being used for reading the FTIR signal. The optical identifier 5 may be a 1D barcode as shown in Fig. 4, a 2D barcode 7 as shown in Fig. 5, or a series of 2D barcodes 7 as shown in Fig. 6 where the series of 2D barcodes 7 may be additionally used as alignment markers, facilitating the image processing. When used as alignment markers detection of optical identifier 5, 7 is used to determine the alignment of the cartridge 1 in relation to the reader 11. Further, the control unit can determine on basis of the alignment whether a detection is started and give a signal in case of uncorrect alignment.

As already mentioned, the barcode areas do not need to be located at the measurement area of the test zone 20 itself, but may well be located at a different position, e.g. at the positions used in the examples of Fig. 1- 3, termed also as single spot FTIR cases, as the optical device of the reader 11 for detecting the presence of an analyte in a biological assay at the test zone 20 is only designed for this matter in these cases, not for reading the optical identifier 5, 7. In this case of the optical identifier 5, 7 located distant from the test zone 20 the optical identifier 7 designed as 2D patterns as described under Fig. 5, 6 can be used as well.

While the invention has been illustrated and described in detail in the drawings and foregoing description, such illustration and description are to be

considered illustrative or exemplary and non-restrictive; the invention is thus not limited to the disclosed embodiments. Variations to the disclosed embodiments can be understood and effected by those skilled in the art and practicing the claimed invention, from a study of the drawings, the disclosure, and the appended claims. In the claims, the word "comprising" does not exclude other elements or steps, and the indefinite article "a" or "an" does not exclude a plurality. A single processor or other unit may fulfill the functions of several items recited in the claims. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures can not be used to advantage. Any reference signs in the claims should not be considered as limiting the scope.

CLAIMS:

1. A method for manufacturing a bio-sensor cartridge (1) including an optical identifier (5, 7), said method comprising the steps of:

(a) printing a bio-marker on a test zone (20) of the bio-sensor cartridge (1) using a printing technique, the bio-marker (10) being for detecting the presence of an analyte in a biological assay applied to the bio-sensor cartridge (1); and

(b) printing the optical identifier (5, 7) identifying cartridge-related information on the bio-sensor cartridge (1) using the printing technique used for printing the bio-marker.

2. The method according to claim 1, wherein the printing technique includes an inkjet printing technique.

3. The method according to claim 1, wherein the optical identifier (5, 7) includes a barcode (5, 7).

4. The method according to claim 3, wherein the barcode (5) is a linear or a 2-dimensional barcode (7).

5. The method according to claim 1, wherein the optical identifier (5, 7) is arranged in the test zone (20) of the bio-sensor cartridge (1).

6. The method according to claim 1, wherein the bio-marker includes magnetic beads.

7. The method according to claim 6, wherein the step of printing the bio-marker includes printing a binding agent for binding the magnetic beads.

8. The method according to claim 1, wherein the printing means comprise different ink cartridges for bio-marker fluid and identifier-ink, respectively.

9. A bio-sensor cartridge (1) comprising a test zone (20) with a bio-marker printed on said test zone (20), and an optical identifier (5, 7) printed on said cartridge (1), the optical identifier (5, 7) identifying cartridge-related information, wherein said bio-marker and said optical identifier (5, 7) are printed using the same printing technique.

10. A bio-sensor cartridge (1) according to claim 9, whereby the optical identifier (5, 7) is used as alignment marker for determining the correct alignment of the cartridge (1) in relation to a reader (11) for connecting with the cartridge (1).

