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(54) **MICRONEEDLE ARRAY DEVICE AND ITS FABRICATION METHOD**

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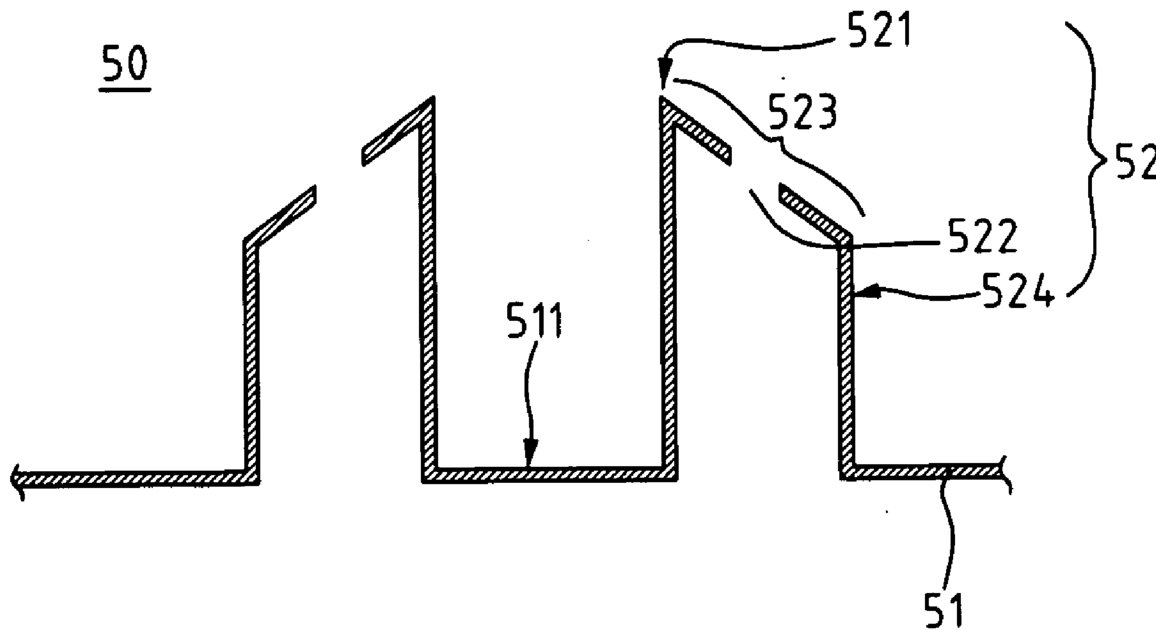
(57) **ABSTRACT**

A microneedle array device and its fabrication method are provided. The microneedle array device comprises a supporting pad and plural of microneedles. Each microneedle has a top portion with a via thereon, thereby the microfluid may flow in or out. The intersection between the top portion and the inner tube of a microneedle forms a convex needle structure, and is almost perpendicular to the upper surface. For each microneedle, a hollow closed tube is formed between the top portion and the supporting pad. The fabrication method uses the substrates with high transmittance and plural of convex area thereon as the upper and lower caps, and applies a photolithography process to fabricate a microneedle array mold. It then sputters or electroplates metal material on the mold. The microneedle array is formed after having taken off the mold. It is a simple fabrication process.



