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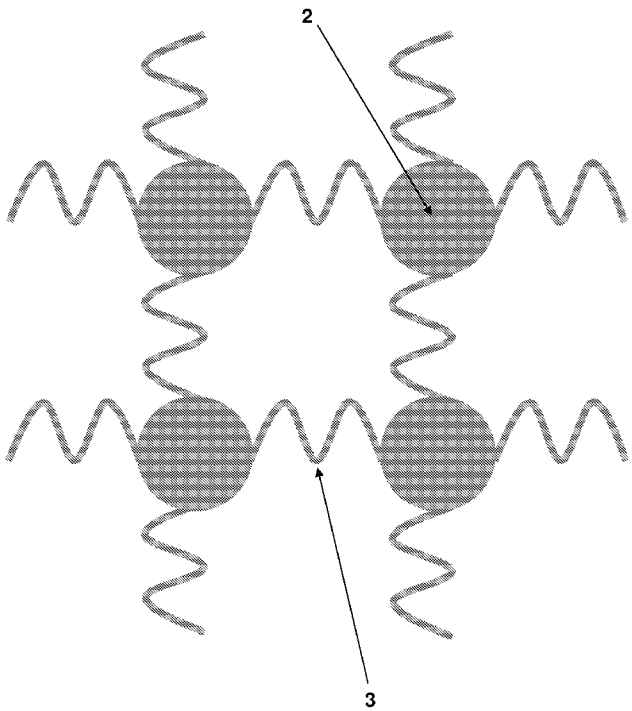
[Continued on next page]

(54) Title: OUT-OF-PLANE MICRONEEDLE MANUFACTURING PROCESS

FIGURE 7



(57) Abstract: Out-of-plane microneedle manufacturing process comprising the simultaneous creation of a network of microneedles and the creation of a polygonal shaped hat (2) above each microneedle (1) under formation, said process comprising the following steps : providing bridges (3) between the hats (3), maintaining the bridges (3) during the remaining microneedle manufacturing steps, removing the bridges (3), together with the hats (2), when the microneedles (1) are formed.

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OUT-OF-PLANE MICRONEEDLE MANUFACTURING PROCESS

Field of invention

The present invention relates to microneedles which are manufactured from a wafer, for instance a silicon wafer. The microneedles according to the invention may advantageously be used in the medical field, for intradermally administering a fluid in the body.

State of the art

MEMS Microneedles may be classified in two groups, namely in-plane microneedles and out-of-plane microneedles. In the first group the microneedle shaft is parallel to the wafer while in the second group the shaft is perpendicular to the substrate. The out-of-plane microneedle group may itself be divided in two sub-groups, i.e. hollow microneedles and solid microneedles. The hollow microneedles have a through hole as described e.g. in patent applications WO 2002/017985 WO0217985 and WO 2003/015860. The microneedle manufacturing processes disclosed in the prior art use different designs and a combination of photolithography and etching (dry and/or wet etching) to obtain different microneedle shapes. A common feature in all those processes is the presence of a protective mask, generally made of silicon dioxide, above each microneedle under formation. This mask is commonly named “hat”.

Some problems are however observed with the state-of-the-art microneedle manufacturing processes. For instance, in the manufacture of out-of-plane microneedles, the yield is limited by the difference of silicon etch rate between the centre and the border of the wafer. Because of this difference some microneedle hats (generally at the periphery of the wafer) fall before the end of the process. The consequence is that the microneedles underneath are no longer protected and as a consequence no longer etched in a controlled manner. Problems therefore arise, in particular microneedle malformation and low production yields.

General description of the invention

The problems discussed in the previous chapter are eliminated or at least notably reduced with the microneedle manufacturing process according to the invention which is characterized by the creation of bridges which link the hats between each others as well as between hats and edges during the manufacturing process.

More exactly the invention concerns an out-of-plane microneedle manufacturing process comprising the simultaneous creation of a network of microneedles and the creation of a polygonal shaped hat above each microneedle under formation, the process comprising the following steps :

- providing bridges between the hats,
- maintaining the bridges during the remaining microneedle manufacturing steps,
- removing the bridges, together with the hats, when the microneedles are formed.

In the present text, the expression "polygonal hat" has to be understood" as a closed figure consisting of straight lines joined end to end.

A "polygonal hat" in the sense of the present text also include a circle. This object May be viewed as a polygone with straight lines tending towards zero.

Like the hats, the bridges are totally removed at the end of the manufacturing process and result in no modification of the microneedle design.

The bridges are preferably made of suspended structures.

They have a design which is compatible with the materials of the suspended structures and the microneedle fabrication process.

The bridges may have many different designs.

In one embodiment they are rectilinear.

In another embodiment they comprise a curved portion.

Advantageously, each bridge consists of a combination of rectilinear segments and of circle portions, e.g. of ½ and ¼ circles.

The bridge dimensions can vary depending on the distance between the microneedles as well as the distance between the microneedles and the edge of the wafer. The thickness of the bridges which is linked to the thickness of the hats can vary between 100nm and 100um: The width of the bridges can vary between 1um and 100um.

Moreover certain physical properties such as the mechanical resistance are affected by the size and shape of the bridges.

The material used must have the appropriate characteristics to support the manufacturing process. For example, for a process requiring an excellent conductivity, metal would be chosen.

Multilayered bridges, in particular with three layers, offer an interesting compromise when different properties are required as for example good conductivity, high selectivity and mechanical resistance to deformation.

Detailed description of the invention

The invention is discussed below in a more detailed way with examples illustrated by the following figures :

Figure 1 shows a microneedle manufacturing process according to the state of the art.

Figure 2 shows a microneedle manufacturing process according to the invention.

Figure 3 is an upper view of the element shown in figure 2.

Figure 4 is a picture of an assembly microneedle-hat according to the state of the art (without bridges)

Figure 5 shows one example of bridges according to the invention.

Figure 6 shows another example of bridges according to the invention.

Figure 7 shows another example of bridges according to the invention.

Figure 8 shows another example of a bridges according to the invention.

Figure 9 is a picture of the example shown on figure 5.

Figure 10 is a picture of microneedles with hats and bridges before removal (status before figure 11)

Figure 11 is a picture of a microneedle obtained with a process according to the invention.

Numerical references used in the figures

1. Microneedle
2. Hat
3. Bridge
4. Wafer
5. Damaged area
6. Rectilinear segment
7. ½ circle
8. ¼ circle
9. Metal layer
10. SiO_2 layer

State of the art MEMS microneedle fabrication process as described in Fig. 1 usually starts with a wafer, preferably a silicon wafer **4**. On top of this silicon wafer a silicon dioxide layer is used as a protective mask to pattern the microneedles.

