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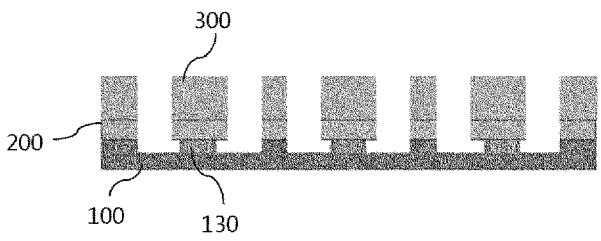
(54) Title: METHOD FOR MANUFACTURING MICROFLUIDIC DEVICE AND THE MICROFLUIDIC DEVICE



(57) Abstract: Disclosed are a method for manufacturing a microfluidic chip and a microfluidic chip capable of mass production and automatic production. The method for manufacturing a microfluidic chip according to an exemplary embodiment of the present invention may include forming a plurality of holes on a glass substrate by punching; and bonding a silicon device to the glass substrate with the plurality of holes, wherein the silicon device forms a bottom and is located below the glass substrate.

Description

Title of Invention: METHOD FOR MANUFACTURING MICROFLUIDIC DEVICE AND THE MICROFLUIDIC DEVICE

Technical Field

[1] The present invention relates to a microfluidic chip, and more particularly, to a method for manufacturing a microfluidic chip and a microfluidic chip capable of mass production and automatic production.

Background Art

[2] A 3D cell culture technology and a drug evaluation technology using a microfluidic system have been stabilized, and as a result, an assay for performing experiments with a large capacity has been demanded. As a related prior art, there is Korean Patent Registration No. 10-0588355.

[3] In the case of a conventional PDMS-based microfluidic chip, a bonding method by contacting two surfaces of a PDMS device and a glass substrate was used. In this case, the PDMS chip configures a microfluidic channel according to a pattern and is used by punching holes manually or using an automatic device or without drilling the holes.

[4] However, in the case of a large chip, a large number of holes is required because of an multi-array, and as a result, an effort required for punching is very increased.

[5] Further, in the case of a conventional plastic-based chip, since bonding between a chip pattern and a bottom is unstable, in many cases, a chip defect rate is largely influenced and an injection mold needs to be fabricated to inject plastic patterns. In this case, in the case of a metal mold, it is not easy to use the metal mold in an initial development stage of a new chip because of high unit cost.

[6] Meanwhile, in the case of a plastic-based chip, since phenotypes of cells may be differently expressed depending on a plastic device, evaluation of cell stability against the plastic device needs to take precedence. Due to the aforementioned reasons, in the plastic-based chip, much many efforts and costs are required until commercialization.

[7] Therefore, studies on a manufacturing technology of the microfluidic chip which can reduce the defective rate in the chip manufacturing and be automatized are required.

Disclosure of Invention

Technical Problem

[8] An object of the present invention is to provide a method for manufacturing a microfluidic chip capable of reducing a defect rate when a chip is manufactured, enabling high-speed automatic production, and manufacturing a large-capacity chip.

[9] Another object of the present invention is to provide a large-capacity microfluidic chip which is manufactured by a high-speed automation system.

Solution to Problem

[10] According to an aspect of the present invention, there is a disclosed a method for manufacturing a microfluidic chip including: forming a plurality of holes on a glass substrate by punching; and bonding a silicon device to the glass substrate with the plurality of holes, wherein the silicon device forms a bottom and is located below the glass substrate.

[11] According to another aspect of the present invention, there is a disclosed a microfluidic chip including a silicon device forming a bottom; and a glass substrate bonded onto the device, wherein the glass substrate has a plurality of holes formed by punching.

Advantageous Effects of Invention

[12] According to the method for manufacturing the microfluidic chip according to the exemplary embodiment of the present invention, it is possible to reduce a defect rate when the chip is manufactured and manufacture a microfluidic chip by a high-speed automatic production method.

