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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 December 2014 (24.12.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/204384 A1

(51) International Patent Classification:
C12M 1/38 (2006.01) *G01K 1/14* (2006.01)

(21) International Application Number:
PCT/SE2014/050728

(22) International Filing Date:
16 June 2014 (16.06.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
1350732-2 17 June 2013 (17.06.2013) SE

(71) Applicant: **GE HEALTHCARE BIO-SCIENCES AB** [SE/SE]; Björkgatan 30, S-751 84 Uppsala (SE).

(72) Inventors: **ÅKERSTRÖM, Patrik**; ., GE Healthcare, Björkgatan 30, S-751 84 Uppsala (SE). **CARLSSON, Lars, Johan**; ., Schottisvägen 1, S-196 37 Kungsängen (SE). **FRICKING, Patric**; ., GE Healthcare, Björkgatan 30, S-751 84 Uppsala (SE). **WAHLNÄS, Håkan**; ., Eksoppsvägen 26, S-756 46 Uppsala (SE).

(74) Agents: **GE HEALTHCARE BIO-SCIENCES AB** et al.; Patent Department, Björkgatan 30, S-751 84 Uppsala (SE).

(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, LT, 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, 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,

[Continued on next page]

(54) Title: BIOREACTOR SYSTEM WITH A TEMPERATURE SENSOR

(57) Abstract: A bioreactor system comprising a base station (11; 17) comprising a control system, a tray (31; 41) arranged to be provided on the base station (11; 17) and arranged to house a bioreactor bag, wherein said base station (11; 17) comprises at least one temperature sensor means (1) and in that said tray (31, 41) comprises at least one opening (33; 43a, 43b) for receiving said temperature sensor means (1) such that it will contact a surface of a bioreactor provided in the tray.

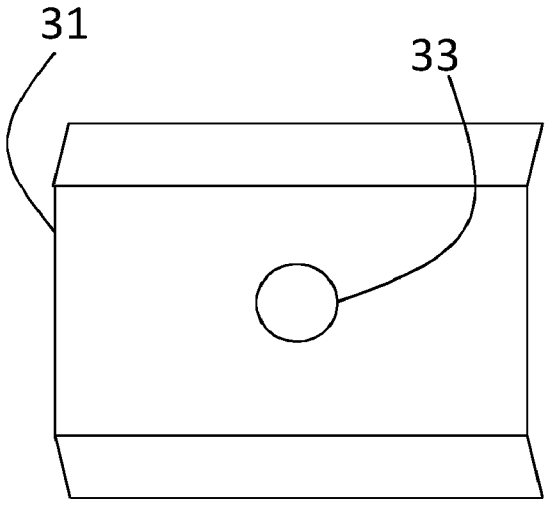

Figure 4a

WO 2014/204384 A1

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))*

BIOREACTOR SYSTEM WITH A TEMPERATURE SENSOR

TECHNICAL FIELD OF INVENTION

The present invention relates to a temperature sensor means and a bioreactor system comprising such a temperature sensor means.

BACKGROUND OF THE INVENTION

Measuring temperatures in bioreactors can be done invasively or noninvasively. Noninvasive measurements are preferred in many cases because the content of the bioreactor should not be contaminated. Temperature sensors provided outside the bioreactor have been used. A problem with such temperature sensors is that ambient temperature will affect the measured temperature.

SUMMARY

The object of the invention is to provide reliable temperature measurements and to provide bioreactor systems that are easy to handle.

This is achieved in a bioreactor system comprising a base station comprising a control system, a tray arranged to be provided on the base station and arranged to house a bioreactor bag, wherein said base station comprises at least one temperature sensor means and in that said tray comprises at least one opening for receiving said temperature sensor means such that it will contact a surface of a bioreactor provided in the tray. Hereby a flexible and easy to handle bioreactor system with reliable temperature measuring capabilities is achieved.

Furthermore the circulation in the bioreactor is not affected by the temperature sensor. Another advantage is that only the base station and not the tray holding the bioreactor need to be considered for calibration. Furthermore a bioreactor system providing reliable temperature measurements with very limited influence from ambient temperature is achieved.

Further embodiments are described in the dependent claims.

