(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 2 072 132 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
24.06.2009 Bulletin 2009/26

(51) Int Cl.:
B01L 3/00 *(2006.01)*

(21) Application number: **07123813.3**

(22) Date of filing: **20.12.2007**

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC MT NL PL PT RO SE SI SK TR
Designated Extension States:
AL BA HR MK RS

(71) Applicant: **Koninklijke Philips Electronics N.V.**
5621 BA Eindhoven (NL)

(72) Inventor: **The designation of the inventor has not yet been filed**

(74) Representative: **Damen, Daniel Martijn**
Philips
Intellectual Property & Standards
P.O. Box 220
5600 AE Eindhoven (NL)

(54) Reactor system in particular for biochemical reactions

(57) A reactor system (1) configured for carrying out a reaction, comprises at least one process chamber (20) and at least one device (40). The process chamber (20) is connected to the device via a first channel (22) and via a second channel (24). The process chamber (20) carries out a reaction forming a product and a waste liquid, and the device (40) receives the product and waste liquid via the first channel (22) and returns the waste liquid to the process chamber (20) via the second channel (24). A method of re-using the process chamber for waste containment is also described.

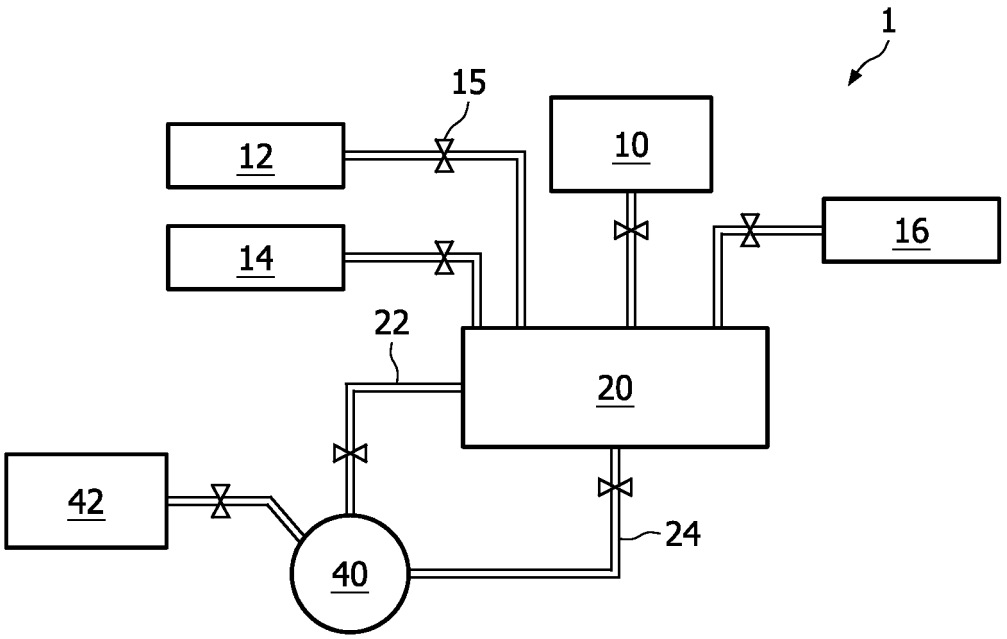

FIG. 1

EP 2 072 132 A1

Description

FIELD OF THE INVENTION:

[0001] The invention relates to a reactor system, in particular to a closed reactor system, more in particular to a closed reactor system capable of carrying out a biochemical reaction.

BACKGROUND OF THE INVENTION:

[0002] For detection of specific bacteria in a fluid sample, a detection method is known based on DNA/RNA amplification process. In this method, the detection is done by performing a number of process steps on different equipments, for example a Biorobot for lysis, washing, mixing and elution, a PCR Cycler for DNA/RNA amplification, and an appropriate optical or electro-magnetic system for detection and identification of the specific amplified DNA/RNA. The fluid samples are handled manually from machine to machine and the detection results are obtained after about 6 hours. An integrated diagnostic device is one in which at least some and preferably all of the above process steps are performed inside a single reactor system without any manual interference. This gives the results sooner and renders the device user-friendly. This device avoids the risk of cross-contamination because all processes are done in a closed reactor system.

[0003] In a closed reactor system all the fluid samples and reagents should be integrated within the reactor system along with a waste liquid generated during the course of lysis, washing mixing, elution and other processes. The waste liquid has to be contained in the reactor system in order to prevent an external dispersion.

[0004] US 7217542 discloses a system, including methods and apparatus, for micro-fluidic analysis of a nucleic acid target in a nucleic acid mixture. In an embodiment of this invention, a cartridge is disclosed that includes internal chambers for carrying out various functions. Internal chambers include two waste chambers designated A and B. Waste chambers receive fluids from reagent reservoirs and from sample input. Internal chambers may include a sample chamber. Such a cartridge with many chambers may not be compact and may need more material for construction.

[0005] It is therefore advantageous to have a reactor system that is compact and occupies less space.

SUMMARY OF THE INVENTION:

[0006] According to a first aspect of the invention, a reactor system, configured for carrying out a reaction, comprises at least one process chamber and at least one device, wherein the process chamber is connected to the device via a first channel and via a second channel, wherein the process chamber is configured for carrying out a reaction forming a product and a waste liquid, and wherein the device is configured to receive the product and waste liquid via the first channel and is configured to return the waste liquid to the process chamber via the second channel.

[0007] The basis of a reactor system, especially of a closed reactor system, is that not only the reactants should be integrated within the reactor system, but also the used fluids also called as waste liquid should be kept inside the reactor system to prevent cross contamination. The process chamber(s) is reused for waste liquid containment after an initial use of carrying out one or more process steps. This ensures that either less or no additional space is needed for the containment of the waste liquid. This results in smaller outer dimensions of the reactor system. The small size of the reactor system saves raw materials used for the production as well as the space needed per reactor system within a logistics system. The smaller the reactor system, the more of them go into a package, which will result in less cost for storage and transportation.

[0008] According to an embodiment of the invention, the reactor system further comprises a plurality of reagent reservoirs, wherein the reagent reservoirs are in fluid communication with the process chamber. The reagent reservoirs dispense the reagents when required to the process chamber.

[0009] According to a preferred embodiment of the invention, the reaction carried out is a chemical reaction, more preferably a biochemical reaction.

[0010] In another embodiment, the invention relates to a biochemical reaction which is an isolation of DNA from a fluid sample. Since the discovery of DNA, the technology relating to the detection of the presence, absence or amount of specific DNA or RNA sequences in a sample has taken an enormous flight. Especially PCR, the Polymerase Chain Reaction, has contributed enormously to the development of assays of all types for the detection of the presence or absence of DNA or RNA sequences. At present, it is possible to collect DNA containing samples from an organism and determine the presence, absence or amount therein of certain specific DNA sequences (target sequences). Technology is available to perform such analysis for multiple target sequences at the same time, so-called multiplex detection of target sequences to thereby increase throughput.

[0011] According to a still further embodiment of the invention, the fist process chamber is loaded with the fluid sample via a sample port.

[0012] According to yet another embodiment of the invention, the reagents comprise lysing reagents for lysing the fluid sample and wash solutions for washing the product formed. The lysing reagents may include, for example, a chaotropic agent, a buffer of high or low ionic strength, one or more ionic or nonionic detergents, an organic solvent and/or the like. The wash solutions may of suitable pH, buffering capacity, ionic strength and solvent composition.

[0013] According to another embodiment of the inven-

tion, the device is a splitter, wherein the splitter splits the product and the waste liquid into two different streams. The stream containing the product is sent for further processing whereas the stream containing the waste liquid is sent back to the process chamber.