This process aims at obtaining microneedles separated from each others and as a consequence the continuous protective mask in step A becomes discontinue at the start of the structuration of the microneedles step B. The parts of this

discontinuous protective mask are called hats **2** and each microneedle is overlooked by a hat, protecting the microneedle and allowing controlled and well defined structuration. Figure 4 shows an example of a microneedle creation **1** under a hat **2**.

This structuration of the microneedles is performed by a sequence of isotropic and anisotropic etches as represented in Fig 1 steps B to E.
The first isotropic etch as represented in Fig 1 step B initiates the tip of the microneedle. The first anisotropic etch (Fig. 1, step C) is used to define the head of the microneedle.
The goal of the second isotropic etch as represented in Fig 1 step D is to initiate the shoulder of the microneedle and to separate the head of the microneedle with the shaft which is obtain thanks to the second anisotropic etch (Fig.1, step E).
Finally comes the last isotropic etch (Fig. 1, step F) which is the most important etch of the process. Thanks to this etch, we pattern the tip of the microneedle, the backside trough holes and the final design of the microneedle,
An oxidation and a silicon oxide etch as represented in Fig.1, step G are then realized to remove the hats and to polish the silicon surface.

Frequently hats may fall before the end of the process (Fig. 1, step F, Ref. 2): This leads to a situation in which the structuration of the microneedle becomes uncontrolled resulting in malformation and low production yields. In addition the fallen hats provoke a bad surface state as shown in Fig. 1 Ref 5.

The present invention provides a way to hold the hats together so that they won't fall before the end of the process. To this effect the hats are linked together and are linked to the edges as displayed in Fig 3. These links (Fig. 2, Ref 3), also named bridges in the present text, will stay in place up to the end of the process and guarantee the stability of each hat until the microneedle fabrication is ended (Fig.2 Step F). When the process has been completed (Fig.1 step G) the hat and

their links are removed revealing perfect microneedles pattern (see e.g. Fig. 11) and chip surface state.

An important advantage of these links is that they do not modify the microneedle structuration parameters. The isotropic and anisotropic etches are the same with or without links.

As described earlier bridges and hats are deeply linked together; as a matter of fact their are made of same materials and have the same thickness.

As far as the design of the bridges is concerned it can take many forms. Simple linear bridge between the hats can be an option as shown schematically in Fig. 5 and on the picture in Fig 9 which represents microneedle process of step B in Fig. 1.

Curved segments as in Fig. 6 and Fig. 7 or combination of rectilinear and curved segments as in Fig. 8 are also possible.

Another aspect of the design of the bridges is the material. Single layer bridges can be appropriate for many processes but depending on the complexity of the process and also on the cleaning steps multilayer bridges can be a better option. Multilayered bridges improve the characteristics of the bridges (Fig. 10). We may associate metal layers (aluminium, tungsten, nickel...) and no conductive layers (silicon dioxide, silicon nitride…). The metal layers improve the thermal conductivity of the bridges and the non conductive layers improve the mechanical resistance and the high selectivity of the bridges.

Claims

1. Out-of-plane microneedle manufacturing process comprising the simultaneous creation of a network of microneedles and the creation of a polygonal shaped hat (2) above each microneedle (1) under formation, said process comprising the following steps :
   - providing bridges (3) between the hats (3),
   - maintaining the bridges (3) during the remaining microneedle manufacturing steps,
   - removing the bridges (3), together with the hats (2), when the microneedles (1) are formed.

2. Process according to claim 1 wherein the bridges (3) are formed simultaneously with the hat formation.

3. Process according to claim 1 or 2 wherein the bridges (3) are made with several layers.

4. Process according to anyone of the previous claims including at least one step for providing a conduit within the microneedles (1).

5. Suspended structure made of hats (2) and bridges (3) in accordance with the process of anyone of the previous claims.

6. Suspended structure according to claim 5 wherein the bridges (3) are multilayered.

7. Suspended structure according to claim 6 wherein the bridges (3) are made of three layers, namely one conductive layer comprised between two non conductive layers.

8. Suspended structure according to claim 7 wherein the conductive layer is made of aluminum and the non conductive layers are made of silicon dioxide.

9. Suspended structure according to anyone of claims 5 to 8 wherein the bridges (3) are rectilinear.

10. Suspended structure according to anyone of claims 5 to 8 wherein the bridges (3) are at least partially curved.

11. Suspended structure according to claim 8 wherein each bridge (3) is made of a combination of rectilinear segments and of circle portions such as ½ circles and ¼ circles.

12. A microneedle assembly manufactured from the same wafer (4) and obtained according to a process according to anyone of claims 1 to 4.