BRIEF DESCRITPION OF THE DRAWINGS

Figure 1 shows schematically a temperature sensor means according to one embodiment of the invention.

Figures 2a and 2b shows schematically a base station of a bioreactor system according to two different embodiments of the invention comprising one or three temperature sensor means.

Figure 3 shows schematically an arm comprising a temperature sensor means according to the invention, said arm being adapted to be used in a base station of a bioreactor system.

Figures 4a and 4b shows schematically trays adapted to be provided on a base station according to the invention and said trays being adapted to hold bioreactor bags.

DETAILED DESCRIPTION

Figure 1 shows schematically a temperature sensor means 1 according to one embodiment of the invention. The temperature sensor means comprises a thermally conducting layer 2 arranged to face the surface to be measured, a thermally insulating layer 3 attached to the thermally conducting layer 2 on the opposite side to the surface to be measured and a temperature sensor 5 provided between the thermally conducting layer 2 and the thermally insulating layer 3 and being completely surrounded on all its sides by either the thermally conducting or thermally insulating layers. The thermally conducting layer is a material with higher thermal conductivity than the thermally insulating layer. It could for example be a metal layer or a thermally conducting graphite or polymer layer. The temperature sensor 5 has a connection 7 through the thermally insulating layer to a control system. The thermally conducting layer 2 will improve the conductivity towards the surface to be measured and the thermally insulating layer 3 will decrease the influence from ambient temperature on the temperature sensor. In another embodiment of the invention the thermally conducting layer and/or the thermally insulating layer could be omitted

Figures 2a and 2b shows schematically two examples of a base station of a bioreactor system according to the invention comprising one and three temperature sensor means as described in relation to Figure 1 respectively. In Figure 2a a base station 11 according to one embodiment of the invention is schematically shown. The base station to a bioreactor system comprises of course many more details but they are omitted in the description of this invention. In this embodiment the base station 11 comprises one temperature sensor means as described in

relation to Figure 1. Suitably the temperature sensor means 1 is provided on an arm 21 as shown in Figure 3. The arm is provided inside the base station 11 under a base station upper surface 13. The arm 21 is provided such that the temperature sensor means can protrude up through an opening 15 in the base station upper surface 13. This can be achieved by providing the arm 21 as a lever. The temperature sensor means 1 is then provided onto one end 22 of the lever 21 and if something pushes down onto the other end 23 of the lever 21 the temperature sensor means 1 will move upwards and protrude through the opening 15 in the base station. Hereby the base station upper surface 13 also needs to be provided with another opening 16 for receiving a pushing means that will push the end of the lever opposite the temperature sensor means downwards. A tray adapted to hold a bioreactor and to be positioned onto the base station may comprise this one or more pushing means. Another possible design would be to provide the temperature sensor means 1 on a resilient arm 21 which protrudes up through the opening 15 in the base station upper surface 13 but easily is pushed back if something presses on the temperature sensor means 1 from above. In Figure 3 an arm 21 with a temperature sensor means 1 is shown. This arm could be provided in the base station as described above either as a lever or as a resilient arm. In Figure 3 a communication connection 7 from the temperature sensor through the thermally insulating layer 3 is shown.

In Figure 2b a base station 17 according to another embodiment of the invention is schematically shown. In this embodiment three arms 21 comprising temperature sensor means are provided. Hereby also three openings 19a,b,c are provided in the base station upper surface. If the arms are of the lever type three openings corresponding to the opening 16 of Fig. 2a should also be provided.

Figures 4a and 4b shows schematically trays adapted to be provided on a base station according to the invention and said trays being adapted to hold bioreactor bags. The tray 31 of Figure 4a can be used in either the base station 11 shown in Figure 2a or the base station 17 shown in Figure 2b. The tray 31 is adapted to hold a bioreactor bag and the tray comprises an opening 33 positioned to align with the opening 15 of the base station 11 of Figure 2a and the middle opening 19b of the base station 17 of Figure 2b. Suitably the opening 33 in the tray is somewhat larger than the temperature sensor means. Hereby the temperature measurements will be less effected by the heaters that often are provided in the trays. When the tray 31 of Figure 4a is used together with the base station 17 of Figure 2b the two other temperature sensor means provided through openings 19a and 19c will not be protruding up through the openings because the tray 31 does not comprise corresponding pushing means for these temperature sensor means arms (if

the lever variant is used). If resilient arms instead are used the temperature sensor means provided through the openings 19a and 19c will be pushed downwards by the tray 31 and not be used.