[13] According to the embodiment of the present invention, it is possible to use a conventional PDMS chip structure which is widely used for cell culture as it is.

[14] According to the exemplary embodiment of the present invention, it is possible to automatically produce a microfluidic chip having a multi array for large-capacity cell culture.

Brief Description of Drawings

[15] The above and other features of the present invention will now be described in detail with reference to certain exemplary embodiments thereof illustrated the accompanying drawings which are given hereinbelow by way of illustration only, and thus are not limitative of the present invention, and wherein:

[16] FIG. 1 illustrates a step of providing a silicon substrate and a glass substrate in a manufacturing process of a microfluidic chip according to an exemplary embodiment of the present invention;

[17] FIG. 2 illustrates a step of performing punching on the glass substrate in the manufacturing process of the microfluidic chip according to the exemplary embodiment of the present invention;

[18] FIG.3 illustrates the glass substrate punched by a sand blasting method according to the exemplary embodiment of the present invention;

[19] FIG. 4 illustrates a PDMS device which is punched to be bonded to the glass substrate of FIG. 3 according to the exemplary embodiment of the present invention;

[20] FIG. 5 illustrates a step of performing a plasma treatment on the surface of the silicon device and the punched surface of the glass substrate in the manufacturing process of

the microfluidic chip according to the exemplary embodiment of the present invention;

[21] FIG. 6 illustrates a step of bonding a surface of the silicon device and a surface of the punched glass substrate which are subjected to the plasma treatment in the manufacturing process of the microfluidic chip according to the exemplary embodiment of the present invention;

[22] FIGS. 7 and 8 illustrate the bonded glass substrate and PDMS device according to the exemplary embodiment of the present invention;

[23] FIG. 9 illustrates a step of performing UV-bonding on an upper surface of the punched glass substrate and a surface of a plastic reservoir to be bonded on the glass substrate in the manufacturing process of the microfluidic chip according to the exemplary embodiment of the present invention;

[24] FIG. 10 illustrates a state in which the plastic reservoir is bonded on the punched glass substrate in the manufacturing process of the microfluidic chip according to the exemplary embodiment of the present invention;

[25] FIG. 11 illustrates a state in which a gel is injected into the completed microfluidic chip according to the exemplary embodiment of the present invention;

[26] FIG. 12 illustrates a state in which a cell culture medium is injected into the completed microfluidic chip according to the exemplary embodiment of the present invention; and

[27] FIG. 13 illustrates the microfluidic chip in which cells are cultured according to the exemplary embodiment of the present invention.

Mode for the Invention

[28] Hereinafter, a method for manufacturing a microfluidic chip and a microfluidic chip according to an exemplary embodiment of the present invention will be described.

[29] Singular expressions used in the present specification include plural expressions unless they have definitely opposite meanings in the context. In the present invention, a term such as "comprising" or "including" should not be interpreted as necessarily including all various components or various steps disclosed in the invention, and it should be interpreted that some component or some steps among them may not be included or additional components or steps may be further included.

[30] FIG. 1 illustrates a step of providing a silicon substrate and a glass substrate in a manufacturing process of a microfluidic chip according to an exemplary embodiment of the present invention.

[31] As illustrated in FIG. 1, in a manufacturing process of a microfluidic chip according to an exemplary embodiment of the present invention, a silicon device 100 is disposed on the lowest side to form a bottom and a glass substrate 200 may be disposed on the silicon device. Hereinafter, a poly dimethyl siloxane stamp (PDMS) device will be

described as an example of the silicon device 100.