[0014] According to a preferred embodiment of the invention the reactor system is a part of a diagnostic system. The isolated DNA is amplified and detected using the diagnostic system.

[0015] According to a second aspect of the invention, a method of re-using a process chamber of a reactor system is provided, wherein the reactor system is configured for carrying out a reaction, wherein the reactor system is provided with at least one process chamber and a device, wherein the process chamber and the device are connected via a first channel and via a second channel, and wherein the method comprises the steps of:

a. carrying out a reaction in the first process chamber;
b. transporting a product and a waste liquid of the reaction from the process chamber to the device via the first channel till the process chamber is empty,
c. splitting the product and the waste liquid into two different streams; and
d. sending the waste liquid from the device to the process chamber via the second channel to the empty process chamber.

[0016] According to another embodiment of the invention, a reactor system configured for carrying out a reaction comprises:

a. a first process chamber and a second process chamber, wherein the first process chamber and the second process chamber are connected via a first channel and via a second channel, and wherein the first process chamber is configured to carry out a reaction to form a product and a waste liquid ;
b. reagent introduction channels, wherein the reagent introduction channels are in fluid communication with the first process chamber and the second process chamber;
c. a fluidic interface in fluid communication with the reagent introduction channel for sampling a plurality of reagents from a plurality of sources of reagents and introducing the reagents into the reagent introduction channel from the sources of the reagents; and
d. a device configured to receive a mixture of a product and a waste liquid from the first process chamber via the second channel, wherein the filter is configured to send the waste liquid to the second process chamber via the second channel.

[0017] The reactor system preferably comprises only the process chambers. Although it is possible to re-use at least one process chambers and include waste chambers for additional waste, the device preferably does not contain any additional waste chambers. This makes the reactor system compact. The second channel provided between the first process chamber and the second process chamber enables a two-way flushing from one chamber to the other allowing the process chamber to act as a waste chamber. The reaction is carried out in the first process chamber. The product and the waste liquid are sent to the device. The product is retained in the device and the waste liquid is sent to the second process chamber leaving the first process chamber completely empty which further can be used for containing waste liquid.

[0018] In another embodiment, the invention relates to a reaction which is a chemical reaction and more preferably a biochemical reaction.

[0019] According to yet another embodiment of the invention, the first process chamber is loaded with the fluid sample via a sample port.

[0020] According to a further embodiment, the invention relates to a method of re-using a first process chamber and a second process chamber of a reactor system, wherein the reactor system is configured for carrying out a reaction, wherein the first process chamber and the second process chamber are connected via a first channel and via a second channel, and wherein the method comprises the steps of:

a. mixing reactants and reagents of the reaction by pumping back and forth from the first process chamber and the second process chamber;
b. carrying out a reaction in the first process chamber;
c. transporting a product of the reaction to a device, wherein the device is configured to receive a mixture of the product and the waste liquid from the first process chamber via the second channel, and wherein the device is configured to send the waste liquid to the second process chamber via the second channel, leading to transport of the waste liquid to process chamber.

According to a preferred embodiment the above-mentioned method is followed by the steps of:

a. transporting the waste liquid from the second process chamber to the first process chamber via the first channel till the second process chamber is empty.
b. washing the product in the device with wash solution;
c. collecting the washed liquid in the empty second process chamber via the second channel.

[0021] This method ensures that the two process chambers are effectively used to handle the waste liquid as well as the washed liquid without requiring any additional waste chambers. This feature reduces the size of the reactor system and makes it compact. This saves raw materials needed for production of the reactor sys-

tem and minimizes space needed per reactor system within a logistics system.

BRIEF DESCRIPTION OF THE FIGURES:

[0022] These and other characteristics, features and advantages of the present invention will become apparent from the following detailed description, taken in conjunction with the accompanying drawings, which illustrate, by way of example, the principles of the invention. This description is given for the sake of example only, without limiting the scope of the invention. The reference figures quoted below refer to the attached drawings.

Fig.1 shows a schematic representation of a reactor system;

Fig.2 shows a reactor system, wherein a product of reaction along with a waste liquid being transported to a device via a first channel;

Fig.3 shows the reactor system of Fig.2, wherein the waste liquid along with washed liquid being sent back to the process chamber via a second channel;

Fig.4 shows a schematic representation of a reactor system with more than one process chamber;

Fig.5 shows a reactor system, wherein a process chamber is being fed with a fluid sample and with reagents and contents being mixed by pumping them back and forth from a first process chamber and a second process chamber;

Fig.6 shows the reactor system of Fig.5, wherein another reagent being added to the first process chamber;

Fig.7 shows the reactor system of Fig.6, wherein the contents are being transferred to the first process chamber leaving the second process chamber empty;

Fig.8 shows the reactor system of Fig.7, wherein the contents are being moved from the first process chamber via a device to the second process chamber;

Fig.9 shows the reactor system of Fig.8, wherein the first process chamber is empty, a product is isolated and the second process chamber is filled with a waste liquid;

Fig.10 shows the reactor system of Fig.9, wherein the waste liquid is moved to the first process chamber rendering the second process chamber empty;

Fig.11 shows the reactor system of Fig.10, wherein the isolated product is being washed with a wash solution and the washed liquid is being collected in the second process chamber;

Fig.12 shows the reactor system of Fig.11, wherein the first process chamber is filled with the waste liquid and the second process chamber is filled with the washed liquid.

DETAILED DESCRIPTION OF THE INVENTION:

[0023] Particular and preferred aspects of the invention are set out in the accompanying independent and dependent claims. Features from the dependent claims may be combined with features of the independent claims and with features of other dependent claims as appropriate and not merely as explicitly set out in the claims.

[0024] The present invention will be described with respect to particular embodiments and with reference to certain drawings but the invention is not limited thereto but only by the claims. Any reference signs in the claims shall not be construed as limiting the scope. The drawings described are only schematic and are non-limiting. In the drawings, the size of some of the elements may be exaggerated and not drawn on scale for illustrative purposes. Where the term "comprising" is used in the present description and claims, it does not exclude other elements or steps. Where an indefinite or definite article is used when referring to a singular noun e.g. "a" or "an", "the", this includes a plural of that noun unless something else is specifically stated.

[0025] Furthermore, the terms first, second, third and the like in the description and in the claims, are used for distinguishing between similar elements and not necessarily for describing a sequential or chronological order. It is to be understood that the terms so used are interchangeable under appropriate circumstances and that the embodiments of the invention described herein are capable of operation in other sequences than described or illustrated herein.

[0026] Moreover, the terms top, bottom, over, under and the like in the description and the claims are used for descriptive purposes and not necessarily for describing relative positions. It is to be understood that the terms so used are interchangeable under appropriate circumstances and that the embodiments of the invention described herein are capable of operation in other orientations than described or illustrated herein.

[0027] A "reaction" in the context of invention may refer to an interaction between elements to form a new substance, a physical change in state of a substance, an extraction/isolation of DNA out of a fluid sample, an amplification reaction or a chemical reaction.

[0028] A "reactor system" is an apparatus or component of an apparatus having micro-fluidic reaction chambers. Typically, at least one reaction chamber will have at least one cross-sectional dimension between about 0.1 μm and about 500 μm.

[0029] A "process chamber" is a chamber (in any form, including a closed channel, a capillary, a trench, groove or the like) on or in a micro-fluidic substrate (a chip, bed, wafer, laminate, or the like having micro-fluidic channels) in which two or more components are mixed. The chamber will have at least one region with a cross sectional dimension of between about 0.1 μm and about 500 μm. The chamber will have a volume of around 2000 μl.