The tray 41 of Figure 4b can be used in the base station 17 shown in Figure 2b. The tray 41 comprises two openings 43a, 43b to receive one temperature sensor means 1 each. In this embodiment the temperature sensor means 1 provided through the middle opening 19b of the base station 17 will not be used and the temperature sensor means provided through the opening 19a will protrude up through the opening 43a of the tray 41 and the temperature sensor means provided through the opening 19c will protrude up through the opening 43b of the tray 41. In this embodiment two bioreactor bags could be provided in the tray 41. The openings in the trays 33, 43a, 43b can in one embodiment be covered by a suitable thin film, for example a plastic film. This could be advantageous in order to keep any spillage in the tray. However this is not necessary.

A control system of the bioreactor system comprises in one embodiment means for measuring the ambient temperature and means for compensating the bioreactor temperature measurement for different ambient temperatures.

With this invention the temperature sensor or sensors are provided in the base station instead of in the different trays. Hereby the trays can be kept simple and without any need for calibration and electrical connections. It is advantageous to have all these functions in the base station.

This written description uses examples to disclose the invention, including the best mode, and also to enable any person skilled in the art to practice the invention, including making and using any devices or systems and performing any incorporated methods. The patentable scope of the invention is defined by the claims, and may include other examples that occur to those skilled in the art. Such other examples are intended to be within the scope of the claims if they have structural elements that do not differ from the literal language of the claims, or if they include equivalent structural elements with insubstantial differences from the literal languages of the claims.

CLAIMS

1. A bioreactor system comprising
   - a base station (11; 17) comprising a control system,
   - a tray (31; 41) arranged to be provided on the base station (11; 17) and arranged to house a bioreactor bag,

   wherein said base station (11; 17) comprises at least one temperature sensor means (1) and in that said tray (31, 41) comprises at least one opening (33; 43a, 43b) for receiving said temperature sensor means (1) such that it will contact a surface of a bioreactor provided in the tray.
2. A bioreactor system according to claim 1, wherein said temperature sensor means (1) is provided in one end of an arm (21) being a lever such that a pushing means provided on the tray will push downwards on the other end of the arm (21) when the tray is provided in the base station and thereby the temperature sensor means will move upwards through the opening (33; 43a, 43b) in the tray (31; 41) such that the temperature sensor means (1) will contact the bioreactor surface but not disturb the bioreactor surface.
3. A bioreactor system according to claim 1 or 2, wherein said base station (11; 17) comprises more than one temperature sensor means (1) and different openings in different trays will decide which temperature sensor means to be contacting the bioreactor surface, whereby the other temperature sensor means will not be protruding through the openings in the tray.
4. A bioreactor system according to claim 3, wherein each temperature sensor means is mounted on a separate arm (21).
5. A bioreactor system according to any one of the claims 1-4, wherein the control system comprises means for compensating the temperature measurement for the ambient temperature.
6. A bioreactor system according to any one of the claims 1-5, wherein the temperature sensor means (1) comprises
   - a thermally conducting layer (2) arranged to face the surface to be measured,
   - a thermally insulating layer (3) attached to the thermally conducting layer (2) on the opposite side to the surface to be measured,
   - a temperature sensor (5) provided between the thermally conducting layer (2) and the thermally insulating layer (3) and being completely surrounded on all its sides by either the thermally conducting or the thermally insulating layers.

7. A bioreactor system according to claim 6, wherein the thermally conducting layer is a material having higher thermal conductivity than the thermally insulating layer.
8. A bioreactor system according to claim 6 or 7, wherein the thermally conducting layer is a metal or a thermally conducting graphite or polymer.
9. A bioreactor system according to any one of the preceding claims further comprising a communication connection (7) provided to the control system from the temperature sensor (5).

