



- (51) **International Patent Classification:**
B01L 9/00 (2006.01) *G01N 27/414* (2006.01)
G01N 27/327 (2006.01)
- (21) **International Application Number:**
PCT/IT2015/000039
- (22) **International Filing Date:**
13 February 2015 (13.02.2015)
- (25) **Filing Language:** Italian
- (26) **Publication Language:** English
- (30) **Priority Data:**
RM2014A000066 14 February 2014 (14.02.2014) IT
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(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, BN, BR, BW, BY, BZ, CA, CH, CL, 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, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, 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, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(54) **Title:** HIGH SENSITIVITY MULTICHANNEL DETECTION DEVICE

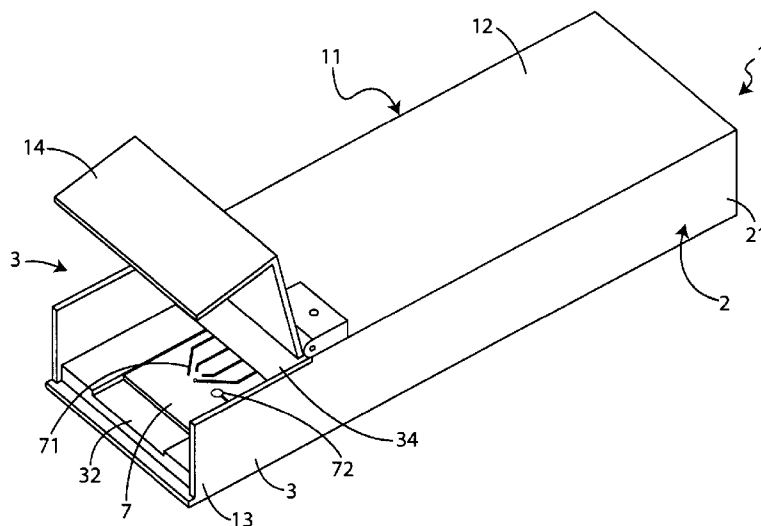


Fig. 1

(57) **Abstract:** The present invention concerns a detection device (1) of a sample to be examined, comprising a processing module (2), a detecting module (3), connected to said processing module (2), a support (7), in which said sample to be examined can be placed, said support (7) comprising a plurality of sensors, preferably biosensors and/or nanosensors, and being insertable within said detecting module (3), and a containment enclosure (11) comprising a body (12), which is arranged within said processing module (2), and a sensor portion (13), in which said detecting module (3) is arranged, characterized in that said processing module (2) comprises a processing unit (4) having a plurality of processing channels (5) and a processor (6), each one of said processing channels (5) being connected to one respective of said sensors and being adapted to amplify and to filter the signals of said sensors, said processor (6) processing said signals amplified and filtered by said processing channels (5).

High sensitivity multichannel detection device.

The present invention relates to a high sensitivity multichannel detection device.

5 More specifically, the invention concerns a device of the above kind, which is fully enclosed in a compact metal housing with electromagnetic protection function, designed to house a card containing sensors (or biosensors), by which it is possible to carry out the observations or the measurements.

10 In the following, the description will be directed to the detection of ion channels, but it is clear that the same should not be considered limited to this specific use.

 As it is well known currently ion channels are responsible for the exchange of transmembrane proteins between intra- and extra-cellular environments. Ion channels play an essential role in many biological processes and their dysfunction are involved in many diseases or serious illnesses.

 Therefore, ion channels are under study for the realization and the preparation of many pharmaceutical compounds.

20 The capacity of ion channels to respond to different chemical-physical stimulations has stimulated the design of hybrid sensors, in which they are adopted as detection unit. This approach has already been used for the detection of molecules in solution and for DNA sequencing.

 For biological purposes, it is essential to characterize the electrical behavior of the ion channel with high accuracy and precision.

25 This is achieved by the low noise acquisition equipment, capable of amplifying the currents of the ion channels that are of the order of picoamperes.

 Current commercially available amplifiers capable of detecting the response of the ion channels provide bulky instrumentation and are limited in the number of channels simultaneously acquired due to the limitations of the discrete electronic architecture, with which they are manufactured.

 It is evident how this procedure is costly in terms of efficiency of use, as well as commercial.

35 A further problem of the portable detection devices according to the prior art is given by the infiltration of liquids and solutions to be tested towards the electronic components, assembled on the printed circuit, on which there are the electronic components. This limits a very much their

diffusion.

In light of the above, it is, therefore, object of the present invention to propose a high sensitivity multichannel detection system, which presents reduced dimensions, so as to allow the portability, and enabling accurate multichannel measures.

Another object of the invention is to provide a packaging that allows easy implementation of the measures and an optimum isolation of the printed circuit from the infiltration of liquid solutions to be examined.

These objects are obtained by the combination of a compact multichannel system for reading the signals of the order of nanoamperes or picoamperes (pA or nA) from sensors coupled to devices that require the use of fluids. This implies both a separation of the "wet" part of the detection system from the electronics, and appropriate measures of electromagnetic shield (shielding) in order to optimize the signal/noise ratio.

It is therefore specific object of the present invention a detection device of a sample to be examined, comprising a processing module, a detecting module, connected to said processing module, a support, in which said sample to be examined can be placed, said support comprising a plurality of sensors, preferably biosensors and/or nanosensors, and being insertable within said detecting module, and a containment enclosure comprising a body, which is arranged within said processing module, and a sensor portion, in which said detecting module is arranged, characterized in that said processing module comprises a processing unit having a plurality of processing channels and a processor, each one of said processing channels being connected to one respective of said sensors and being adapted to amplify and to filter the signals of said sensors, said processor processing said signals amplified and filtered by said processing channels.

Always according to the invention, said processing module could be placed in said body of said containment enclosure, could be provided with a printed circuit board, in which an input connector is arranged, which has a plurality of terminals, preferably spring type, and an output connector, preferably USB type, connected to said processor, for the connection to a personal computer or processor, said containment enclosure preferably being made of conductive material, such as metal or the like.

Still according to the invention, each one of said processing

channels could comprise an analog part, which includes an amplifier having an input connected to said input connector, an adder, interposed between said amplifier and a differentiator or active high-pass filter, and a digital part, which includes an analog to digital converter, having its output
5 connected to said processor, and a second digital to analog converter, having its input connected to said processor and the output connected both to said adder, and to the input of said amplifier, so as to realize a control system of the potential applied to the input connector.

Further according to the invention, said processing channels,
10 preferably four, could be integrated into one or more electronic devices, realized in ASIC (Application-Specific Integrated Circuit), and in that said processor is an FPGA (Field Programmable Gate Array).

Advantageously according to the invention, said sensor portion of said containment enclosure could comprise a door coupled or hinged to
15 said containment enclosure that can be opened and closed.

Always according to the invention, said sensor module could comprise a base, arranged partially below said printed circuit board, in correspondence of said input connector, on said base being obtained a guide, which is insertable in said support, and a blocking element, which
20 forms with the latter a housing (35), in which said input connector is placed.

Still according to the invention, said base of said detecting module could have a first longitudinal groove, intended to house a first seal, arranged in contact with a first face of said printed circuit board, and said
25 blocking element of said detection module could have a second longitudinal groove, intended to house a second seal, arranged in contact with a second face, opposite to said first face of said printed circuit board.

Further according to the invention, said base and/or said blocking element could be made of hydrophobic plastic material.

30 Advantageously according to the invention, said containment enclosure could have at least one inspection opening to which a microscope for optical control could be applicable and/or through which it is possible to provide solutions for performing experiments and measurements.

35 Always according to the invention, said inspection opening could be obtained in said sensor portion, below said base, and in that said base could have further opening arranged in correspondence of said inspection

opening.

Still according to the invention, said support could be double layer type, comprising an upper layer, having a plurality of main holes, a common hole and a series of superficial contacts, and a lower layer, on which a plurality of electrodes are arranged, each arranged in a respective main hole of said upper layer, each one of said electrodes being connected to one respective of said sensors, and a further common electrode, arranged in correspondence of said common hole, said electrodes and said common electrode being connected to said superficial contacts.

Advantageously according to the invention, when said support is inserted in said guide of said base, each one of said superficial contacts could come in contact with a corresponding terminal of said input connector.