[0030] A "channel" is a channel (in any form, including

a closed channel, a capillary, a trench, groove or the like) on or in a micro-fluidic substrate (a chip, bed, wafer, laminate, or the like having micro-fluidic channels) through which components are transported (typically suspended or dissolved in a fluid). The channel will have at least one region with a cross sectional dimension of between about 0.1 μm and about 500 μm.

[0031] Waste liquid is any fluid component, complex, aggregate or particulate that does not correspond to the DNA of interest. Further, waste liquid may include cell or viral debris, unbroken cells or virus particles, cell membranes, cytoplasmic components, soluble non-DNA materials, insoluble non-DNA materials, nucleic acids that are not of interest, and/or the like. Waste material also may be a fluid, removal of which concentrates the DNA.

[0032] Washed liquid is that liquid generated after washing a product of a reaction with wash solution.

[0033] Note that the terms first process chamber and second process chamber do not relate to specific functions, but merely as ordinal numbers to discern the two. The names may be interchanged, as may the functions.

[0034] As shown in Figures 1-3, the reactor system 1 includes a process chamber 20 and a device 40. The process chamber 20 and the device 40are connected to each other via a first channel 22 and via a second channel 24. Valves 15 are represented by solid bowties (closed) or by unfilled bowties (open). Reagent reservoirs 12, 14 and 16 and 42 (only few reagent reservoirs out of a plurality of reagent reservoirs are shown) are pre-loaded with reagents. A fluid sample is introduced into the process chamber 20 via a sampling port 10. The sampling port 10 has been indicated only very diagrammatically as a kind of introduction channel. In principle, any desired introduction device known in the state of the art may be provided. The sampling port 10 may be closeable by means of a valve. Note that, when the valve is closed, the reactor system 1 comprises a completely closed system. This greatly reduces the risk of contamination.

[0035] The fluid sample from the sampling port 10 and the reagents from the reagent reservoirs 12, 14 and 16 are introduced into the process chamber 20. The required conditions are provided in the process chamber 20 and the reaction takes place. As illustrated in Fig.2, the product of the reaction along with the waste liquid is transported to the device 40 via the first channel 22. This leaves the process chamber 20 empty. The device 40 is a splitter or a similar kind of device which is capable of splitting the product and the waste liquid into two different streams.

[0036] The waste liquid is returned to the process chamber 20 via the second channel 24 thus re-using the process chamber as a waste chamber. The product is washed with wash solution that is contained in the reservoir 42. The washed liquid is also collected in the process chamber 20 via the second channel. This is illustrated in Fig.3.

[0037] The reactor system 100 shown in Figures 4 -12 includes a first process chamber 120 and a second process chamber 130. The first process chamber 120 and the second process chamber 130 are connected to each other via a first channel 132 and via a second channel 122. Valves 105 are represented by solid bowties (closed) or by unfilled bowties (open). Reagent reservoirs 112, 114 and 116 and 142 (only few reagent reservoirs out of a plurality of reagent reservoirs are shown) are pre-loaded with reagents. The reactor system 100 is provided with a device 140 which is coupled to the first process chamber 120 and the second process chamber 130 via the second channel 122. A fluid sample is introduced into the first process chamber 120 via a sampling port 110. The sampling port 110 has been indicated only very diagrammatically as a kind of introduction channel. In principle, any desired introduction device known in the state of the art may be provided. The sampling port 110 may be closeable by means of a valve. Note that, when the valve is closed, the reactor system 1 comprises a completely closed system.

[0038] As shown in Fig.5, the fluid sample is introduced into the first process chamber 120 via the sampling port 110. In the first process chamber 120, the fluid sample is mixed with reagent 1 and reagent 2 from reagent reservoirs 112 and 114. This mixing is further enhanced by pumping it back and forth to the second process chamber 130. The pre-loaded reagent reservoirs may carry the lysing reagents for lysing the fluid sample and wash solution for washing the product formed. The lysing reagents may include, for example, a chaotropic agent, a buffer of high or low ionic strength, one or more ionic or nonionic detergents, an organic solvent and/or the like. The wash solution may of suitable pH, buffering capacity, ionic strength, solvent composition etc.

[0039] The fluid sample is heated in the first process chamber 120 and mixed with reagent 3 from the reagent reservoir 116 as is shown in Fig. 6. Again the fluid sample along with the reagent 3 is pumped back and forth to the second process chamber 130 for ensuring a thorough mixing.

[0040] Later, as shown in Fig.7, the mixture of fluid sample and reagents is transferred to the first process chamber 120 ensuring that the first process chamber 120 is completely filled and the second process chamber 130 is fully empty.

[0041] Then the fluid sample is flushed through the device 140 according to the Figures 8 and 9. The device 140 is a filter or such kind of a device which can isolate the product. In case of a biochemical reaction, the device 140 is a filter which filters the DNA out of the fluid sample. The filter 140 mechanically retains cells, particles, debris and/or the like. The filter removes particles that might interfere with further processing steps. The waste liquid after isolation of DNA is sent to the second process chamber 130, but via the second channel 122. This is controlled by the valves 105. The valves are electrically activated or mechanically operated by electrically activated valve actuators. This step is continued till the first process chamber 120 is empty. The waste liquid is collected in

the second process chamber 130.

[0042] The next step as shown in Fig.10 is to pump the waste liquid, which is no longer needed for the process, back to the first process chamber 120, where it is kept for waste containment. This results in a completely filled first process chamber 120 and an empty second process chamber 130.

[0043] The product of the reaction, which may be isolated DNA, is washed with the wash solution contained in the reservoir 142 as shown in Fig.11. The wash solution is stored in the reagent reservoir 142, which is integrated in the reactor system 100. The fluids are sequentially flushed through the filter 140 for washing the product. The product is sent for further detection or for further processing. The second process chamber 130 is then used for the containment of the washed liquid. The washed liquid is directed by the valves 105 to the second process chamber 130, where the washed liquid is kept for the waste containment.

[0044] The reactor system 100 as shown in Fig.12 has the first process chamber 120 filled with the waste liquid and has the second process chamber 130 filled with the washed liquid. The waste generated during the course of the reaction is contained within the process chambers 120 and 130, thus re-using them after being used for carrying out a reaction, for mixing the contents of the reaction or for any other process.

[0045] This flow strategy can be extended with more fluid samples or other process flows, depending on the needed bio chemical sequence or other requirements. Also more process chambers can be used in the above described way by adding additional pathways from one process chamber to the other process chambers, so that the fluids can be flushed in two ways.

[0046] The reactor system is not limited to the field of molecular diagnostics. In all systems, where closed fluidic reactor systems are used and there is a need for waste containment within the reactor system, this invention can be used.

[0047] It is to be understood that although preferred embodiments, specific constructions and configurations have been discussed herein according to the present invention, various changes or modifications in form and detail may be made without departing from the scope and spirit of this invention.

Claims

1. A reactor system (1) configured for carrying out a reaction, wherein the reactor system (1) comprises at least one process chamber (20) and at least one device (40), wherein the process chamber (20) is connected to the device via a first channel (22) and via a second channel (24), wherein the process chamber (20) is configured for carrying out a reaction forming a product and a waste liquid, and wherein the device (40) is configured to receive the product and the waste liquid via the first channel (22) and is configured to return the waste liquid to the process chamber (20) via the second channel (24).

2. The reactor system (1) of claim 1, wherein the reactor system further comprises a plurality of reagent reservoirs (12, 14, 16, 42), wherein the reagent reservoirs are in fluid communication with the process chamber (20).