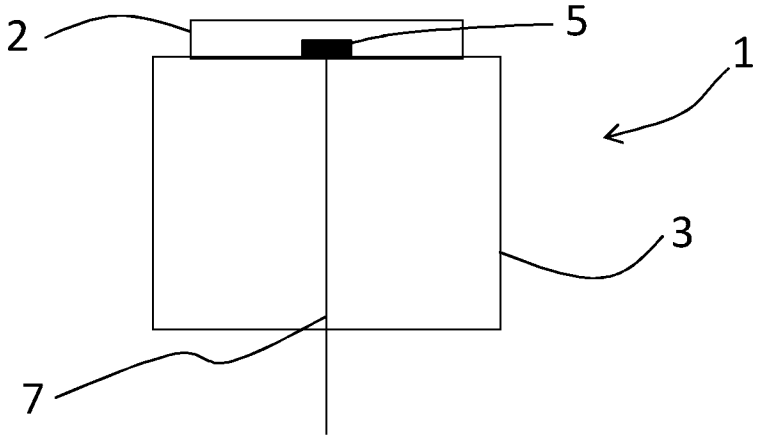

Fig. 1

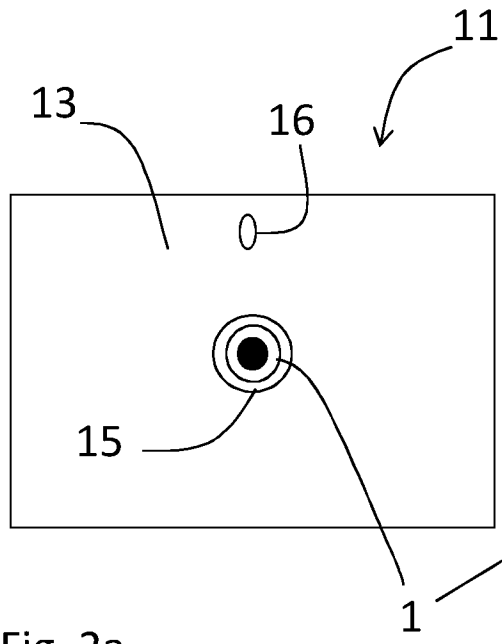

Fig. 2a

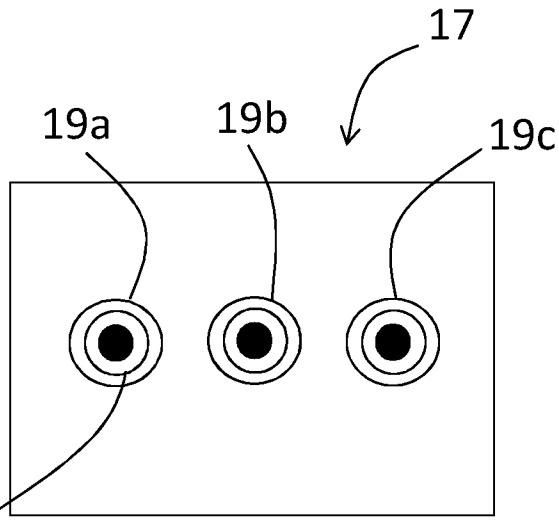

Fig. 2b

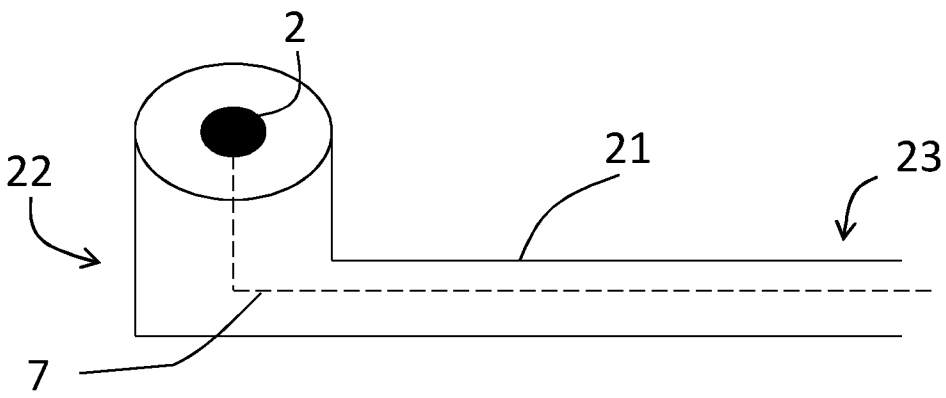

Figure 3

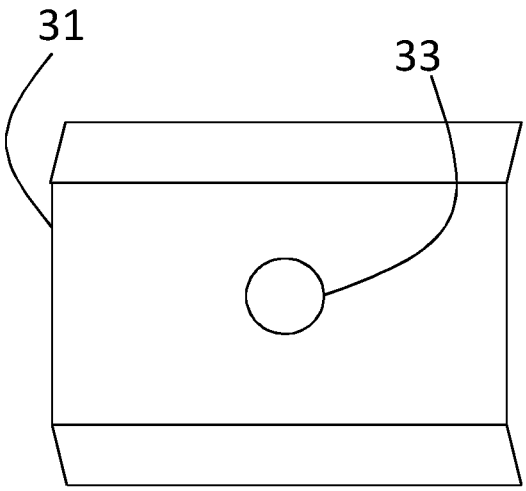

Figure 4a

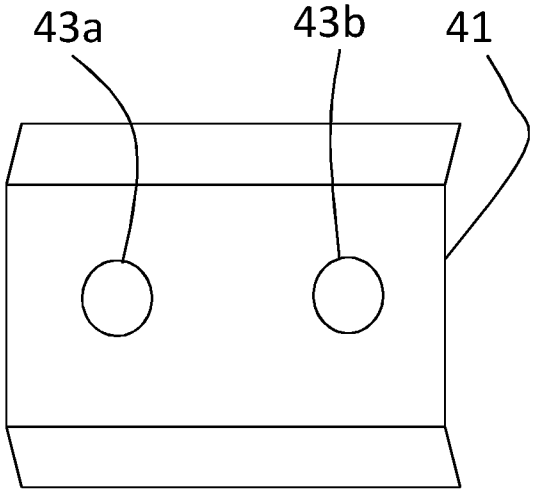

Figure 4b

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2014/050728

A. CLASSIFICATION OF SUBJECT MATTER

IPC: see extra sheet

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)

IPC: C12M, G01K

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

SE, DK, FI, NO classes as above

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

EPO-Internal, PAJ, WPI data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 20120258441 A1 (GE HEALTCARE BIO SCIENCES AB), 11 October 2012 (2012-10-11); whole document; figures; claims --	1-9
A	US 20050272146 A1 (XCELLEREX INC), 8 December 2005 (2005-12-08); whole document; figures; claims --	1-9
A	WO 2008102249 A1 (MCCORMICK MARK), 28 August 2008 (2008-08-28); whole document; claims --	1-9
A	JP 2007174982 A (MEDEII KON INTERNAT KK), 12 July 2007 (2007-07-12); whole document; figures -- --------	1-9