Further according to the invention, said detection device could comprise electromagnetic shielding means.

Always according to the invention, said shielding means could be arranged close to or on said one or more electronic devices and are connected to a common potential different from said analogical ground and/or said digital ground, preferably said common potential is comprised between 1 Volt and 2 volts, more preferably equal to about 1,65 Volts, so as to maximize the shielding effect, said common potential being used internally to said one or more electronic devices in which said processing channels are integrated as a reference for all other voltages of said detection device.

Still according to the invention, said processing module could comprise an analogical ground and a digital ground.

Further according to the invention, said electromagnetic shielding means could comprise a ferrite for the connection between said analog ground and said digital ground, said containment enclosure being connected to said analog ground.

Advantageously according to the invention, said input connector and said analog part of said processing channels could be enclosed by a analogical ground plane on an inner layer of said printed circuit board, which constitutes said analog ground or are connected to a common potential, and said shielding means comprise a first metal or Faraday cage, and the digital part of said processing channels and said processor

could be enclosed by a digital ground plane within the printed circuit board, which constitutes said digital ground, and said shielding means comprise a second Faraday cage above and below said printed circuit board.

5 The present invention will be now described, for illustrative but not limitative purposes, according to its preferred embodiments, with particular reference to the figures of the enclosed drawings, wherein:

figure 1 shows a perspective overall view of a high sensitivity multichannel detection device according to the present invention;

10 figure 2 shows a perspective view in transparency of the device according to figure 1; and

figure 3 shows a seat for the insertion of a sample to be examined in the device according to figure 1;

15 figure 4 shows a detail of an electrical connector of the device according to figure 1;

figure 5 shows the circuit diagram of the detection device according to the present invention;

20 figures 6 and 7 show the steps for inserting a support for a sample to be analyzed in a multichannel detection device according to the invention;

figure 8 shows a perspective assembly view of a second embodiment of a high sensitivity multichannel detection device according to the present invention;

25 figure 9 shows the detection device into which a support for a sample to be analyzed is inserted;

figure 10 shows a perspective assembly view of a third embodiment of a high sensitivity multichannel detection device according to the present invention; and

30 figure 11 shows a view in transparency of a detail of the detection device according to figure 10.

In the various figures, similar parts will be indicated by the same reference numbers.

35 Referring to figures 1-4, it is seen a high sensitivity multichannel detection device 1 according to the invention, essentially comprising a processing module 2, and a detection module 3, connected to said processing module 2, both arranged in a containment enclosure 11. Said containment enclosure 11 is preferably made of metal and has a body 12

and a sensor portion 13, which provides a door 14, coupled with said containment casing 11 and possibly hinged to it.

5 The processing module 2 comprises a processing unit 4 placed in the body 12 of said containment enclosure 11, provided with a printed circuit 41, in which an input connector 42 is arranged. Said input connector 42 is in its turn provided with a plurality of terminals 42' of the spring-type. Said processing unit 4 also includes an output connector 43 of USB-type, for the connection of the device 1 to a personal computer or processor.

10 Said processing unit 4, whose processing circuit diagram is shown in figure 5, also includes four processing channels 5 (in figure 5 the diagram of a single processing channel 5 is shown) and a processor 6, connected in output to said output connector 43.

Each one of said processing channels 5 comprises an amplifier 51, preferably an operational amplifier having its inverting input connected to said input connector 42, an adder 52, interposed between said amplifier 15 51, and a differentiator 53 or high-pass active filter. Connected to said differentiator 53, said processing channel 5 comprises an analog/digital converter 54, having its output connected to said processor 6. Finally, each of said processing channels 5 comprises a second digital/analog 20 converter 55, having the input connected to said processor 6 and the output connected both to said adder 52, in the inverting terminal, and in input to said amplifier 51, to the non-inverting terminal.

The processing channels 5, which in this case are four, are integrated in a single electronic device, made as an ASIC (Application 25 Specific Integrated Circuit), while said processor 6 is a FPGA (Field Programmable Gate Array), i.e. an integrated circuit whose features are programmable by software.

30 Figure 5 also shows the schematic arrangement of a Faraday cage 8 (see the dashed line), which protects the four processing channels 5 of the detection device 1.

The above enables to minimize interference from outside and interference from the digital circuitry of the processor 6. In other words, the Faraday cage 8 allows to obtain the signal to noise ratio (S/N) appropriate and necessary to discriminate signals otherwise hidden by noise.

35 The detection device 1 includes, in a preferred embodiment, shielding means, and is provided for the separation between analog ground and digital ground, connected each other together by means of a

ferrite core (not shown in the figure). Furthermore, the external containment enclosure 11 is connected to the analog ground.

The input connector 42 with terminals 42' of spring type and the elements of the analog processing channels 5 (i.e. the amplifier 51, the adder 52 and the differentiator 53) are enclosed by an analog ground plane, on an inner layer of the printed circuit 41 where electronics is mounted. It is also provided a metal cage above, i.e. the aforementioned Faraday cage 8, so as to totally enclose the sensitive part with a shield to the analog ground. More particularly, said Faraday cage can be connected to a common fixed potential, different from said the analog ground and/or to said digital mass, preferably comprised between 1 Volt and 2 volts, more preferably equal to about 1,65 Volts. Said common potential, which is connected to said Faraday cage, is used internally of the electronic device, in which said processing channels 5 are integrated and is used as a reference for all other voltages of the detection device 1. The chosen value of 1,65 indicated Volts equals or $V_{dd}/2$, i.e. to half of the power supply potential of said electronic device.

All of the digital part of the processing channels 5 (i.e. the Analog/Digital converter 54 and the second Digital/Analogue converter 55) and said processor 6 are connected, in a similar way, from a digital ground plane to the printed circuit 41.

It is considered that for reading signals of so small intensity is necessary to adopt such special technique of shielding (shielding), it is not sufficient a simple separation of the masses (grounding).

Experimentally, in fact, it was observed that only optimizing the shielding, the performances required for this type of systems (low-noise readout) are obtained. In particular, by placing appropriately said Faraday cage 8 in direct contact with said electronic device, made in ASIC technology the desired signal/noise ratio characteristics are obtained.

Furthermore, this particular shielding turns out to be at an analog potential different from one of the two masses (both analog and digital). This differentiates the system concerned by normal grounding systems. This shielding technique can be extended to all applications that use low-noise readout chip with mixed signals (mixed analog/digital signal).

The sensing module 3 is arranged in the portion of the sensor 13 of the containment enclosure 11, in correspondence of said door 14, and internally comprises a base 31, arranged partially below said printed circuit

board 41, at said input connector 42, and a blocking element 34 partially overlapped on said base 31, which form with the latter a housing 35, into which said input connector 42 is placed.

On said base 31 a guide 32 is obtained, which is insertable in a double-layer support 7 for a sample to be analyzed. Said double-layer support 7 comprises an upper layer, having four main holes 71, a common hole 72 and a set of superficial contacts 73; and a lower layer, on which four electrodes are arranged (not shown in the figures), each arranged in correspondence with a respective main hole 71, and a further and common electrode (not shown in the figures), arranged in correspondence with said common hole 72.

The array of electrodes mentioned above are respectively connected to an array of sensors or biosensors and/or nanosensors, which come into contact with the sample to be examined or measured, as a result of the arrangement on said double-layer support 7 of the same sample to be examined (not shown in the figures), possibly also in liquid form or in solution.

Naturally, said electrodes are connected to corresponding superficial contacts 73. When the double-layer support 7 is completely inserted in said guide 32, each one of the superficial contacts 73 come into contact with a corresponding terminal 42' of said input connector 42.

The operation of the high sensitivity multichannel detection device 1 described above is as follows.

Preliminarily, some drops of a solution of which carrying out the analysis is necessary, such as solutions containing specific single molecular species or drugs of interest, is placed on said double-layer support 7. In this way, due to microfluidity phenomena, e.g. by capillarity, said solution passes through or is in contact with sensors or nanosensors, such as proteins, ion channels, cells and the like. Consequently, appropriate electrical signals are detectable on the electrodes corresponding to the holes 71 and 72 and, therefore, on said surface contacts 73.