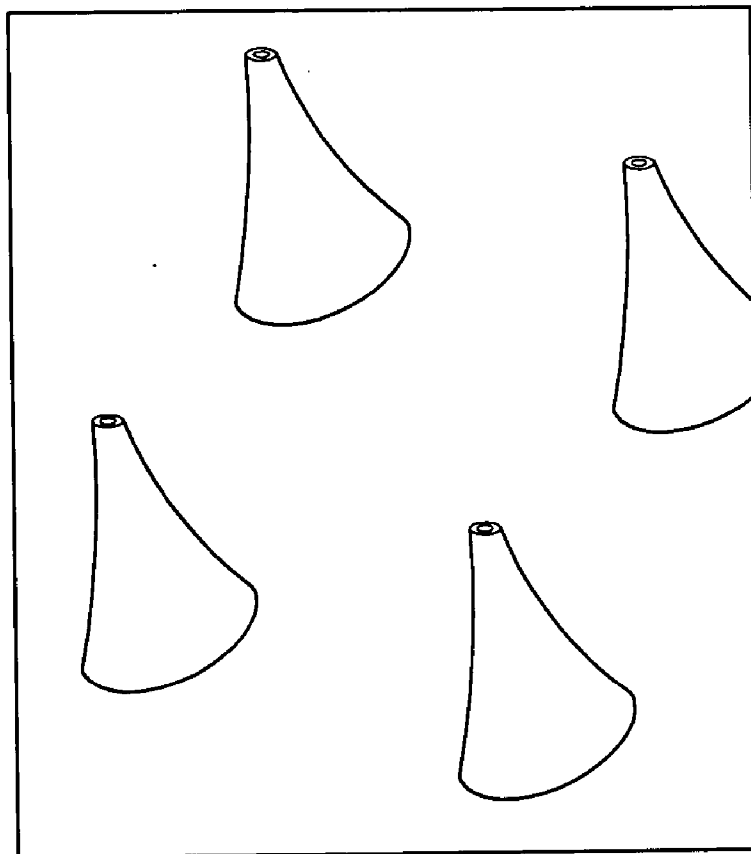


FIG. 1

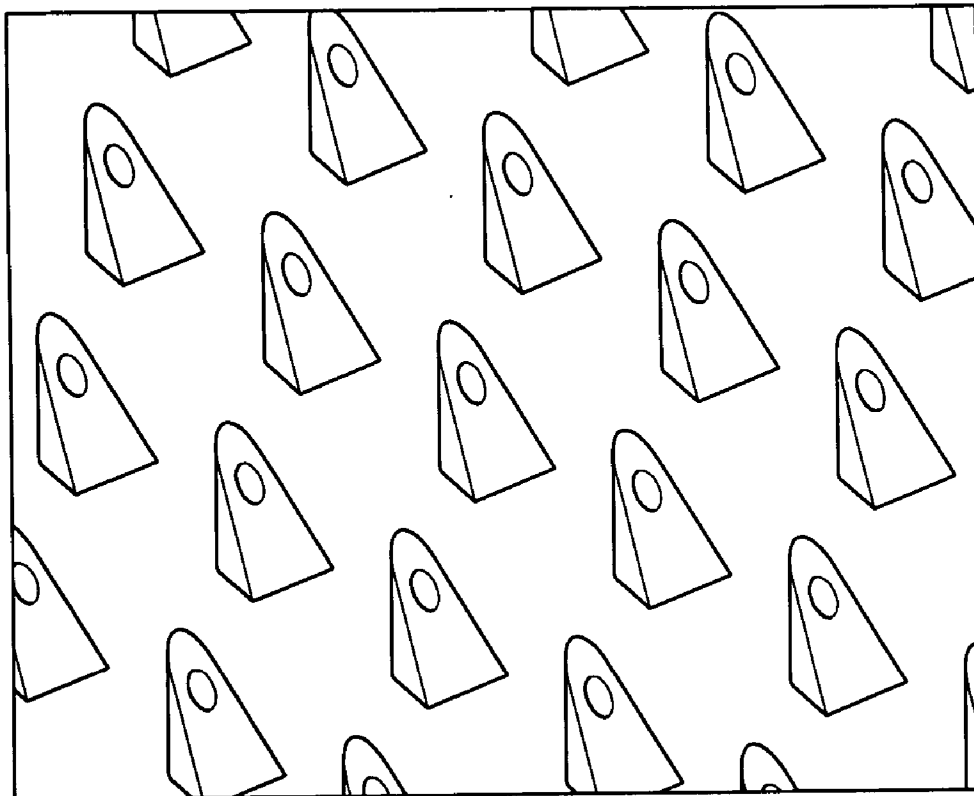


FIG. 2

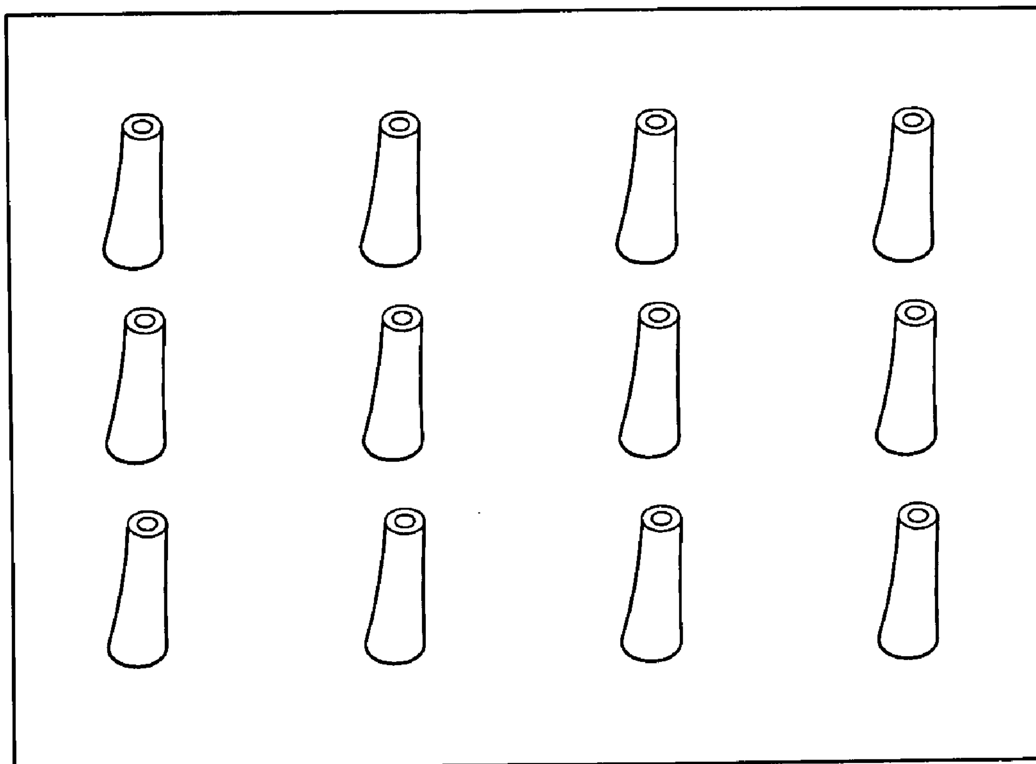


FIG. 3

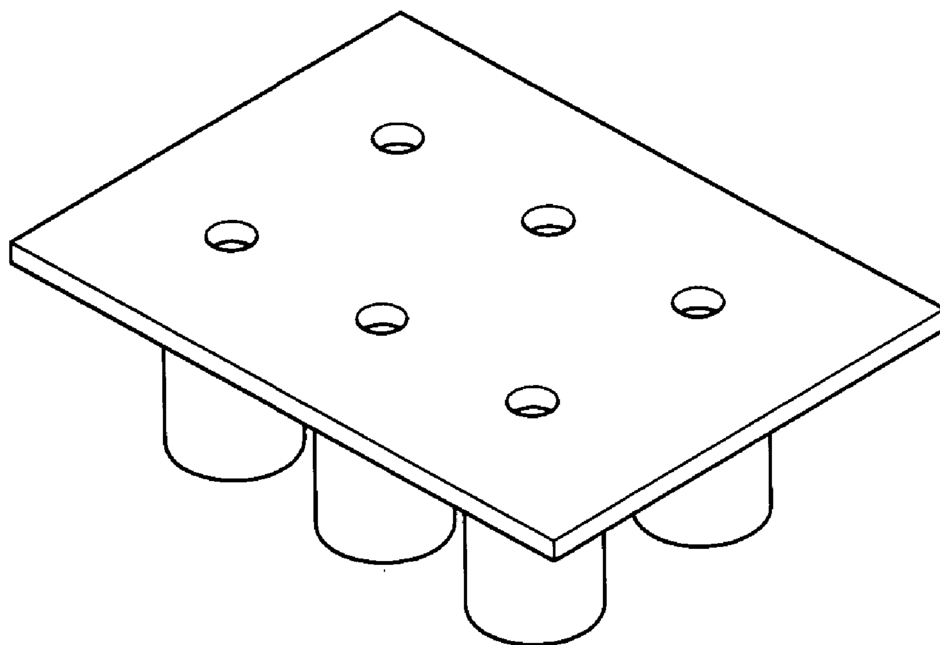


FIG. 4

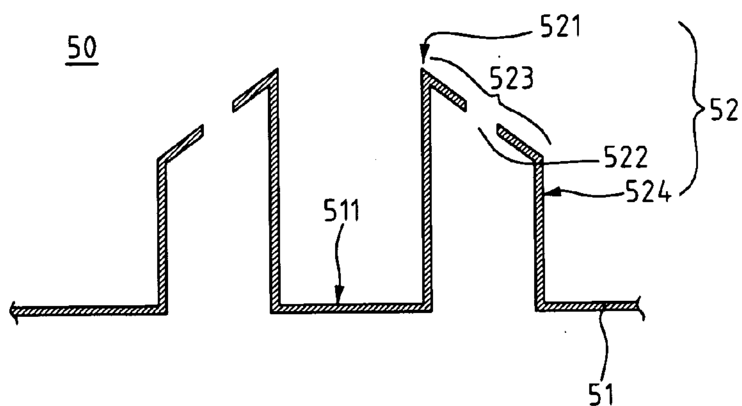


FIG. 5A

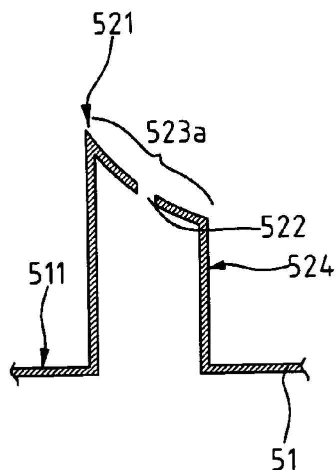


FIG. 5B

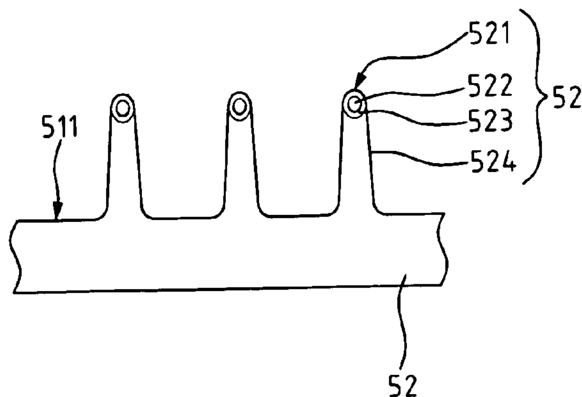


FIG. 5C

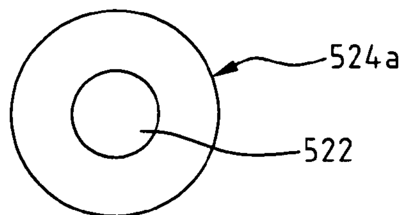


FIG. 6A

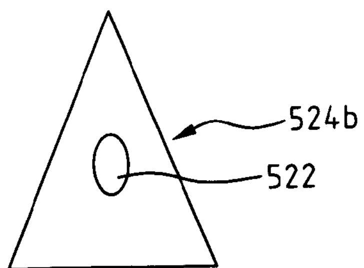


FIG. 6B

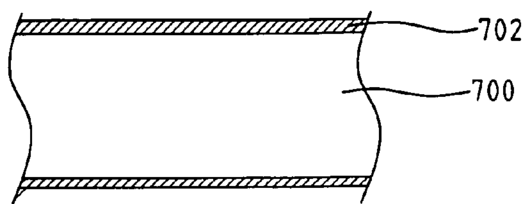