3. The reactor system (1) of claim 1, wherein the reaction carried out is a chemical reaction, more preferably a biochemical reaction.

4. The reactor system (1) of claim 3, wherein the biochemical reaction is an isolation of DNA from a fluid sample.

5. The reactor system (1) of claim 1, wherein the fist process chamber (20) is loaded with the fluid sample via a sample port (10).

6. The reactor system (1) of claim 1, wherein the reagents comprise lysing reagents for lysing the fluid sample and wash solution for washing the product formed.

7. The reactor system (1) of claim 1, wherein the device (40) is a splitter, wherein the splitter splits the product and the waste liquid into two different streams.

8. A diagnostic system comprising a reactor system (1) of claim 1.

9. A method of re-using a process chamber (20) of a reactor system (1), wherein the reactor system (1) is configured for carrying out a reaction, wherein the reactor system (1) is provided with at least one process chamber (20) and a device (40), wherein the process chamber (20) and the device (40) are connected via a first channel (22) and via a second channel (24), and wherein the method comprises the steps of:

a. carrying out a reaction in the first process chamber (20);
b. transporting a product and a waste liquid of the reaction from the process chamber (20) to the device (40) via the first channel (22) till the process chamber (20) is empty,
c. splitting the product and the waste liquid into two different streams; and
d. sending the waste liquid from the device (40) to the process chamber (20) via the second channel (24) to the empty process chamber (20).

10. A reactor system (100) configured for carrying out a reaction, wherein the reactor system (100) compris-

es:

a first process chamber (120) and a second process chamber (130), wherein the first process chamber (120) and the second process chamber (130) are connected via a first channel (132) and via a second channel (122), and wherein the first process chamber (120) is configured to carry out a reaction to form a product and a waste liquid ;
a plurality of reagent reservoirs (112,114,116,142), wherein the reagent reservoirs are in fluid communication with the first process chamber (120) and the second process chamber (130); and
a device (140) configured to receive a mixture of a product and a waste liquid from the first process chamber (120) via the second channel (122), wherein the device (140) is configured to send only the waste liquid to the second process chamber (130) via the second channel (122).

11. The reactor system (100) of claim 10, wherein the reaction carried out is a chemical reaction, more preferably a biochemical reaction.

12. The reactor system (100) of claim 10, wherein the fist process chamber (120) is loaded with the fluid sample via a sample port (110).

13. A method of re-using a first process chamber of a reactor system (100), wherein the reactor system (100) is configured for carrying out a reaction, wherein a first process chamber (120) and a second process chamber (130) are connected via a first channel (132) and via a second channel (122), and wherein the method comprises the steps of:

a. mixing reactants and reagents of the reaction by pumping back and forth from the first process chamber (120) and the second process chamber (130);
b. carrying out a reaction in the first process chamber (120);
c. transporting a product of the reaction to a device (140), wherein the device is configured to receive a mixture of the product and the waste liquid from the first process chamber (120) via the second channel (122), and wherein the device (140) is configured to send the waste liquid to the second process chamber (130) via the second channel (122), leading to transport of the waste liquid to process chamber (130).

14. A method according to claim 13 further comprising the steps of :

a. transporting the waste liquid from the second process chamber (130) to the first process chamber (120) via the first channel (132) till the second process chamber (130) is essentially empty.
b. washing the product in the device (140) with wash solution contained the reagent reservoir (142);
c. collecting the washed liquid in the second process chamber (130) via the second channel (122).