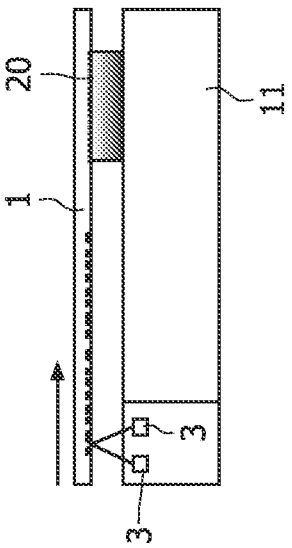


FIG. 1

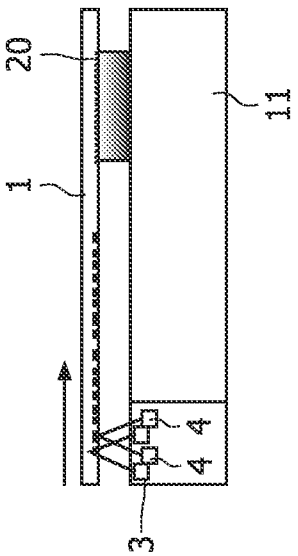
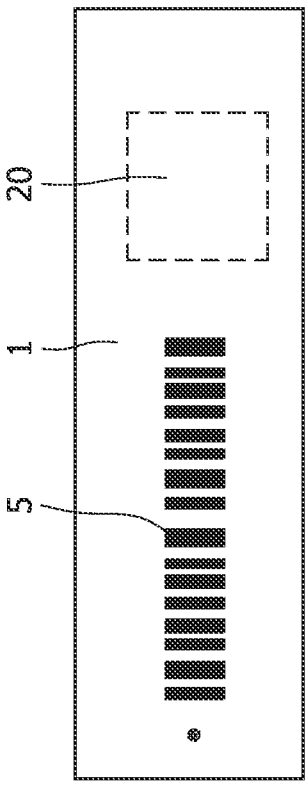
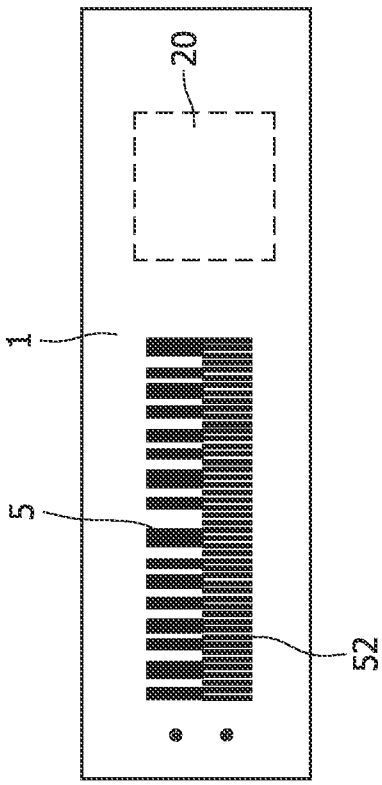


FIG. 2





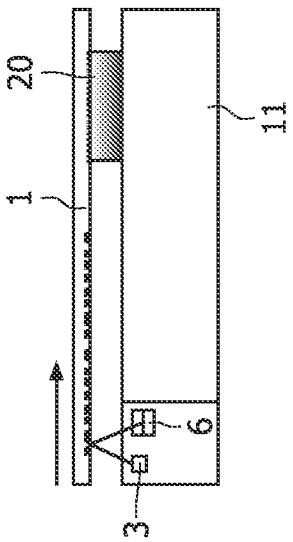


FIG. 3

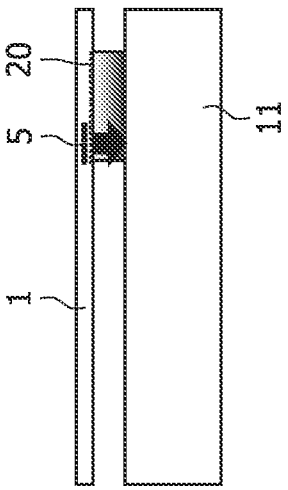
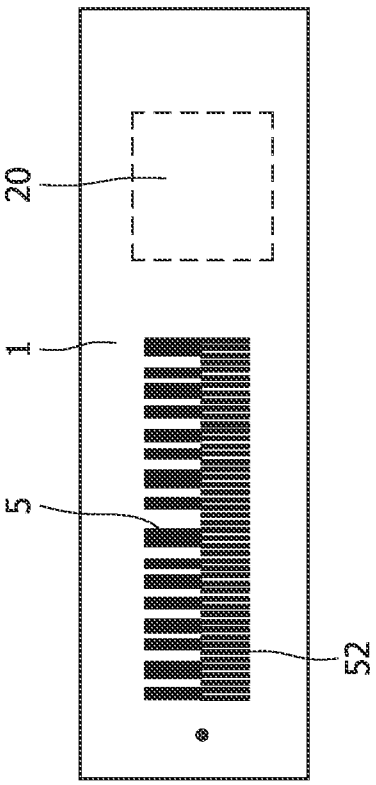
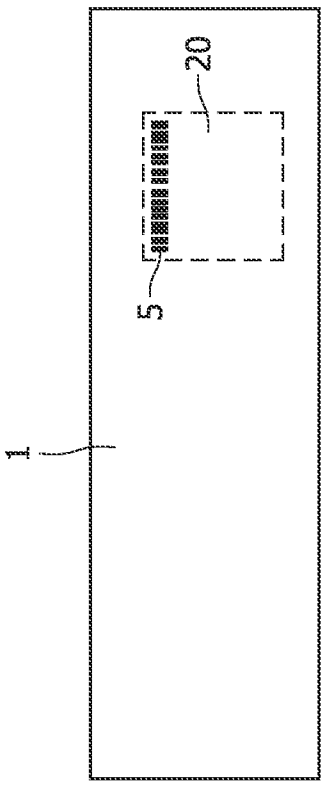