[32] In the case of a conventional PDMS-based microfluidic chip, a glass substrate forms the bottom and a PDMS mold is bonded onto the glass substrate. In this case, the PDMS device is used by manually punching holes according to a chip pattern. However, in the case of a large-sized and large-capacity chip for a high-throughout experiment, the number of holes to be punched increases exponentially and thus it is not easy to punch the holes by hands one by one. Accordingly, in the exemplary embodiment, the microfluidic chip is manufactured by a method of performing punching on the glass substrate 200 without punching the holes on the surface of the PDMS device 100. The punching may be performed according to a punching line. In addition, in the PDMS device 100, a cell fluid to be cultured may be injected, stored, and flowed, and a cell culturable pattern 110 may be formed. In the PDMS device 100, a post 120 may be formed. The post 120 can prevent leakage of fluid.

[33] FIG. 2 illustrates a step of performing punching on the glass substrate in the manufacturing process of the microfluidic chip according to the exemplary embodiment of the present invention.

[34] As illustrated in FIG. 2, in the exemplary embodiment, unlike a conventional method, the PDMS device 100 is located at the lowest part of the microfluidic chip, and in the glass substrate 200 bonded to the PDMS device 100, the punching may be performed at a part requiring the holes using sandblasting or other punching methods (for example, laser cutting, drilling, EDM, etc.).

[35] FIG.3 illustrates the glass substrate punched by a sand blasting method according to the exemplary embodiment of the present invention and FIG. 4 illustrates a PDMS device which is punched to be bonded to the glass substrate of FIG. 3 according to the exemplary embodiment of the present invention.

[36] As illustrated in FIGS. 3 and 4, in the exemplary embodiment, in the glass substrate 200, the punching is performed by the sandblasting method and in the PDMS device 100, the punching is not performed.

[37] FIG. 5 illustrates a step of performing a plasma treatment on the surface of the silicon device and the punched surface of the glass substrate in the manufacturing process of the microfluidic chip according to the exemplary embodiment of the present invention.

[38] As illustrated in FIG. 5, the surface of the PDMS device 100 with the pattern 110 and the surface of the glass substrate 200 are surface-modified by using a plasma cleaner and then the two surfaces are bonded to each other by contacting each other.

[39] FIG. 6 illustrates a step of bonding the surface of the silicon device and the punched surface of the glass substrate which are subjected to the plasma treatment in the manufacturing process of the microfluidic chip according to the exemplary embodiment of the present invention.

[40] As illustrated in FIG. 6, the surface of the PDMS device 100 and the surface of the glass substrate 200 are subjected to the plasma treatment and then may be bonded to each other by contacting each other. When the surface of the PDMS device 100 and the surface of the glass substrate 200 are subjected to the plasma treatment, bonding force between the glass substrate 200 and the PDMS device 100 is enhanced to prevent the cell culture solution from being leaked.

[41] FIGS. 7 and 8 illustrate the bonded glass substrate and PDMS device according to the exemplary embodiment of the present invention.

[42] FIG.7 is a photograph of the bonded glass substrate 200 and PDMS device 100 taken at the top and FIG. 8 is a photograph of the bonded glass substrate 200 and PDMS device 100 taken at the top.

[43] As confirmed by FIGS. 7 and 8, when the plasma treatment is performed, the PDMS device 100 and the glass substrate 200 are strongly bonded to each other so as not to be distinguished.

[44] FIG. 9 illustrates a step of performing UV-bonding on an upper surface of the punched glass substrate and a surface of a plastic reservoir to be bonded on the glass substrate in the manufacturing process of the microfluidic chip according to the exemplary embodiment of the present invention and FIG. 10 illustrates a state in which the plastic reservoir is bonded on the punched glass substrate in the manufacturing process of the microfluidic chip according to the exemplary embodiment of the present invention.

[45] As illustrated in FIGS. 9 and 10, the surface of the glass substrate 200 and the surface of the plastic reservoir 300 are subjected to UV-bond treatment to be bonded to each other by contacting each other. The reservoir 300 may be bonded to the top of the glass substrate so that a plurality of holes formed in the glass substrate 200 may be exposed upward. The reservoir 300 may be made of a material having a smaller density than the glass substrate 200. For example, the reservoir 300 may be made of a plastic material. Further, the reservoir 300 may include a bottomless multi well plate. Since the glass substrate 200 has a relatively larger weight and relatively higher punching cost than the reservoir 300, a separate reservoir is not used, and when a thickness of the glass substrate 200 is increased to form the reservoir, the process cost may be increased and the cells may also be damaged due to the weight thereof. However, when a separate reservoir 300 having a smaller mass than the glass substrate 200 is bonded onto the glass substrate 200, it is possible to prevent the call damage while reducing the process cost.