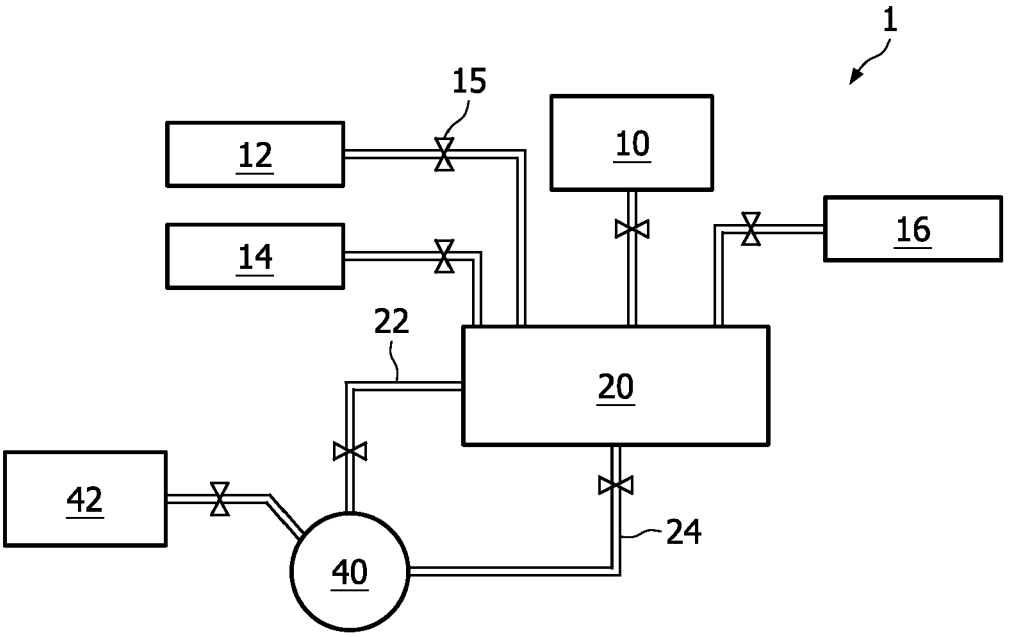

FIG. 1

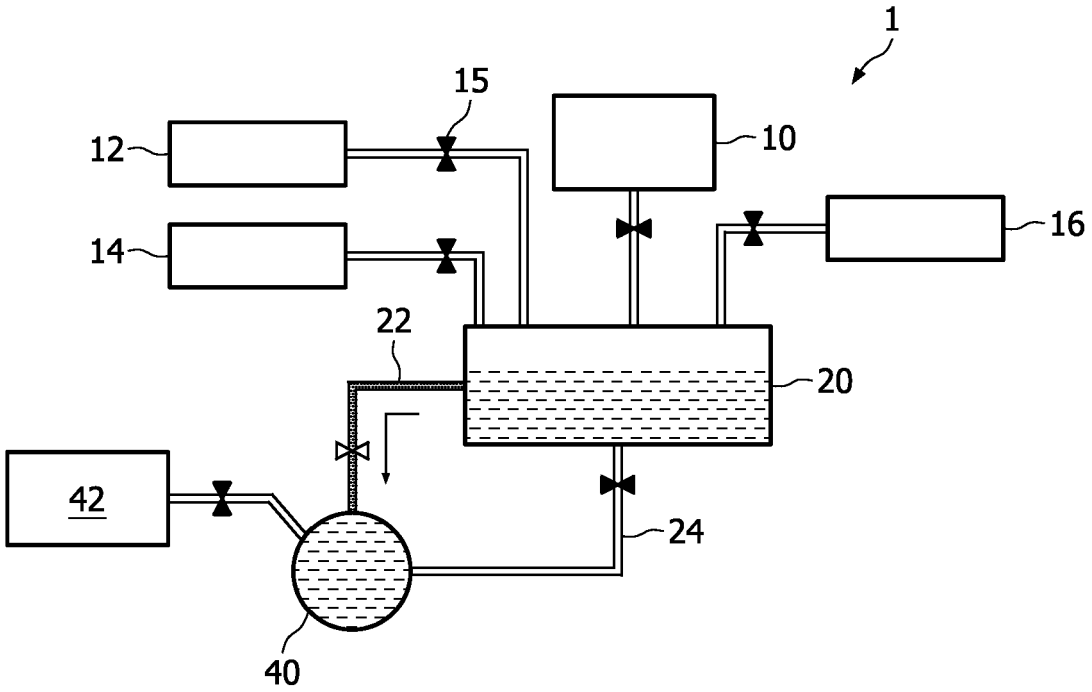

FIG. 2

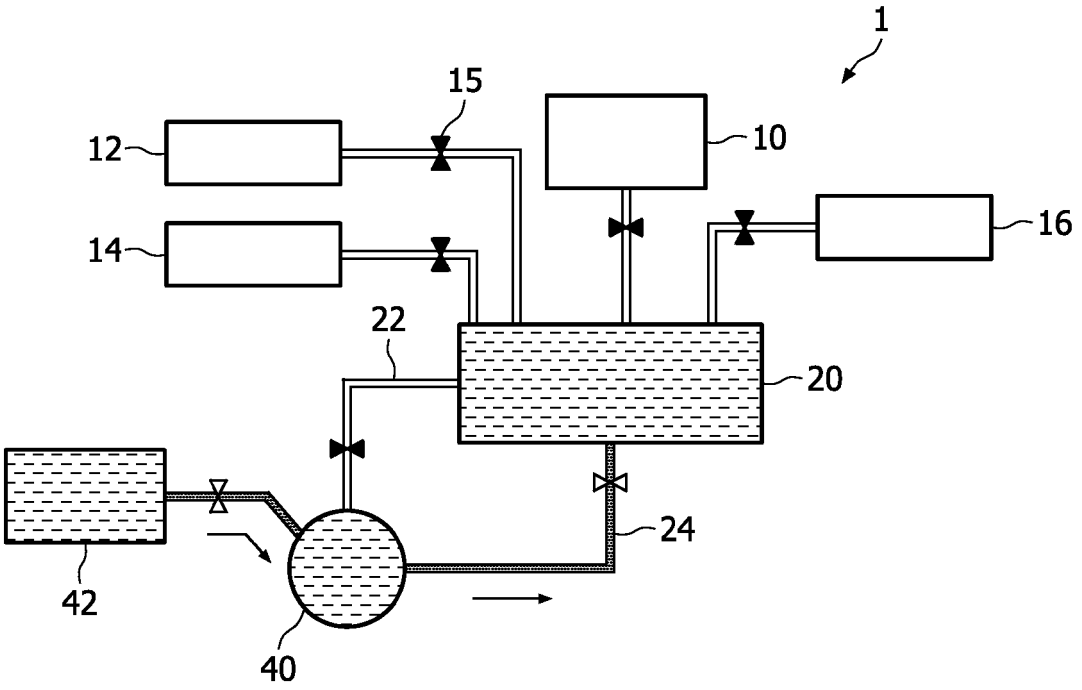
1
15
12
10
16
14
22
20
24
42
40

FIG. 3

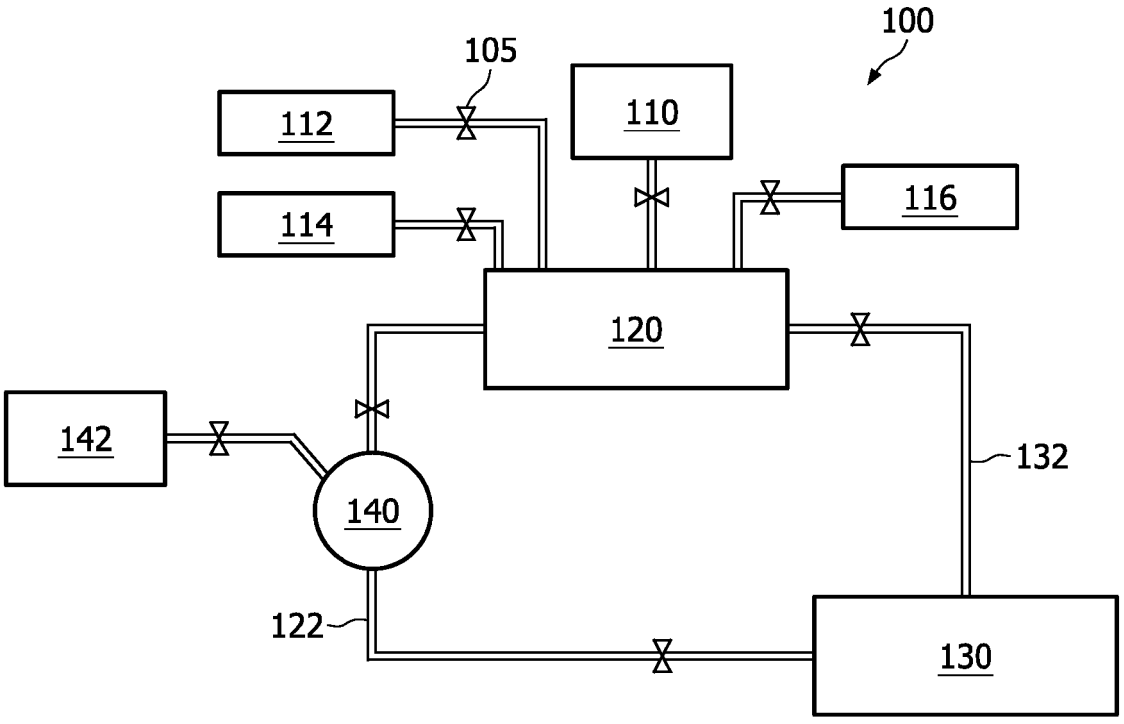
100
105
112
110
116
114
120
142
132
140
122
130

FIG. 4

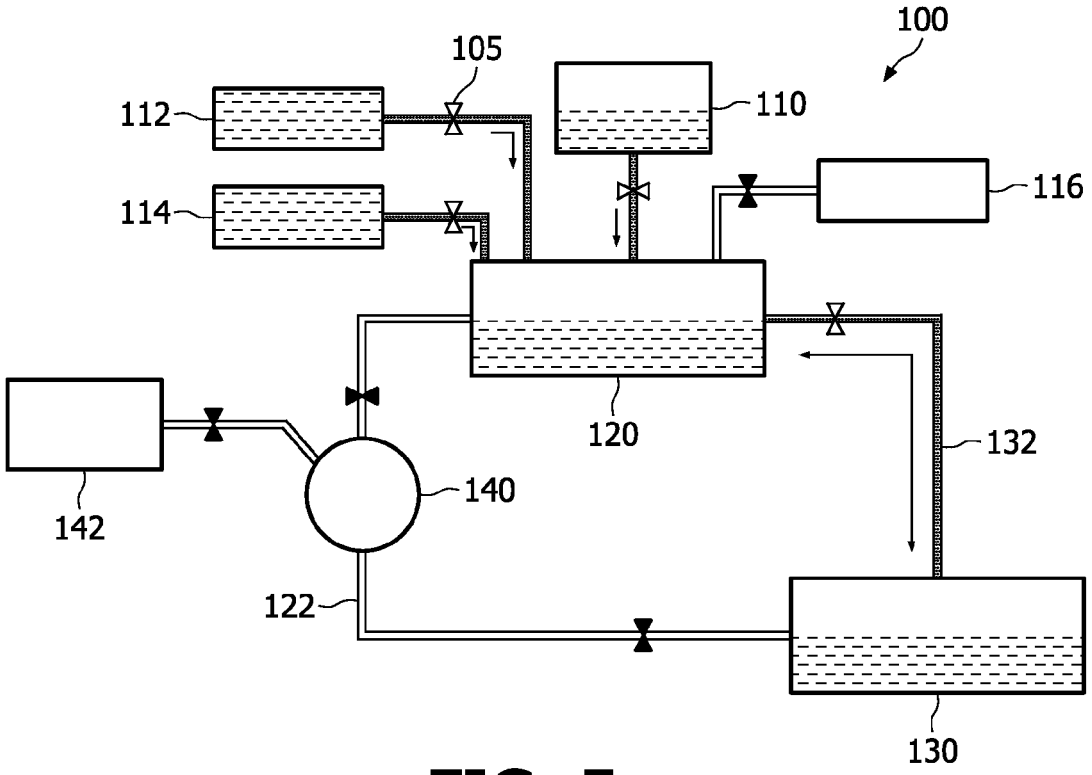
100
105
112
110
114
116
120
132
140
142
122
130