When the double-layer support 7 is inserted in the guide 32 (see also figures 6 and 7), after opening said door 14, the electrodes are inserted below said input connector 42, so that said terminals 42' can be in contact with said superficial contacts 73.

Subsequently said door 14 is closed so as to protect the sample

from the surrounding electromagnetic environment.

The detected signals of said terminals 42' of the input connector 42 are amplified by said amplifier 51, filtered by said differentiator 53 and converted by said Analog/Digital converter 54, to be subsequently
5 processed by said processor 6. Once carried out the different (in this case four) measures and obtained the characteristic responses of each biosensor, result signals can be easily detected by said output connector 43.

Figures 8 and 9 show a second embodiment of the detection device
10 1, in which the containment enclosure 11 has a circular opening 15 obtained in the portion of the sensor 13, under the base 31. In addition, also the base 31 has a circular opening 33, arranged in correspondence with said opening 15.

These apertures 15 and 33 allow the viewing by a microscope,
15 allowing to have a small system (and therefore easily interfaced to different experimental setups) that allows a double investigation by analyzing simultaneously both the electrical properties and the optical one of the possible biosensor object of study.

Referring now to figures 10 and 11, a high sensitivity multichannel
20 detection device 1 is shown, in which there is a particular structure intended to prevent the infiltration of the test solution, placed on the double-layer support 7.

In particular, the base 31 of said detection module 3 has a first longitudinal groove 31', intended to house a corresponding first insulating
25 seal 36, preferably made of rubber, which is in contact with the lower face of said printed circuit 41, while the blocking element 34, in its turn, has a second longitudinal seal 34', intended to house a corresponding second insulating seal 37, also preferably made of rubber, which is in contact with the upper face of said printed circuit board 41.

30 Said first longitudinal groove 31' and said second longitudinal groove 34' can possibly be arranged parallel and overlapping.

Among other things, said base 31 and said blocking element 34 are made of hydrophobic plastic material, so as to prevent any infiltration.

Using the assembly described, there is a high degree of prevention
35 of the infiltration of liquids and solutions deposited on said double-layer support 7 toward the electronic components mounted on the printed circuit uprights 41.

An advantage of the present invention is that the integration of the circuits of the processing channels 5 in a single chip made by ASIC technology together with the presence of the Faraday cage, allows to obtain a very high level of sensitivity of the instrument.

5 Another advantage according to the invention is that the described configuration allows to have supports with more than one sensor in a very small space, thereby minimizing the parasitic capacitances on the lines of measurement, and consequently the measurement noise that is proportional.

10 It is also advantage of the present invention the minimization of parasitic capacitance on the input line so as to read signals of the order of pA (or nA) from different types of sensors, in addition to the possibility of more contemporary measures and in real time.

15 It is further advantage of the present invention, the portability of the detection device, in addition to not necessity of an external power supply and the use of the same device with different sensor systems also interchangeable.

20 The present invention has been described for illustrative but not limitative purposes, according to its preferred embodiments, but it is to be understood that modifications and/or changes can be introduced by those skilled in the art without departing from the relevant scope as defined in the enclosed claims.

25

CLAIMS

1. Detection device (1) of a sample to be examined, comprising
a processing module (2),
a detecting module (3), connected to said processing module (2),
5 a support (7), in which said sample to be examined can be placed,
said support (7) comprising a plurality of sensors, preferably biosensors
and/or nanosensors, and being insertable within said detecting module (3),
and
a containment enclosure (11) comprising a body (12), which is
10 arranged within said processing module (2), and a sensor portion (13), in
which said detecting module (3) is arranged,
characterized in that said processing module (2) comprises a
processing unit (4) having a plurality of processing channels (5) and a
processor (6), each one of said processing channels (5) being connected
15 to one respective of said sensors and being adapted to amplify and to filter
the signals of said sensors, said processor (6) processing said signals
amplified and filtered by said processing channels (5).
2. Detection device (1) according to claim 1, characterized in that
said processing module (2) is placed in said body (12) of said containment
20 enclosure (11), is provided with a printed circuit board (41), in which an
input connector (42) is arranged, which has a plurality of terminals (42'),
preferably spring type, and an output connector (43), preferably USB type,
connected to said processor (6), for the connection to a personal computer
or processor, said containment enclosure (11) preferably being made of
25 conductive material, such as metal or the like.
3. Detection device (1) according to claim 2, characterized in that
each one of said processing channels (5) comprises
an analog part, which includes an amplifier (51) having an input
connected to said input connector (42), an adder (52), interposed between
30 said amplifier (51) and a differentiator (53) or active high-pass filter, and
a digital part, which includes an analog to digital converter (54),
having its output connected to said processor (6), and a second digital to
analog converter (55), having its input connected to said processor (6) and
the output connected both to said adder (52), and to the input of said
35 amplifier (51), so as to realize a control system of the potential applied to
the input connector.
4. Detection device (1) according to anyone of the preceding

claims, characterized in that said processing channels (5), preferably four, are integrated into a one or more electronic devices, realized in ASIC (Application-Specific Integrated Circuit), and in that said processor (6) is an FPGA (Field Programmable Gate Array).

5 5. Detection device (1) according to anyone of the preceding claims, characterized in that said sensor portion (13) of said containment enclosure (11) comprises a door (14) coupled or hinged to said containment enclosure (11) that can be opened and closed.

10 6. Detection device (1) according to anyone of claims 2-5, characterized in that said sensor module (3) comprises

 a base (31), arranged partially below said printed circuit board (41), in correspondence of said input connector (42), on said base (31) being obtained a guide (32), which is insertable in said support (7), and

15 a blocking element (34), which forms with the latter a housing (35), in which said input connector (42) is placed.

 7. Detection device (1) according to claim 6, characterized

 in that said base (31) of said detecting module (3) has a first longitudinal groove (31'), intended to house a first seal (36), arranged in contact with a first face of said printed circuit board (41), and

20 in that said blocking element (34) of said detection module (3) has a second longitudinal groove (34'), intended to house a second seal (37), arranged in contact with a second face, opposite to said first face of said printed circuit board (41).

25 8. Detection device (1) according to anyone of claims 6 or 7, characterized in that said base (31) and/or said blocking element (34) are made of hydrophobic plastic material.

30 9. Detection device (1) according to anyone of the preceding claims, characterized in that said containment enclosure (11) has at least one inspection opening to which a microscope for optical control is applicable and/or through which it is possible to provide solutions for performing experiments and measurements.

35 10. A detection device (1) according to claim 9, when dependent on anyone of claims 6-8, characterized in that said inspection opening (15) is obtained in said sensor portion (13), below said base (31), and in that said base (31) has a further opening (33) arranged in correspondence of said inspection opening (15).

 11. Detection device (1) according to anyone of the preceding

claims, characterized in that said support (7) is double layer type, comprising

an upper layer, having a plurality of main holes (71), a common hole (72) and a series of superficial contacts (73), and

5 a lower layer, on which a plurality of electrodes are arranged, each arranged in a respective main hole (71) of said upper layer, each one of said electrodes being connected to one respective of said sensors, and a further common electrode, arranged in correspondence of said common hole (72), said electrodes and said common electrode being connected to
10 said superficial contacts (73).

12. Detection device (1) according to claim 11, when dependent on anyone of claims 6-11, characterized in that when said support (7) is inserted in said guide (32) of said base (31), each one of said superficial contacts (73) come in contact with a corresponding terminal (42') of said
15 input connector (42).

13. Detection device (1) according to anyone of the preceding claims, characterized in that it comprises electromagnetic shielding means (8).

14. Detection device (1) according to claim 13, when dependent on
20 claim 4, characterized in that said shielding means are arranged close to or on said one or more electronic devices and are connected to a common potential different from said analogical ground and/or said digital ground, preferably said common potential is comprised between 1 Volt and 2 volts, more preferably equal to about 1,65 Volts, so as to maximize the shielding
25 effect, said common potential being used internally to said one or more electronic devices in which said processing channels (5) are integrated as a reference for all other voltages of said detection device (1).

15. Detection device (1) according to anyone of the preceding claims, characterized in that said processing module (2) comprises an
30 analogical ground and a digital ground.