FIG. 7A

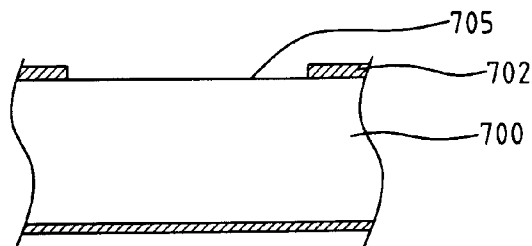


FIG. 7B

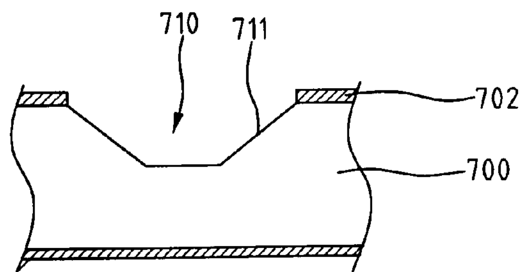


FIG. 7C

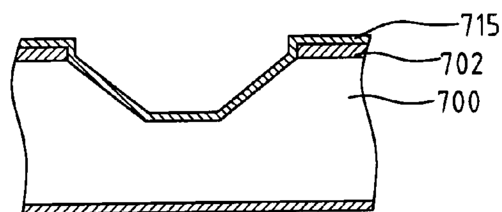


FIG. 7D

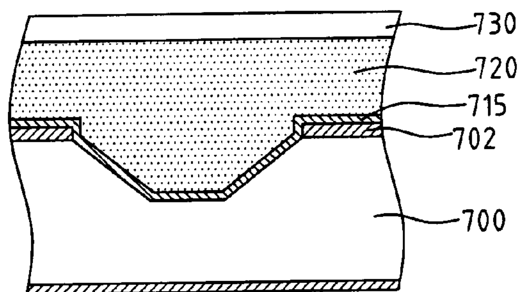


FIG. 7E

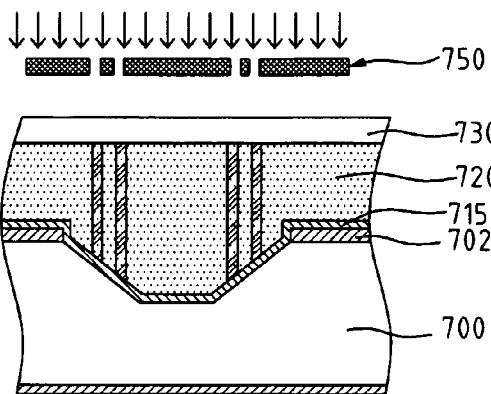


FIG. 7F

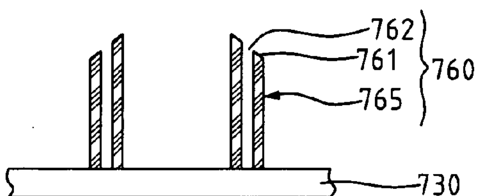


FIG. 7G

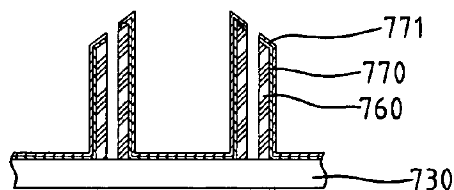


FIG. 7H

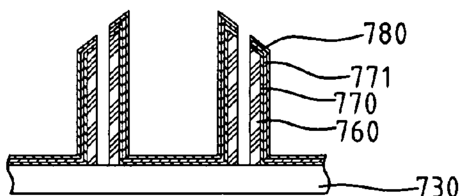


FIG. 7I

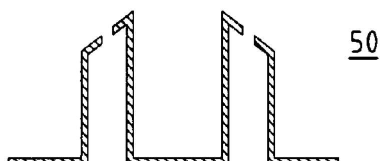


FIG. 7J