FIG. 5

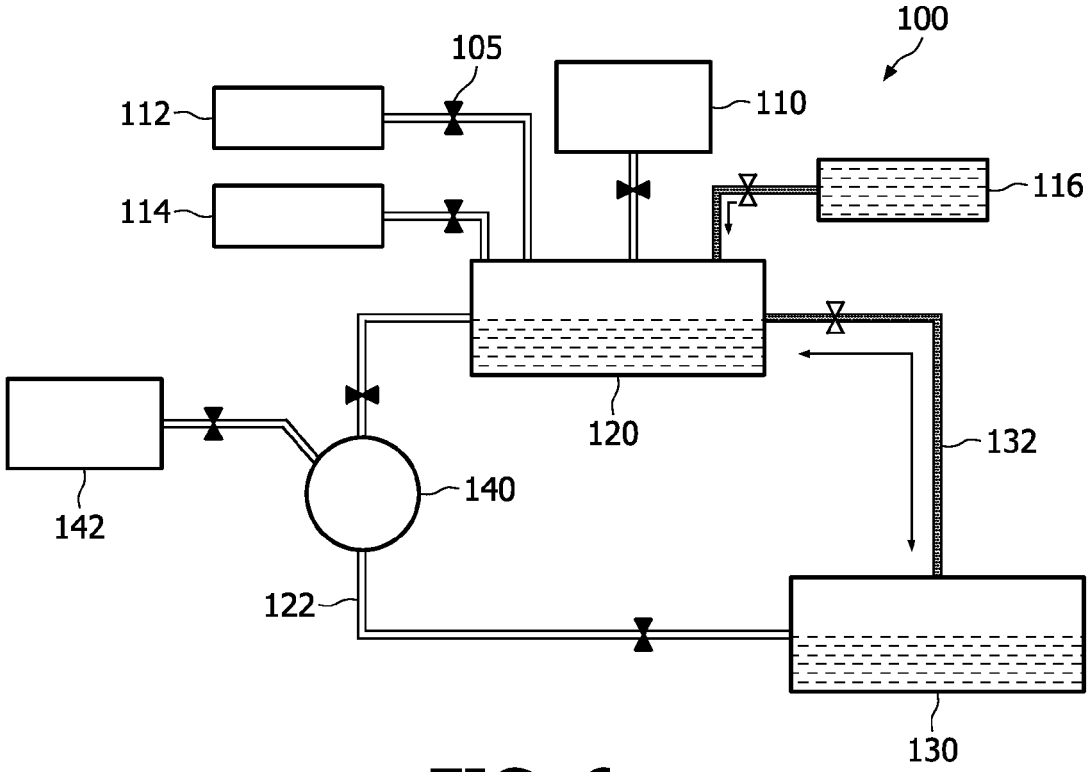
100
105
112
110
114
116
120
132
140
142
122
130

FIG. 6

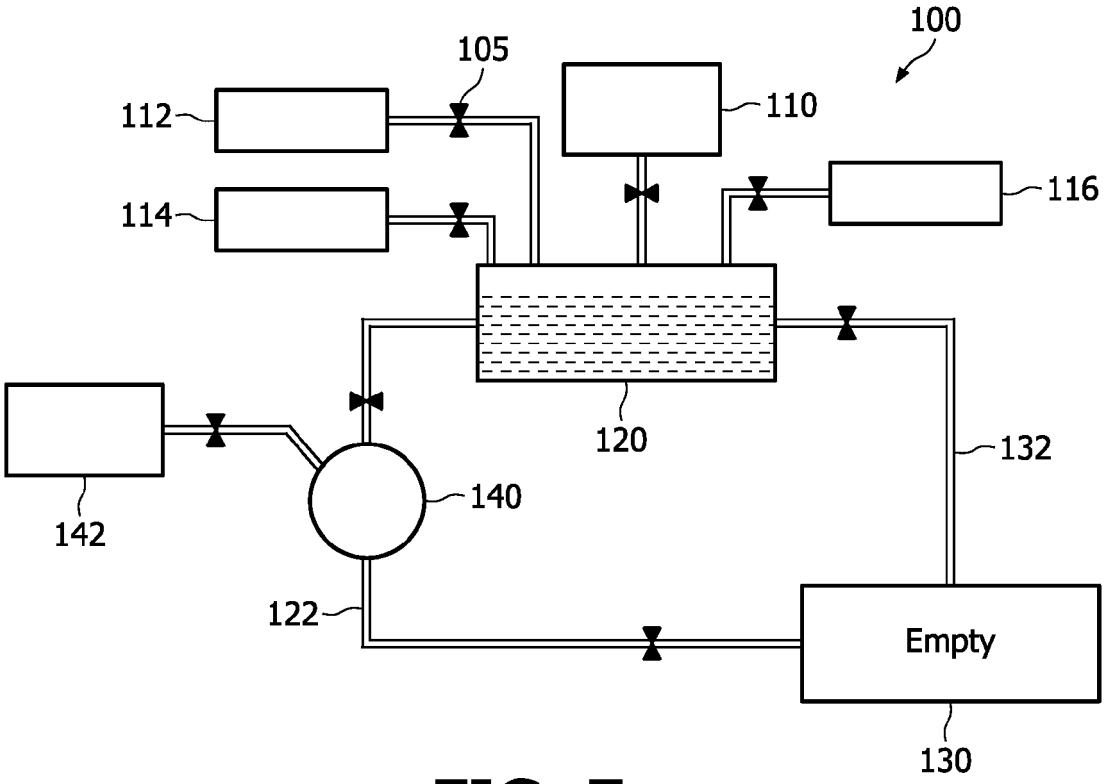
100
105
112
110
114
116
120
132
140
142
122
Empty
130