[46] FIG. 11 illustrates a state in which a gel is injected into the completed microfluidic chip according to the exemplary embodiment of the present invention.

[47] As illustrated in FIG. 11, the gel 130 may be injected into a space between the posts

120 and the gel 130 may be fixed due to surface tension between posts.

[48] FIG. 12 illustrates a state in which a cell culture medium is injected into the completed microfluidic chip according to the exemplary embodiment of the present invention.

[49] As illustrated in FIG. 12, the cell culture medium 400 may be injected into a cell culture solution storage space generated by the PDMS device 100, the glass substrate 200, and the reservoir 300.

[50] FIG. 13 illustrates the microfluidic chip in which cells are cultured according to the exemplary embodiment of the present invention.

[51] As illustrated in FIG. 13, in the case of the internal structure of the microfluidic chip manufactured according to the embodiment of the present invention, since the PDMS element and the glass structure are present as they are, the hydrophobicity is maintained in the chip. Accordingly, a gel or other fluids may be filled in the chip and the cell culture is possible.

[52] As described above, according to the method for manufacturing the microfluidic chip according to the exemplary embodiment of the present invention, it is possible to reduce a defect rate when the chip is manufactured and manufacture a microfluidic chip by a high-speed automatic production method.

[53] According to the exemplary embodiment of the present invention, it is possible to automatically produce a microfluidic chip having a multi array for large-capacity cell culture.

[54] In the method for manufacturing the microfluidic chip and the microfluidic chip described above, the configurations and the method of the described exemplary embodiments may be limitedly applied, but the exemplary embodiments may also be configured by combining selectively all or some of the exemplary embodiments so that various modifications may be made.

Claims

[Claim 1] A method for manufacturing a microfluidic chip, comprising:
forming a plurality of holes on a glass substrate by punching; and
bonding a silicon device to the glass substrate with the plurality of holes, wherein the silicon device forms a bottom and is located below the glass substrate.

[Claim 2] The method for manufacturing a microfluidic chip of claim 1, wherein the silicon device includes a poly dimethyl siloxane stamp (PDMS) device.

[Claim 3] The method for manufacturing a microfluidic chip of claim 2, further comprising:
bonding a reservoir onto the glass substrate so that the plurality of holes formed on the glass substrate may be exposed upward, wherein the reservoir has a relatively smaller density than the glass substrate.

[Claim 4] The method for manufacturing a microfluidic chip of claim 3, wherein the bonding of the silicon device to the glass substrate includes bonding the surface of the device to the surface of the glass substrate by plasma-treating the surface of the device to the surface of the glass substrate, respectively.

[Claim 5] The method for manufacturing a microfluidic chip of claim 3, wherein the punching performed on the glass substrate includes at least one of sandblasting, drilling, and an EDM method.

[Claim 6] The method for manufacturing a microfluidic chip of claim 3, wherein in the silicon device, a cell fluid to be cultured is injected, stored, and flowed, and a cell culturable pattern is formed.

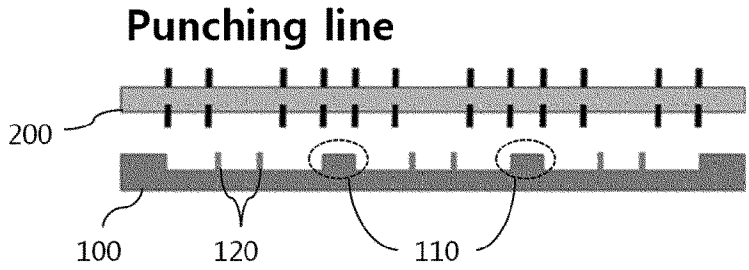
[Claim 7] A microfluidic chip, comprising:
a silicon device forming a bottom; and
a glass substrate bonded onto the device, wherein the glass substrate has a plurality of holes formed by punching.