FIG. 4





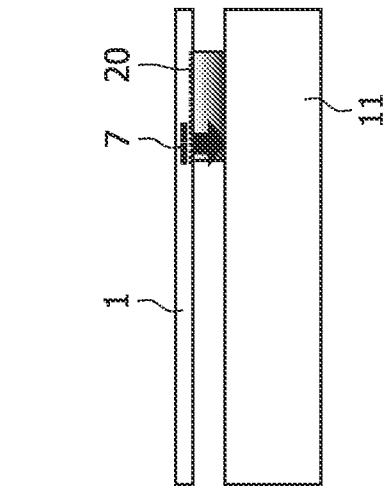
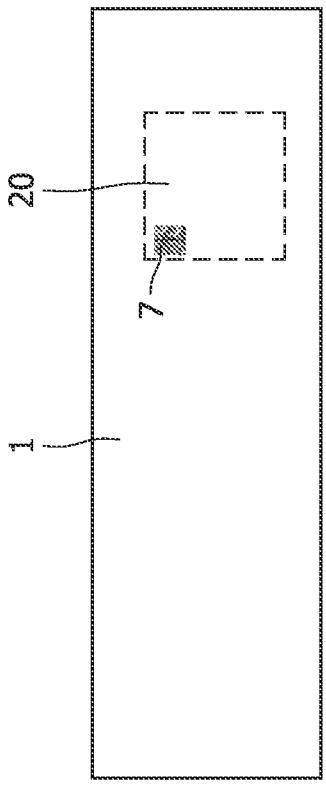


FIG. 5



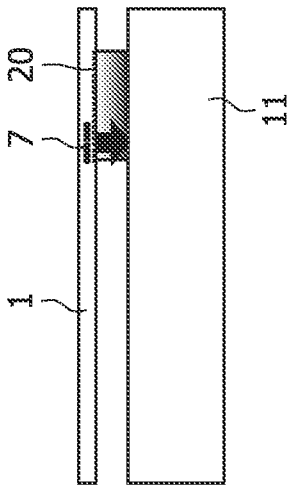
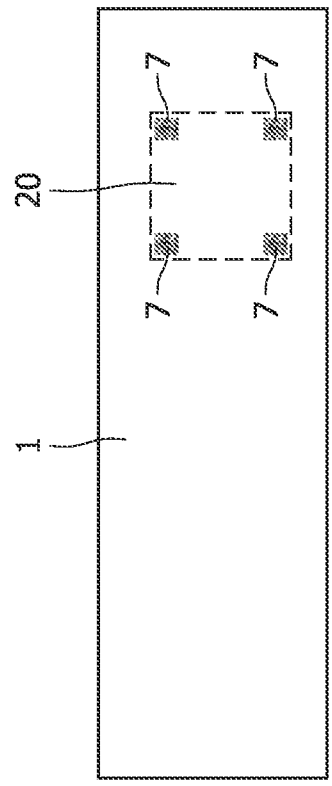


FIG. 6



INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2008/054686

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/558 B01J19/00

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)
G01N

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 practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97/26539 A (BECKMAN INSTRUMENTS INC [US]) 24 July 1997 (1997-07-24) page 17, lines 19-34 page 3, lines 11-18	1-10
X	WO 02/088739 A (ISCHEMIA TECH INC [US]) 7 November 2002 (2002-11-07) cited in the application	9,10
Y	page 4, lines 22,23; figure 1	1-8
X	EP 0 492 326 A (BOEHRINGER MANNHEIM GMBH [DE]) 1 July 1992 (1992-07-01)	9,10
Y	figure 2	1-8
Y	US 5 968 839 A (BLATT JOEL M [US] ET AL) 19 October 1999 (1999-10-19) column 12, lines 12-14	1-8

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"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	Date of mailing of the international search report
9 February 2009	25/02/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Lanzrein, Markus

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2008/054686

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 424 220 A (GOERLACH-GRAW ADA [DE] ET AL) 13 June 1995 (1995-06-13) column 6, line 55 - column 7, line 15	1-8

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2008/054686

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9726539	A	24-07-1997	AU	734126 B2	07-06-2001
			AU	1530497 A	11-08-1997
			EP	0819256 A1	21-01-1998
			JP	11502937 T	09-03-1999
			JP	2005121675 A	12-05-2005
			JP	2005181344 A	07-07-2005
			JP	2005148080 A	09-06-2005
			US	2006057029 A1	16-03-2006
			US	2005271552 A1	08-12-2005
			US	2002182117 A1	05-12-2002
			US	2006045812 A1	02-03-2006
			US	6660233 B1	09-12-2003
WO 02088739	A	07-11-2002	CA	2446329 A1	07-11-2002
			DE	02766865 T1	15-07-2004
			EP	1390752 A1	25-02-2004
			JP	2004527755 T	09-09-2004
			US	2003124738 A1	03-07-2003
EP 0492326	A	01-07-1992	AT	119292 T	15-03-1995
			DE	4041905 A1	02-07-1992
			ES	2071198 T3	16-06-1995
			GR	3015727 T3	31-07-1995
			JP	7005109 A	10-01-1995
			JP	7035998 B	19-04-1995
			US	5281395 A	25-01-1994
US 5968839	A	19-10-1999	CA	2254075 A1	19-11-1998
US 5424220	A	13-06-1995	AT	170290 T	15-09-1998
			DE	4202850 A1	05-08-1993
			EP	0553770 A2	04-08-1993
			ES	2123578 T3	16-01-1999
			JP	2952269 B2	20-09-1999
			JP	5281231 A	29-10-1993