FIG. 7

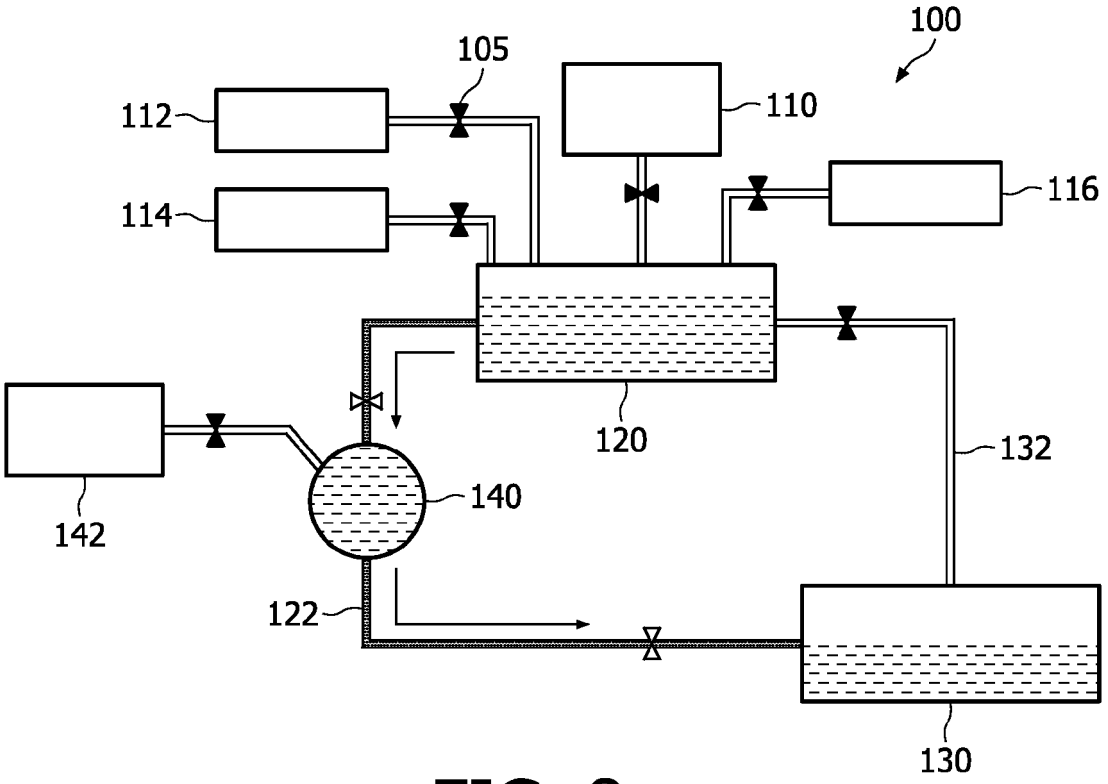
100
105
112
110
114
116
120
132
140
142
122
130

FIG. 8

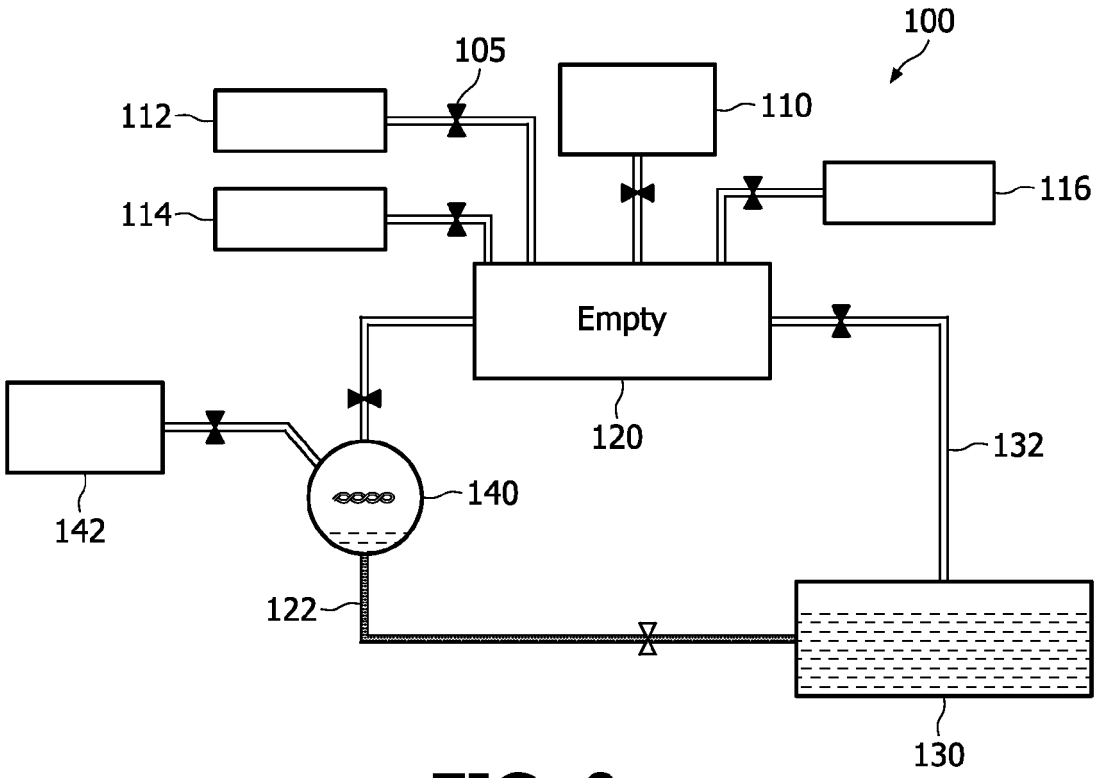
100
105
112
110
116
114
Empty
120
132
140
142
122
130

FIG. 9

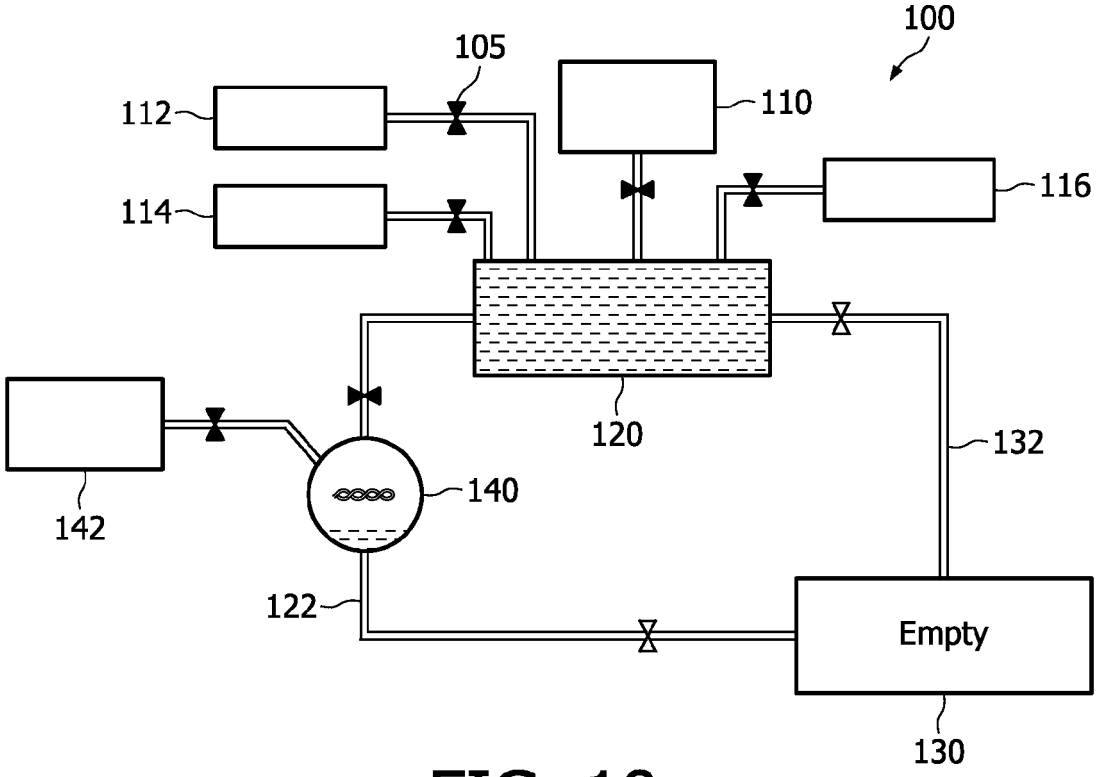
100
105
112
110
116
114
120
132
140
142
122
Empty
130

