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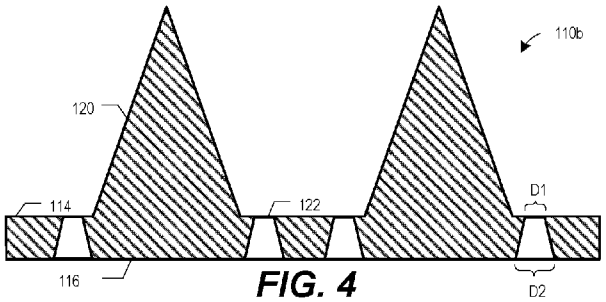

FIG. 4

(57) Abstract: This disclosure describes methods and systems for manufacturing an array of microneedles having a layer that defines a plurality of openings extending between and through first and second sides of the layer outside bases of the microneedles. For example, at least one of the openings can be tapered between the first and second sides, at least one opening can be occupied by a hydrophilic material, and/or two or more of the openings can be positioned between two neighboring microneedles. This disclosure also includes methods and systems for manufacturing articles of manufacture, such as one or more layers of polymers with microneedles, formed by such methods and systems.

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METHODS AND SYSTEMS OF PRODUCING MICRONEEDLE ARRAYS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of U.S. Provisional Patent Application No. 62/561,982 filed September 22, 2017, which is hereby incorporated by reference in its entirety.

BACKGROUND

1. Field of Invention

[0002] The present disclosure relates generally to microneedle arrays, and, but not by way of limitation, to methods and systems for producing microneedles.

2. Description of Related Art

[0003] Health and wellness monitoring of a patient often requires sampling fluid (*e.g.*, blood or interstitial fluid). For example, individuals with diabetes often use a lancing device to puncture tissue and draw blood provided to a test device (*e.g.*, a blood glucose meter). As another example, a syringe is used to acquire fluid from a patient. Depending on an individual's health, multiple fluid samples may be acquired per day and, in severe situations, continuous sampling and monitoring may be warranted, which is often painful, uncomfortable (*e.g.*, causes skin sensitivity), and inconvenient. A microneedle array has potential to provide a pain-free or reduced-pain alternative to a syringe for sampling fluid. As used in this disclosure, a "hollow" microneedle is a microneedle with an internal channel extending through at least a portion of the length of the microneedle and opening through at least one outer surface of the microneedle to permit fluid communication through the microneedle. In contrast, a "solid" microneedle is a microneedle that does not include a channel extending through an exterior surface of the microneedle, such that fluid communication is not permitted through the microneedle.

[0004] Manufacturing of microneedle arrays has met many challenges. For example, given the relatively small sizes of microneedles and features thereof, expensive production processes are needed. To illustrate, a particular microneedle array manufacturing process includes laser drilling to form a channel through a center of a microneedle. In another microneedle array manufacturing process, silicon etching is used, which is difficult to scale up for mass production and is also expensive. In addition to complexity of different manufacturing techniques, hollow microneedles having a channels through the microneedles are susceptible to blockage from skin or tissue during insertion and have reduced tip sharpness as compared to

similarly sized solid microneedles.

[0005] U.S. Patent No. 6,312,612 describes a microneedle array having solid microneedles and a single cylindrical hole between two neighboring microneedles. A chamber filled with a hydrogel is coupled to a backside of the microneedle array. Fluid transfer through the microneedle array into the chamber is constrained by dimensions the cylindrical holes. To enhance a transport rate of fluids, U.S. Pat. No. 6,312,612 describes using additional devices—*i.e.*, a pump or a device that generates an electric field to induce a current through skin. Use of these additional devices in conjunction with the microneedle array increases the complexity and cost to use the array.

SUMMARY

[0006] The present disclosure describes methods and systems for producing microneedle arrays. The present microneedle arrays include a plurality of microneedles (*e.g.*, spikes) extending from a layer (*e.g.*, of polymer), and a plurality of openings extending through the layer, outside of respective bases of individual microneedles. In some implementations, at least one opening is tapered from a first side of the layer to a second side. Relative to a cylindrical opening, a tapered opening can improve a capillary effect to cause fluid to enter or pass through the opening, and/or can improve manufacturability of the microneedle array by facilitating removal of the microneedle array from a mold or tool. Additionally, or alternatively, at least one opening can be occupied by a hydrophilic material. Openings that are at least partially occupied by a hydrophilic material benefit from improved collection and storage of fluid, such as for analysis and/or sensing of a property of the fluid, relative to openings that are not occupied by a hydrophilic material. Additionally, or alternatively, at least two openings can be positioned between two neighboring or adjacent microneedles. A microneedle array with at least two openings positioned between two neighboring microneedles can provide faster localized collection of fluid relative to a microneedle array in which only a single opening is positioned between two neighboring needles.