FIGURE 1

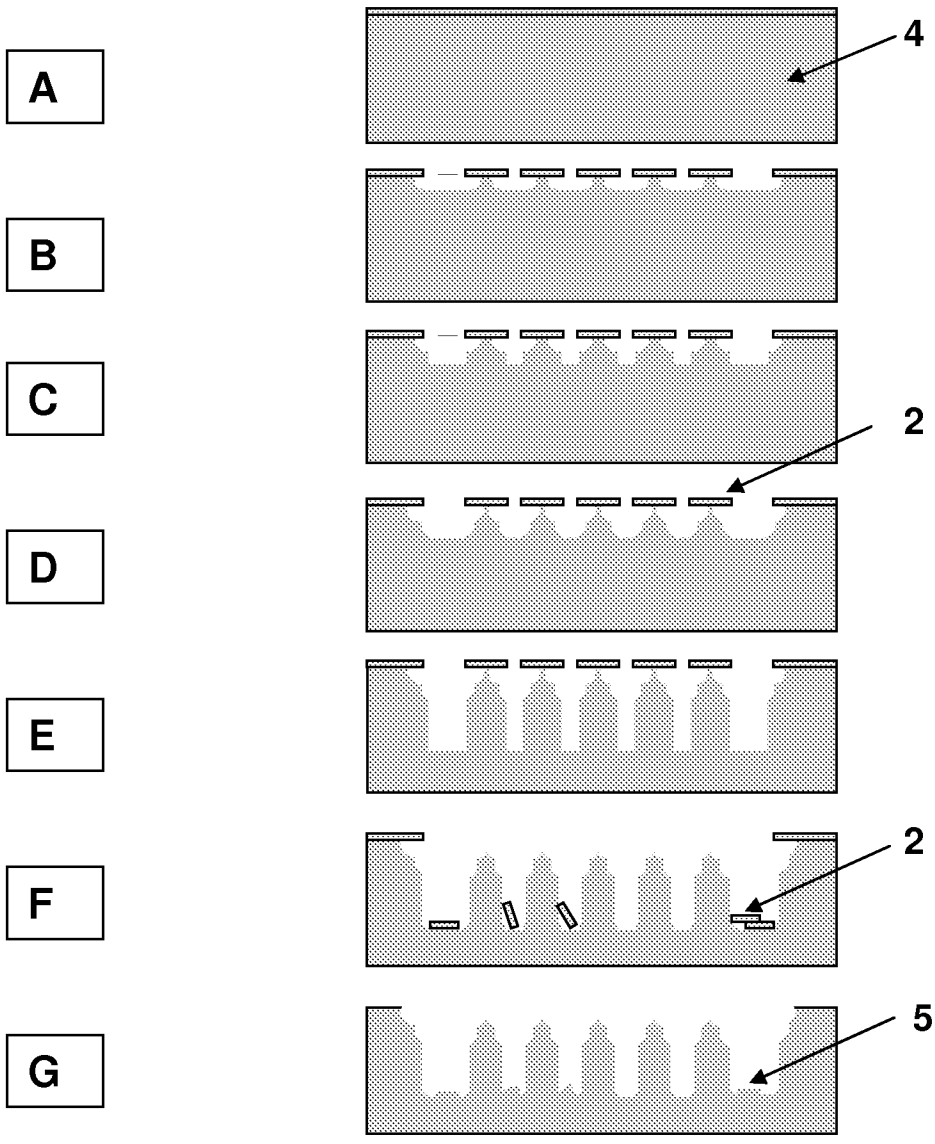


FIGURE 2 (AA')