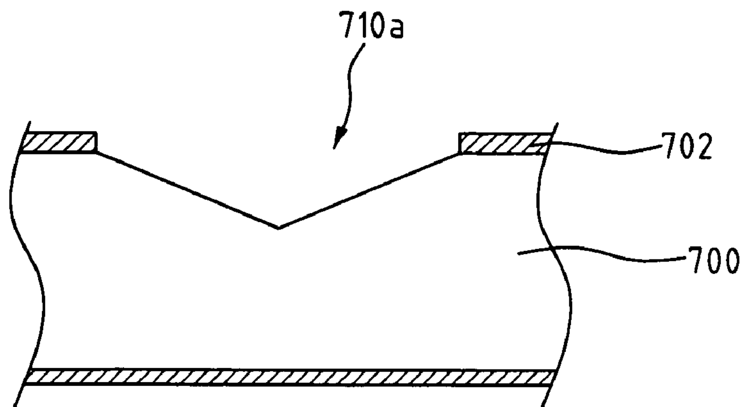


FIG. 8A

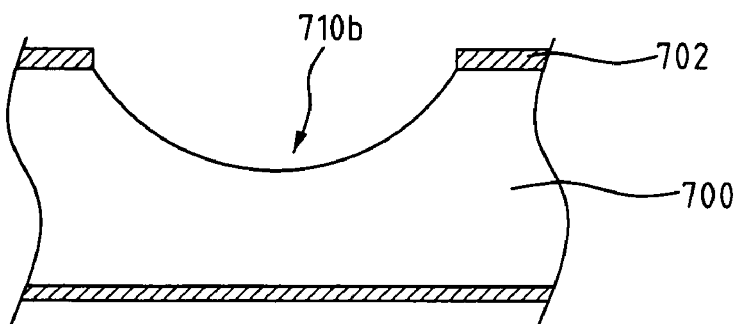


FIG. 8B

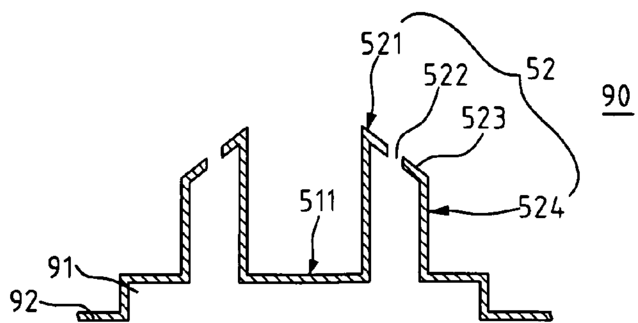


FIG. 9A

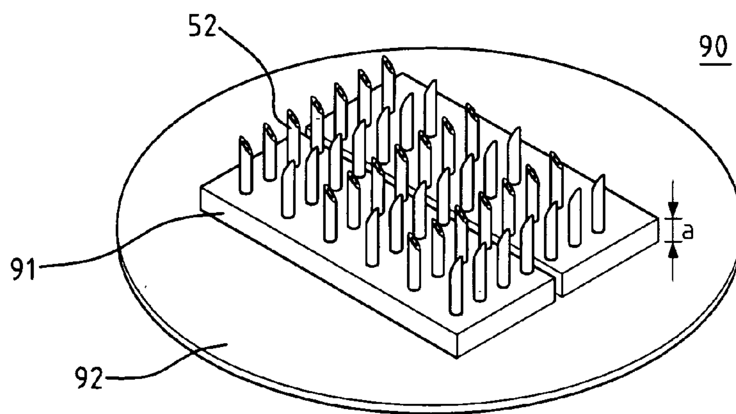


FIG. 9B

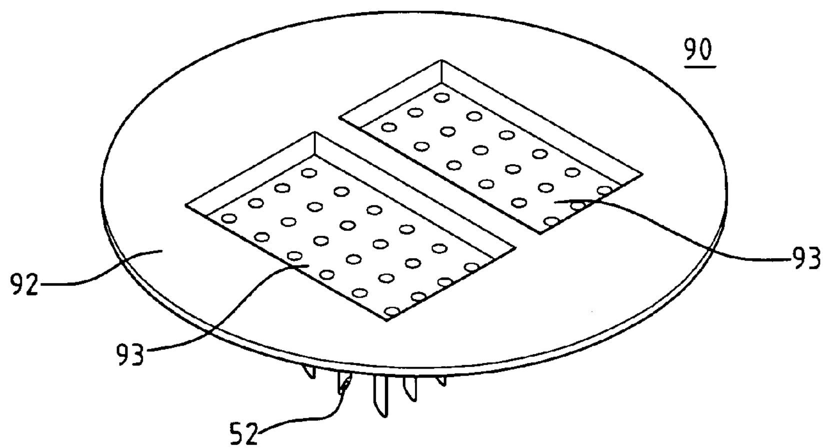


FIG. 9C

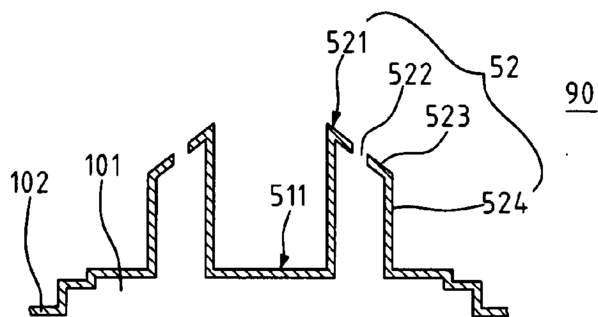


FIG. 10A

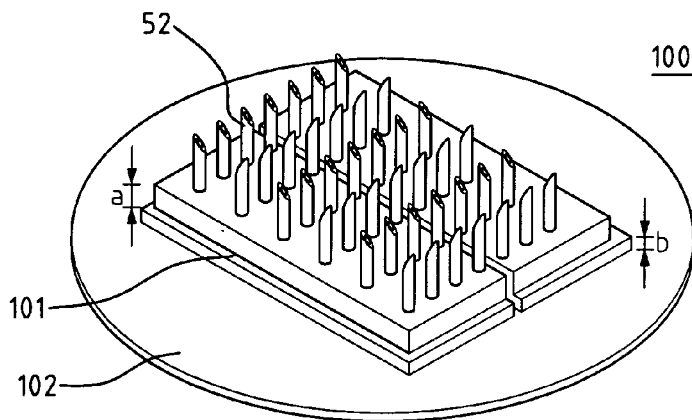


FIG. 10B

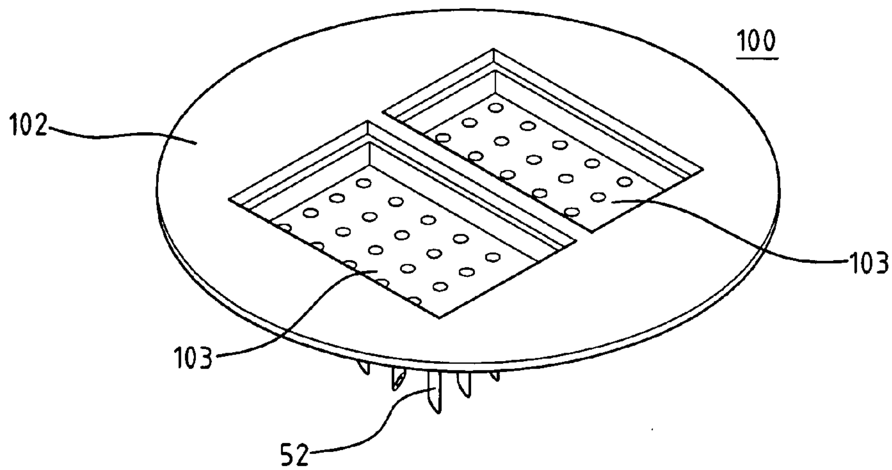


FIG. 10C

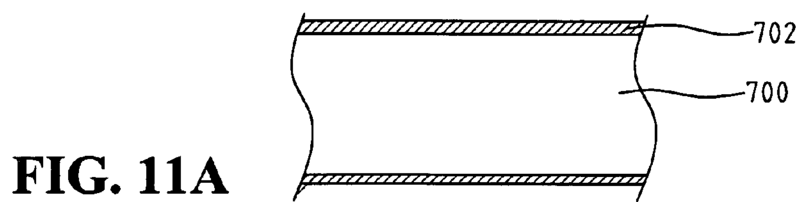


FIG. 11A

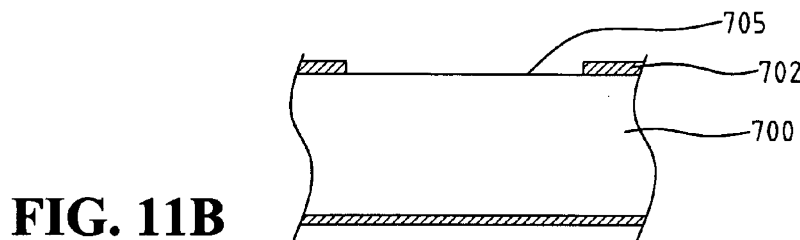