16. Detection device (1) according to claim 15, when depending on anyone of claims 13 or 14, characterized in that said electromagnetic shielding means (8) comprise a ferrite for the connection between said analog ground and said digital ground, said containment enclosure (11)
35 being connected to said analog ground.

17. Detection device (1) according to anyone of claims 13-16, when dependent on claim 2, characterized

in that said input connector (42) and said analog part of said processing channels (5) are enclosed by a analogical ground plane on an inner layer of said printed circuit board (41), which constitutes said analog ground or are connected to a common potential, and said shielding means
5 (8) comprise a first metal or Faraday cage (8), and

in that the digital part of said processing channels (5) and said processor (6) are enclosed by a digital ground plane within the printed circuit board (41), which constitutes said digital ground, and said shielding means (8) comprise a second Faraday cage above and below said printed
10 circuit board (41).

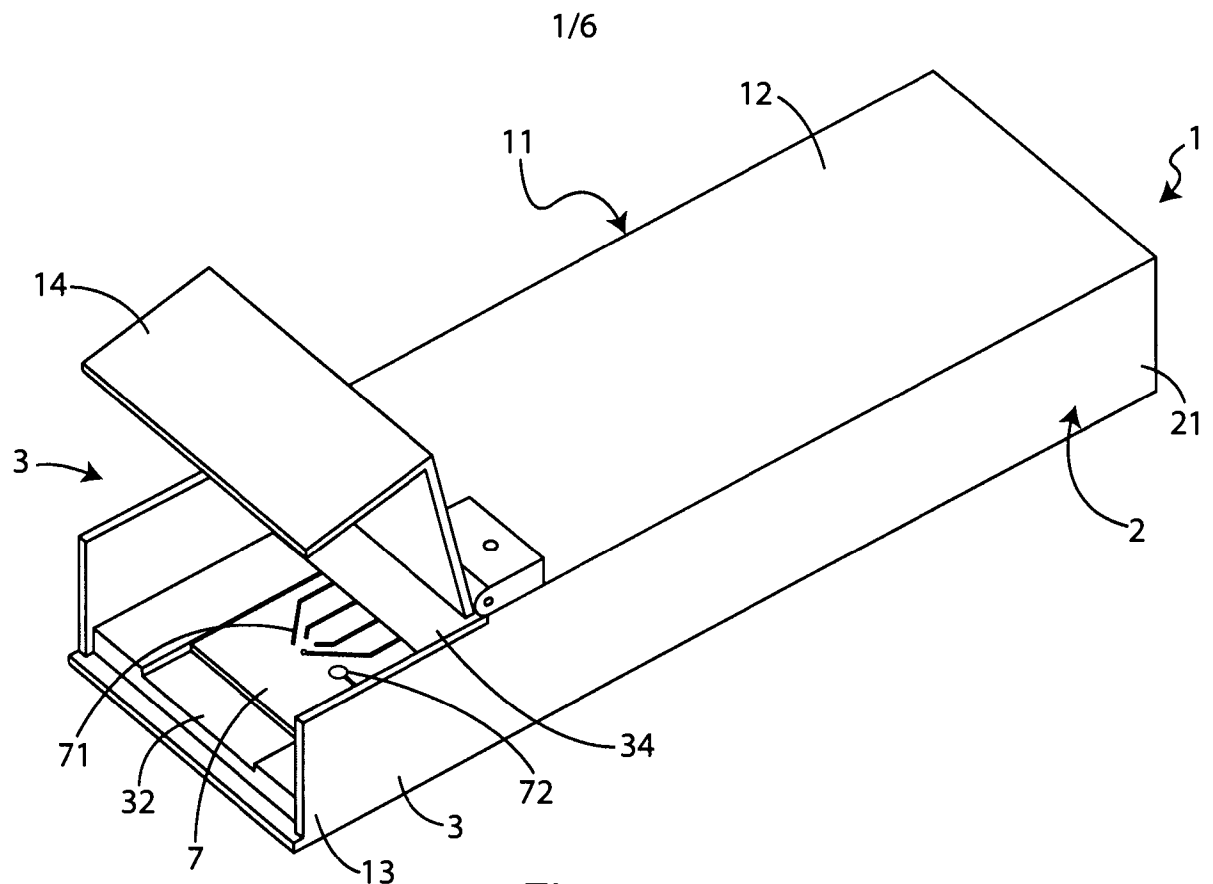


Fig. 1

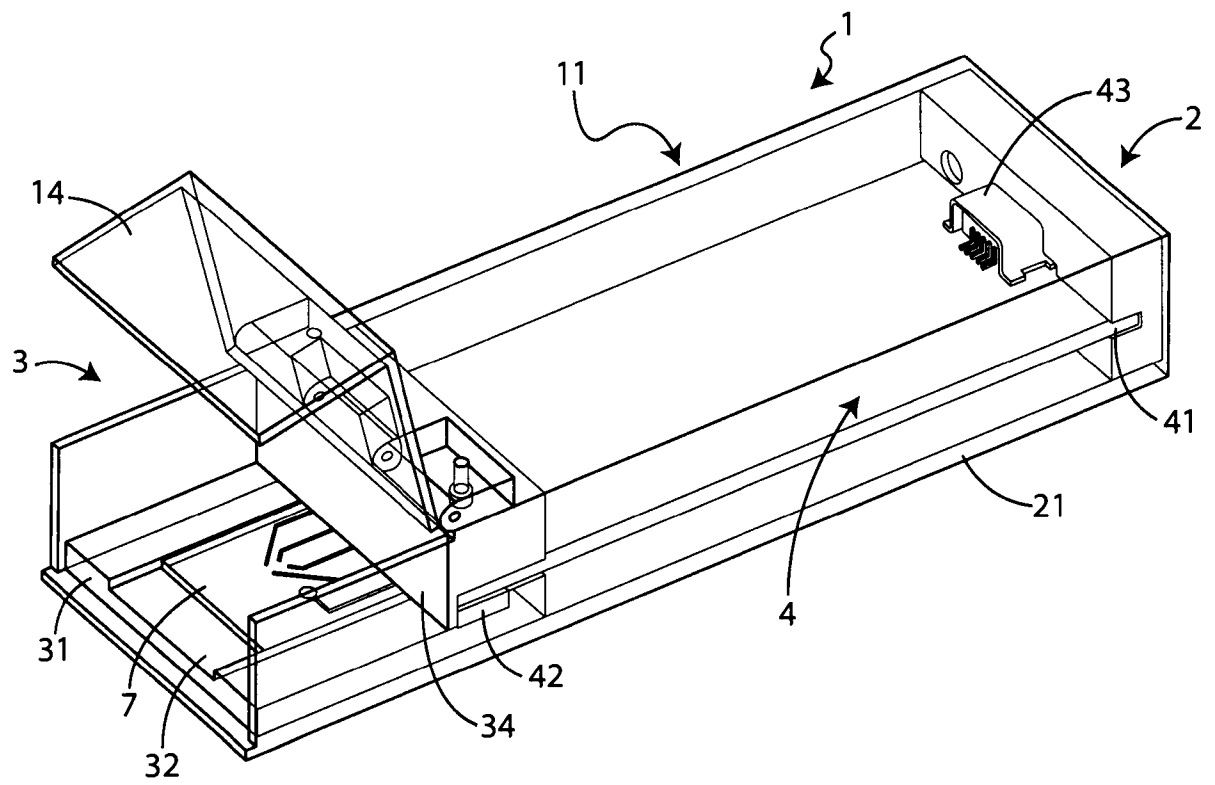


Fig. 2

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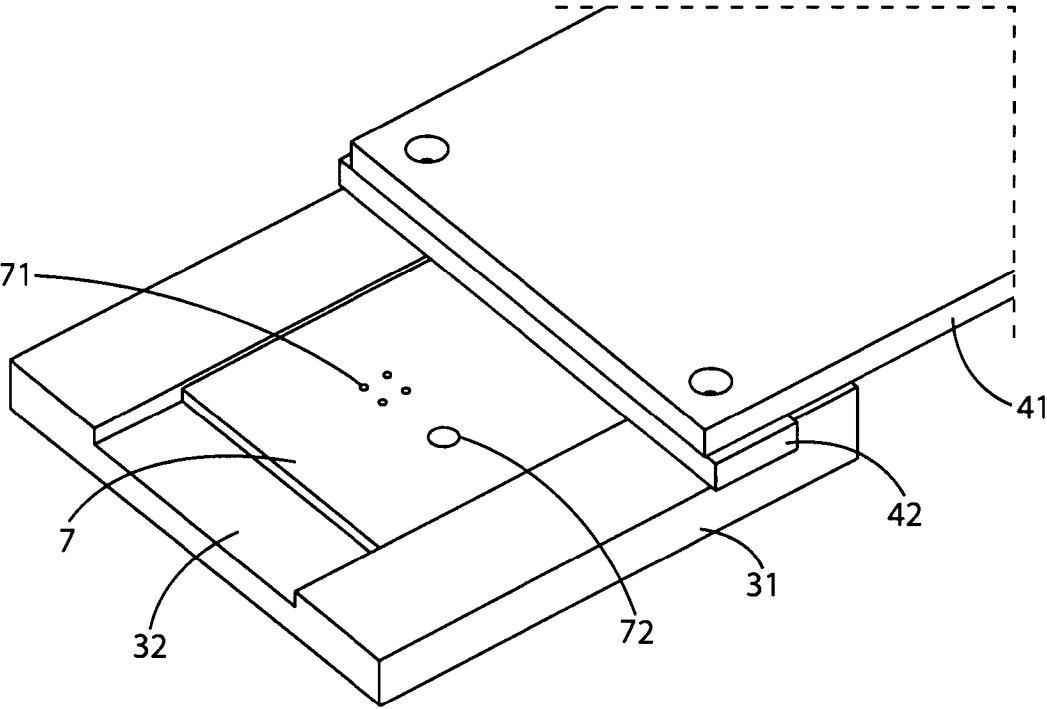