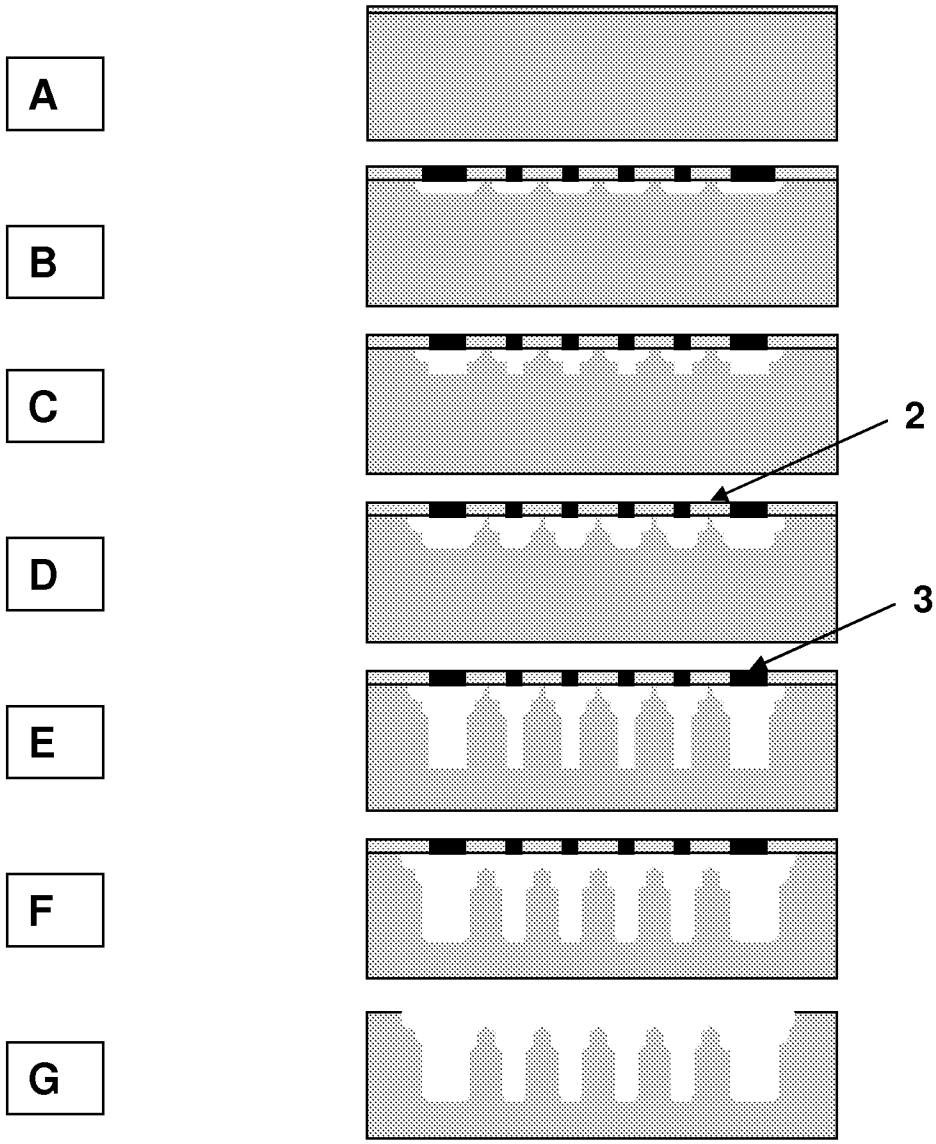


FIGURE 3

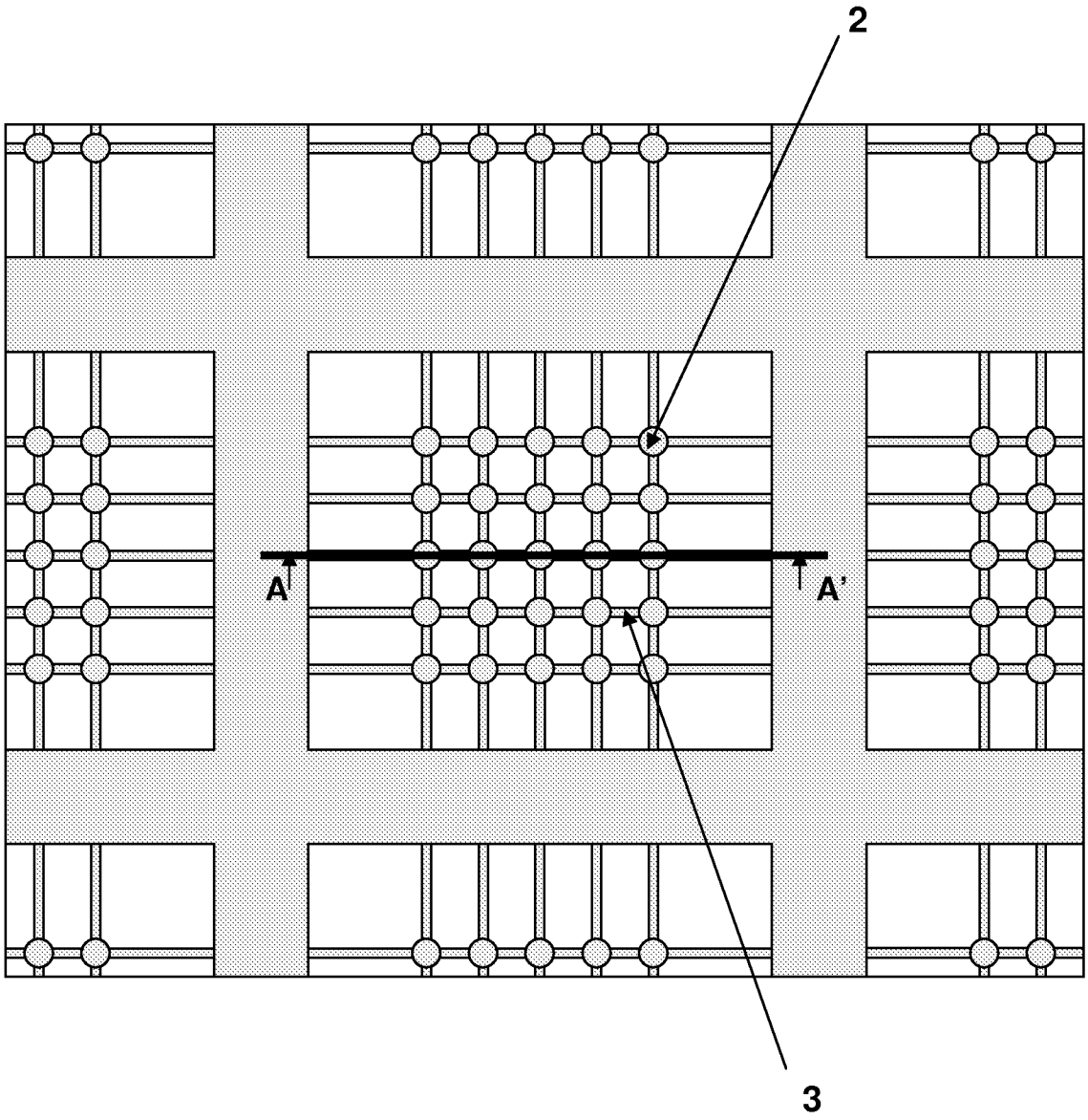


FIGURE 4

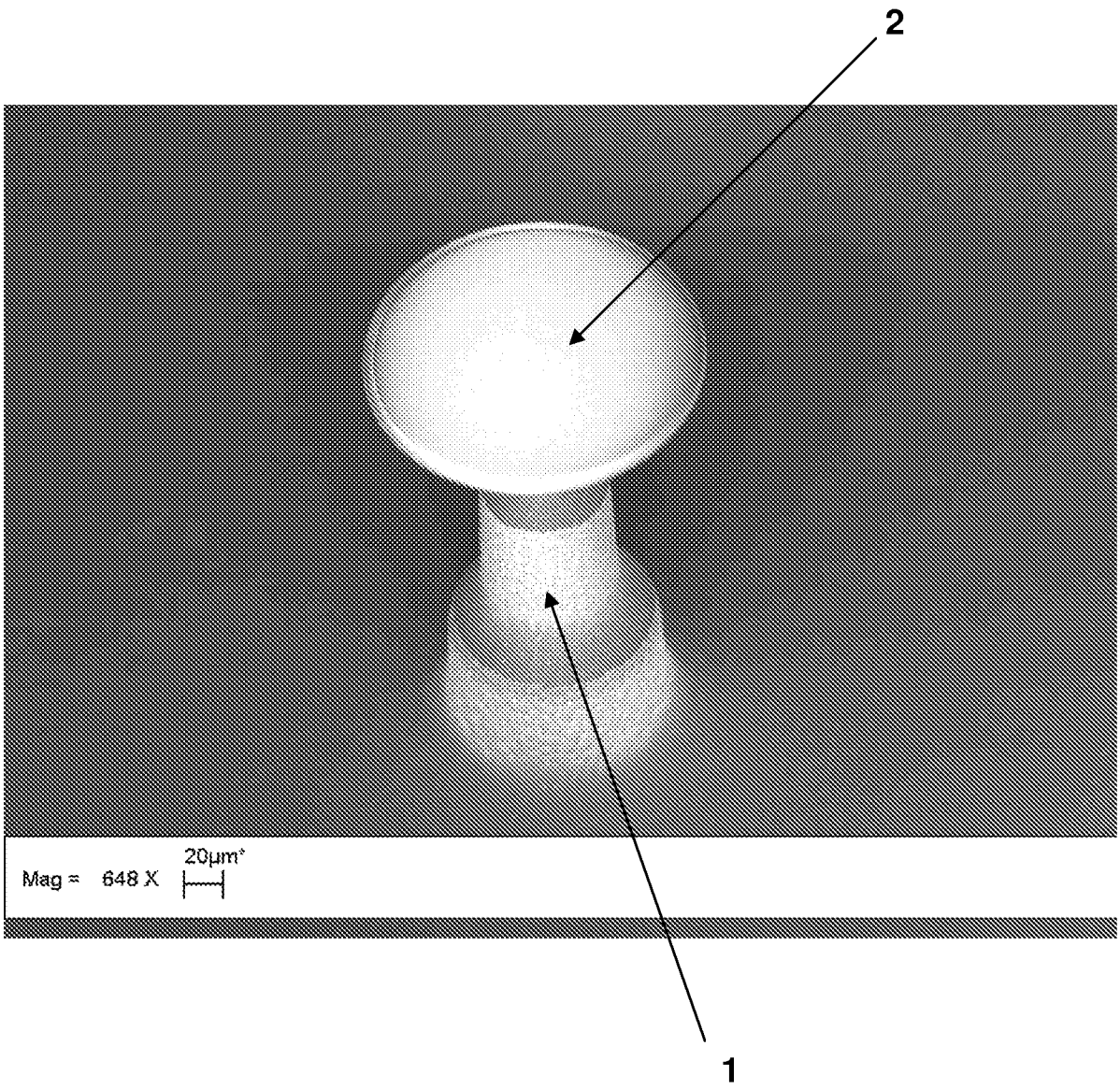


FIGURE 5

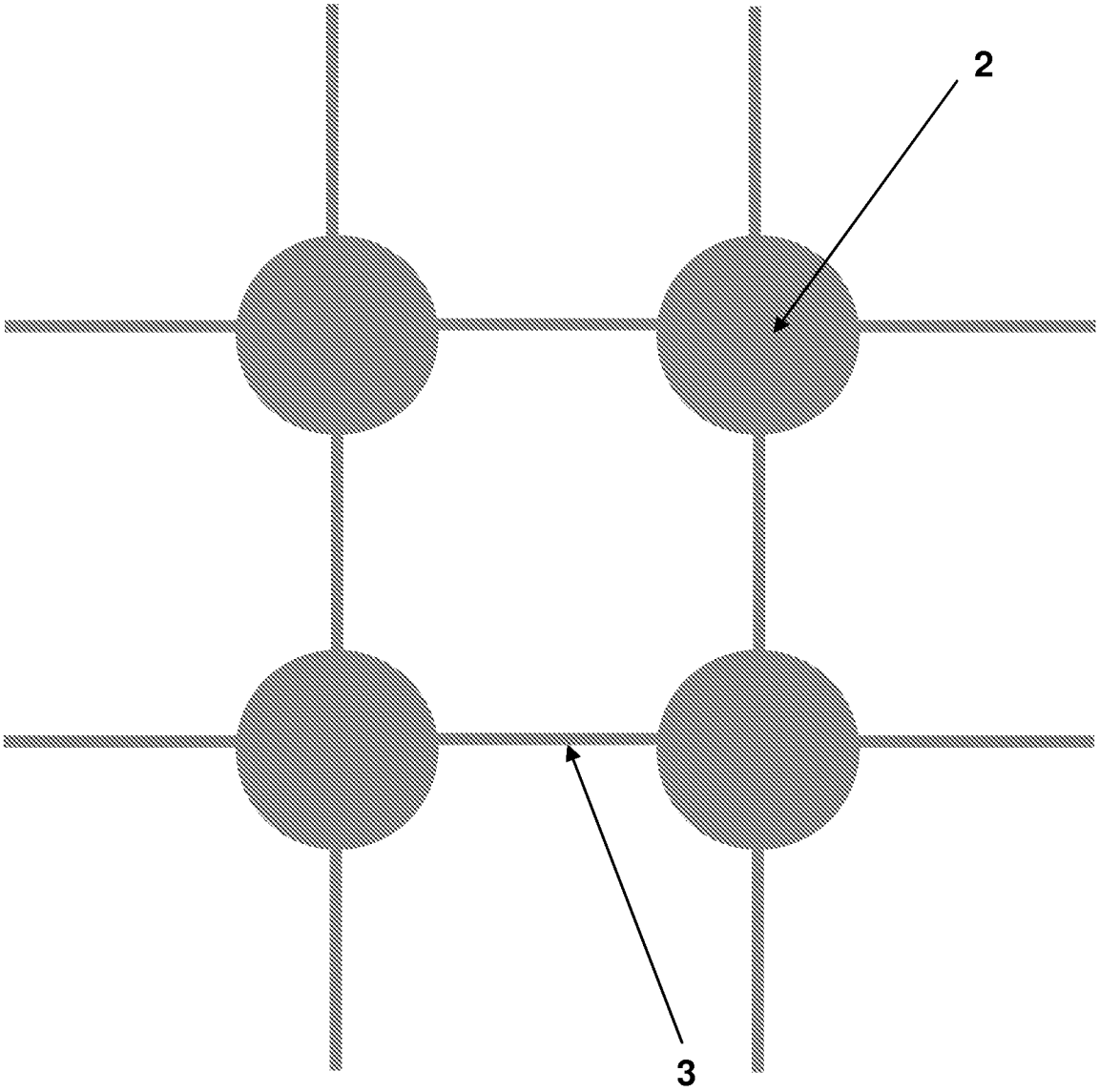


FIGURE 6

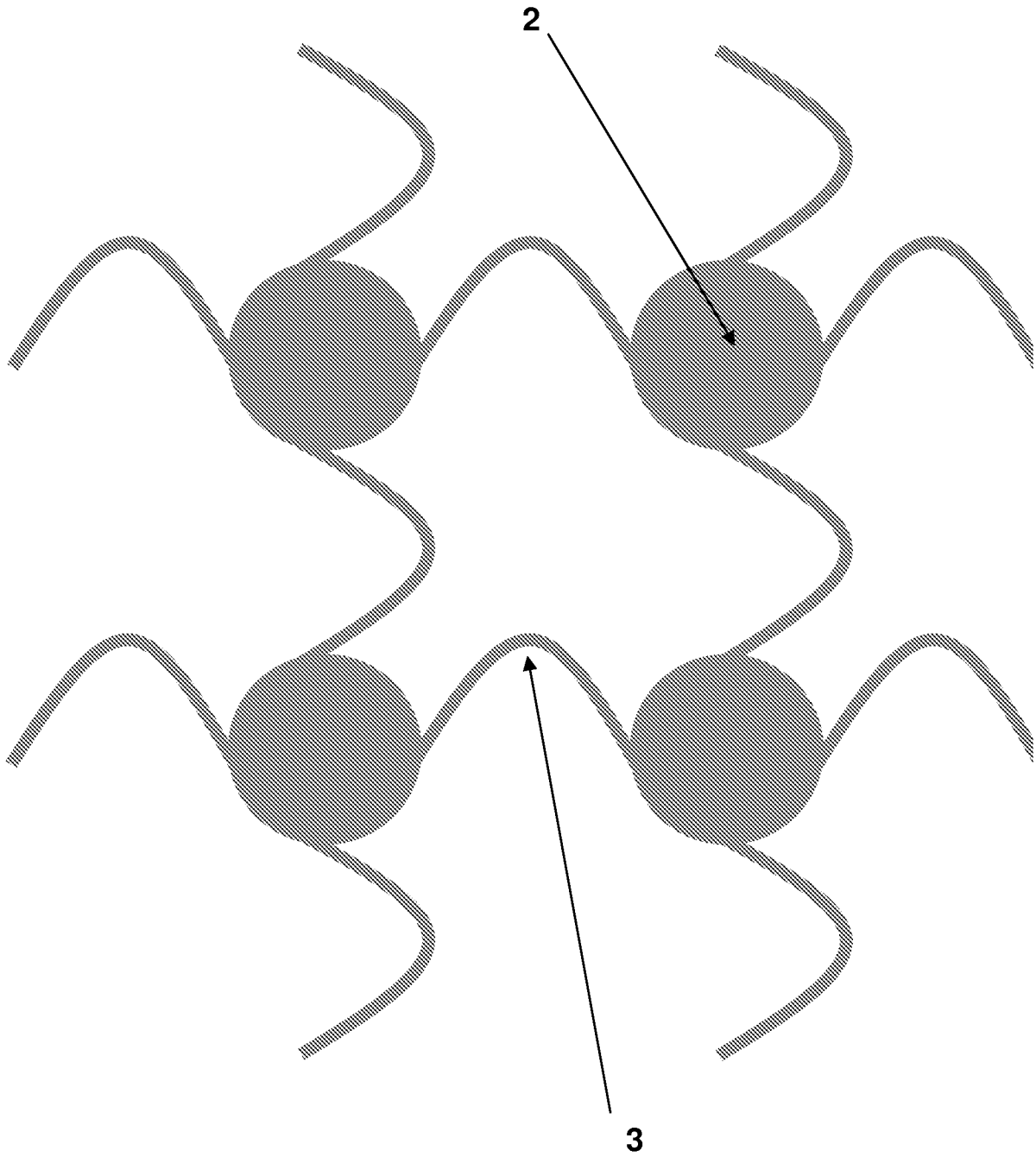


FIGURE 7

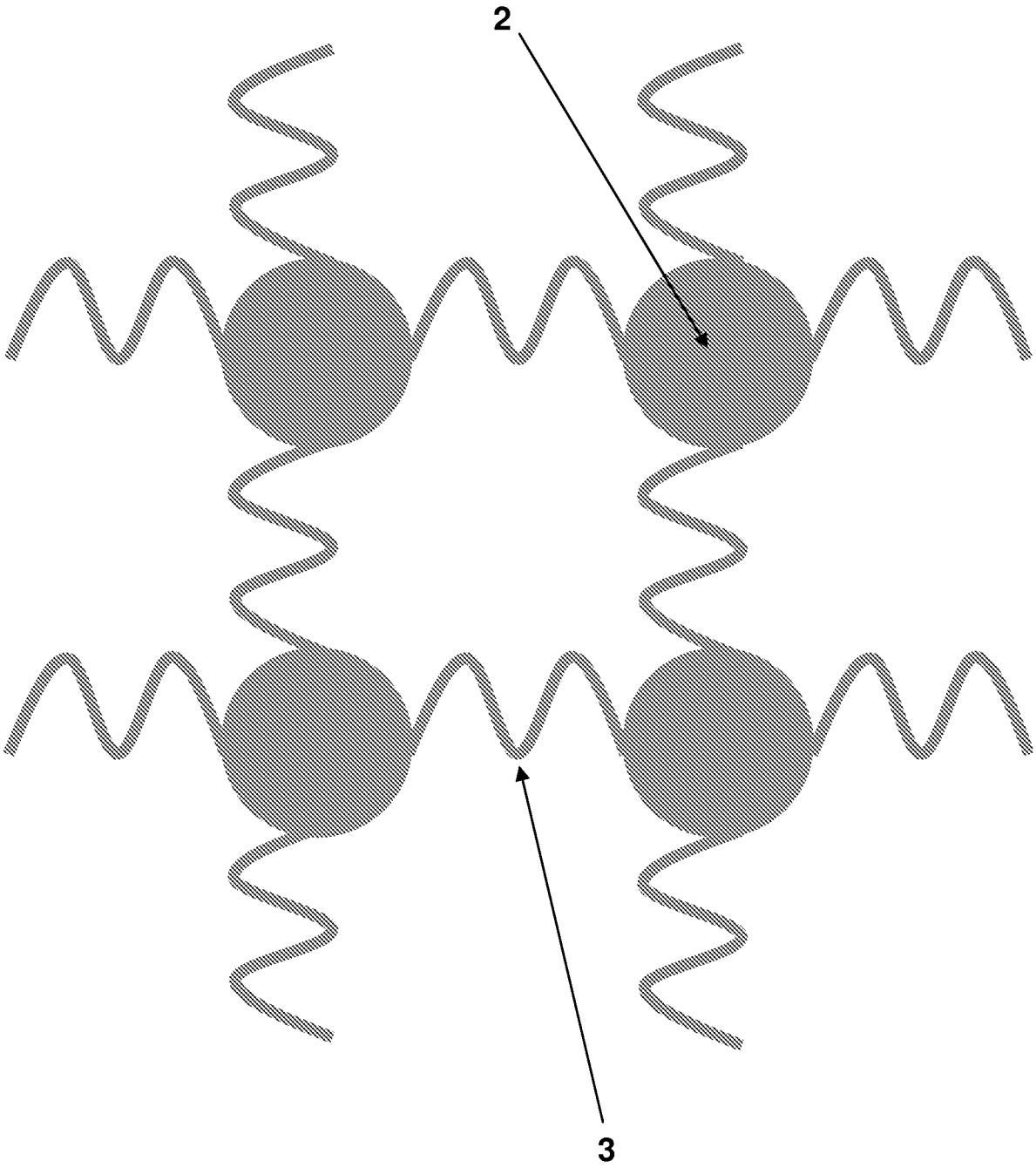


FIGURE 8

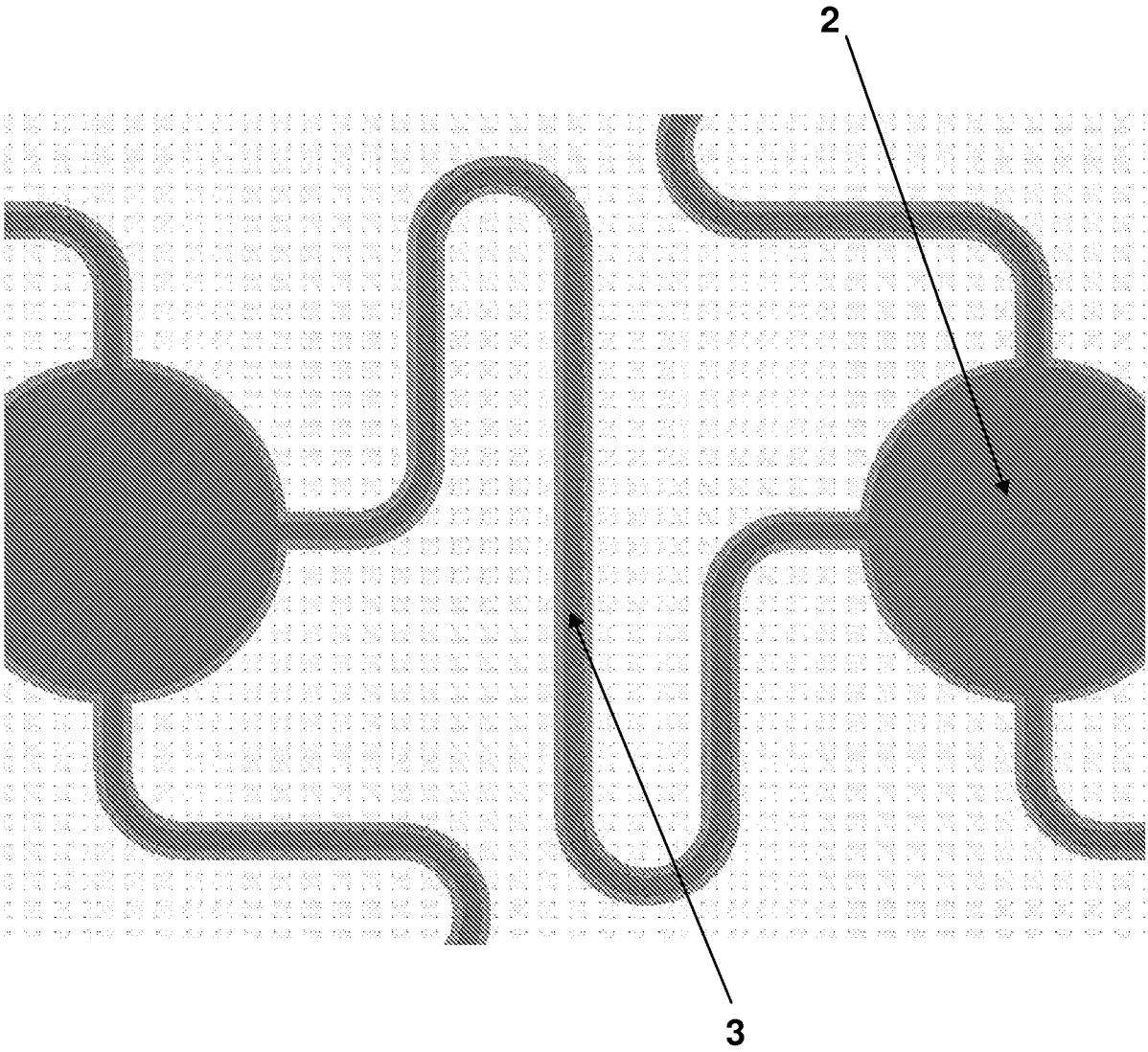