FIG. 11B

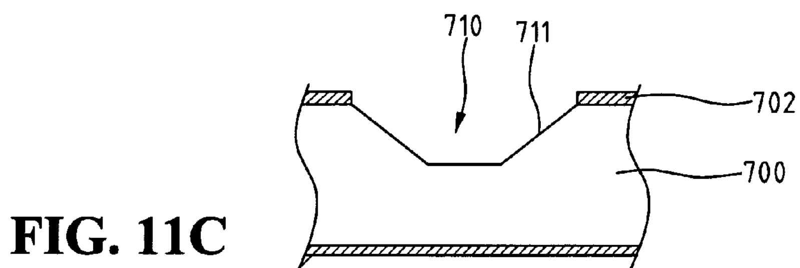


FIG. 11C

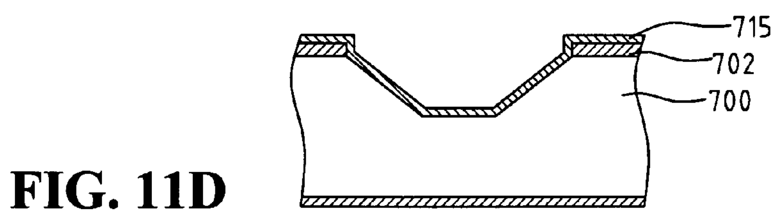


FIG. 11D

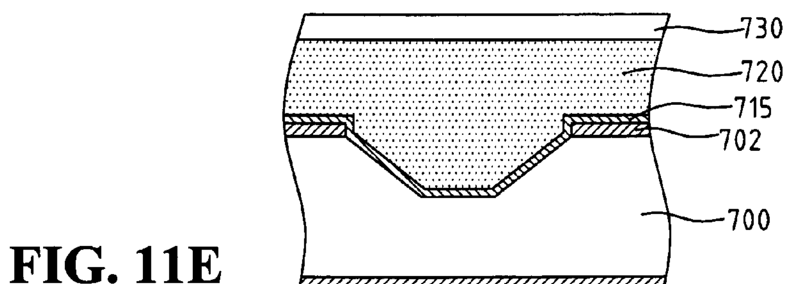


FIG. 11E

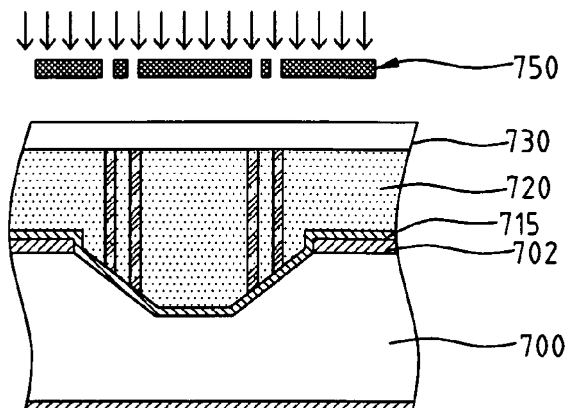


FIG. 11F

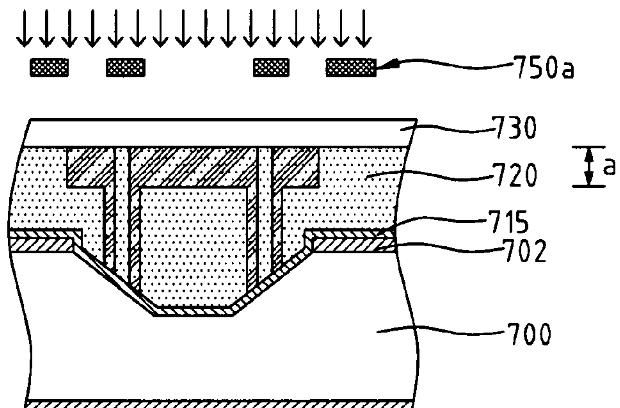


FIG. 11G

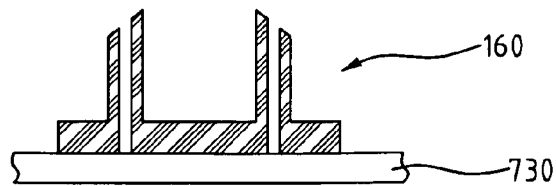


FIG. 11H

FIG. 11I

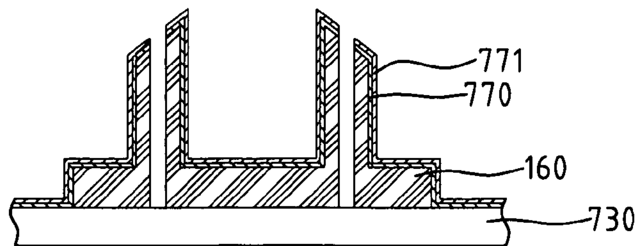


FIG. 11J

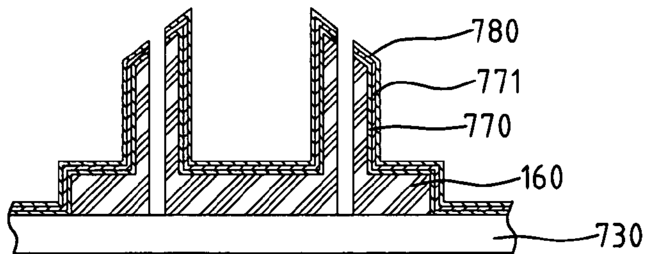
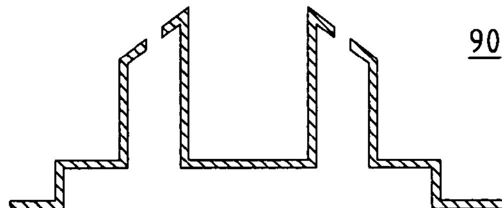