[Claim 8] The microfluidic chip of claim 7, wherein the silicon device includes a poly dimethyl siloxane stamp (PDMS) device.

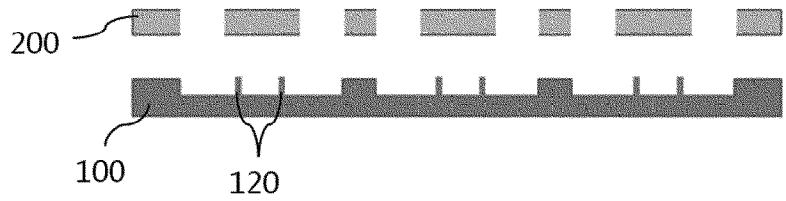
[Claim 9] The microfluidic chip of claim 8, further comprising:
a plastic reservoir bonded onto the glass substrate.

[Claim 10] The microfluidic chip of claim 8, wherein the silicon device has a pattern in which a cell fluid to be culture is injected and fixed.

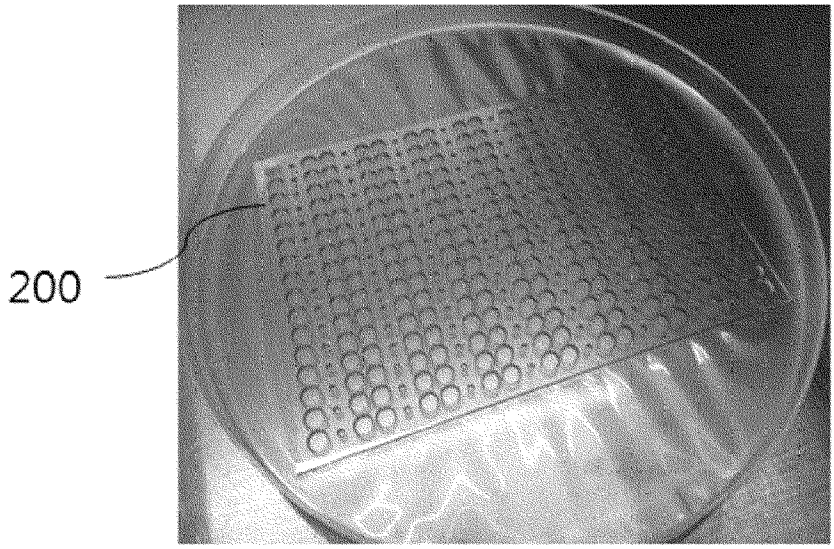
[Fig. 1]



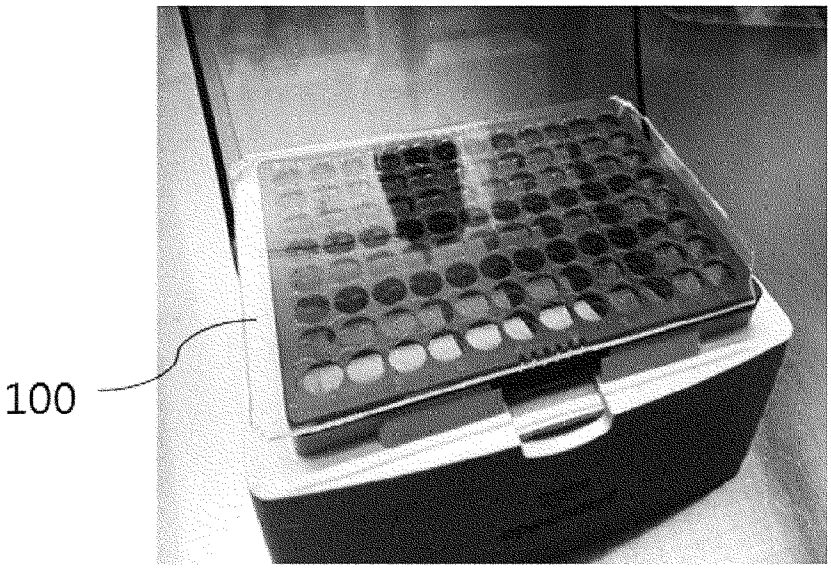
[Fig. 2]