Fig. 3

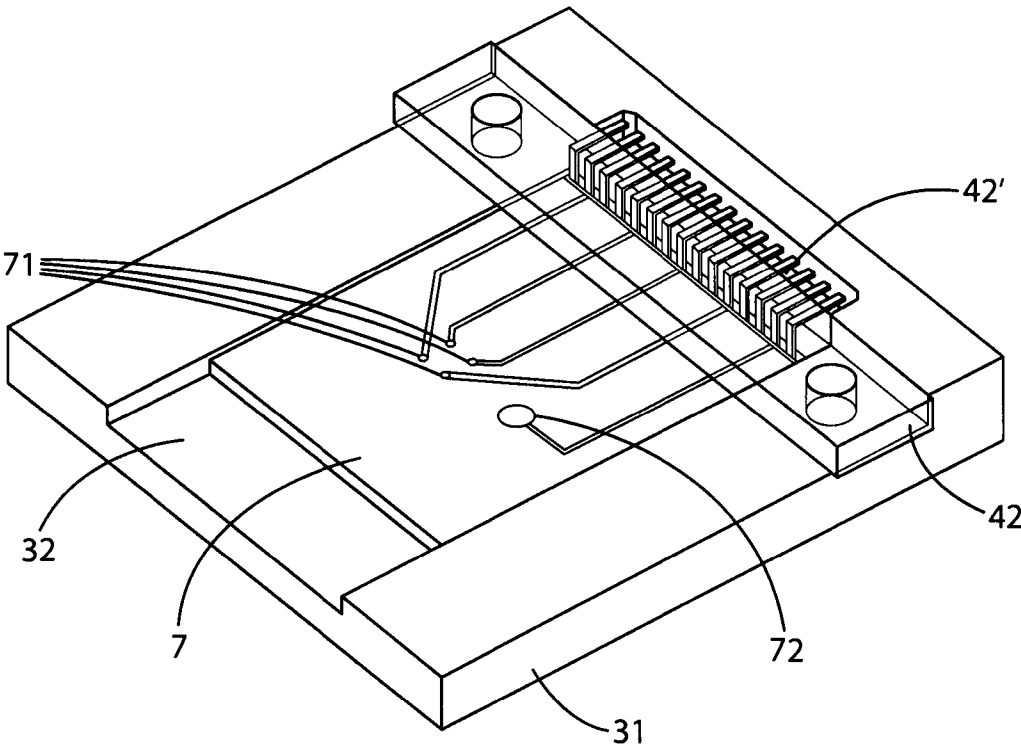


Fig. 4

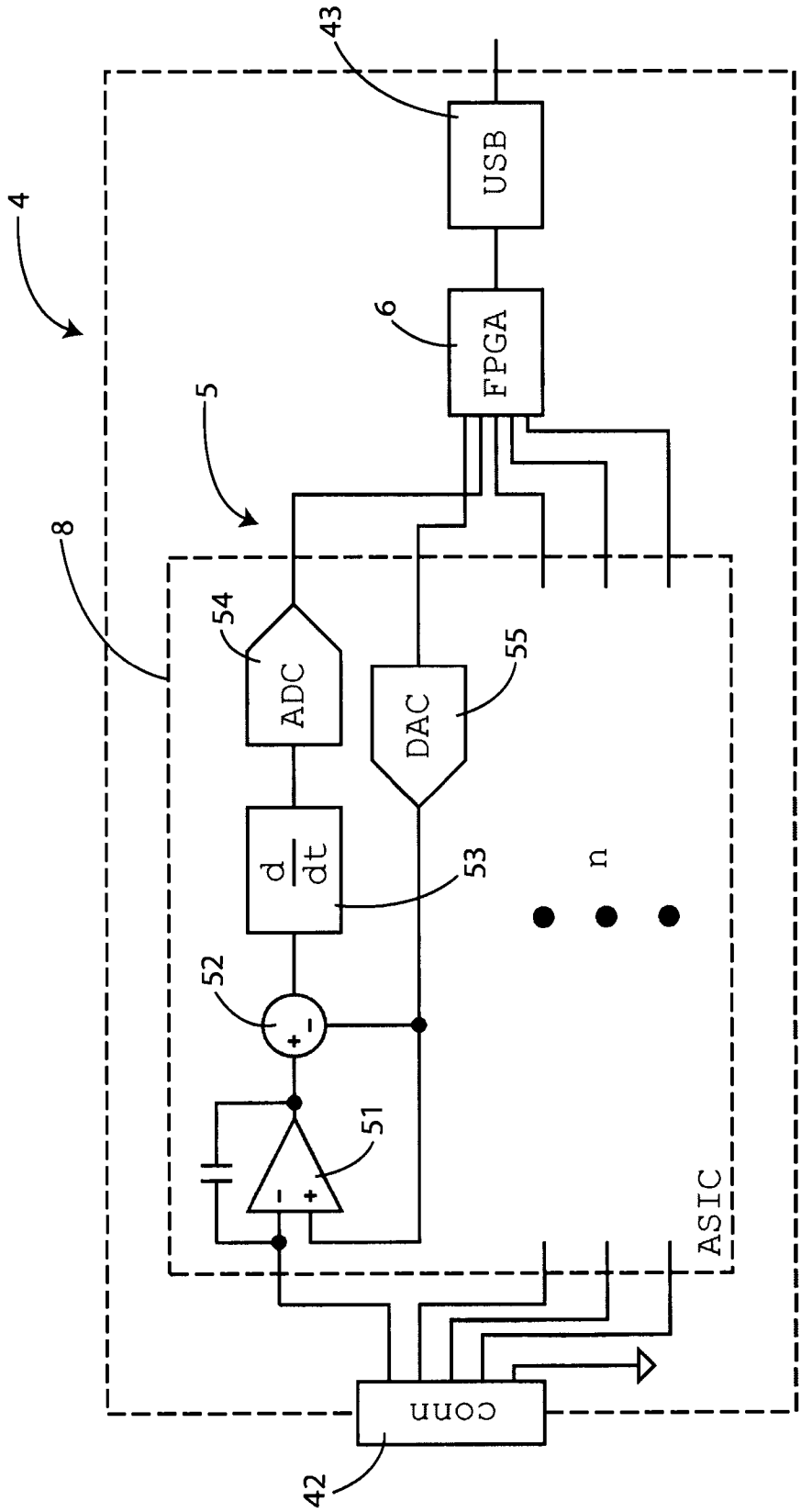


Fig. 5