FIG. 11K



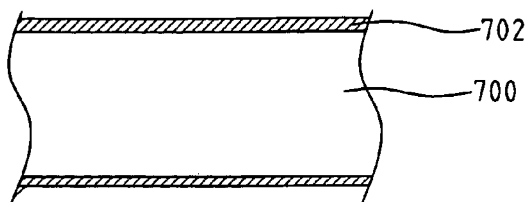


FIG. 12A

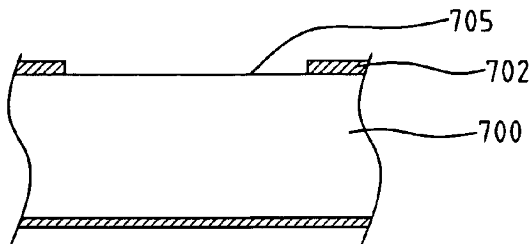


FIG. 12B

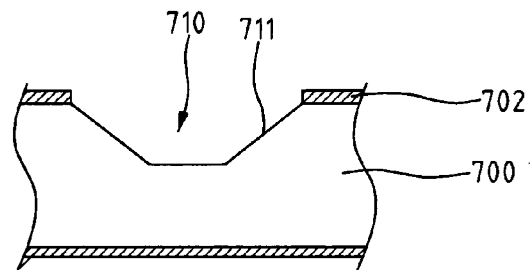


FIG. 12C

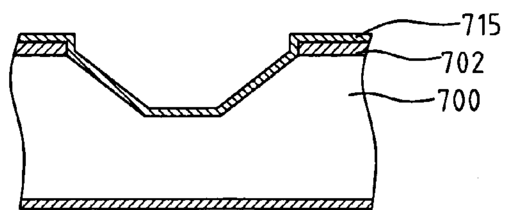


FIG. 12D

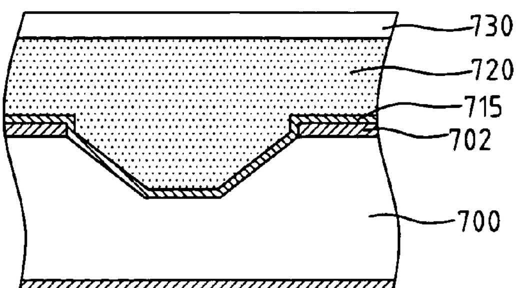


FIG. 12E

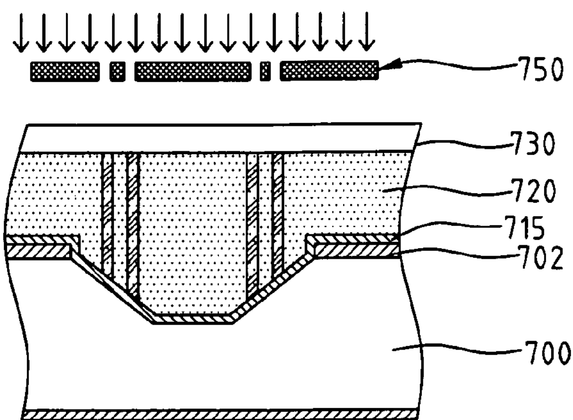


FIG. 12F

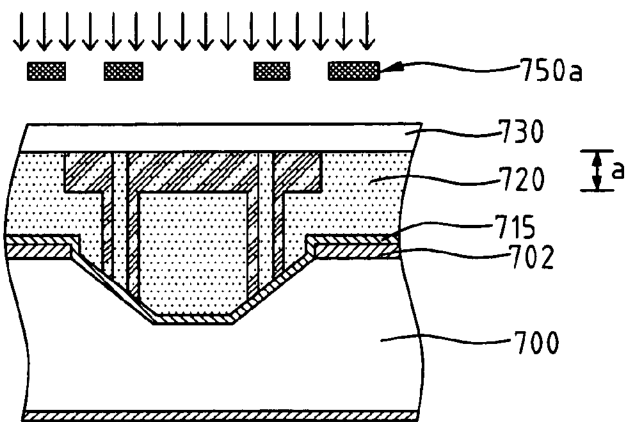


FIG. 12G

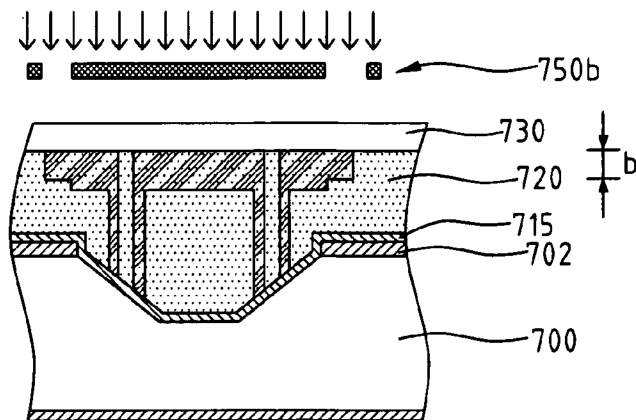


FIG. 12H

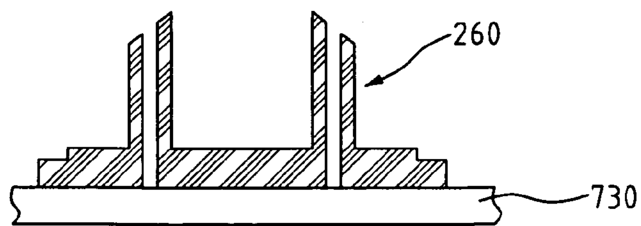


FIG. 12I

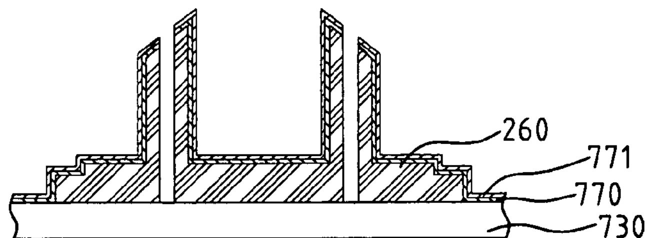


FIG. 12J

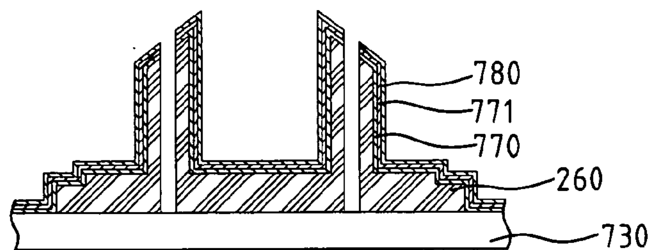


FIG. 12K

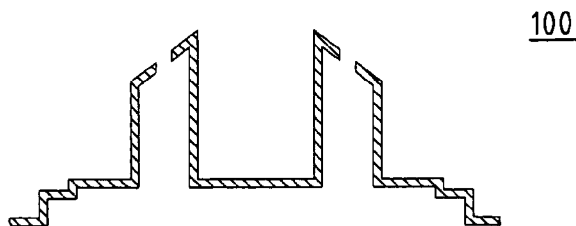


FIG. 12L

MICRONEEDLE ARRAY DEVICE AND ITS FABRICATION METHOD

FIELD OF THE INVENTION

[0001] The present invention generally relates to a microneedle array structure, and more specifically to a microneedle array device, and a method of forming the same.

BACKGROUND OF THE INVENTION

[0002] The current microneedle array may be made of silicon (Si substrate), metal or polymer. The manufacturing methods of Si substrate microneedle array can further be categorized as using wet etching or dry etching. The manufacturing process of metal microneedle array can further be categorized as using electroplating or deposition. The manufacturing process of polymer microneedle array can be further categorized as using molding or photolithography.

[0003] Among the methods of microneedle array, the most widely adopted is using Si substrate to fabricate the hollow needles or mold. However, the fabrication process of using Si substrate is more complicated, as disclosed in WO0217985, and requires many steps of wet/dry etching and thin film deposition. As it takes a longer time to fabricate, the yield rate is low and the cost is high. U.S. Pat. No. 6,334,856 disclosed a method of fabricating a microneedle array having flat needle tips and tapered tube, as shown in **FIG. 1**. This type of design limits the width of the flow channel and the flexibility of the needle. To fabricate the needle higher than 100 um, the needle density must be restricted in compromise for an appropriate size of aperture and strength of needle structure. The restriction of low needle density further causes the problem of insufficient sampling. In addition, the Si substrate microneedles are brittle and break easily.

[0004] The tip of the hollow microneedle in most prior arts is designed as flat, except the design disclosed in WO0217985 (see **FIG. 2**), which is a slant. This is because a slant tip is easier to penetrate the human skin for microsampling than the flat tip, as the human skin is flexible.

[0005] Kim et al. disclosed a method for fabricating metal microneedle array in Journal of Micromechanics and Micro engineering in 2004. They spread two layers of SU-8 on a glass substrate and used a back exposure to separately bake the two layers of SU-8. They also used reactive ion etching to obtain an SU-8 pillar array structure, and then used sputtering, electroplating, planarization and polishing to fabricate a tapered metal hollow microneedle array, as shown in **FIG. 3**. However, the method requires multiple layers of SU-8 to achieve the layered effect and the high aspect ratio of the pillar is prone to slant or twist. The fabrication process is difficult to maintain the quality.

[0006] U.S. Pat. No. 6,663,820 disclosed another method of using lithography and photolithography to fabricate polymer microneedle array, as shown in **FIG. 4**. This method has the advantages of rapid fabrication of micromold and microneedle, and low fabrication cost of the material and process. However, the flat-tip microneedles are still limited in the application. In addition, the polymer microneedles of this method do not have microchannels or reservoirs, and require additional fabrication process to attach the microchannels and reservoirs, if necessary. It is, therefore, difficult to have this method applied for mass production.

[0007] Numerous methods of fabricating microneedle array have been proposed. Regardless of the material used, the object of the microneedle array includes the capability to penetrate the human skin for micro-injection or microsampling painlessly, easy to fabricate, low in fabrication cost and safe to use.

SUMMARY OF THE INVENTION

[0008] The present invention has been made to overcome the aforementioned drawback of conventional bonding methods of fabricating microneedle array. The primary object of the present invention is to provide a microneedle array device, including a supporting pad and a plurality of microneedles. The supporting pad has an upper surface. Each microneedle has a slant or concave top portion with a via thereon, thereby the microfluid may flow in or out. The intersection between the top portion and the inner tube of a microneedle forms a convex needle structure. Each microneedle stands on the upper surface of the supporting pad and is almost perpendicular to the upper surface. A hollow closed tube is formed between the top portion and the supporting pad.

[0009] The supporting pad further includes a bottom portion and at least a layer of reservoir. The reservoir is located above the bottom portion and below the microneedle. The reservoir can be further divided, if necessary, into a plurality of reservoir units, with reservoir units separated from one another to prevent the microfluid flowing from one unit to another. The monolithic metal structure of the present invention includes convex needle structure formed by the intersection of the slant or concave top portion of each microneedle and the inner tube of a microneedle. The main feature of the present invention includes the safety of use and the improvement of pain. Furthermore, the rigidity and the slant uniformity of the microneedle with slant top portion are both improved so that it is suitable for molding and mass production.

[0010] Another object of the present invention is to provide a method of fabricating a microneedle array device, including the steps of: (1) providing a substrate, and forming a plurality of concave areas on a surface of the substrate; (2) spreading a layer of photo-sensitive material on the substrate and covering a layer of light transmission material on top of the photo-sensitive material; (3) using a patterned mask for exposing and lithography of the light transmission material to obtain a polymer hollow microneedle array mold based on the light transmission material; and (4) using the polymer hollow microneedle array mold to form a microneedle array device.

[0011] According to the present invention, there are several techniques to be used in step (1) of forming a plurality of concave areas, including etching, X-ray photo-etching, ultra-violet etching, ion beam etching and excimer laser micromachining. Step (4) of the method further includes the following substeps: (4a) coating a layer of metal on the outer surface of the polymer hollow microneedle array mold and the light transmission material to form a microneedle array; and (4b) removing the polymer hollow microneedle array mold from the microneedle array. In step (4), the techniques for coating metal to the surface of the polymer hollow microneedle array mold include electroplating, electroless plating, evaporation, and sputtering. The metal used can be

Cu, Cr, Ni, Fe, Au, Pt, Pd, stainless steel and their alloys. The present invention uses the coating of photo-sensitive polymer on the concave areas of the substrate and covering with a light transmission material, which is exposed to define an outline of the microneedle and using lithography to obtain a polymer hollow microneedle array mold using the high light transmission material as the base for further fabrication of a metal microneedle array. The advantages of the fabrication method of the present invention are simple process and low in cost.

[0012] The foregoing and other objects, features, aspects and advantages of the present invention will become better understood from a careful reading of a detailed description provided herein below with appropriate reference to the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] **FIG. 1** shows a conventional flat-top microneedle array made of Si substrate.