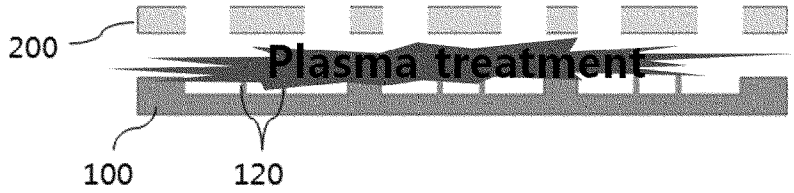
[Fig. 3]



[Fig. 4]

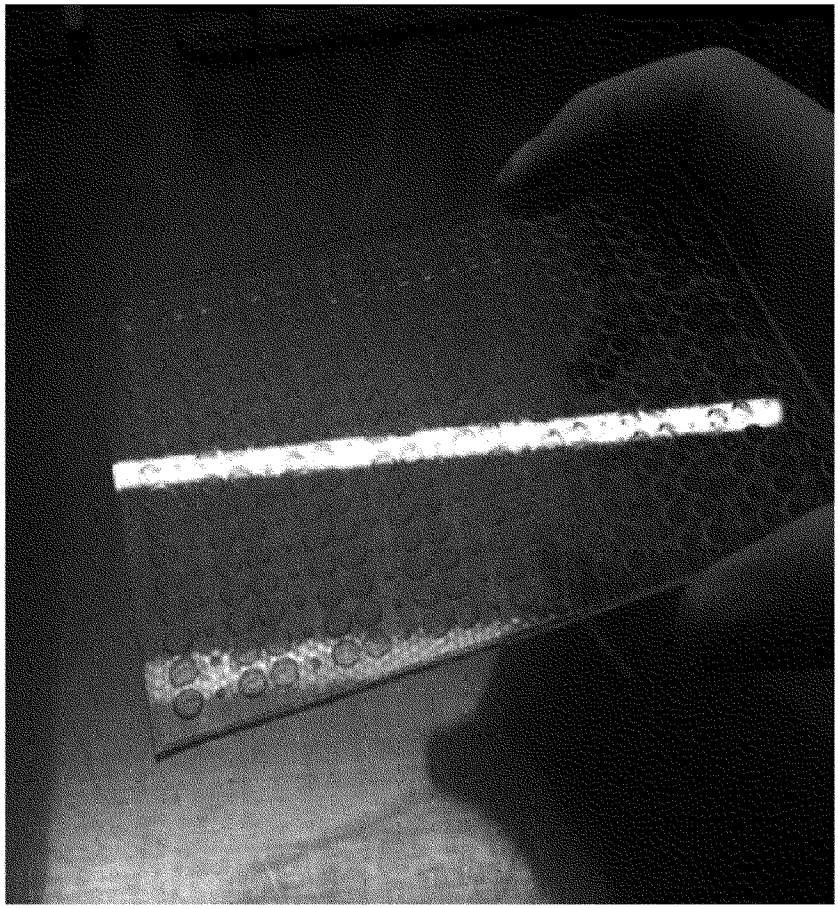


[Fig. 5]