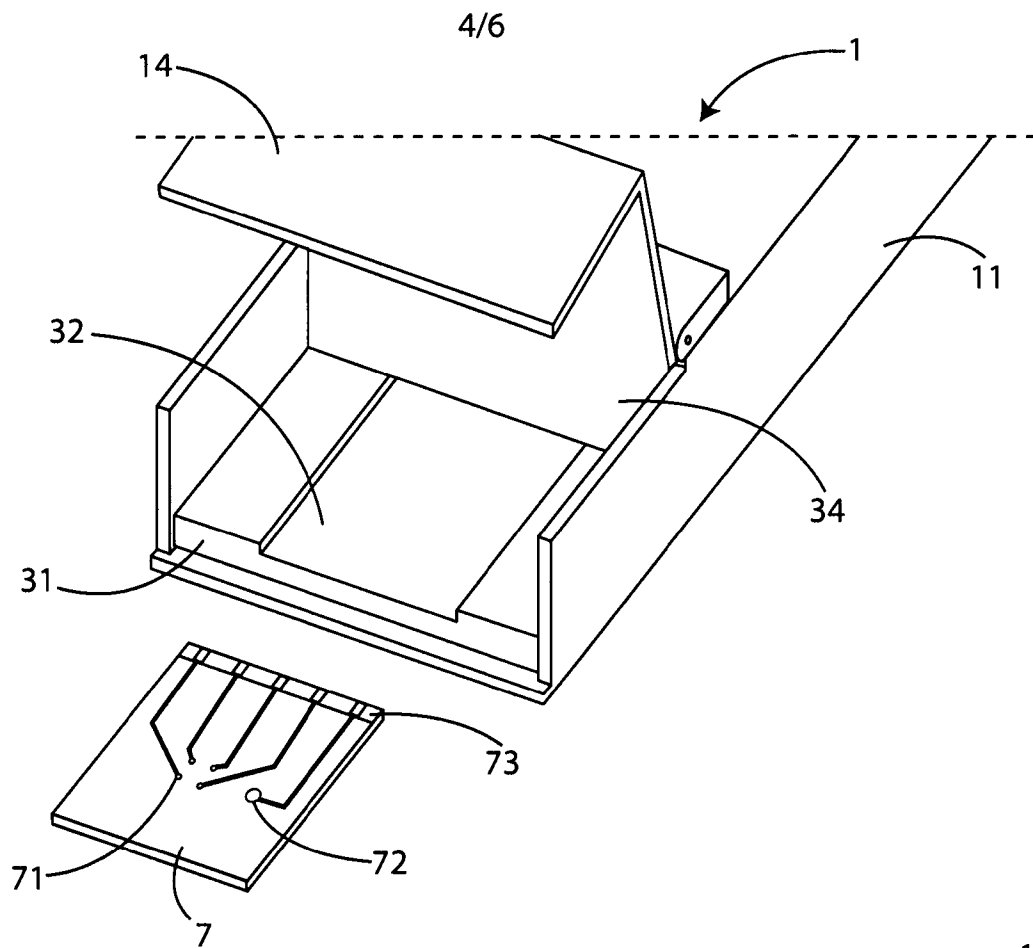


Fig. 6

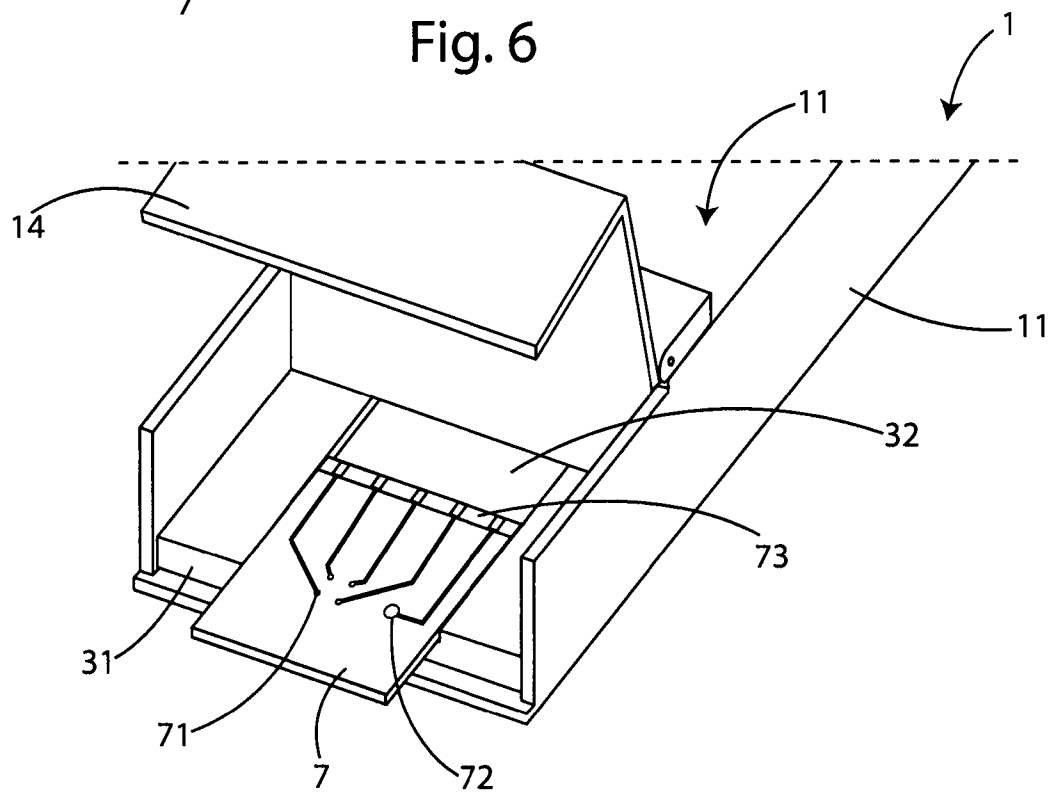


Fig. 7

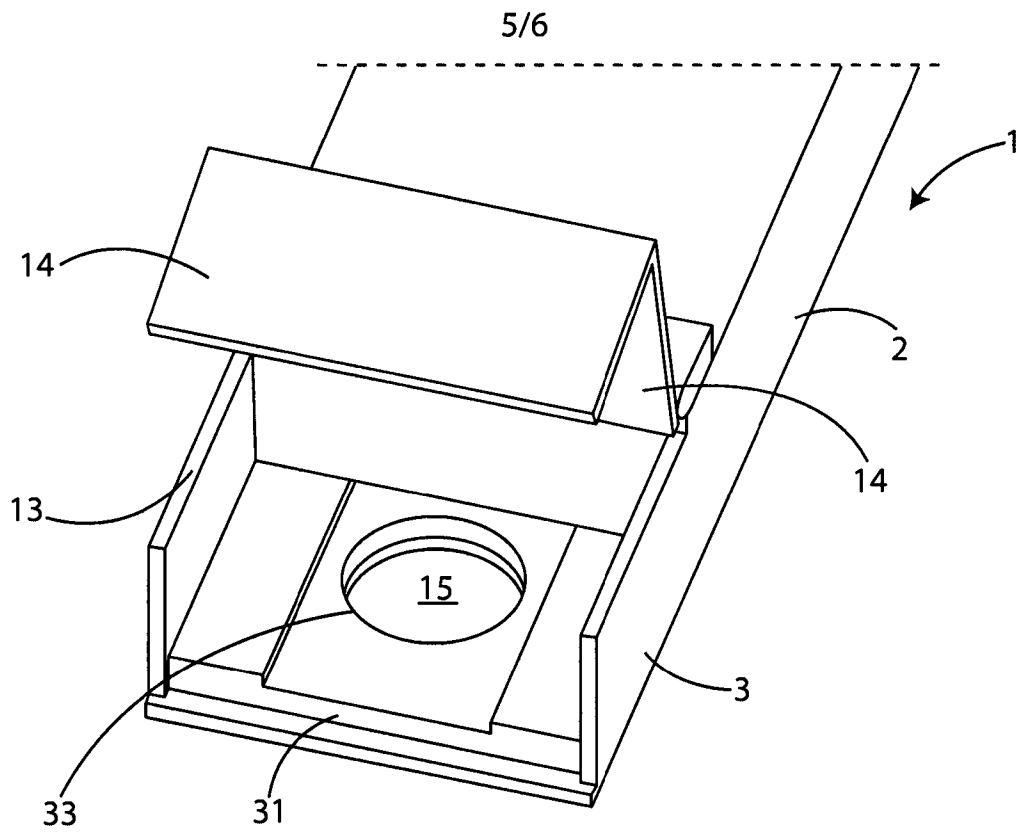