FIG. 10

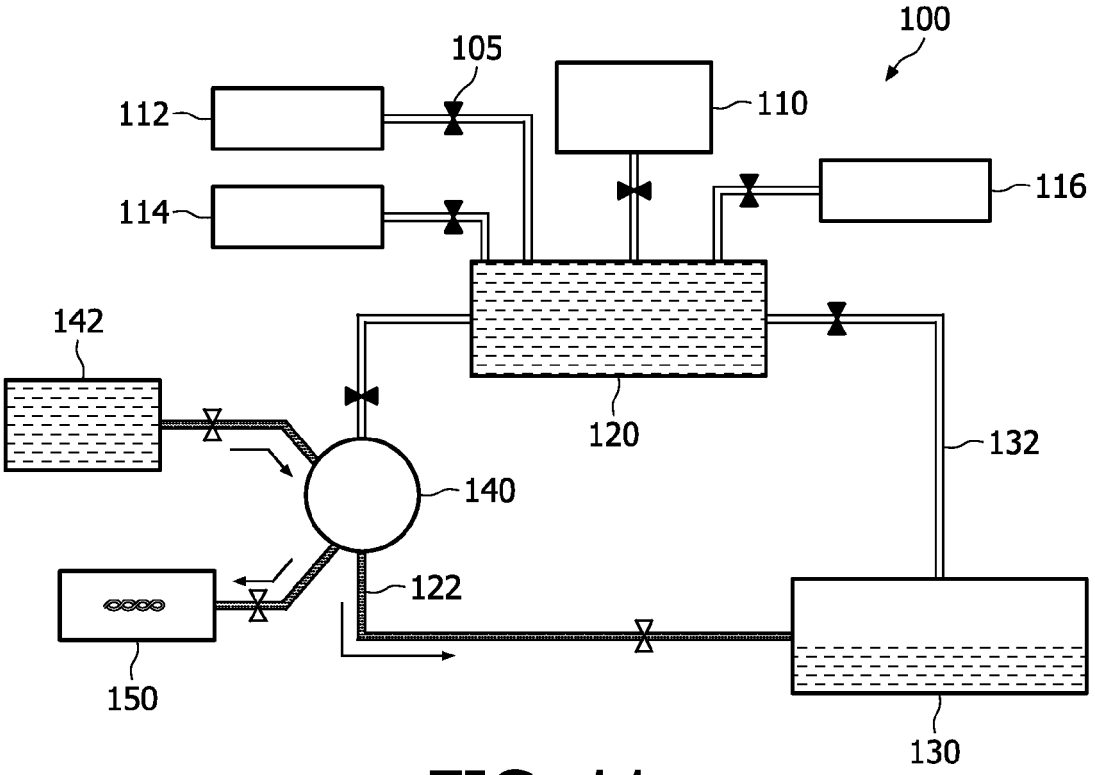
100
105
112
110
116
114
142
120
132
140
122
150
130

FIG. 11

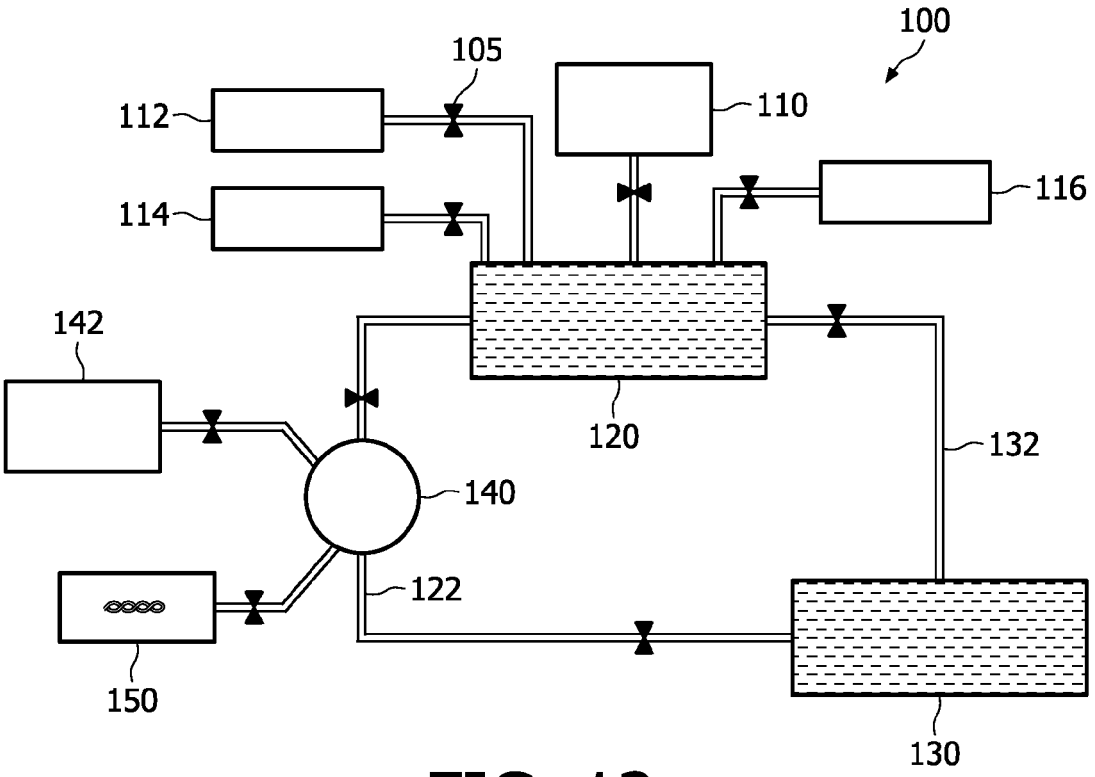
100
105
112
110
116
114
142
120
132
140
122
150
130

FIG. 12

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 07 12 3813

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X Y	WO 2006/060783 A (CYTONOME INC [US]; GILBERT JOHN R [CA]; LEWIS HUGH [ZA]; BEAUPRE DEREK) 8 June 2006 (2006-06-08) * page 7, line 4 - line 11; figures 5,7-10 * * page 10, line 23 - line 26 *	1,2 13,14	INV. B01L3/00
X	US 2006/216812 A1 (OKADA JUN [JP] ET AL) 28 September 2006 (2006-09-28) * figure 4 *	1-6,8	
Y	US 2002/155586 A1 (CHENG JING [CN] ET AL CHENG JING [CN] ET AL) 24 October 2002 (2002-10-24) * paragraph [0066]; figure 7 *	13,14	
D,A	US 7 217 542 B2 (TYVOLL DAVID [US] ET AL) 15 May 2007 (2007-05-15) * figures 9,11-16 *	1-14	
			TECHNICAL FIELDS SEARCHED (IPC) B01L

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
Munich	23 May 2008	de Biasio, Arnaldo

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 07 12 3813

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

23-05-2008

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006060783 A	08-06-2006	AU 2005311631 A1	08-06-2006
		CA 2588753 A1	08-06-2006
		CN 101099082 A	02-01-2008
		EP 1817568 A2	15-08-2007
		KR 20070104347 A	25-10-2007
US 2006216812 A1	28-09-2006	JP 2005261298 A	29-09-2005
US 2002155586 A1	24-10-2002	NONE	
US 7217542 B2	15-05-2007	CA 2444200 A1	30-04-2004
		CN 1499195 A	26-05-2004
		EP 1418243 A2	12-05-2004
		JP 2004147658 A	27-05-2004
		KR 20040038878 A	08-05-2004
		SG 120120 A1	28-03-2006
		TW 271218 B	21-01-2007
		US 2004086870 A1	06-05-2004

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 7217542 B **[0004]**