[0014] **FIG. 2** shows a conventional slant top microneedle array made of Si substrate.

[0015] **FIG. 3** shows a conventional flat-top microneedle array made of metal.

[0016] **FIG. 4** shows a conventional flat-top microneedle array made of polymer.

[0017] **FIG. 5A** shows a cross-sectional view of the first embodiment of a microneedle array device of the present invention.

[0018] **FIG. 5B** shows a schematic view of the concave top of a microneedle of the present invention.

[0019] **FIG. 5C** shows a schematic view of the first embodiment of a microneedle array device of the present invention.

[0020] **FIGS. 6A and 6B** show respective top views of the microneedles having different inner tube shapes.

[0021] **FIGS. 7A-7J** show the fabrication method of the first embodiment of a microneedle array device of the present invention.

[0022] **FIGS. 8A and 8B** show respective top cross-sectional views of the different shapes of concave areas of Si substrate of the present invention.

[0023] **FIG. 9A** shows a cross-sectional view of the second embodiment of a microneedle array device of the present invention.

[0024] **FIG. 9B** shows a schematic view of the second embodiment of a microneedle array device of the present invention.

[0025] **FIG. 9C** shows a top view of **FIG. 9B**.

[0026] **FIG. 10A** shows a cross-sectional view of the third embodiment of a microneedle array device of the present invention.

[0027] **FIG. 10B** shows a schematic view of the third embodiment of a microneedle array device of the present invention.

[0028] **FIG. 10C** shows a top view of **FIG. 10B**.

[0029] **FIGS. 11A-11K** show the fabrication method of the second embodiment of the present invention.

[0030] **FIGS. 12A-12L** show the fabrication method of the third embodiment of the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0031] **FIG. 5A** shows a cross-sectional view of a microneedle array device **50** of the present invention. As shown in **FIG. 5A**, microneedle array device **50** includes a supporting pad **51** and a plurality of microneedles **52**. Supporting pad **51** includes an upper surface **511**. For the purpose of safety and effective skin penetration, the top portion of each microneedle **52** includes a convex needle structure **521**. The top portion of microneedle **52** can be a slant **523** or a concave surface **523***a*, as shown in **FIG. 5B**. The top portion of microneedle **52** intersects with tube wall **524** to form convex needle structure **521**. In addition, top portion **523** or **523***a* includes a via **522**, which allows the follow of a microfluid, for example, a medicine to flow out or a blood to flow in. According to the present invention, the microneedle array is a monolithic metal structure with each microneedle **52** standing on and perpendicular to the upper surface **511** of supporting pad **51**, and a hollow closed tube being formed between top portion **523** (**523***a*) and supporting pad **51**.

[0032] **FIG. 5C** shows a schematic view of the structure of microneedle array device **50** of the present invention. The top portion **523** of each microneedle **52** is a slant, and the cross-section of tube wall **524** forms a closed oval, circular, or triangular shape, as shown in **FIG. 6A** and **FIG. 6B**, respectively. The metal for fabricating microneedle array can be Cu, Cr, Ni, Fe, Au, Pt, Pd, stainless steel, or their alloys. The range of the aperture of each microneedle is 10-70 um, the outer circumference is 80-250 um, and the height is 100-600 um.

[0033] **FIGS. 7A-7J** shows the fabrication method of the first embodiment of the present invention. First, a substrate is provided, which including a plurality of concave areas on the surface. According to the present invention, there are several techniques for forming a plurality of concave areas, including etching, X-ray photo-etching, ultra-violet etching, ion beam etching and excimer laser micromaching. The present embodiment uses an anisotropic wet etching for explanation.

[0034] As shown in **FIG. 7A**, a single crystal silicon with a grainorientation [1,0,0] is used as a substrate **700**, and a protective layer **702** is deposited on the surface. Protective layer **702** can be made of Si_3N_4. The wet etching areas **705** are defined, as shown in **FIG. 7B**, followed by wet etching. The solution commonly used in silicon anisotropic wet etching includes potassium hydroxide (KOH) and Tetramethyl-ammonium hydroxide (TMAH). After etching the silicon, a plurality of concave areas **710** are formed. Each concave area **710** has two slants **711**, as shown in **FIG. 7C**. Slant **711** defines a slant top **523** of each microneedle. The shape of the plurality of concave areas can vary in accordance with the fabrication process, for example, a V-shape **710***a* or U-shape **710***b*, as shown in **FIG. 8A** and **FIG. 8B**, respectively. In other words, a U-shaped concave area **710** defines a concave curvy top portion **523***a* of a microneedle.

[**0035**] Before the coating of photo-sensitive material **720**, a sacrificial layer or mold release layer **715** is coated on top of substrate **700** for the subsequent mold release, as shown in **FIG. 7D**. The commonly used material for the sacrificial or mold release layer includes Su-8, Al, Au, silicon rubber and Teflon.

[**0036**] The next step is to spread a photo-sensitive material **720** on top of sacrificial layer **715**, and a light transmission material **730** on top of photo-sensitive material layer **720**, as shown in **FIG. 7E**. Photo-sensitive material **720** used in the present invention is SU-8, a negative photo-resist developed by Microlithography Chemical Corporation (USA), or JSR 430N, a positive or negative photo-resist developed by Japanese Synthetic Rubber (Japan). Light transmission material can be either glass or PMMA.

[**0037**] The next step is exposure and lithography to obtain a polymer hollow microneedle array mold **760** using light transmission material **730** as a base. As shown in **FIG. 7F**, a patterned mask **750** defining the shape of tube wall **524** and via **522** of microneedle **52** is used before the exposure. The shapes can be either oval, circular **524***a*, or triangular **524***b*, as shown in **FIG. 5C**, **FIG. 6A**, and **FIG. 6B**, respectively. If SU-8 negative photo-resist is used as photo-sensitive material **720**, the bond forms at a later stage of the exposure to light and stays during the development. The un-exposed part is dissolved. After the mold release, a polymer hollow microneedle array mold **760** having a plurality of polymer microneedles is obtained for subsequent metal plating, as shown in **FIG. 7G**. Because the present invention directly applies photo-sensitive material **720** on the slant of concave areas **710** on substrate or the concave curvy top, the top portion **761** of polymer microneedle **765** is also slant or concave curvy surface. Microneedle **765** has a via **762** reaching light transmission material **730**.

[**0038**] Finally, polymer hollow microneedle array mold **760** is used to form a microneedle array device **50**, as shown in **FIG. 7J**. The forming of a microneedle array device step further includes the following two substeps: (a) coating a metal layer **780** on the outer surfaces of polymer hollow microneedle array mold **760** and light transmission material layer **730** to form a microneedle array device **50**, and (b) removing polymer hollow microneedle molde **760** from microneedle array device **50**.

[**0039**] Similarly, before the coating of metal layer **780** in sub-step (a), a sacrifical layer or mold release layer **770** is deposited on the outer surfaces of polymer hollow microneedle array mold **760** and light transmission material layer **730**, and a starting layer **771** (**FIG. 7H**) is electroplated to electro-cast. The material for sacrificial layer **770** includes either Cu, Al, or Au. The material for starting layer **771** is any metal.

[**0040**] In sub-step (a), the electroplating, electroless plating, evaporation and sputtering is used to plate metal layer **780** on the upper surface (**FIG. 7I**) of strating layer **771**. The metal for plating metal layer **780** may include Cu, Cr, Ni, Fe, Au, Pt, Pd, stainless steel, and their alloys.

[**0041**] In sub-step (b), the technique for removing polymer hollow microneedle array mold **760** from microneedle array device **50** is to remove sacrificial layer **770** deposited on the outer surfaces of polymer hollow microneedle array mold **760** and light transmission material layer **730**. The technique includes oxygen plasma removal, thermal removal, solvent removal, aqueous removal or photo-degradation removal.