Fig. 8

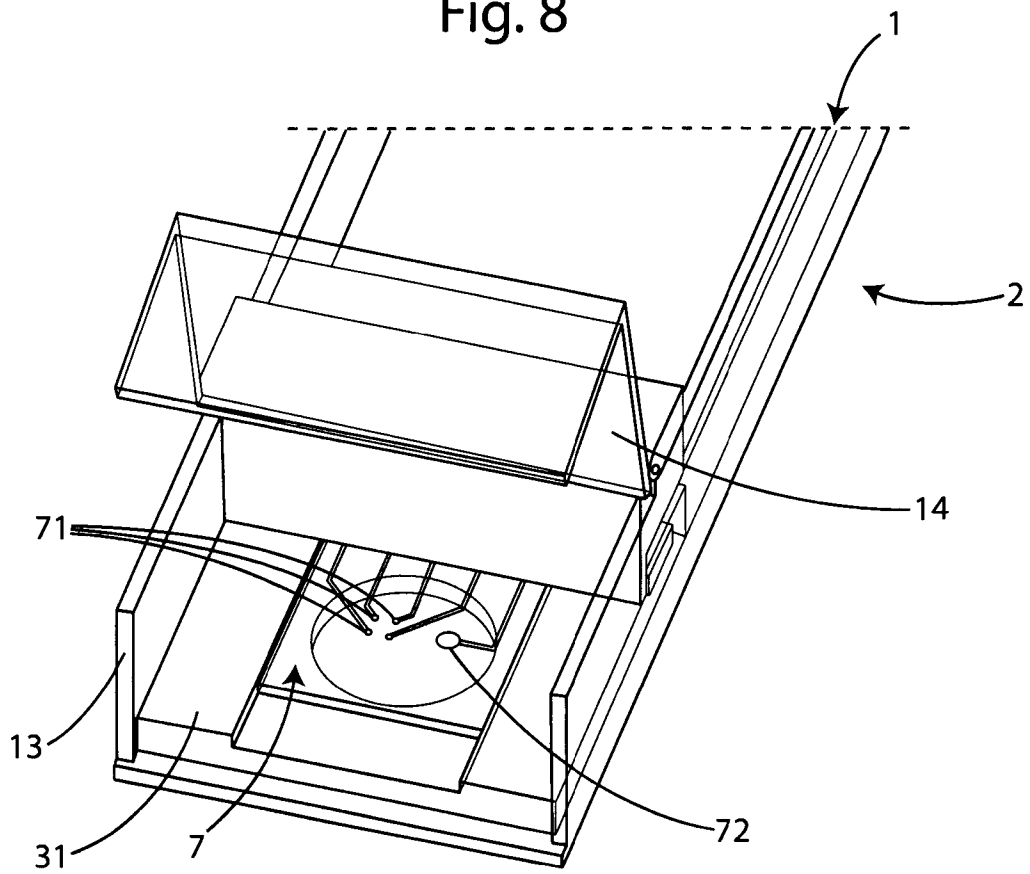
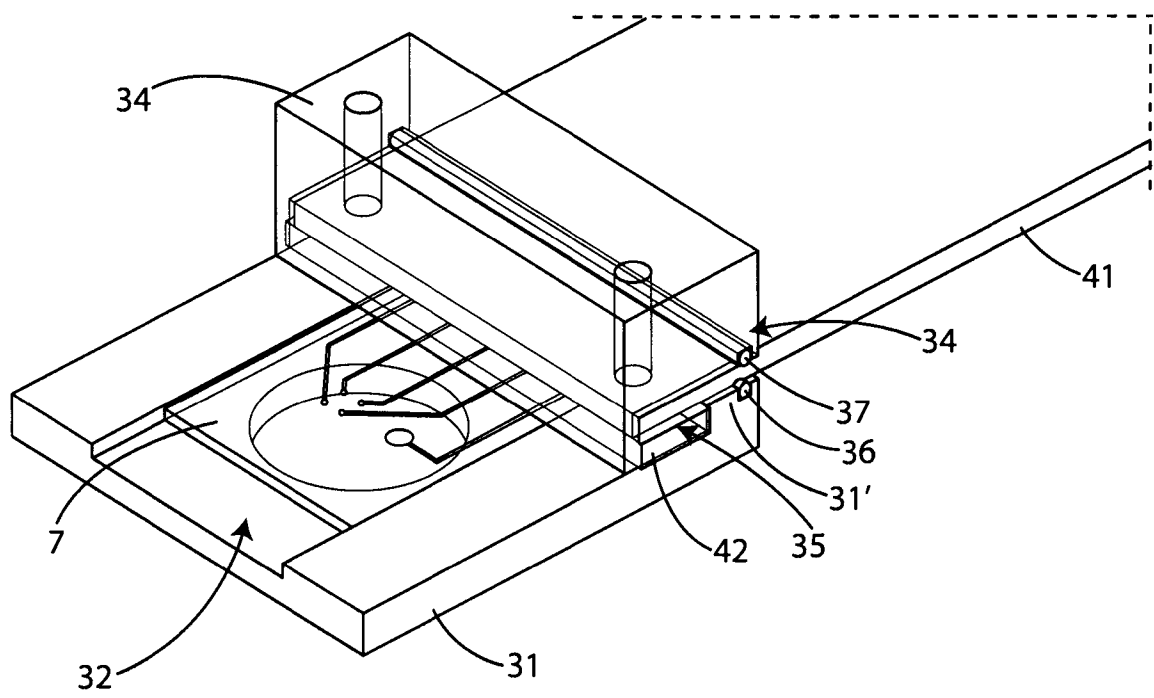
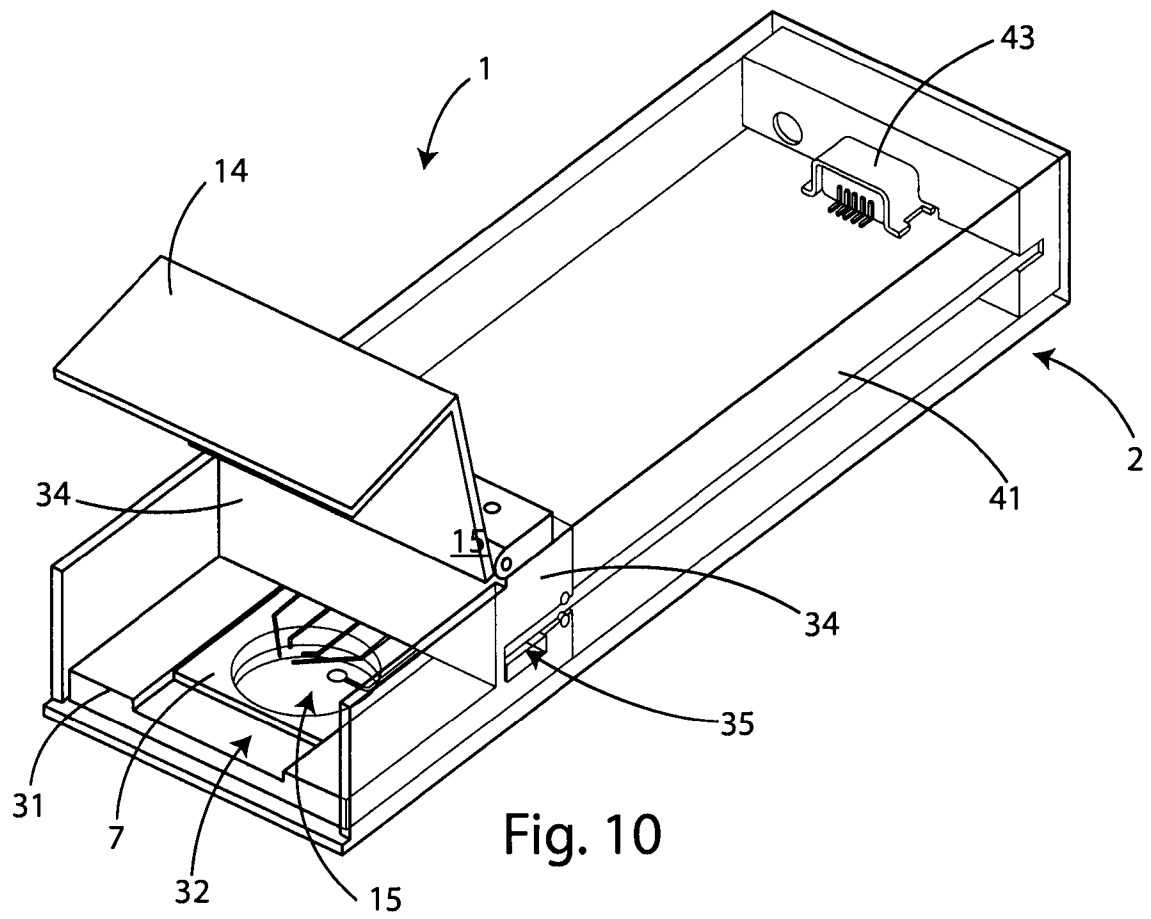