FIGURE 9

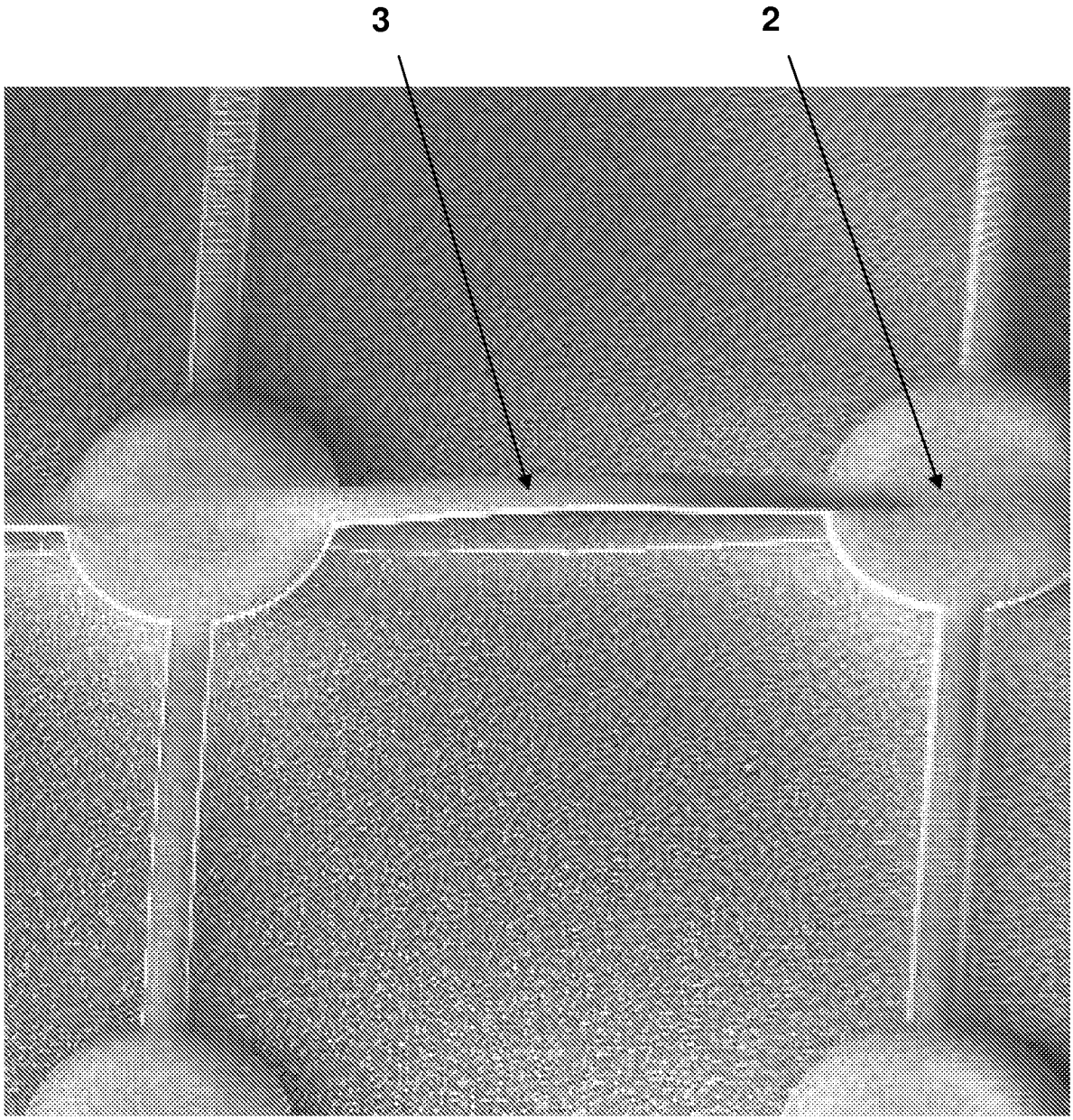


FIGURE 10

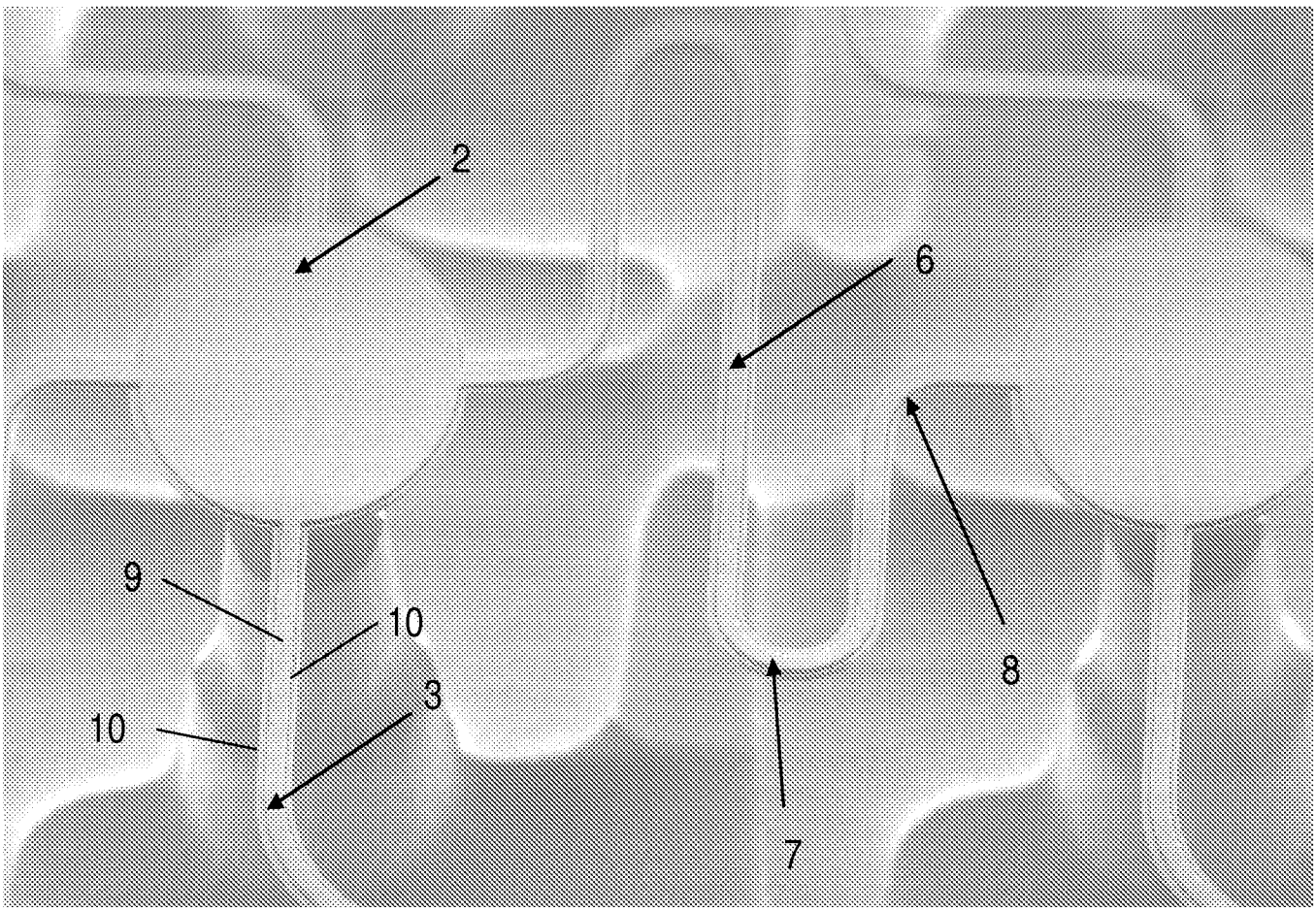
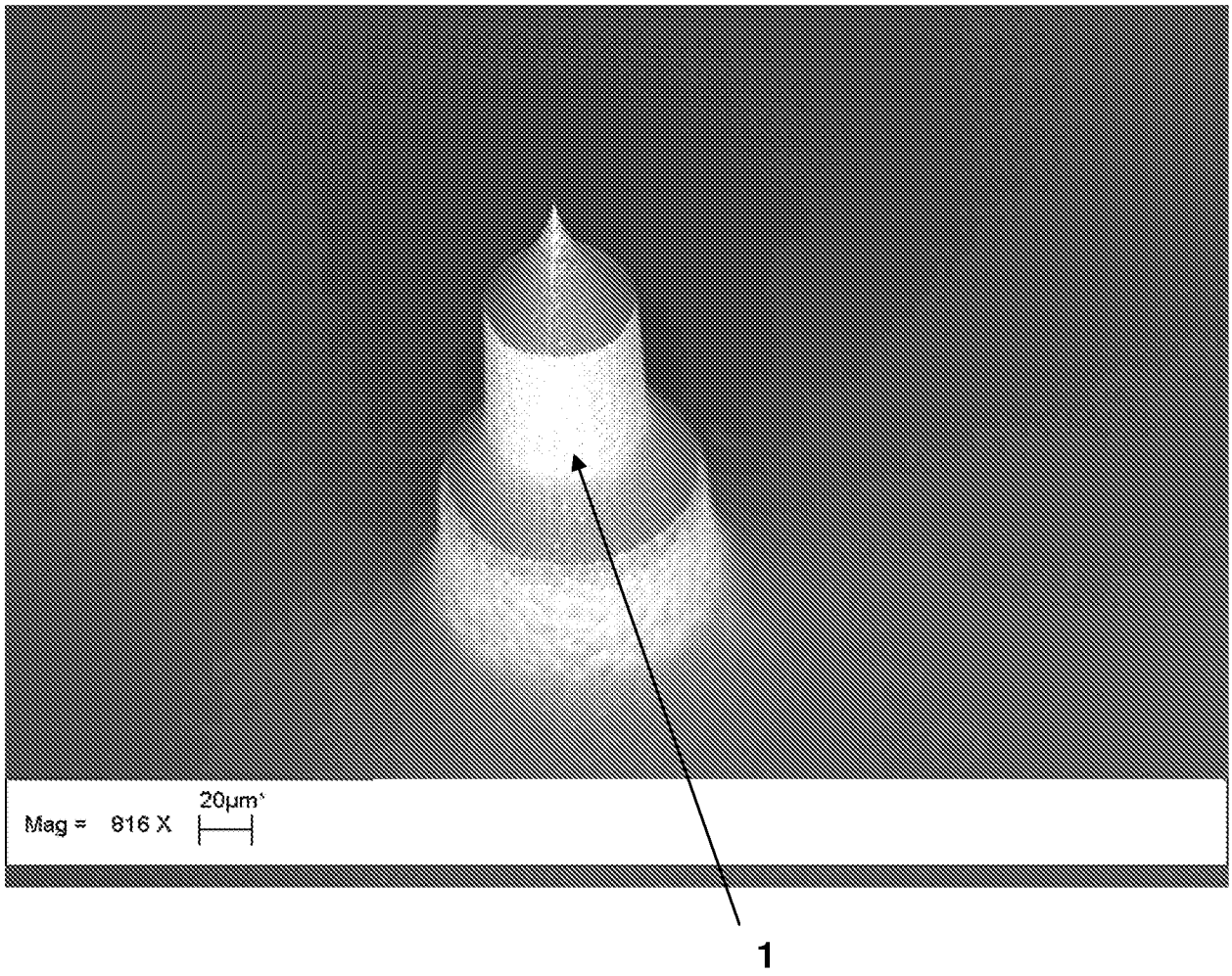


FIGURE 11



INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2008/054280

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M37/00 B81C1/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M B81C G03F

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	EP 0 597 302 A (RICOH SEIKI CO LTD [JP]) 18 May 1994 (1994-05-18) column 4, line 49 - column 6, line 5; figures 2A-2E	1,2,4,5
P,X	WO 2008/003564 A (BOSCH GMBH ROBERT [US]; STUMBER MICHAEL [DE]; REICHENBACH RALF [DE]; F) 10 January 2008 (2008-01-10) the whole document	1-7,12

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

[X] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
5 May 2009	13/05/2009

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2008/054280

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 03/015860 A (BONSENS AB [SE]; STEMME GOERAN [SE]; GRISS PATRICK [SE]) 27 February 2003 (2003-02-27) cited in the application the whole document	1-12
A	LANG W: "Silicon microstructuring technology" MATERIALS SCIENCE AND ENGINEERING R: REPORTS, ELSEVIER SEQUOIA S.A., LAUSANNE, CH, vol. 17, no. 1, 1 September 1996 (1996-09-01), pages 1-55, XP004013096 ISSN: 0927-796X the whole document	1-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

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