☐ 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	Date of mailing of the international search report
16-09-2014	16-09-2014

Name and mailing address of the ISA/SE	Authorized officer
Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. + 46 8 666 02 86	Erika Stenroos Telephone No. + 46 8 782 25 00

International application No.
PCT/SE2014/050728

Continuation of: second sheet

International Patent Classification (IPC)

C12M 1/38 (2006.01)
G01K 1/14 (2006.01)

US	20120258441	A1	11/10/2012	CA	2784519	A1 30/06/2011
				CN	102656282	A 05/09/2012
				EP	2516682	A1 31/10/2012
				JP	2013514804	A 02/05/2013
				WO	2011078773	A1 30/06/2011
US	20050272146	A1	08/12/2005	AU	2005250500	A1 15/12/2005
				BR	PI0510648	A 20/11/2007
				CA	2569405	C 03/05/2011
				CN	101001945	B 08/02/2012
				CN	102492607	A 13/06/2012
				CR	8769	A 28/08/2007
				EP	1773976	A2 18/04/2007
				HK	1112479	A1 09/11/2012
				JP	2008501347	A 24/01/2008
				JP	4680990	B2 11/05/2011
				KR	20070053200	A 23/05/2007
				KR	101021203	B1 11/03/2011
				MX	PA06014099	A 09/05/2007
				NO	20070069	A 05/03/2007
				US	7629167	B2 08/12/2009
				WO	2005118771	A3 02/02/2006
WO	2008102249	A1	28/08/2008	NONE		
JP	2007174982	A	12/07/2007	JP	4310653	B2 12/08/2009