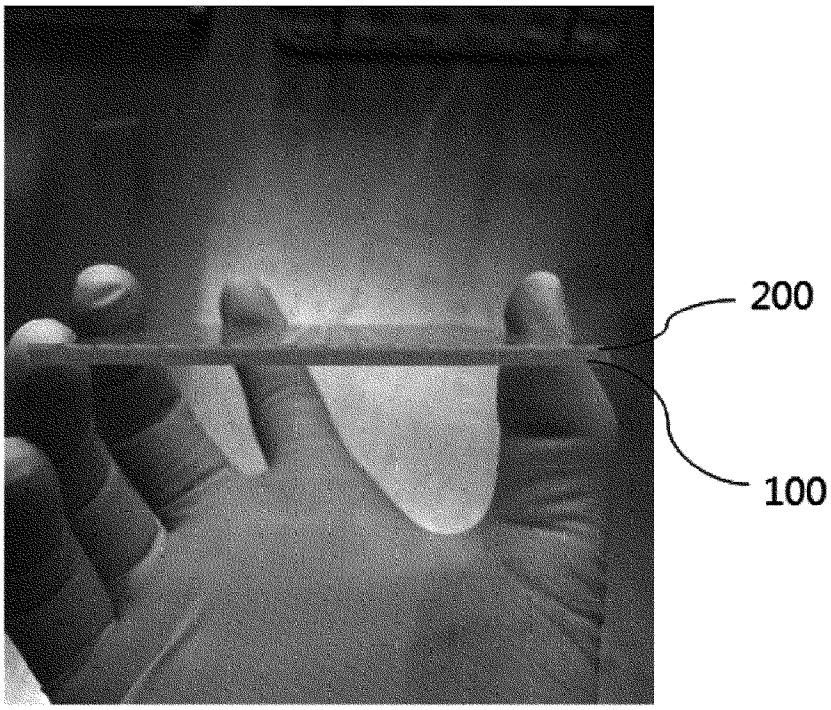


[Fig. 6]

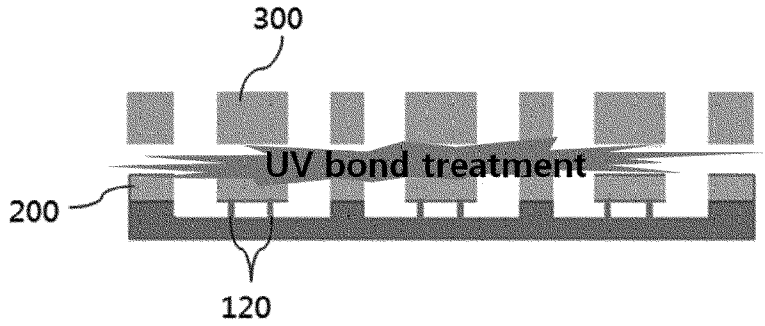
[Fig. 7]



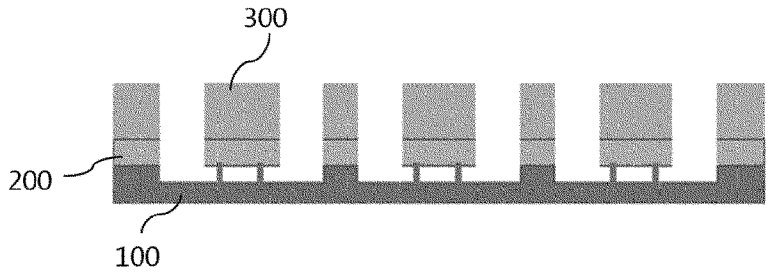
[Fig. 8]



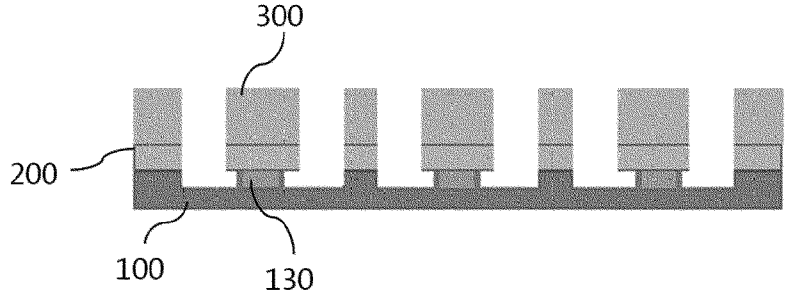
[Fig. 9]