[**0042**] **FIG. 9A** and **FIG. 10A** show the second and the third embodiments of a microneedle array device of the present invention, respectively.

[**0043**] **FIG. 9A** is similar to the structure shown in **FIG. 5A**. The difference lies in microneedle array device **90** in **FIG. 9A** has a reservoir layer **91** below a plurality of microneedles **52** and above bottom portion **92**. Reservoir layer **91** is for storing or mixing the medicine or collecting blood sample. As shown in **FIG. 9B** and **FIG. 9C**, reservoir **91** may be further divided into a plurality of reservoir unit **93**. Reservoir units **93** are separate from one another to block the flow of microfluid. They may be used for blood analysis.

[**0044**] Similarly, microneedle array device **100** in **FIG. 10A** has two reservoir layers **101** below a plurality of microneedles **52** and above bottom portion **102**. Reservoir layer **91** is for storing or mixing the medicine or collecting blood sample. As shown in **FIG. 10B** and **FIG. 10C**, reservoir layers **101** may be further divided into a plurality of reservoir unit **103**. Reservoir units **103** are separate from one another to block the flow of microfluid.

[**0045**] **FIGS. 11A-11K** show the fabrication method of the second embodiment of the present invention.

[**0046**] The fabrication method of the second embodiment is similar to that of first embodiment. The only difference is in the exposure and development step. Because the second embodiment has a reservoir layer **91** in the structure, the second embodiment requires an additional exposure than the first embodiment. During the second exposure, a corresponding patterned mask **750***a* is used to define reservoir layer **91** and the shape of reservoir units **93** within. By adjusting the exposure dosage to control the depth "a" of the reservoir layer, the result of this step is to obtain a polymer hollow microneedle array mold **160**. The remaining steps of the fabrication are identical to those in **FIG. 7A-7J**.

[**0047**] **FIGS. 12A-12L** show the fabrication method of the third embodiment of the present invention.

[**0048**] The fabrication method of the third embodiment is also similar to that of first embodiment The only difference is still in the exposure and development step. Similarly, because the third embodiment has two more reservoir layers **101** in the structure, the third embodiment requires two additional exposures than the first embodiment. During the second and third exposures, a corresponding patterned mask **750***a*, **750***b* is used to define, respectively, each reservoir layer **101** and the shape of reservoir units **103** within. By adjusting the exposure dosage to control the depths "a" and "b" of the reservoir layers, the result of this step is to obtain a polymer hollow microneedle array mold **260**. Therefore, according to the present invention, the first exposure is to form the shape and the structure of the microneedles, and the second and subsequent exposures are for forming the shape and the structure of the reservoir layer. The remaining steps of the fabrication are identical to those in **FIG. 7A-7J**.

[**0049**] In summary, compared to the other molding techniques, the present invention directly applies photo-sensitive polymer on the concave areas of the substrate to form a polymer hollow microneedle array mold having slants and

concave curvy surface. Then, the polymer hollow microneedle array mold is used with the evaporation and electroplating techniques to fabricate metal microneedle array device. This method greatly reduces the complexity of the fabrication and the cost of the material. The metal microneedle array electroplated on the polymer hollow microneedle array mold has a good rigidity and slant uniformity, and is suitable for mass production. The present invention may be widely used in blood sampling, micro-sampling and medication injection systems.

[0050] Although the present invention has been described with reference to the preferred embodiments, it will be understood that the invention is not limited to the details described thereof. Various substitutions and modifications have been suggested in the foregoing description, and others will occur to those of ordinary skill in the art. Therefore, all such substitutions and modifications are intended to be embraced within the scope of the invention as defined in the appended claims.

What is claimed is:

1. A microneedle array device having a monolithic structure, comprising:

a supporting pad having an upper surface; and

a plurality of microneedles, each microneedle having a slant or concave curvy top portion, said top portion having a via for microfluid to flow, a hollow closed tube being formed between said top portion to said supporting pad, said top portion intersecting with wall of said tube wall to form a convex needle structure, each microneedle standing on said upper surface of said supporting pad, and said microneedle being perpendicular to said upper surface of said supporting pad.

2. The device as claimed in claim 1, wherein said tube wall of each microneedle toruses to form an oval, circular or triangular shape.

3. The device as claimed in claim 1, wherein said supporting pad further comprises a bottom portion and at least a reservoir layer, said reservoir layer is located above said bottom portion and below said plurality of microneedles.

4. The device as claimed in claim 3, wherein said at least reservoir layer is further divided into a plurality of reservoir units, said reservoir units are separate from one another to prevent microfluid stored in said reservoir units from flowing among said reservoir units.

5. The device as claimed in claim 1, wherein said metal structure is made of a metal selected from one of the Cu, Cr, Ni, Fe, Au, Pt, Pd, stainless steel, and their alloy.

6. The device as claimed in claim 1, wherein the aperture of said microneedle ranges from 10 um to 60 um.

7. The device as claimed in claim 1, wherein the circumference of said microneedle ranges from 70 um to 250 um.

8. The device as claimed in claim 1, wherein the height of said microneedle ranges from 100 um to 600 um.

9. A method of fabricating a microneedle array device, comprises the steps of:

(1) providing a substrate, and forming a plurality of concave areas on a surface of said substrate;

(2) coating a layer of photo-sensitive material on top of said substrate, and coating a layer of light transmission material on top of said photo-sensitive material;

(3) using a patterned mask for exposure and development on said light transmission material to obtain a polymer hollow microneedle array mold using said light transmission material as a base; and

(4) forming a microneedle array device using said polymer hollow microneedle array mold.

10. The method as claimed in claim 9, wherein said substrate in step (1) is made of silicon.

11. The method as claimed in claim 9, wherein said plurality of concave areas on said substrate in step (1) are formed by an etching technique.

12. The method as claimed in claim 11, wherein said etching technique is anisotropic wet etching technique.

13. The method as claimed in claim 9, wherein said plurality of concave areas on said substrate in step (1) are formed by X-ray etching, ultra-violet etching, ion beam etching, or excimer laser micromachining.

14. The method as claimed in claim 9, wherein said plurality of concave areas on said substrate in step (1) are formed by micro electro discharge machining technique.

15. The method as claimed in claim 9, wherein said photo-sensitive material in said step (2) is SU-8 or JSR430N.

16. The method as claimed in claim 9, wherein said light transmission material in said step (2) is PMMA or glass.

17. The method as claimed in claim 9, wherein said step (3) further comprises a step of using a patterned mask to define the shape of microneedles.

18. The method as claimed in claim 17, wherein patterned mask comprises a plurality of pairs of closed curves, each said pair of closed curves comprise a first closed curve and a second closed curve, said first closed curve encompasses said second closed curve, said second closed curve has a circumference smaller than that of said first closed curve, and remaining areas are masked except the area between said first and said second closed curves.

19. The method as claimed in claim 17, wherein said step (3) further comprises a step of forming at least a reservoir layer.

20. The method as claimed in claim 19, wherein the shape of each said reservoir layer is defined by using a corresponding patterned mask.

21. The method as claimed in claim 19, wherein the depth of each said reservoir layer is controlled by adjusting exposure dosage of light.

22. The method as claimed in claim 9, wherein said step (4) further comprises the following sub-steps of:

(4a) coating a metal layer on outer surfaces of said polymer hollow microneedle array mold and said light transmission material to form said microneedle array device; and

(4b) removing said polymer hollow microneedle array mold from said microneedle array device.

23. The method as claimed in claim 22, wherein said coating of metal or other material in said step (4a) is by electroplating, electroless plating, evaporation, or sputtering.

24. The method as claimed in claim 22, wherein said metal is chosen from one of the Cu, Cr, Ni, Fe, Au, Pt, Pd, stainless steel and their alloys.

25. The method as claimed in claim 22, wherein said removing said polymer hollow microneedle array mold in said step (4b) uses one of oxygen removal, thermal removal, solvent removal, aqueous removal, photo-degradation removal, and their combinations.

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