Fig. 9

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IT2015/000039

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01L9/00 G01N27/327 G01N27/414
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)
B01L 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 practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007/263046 A1 (IWASA KOICHIRO [JP] ET AL) 15 November 2007 (2007-11-15)	1-5,9-12
Y	paragraphs [0166] - [0189]; figures 1,3,	13,15-17
A	4-4c,5,7	6-8

X	US 2002/177135 A1 (DOUNG HAU H [US] ET AL) 28 November 2002 (2002-11-28)	1-4,9-12
Y	paragraph [0081] - paragraph [0100]	13,15-17
A	paragraph [0316] - paragraph [0357] abstract; figures	5-8

	-/--	



Further documents are listed in the continuation of Box C.



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 application or patent 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

1 July 2015

Date of mailing of the international search report

17/07/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
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Authorized officer

Smith-Hewitt, Laura

INTERNATIONAL SEARCH REPORT

International application No
PCT/IT2015/000039

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Walter Kester ET AL: "Grounding in Mixed Signal Systems", Hardware Design Techniques, 7 October 2009 (2009-10-07), pages 10.1-10.14, XP055142321, Norwood, MA, USA Retrieved from the Internet: URL:https://web.archive.org/web/20091007200316/http://www.analog.com/static/imported-files/analog_dialogue/5467026043687049331665676350Grounding.pdf [retrieved on 2014-09-24] the whole document	13,15-17
A	----- US 2009/026082 A1 (ROTHBERG JONATHAN M [US] ET AL) 29 January 2009 (2009-01-29) paragraphs [0200] - [0217]; figures 13-17 -----	13,15-17
A	US 6 153 069 A (POTTGEN PAUL A [US] ET AL) 28 November 2000 (2000-11-28) figure 8 -----	3
A	US 6 197 503 B1 (VO-DINH TUAN [US] ET AL) 6 March 2001 (2001-03-06) figures 5,9,10 -----	3
A	WO 01/33207 A1 (CANTOR HAL C [US]; HOWER ROBERT W [US] ADVANCED SENSOR TECHNOLOGIES I) 10 May 2001 (2001-05-10) page 19, line 25 - page 24, line 13 -----	3
A	US 2009/114044 A1 (GODFREY DANIEL PETERSON [GB] ET AL) 7 May 2009 (2009-05-07) paragraphs [0048], [0077], [0107] -----	12
A	WO 96/30752 A1 (HEALTH CRAFT INTERNATIONAL INC [US]) 3 October 1996 (1996-10-03) figures -----	1-12
A	US 5 955 028 A (CHOW CALVIN Y H [US]) 21 September 1999 (1999-09-21) figures -----	6

INTERNATIONAL SEARCH REPORT

International application No.
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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 14
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 14

Without knowing what electronic devices /sensors were to be used, the skilled person could not know how to arrange the shielding means on the devices or close to the devices as required by present claim 14. Furthermore, claim 14 encompasses devices being connected to a common potential of preferably between 1V and 2V, more preferably equal to 1,65 V. However, the type of processor, the types of sensors to be used (biosensors or nanosensors) and electronic devices are not specified at all in either claim 14 or any antecedent claim. The only further specification is that of the desired function of "maximising the shielding effect", contrary to the requirements of clarity of Article 6 PCT, because this result-to-be-achieved type of definition does not allow the scope of the claim to be ascertained. The fact that any electronic device/biosensor/nanosensor could be used does not overcome this objection, as the skilled person would not have knowledge beforehand as to whether it would fall within the scope claimed, i.e. whether the potential of e.g. between 1 and 2 V would maximise a purported shielding effect, or how with unknown devices a shielding effect could be maximised. Undue experimentation would be required to test out combinations of sensors randomly.

The non-compliance with the substantive provisions is to such an extent that no meaningful search of claim 14 could be carried out at all (Article 17(2) PCT).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IT2015/000039

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2007263046 A1	15-11-2007	CA 2601078 A1 CN 101031802 A EP 1852703 A1 JP 4053081 B2 RU 2377571 C2 US 2007263046 A1 WO 2006080186 A1	03-08-2006 05-09-2007 07-11-2007 27-02-2008 27-12-2009 15-11-2007 03-08-2006
US 2002177135 A1	28-11-2002	US 2002177135 A1 US 2006160205 A1	28-11-2002 20-07-2006
US 2009026082 A1	29-01-2009	US 2009026082 A1 US 2011230375 A1 US 2011241081 A1 US 2011247933 A1 US 2011248319 A1 US 2012071363 A1 US 2013015505 A1 US 2013015506 A1 US 2013017959 A1 US 2013210641 A1 US 2013217587 A1 US 2013244908 A1 US 2013338046 A1	29-01-2009 22-09-2011 06-10-2011 13-10-2011 13-10-2011 22-03-2012 17-01-2013 17-01-2013 17-01-2013 15-08-2013 22-08-2013 19-09-2013 19-12-2013
US 6153069 A	28-11-2000	US 6153069 A US 6413411 B1 US 2003159944 A1	28-11-2000 02-07-2002 28-08-2003
US 6197503 B1	06-03-2001	AT 234367 T AU 1609399 A CA 2311466 A1 DE 69812158 D1 DE 69812158 T2 EP 1034305 A1 EP 1236807 A2 ES 2194377 T3 US 6197503 B1 US 6448064 B1 WO 9927140 A1	15-03-2003 15-06-1999 03-06-1999 17-04-2003 08-01-2004 13-09-2000 04-09-2002 16-11-2003 06-03-2001 10-09-2002 03-06-1999
WO 0133207 A1	10-05-2001	AU 1466301 A EP 1230539 A1 JP 2003513275 A WO 0133207 A1	14-05-2001 14-08-2002 08-04-2003 10-05-2001
US 2009114044 A1	07-05-2009	AT 535799 T EP 1864120 A2 US 2009114044 A1 WO 2006103440 A2	15-12-2011 12-12-2007 07-05-2009 05-10-2006
WO 9630752 A1	03-10-1996	AU 2122895 A WO 9630752 A1	16-10-1996 03-10-1996
US 5955028 A	21-09-1999	AT 298631 T AU 717981 B2 AU 3815697 A CA 2259929 A1	15-07-2005 06-04-2000 25-02-1998 12-02-1998

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IT2015/000039

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		CN 1226845 A	25-08-1999
		DE 69733663 D1	04-08-2005
		DE 69733663 T2	04-05-2006
		EP 0952890 A1	03-11-1999
		EP 1426109 A1	09-06-2004
		JP 3686932 B2	24-08-2005
		JP 2000515630 A	21-11-2000
		US 5955028 A	21-09-1999
		US 6071478 A	06-06-2000
		US 6399023 B1	04-06-2002
		US 6399025 B1	04-06-2002
		US 2002015667 A1	07-02-2002
		US 2002192112 A1	19-12-2002
		WO 9805424 A1	12-02-1998
		ZA 9706887 A	11-05-1998