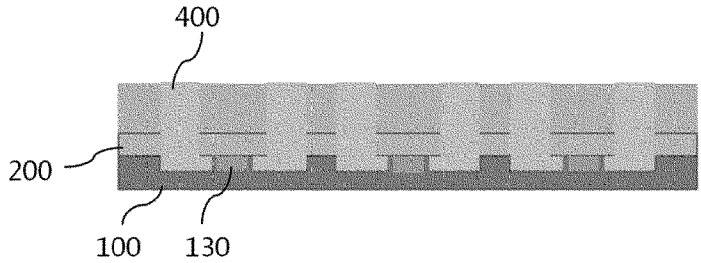
[Fig. 10]



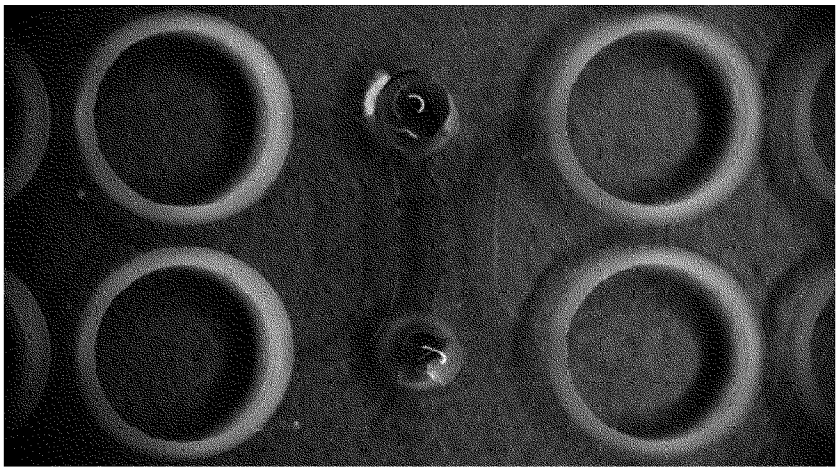
[Fig. 11]



[Fig. 12]



[Fig. 13]



INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2018/001700

A. CLASSIFICATION OF SUBJECT MATTER

C12M 3/06(2006.01)i, B01L 3/00(2006.01)i

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)
C12M 3/06; C25B 9/00; C12N 5/071; B01J 13/00; C12N 5/07; B32B 31/20; B01F 5/00; B32B 5/02; B29C 65/00; B01L 3/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: microfluidic chip, holes, glass substrate, punching, PDMS, reservoir

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP 2010-029790 A (DAINIPPON PRINTING CO., LTD.) 12 February 2010 See paragraphs [0007], [0024], [0044]-[0063]; claims 1-10; figure 1.	1-10
X	US 2010-0323447 A1 (TAKAYAMA, SHUICHI et al.) 23 December 2010 See paragraphs [0048]-[0076]; claims 32-37; figure 1.	1-10
X	US 2004-0200724 A1 (FUJII, TERUO et al.) 14 October 2004 See paragraphs [0043], [0061], [0093]; claims 1-18; figure 1.	1-10
A	US 5882465 A (MCREYNOLDS, RICHARD J.) 16 March 1999 See the whole document.	1-10
A	KR 10-2012-0118680 A (INDUSTRY-UNIVERSITY COOPERATION FOUNDATION HANYANG UNIVERSITY ERICA CAMPUS) 29 October 2012 See the whole document.	1-10

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 June 2018 (29.06.2018)	**29 June 2018 (29.06.2018)**

Name and mailing address of the ISA/KR
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR2018/001700

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