[0007] In a particular implementation, the openings includes multiple tapered openings positioned between two neighboring microneedles. Relative to implementations of a microneedle arrays having a single cylindrical opening positioned between two neighboring microneedles, the multiple tapered openings can improve flow of fluid through the microneedle array, can improve a capillary effect to permit fluid to enter or pass through the openings, and/or improve manufacturability of the microneedle array. In some implementations, the

multiple tapered openings are at least partially occupied by a hydrophilic material. The hydrophilic martial can advantageously improve collection and storage of fluid during use of the microneedle array.

[0008] In another implementation, the plurality of openings includes a tapered opening and that is at least partially occupied by a hydrophilic material. Relative to an implementation of an array having a single cylindrical opening (with no hydrophilic included therein), the tapered opening can improve flow of fluid through microneedle array, can improve a capillary effect to cause fluid to enter or pass through openings, and/or can improve manufacturability of microneedle array by facilitating removal of microneedle array from a mold or tool, while the hydrophilic material can improve collection and storage of fluid during use of the microneedle array.

[0009] In an alternative implementation, the plurality of openings includes multiple opening positioned between two neighboring microneedles, and each of the multiple openings at least partially occupied by a hydrophilic material. Relative to an implementation of an array having a single cylindrical opening (with no hydrophilic included therein) positioned between two neighboring microneedles, multiple openings positioned between two neighboring microneedles can improve flow of fluid through the array, and the hydrophilic material can improve collection and storage of fluid during use of the microneedle array.

[0010] The present disclosure also includes systems and methods for manufacturing the present microneedle arrays. For example, the microneedle arrays can be manufactured using an embossing process (*e.g.*, a roll embossing process), an injection molding process, an extrusion process, a three-dimensional printing process, or another process. Such methods allow arrays (*e.g.*, large arrays) of microneedles to be manufactured more rapidly than prior art methods. For example, the present embossing process can involve unrolling one or more sheets of polymer material from a dispenser roll, pressing the one or more sheets between a tool (*e.g.*, a mold) and a roller to form microneedles on a side of the sheet(s), and rolling the formed or molded sheet(s) onto a receiver roll. As another result, microneedle arrays formed with the present systems and methods need not be singular, discrete arrays, but can instead include one or more arrays extending along an elongated sheet or layer of polymer. For example, a sheet of polymer with a length that is five or more times its width can have multiple microneedle arrays extending along a majority of its length. Additionally, one or more tools or molds may be configured or designed to form tapered openings (as described above) and facilitate removal of microneedle arrays from the tools or molds. By facilitating removal of the arrays, the present

methods improve a manufacturability of microneedle arrays that have a reduced number of defects and increase a manufacturing yield relative to techniques that form microneedle arrays that do not have tapered openings.

[0011] Some embodiments of the present methods (*e.g.*, of manufacturing a microneedle array) comprise: disposing a polymer between a pressing device and a surface of a tool with a temperature of at least a portion of the polymer in contact with the tool above a glass transition temperature of the polymer, the tool defining a plurality of cavities, each of the cavities extending from a base at the surface to a distal end within the tool to define a negative mold of a microneedle, the base of each of the cavities having a cross-sectional area larger than that of the respective distal end; and pressurizing at least a portion of the polymer between the pressing device and the tool such that the polymer: defines a layer of polymer between the pressing device and the surface of the tool, the layer having a first side facing the tool and a second side facing the pressing device; and flows into the cavities until the polymer substantially fills the cavities to form a plurality of microneedles on the first side of the layer; where at least one of the surface of the tool and a distal side of the pressing device includes a plurality of projections that extend through the layer to define a plurality of openings extending between and through the first and second sides of the layer outside the bases of the microneedles, the plurality of openings including one or more characteristics (including combinations of the characteristics) selected from the group of characteristics consisting of: at least one opening tapered from the first side to the second side, at least one opening configured to be occupied by a hydrophilic material, and at least a portion of multiple openings positioned between two neighboring microneedles.

[0012] In some of the foregoing embodiments of the present methods, at least a portion of the plurality of openings are each between microneedles. Additionally, or alternatively, at least a portion of the plurality of openings extend through a portion of the first side of the layer that, when the layer is disposed flat against a planar supporting surface, is substantially planar and parallel to a planar portion of the second side.

[0013] In some of the foregoing embodiments of the present methods, each of the plurality of openings is tapered from a first end at the first side having a first cross-sectional area to a second end at the second side having a second cross-sectional area that is larger than a first cross-sectional area. In some such embodiments, the first and second ends of each of the plurality of openings have a circular cross-sectional shape.

[0014] In some of the foregoing embodiments of the present methods, the layer of polymer comprises a first layer, the pressing device comprises a first pressing device, and the present methods further comprise: disposing a hydrophilic material between a second pressing device and the second side of the first layer with a temperature of at least a portion of the hydrophilic material in contact with the first layer above a glass transition temperature of the hydrophilic material but below the glass transition temperature of the polymer; and pressurizing at least a portion of the hydrophilic material between the second pressing device and the first layer such that the hydrophilic material: defines a layer of hydrophilic material between the second pressing device and the second side of the first layer; and flows into the openings in the first layer until the hydrophilic material substantially fills at least a portion of the openings.

[0015] In some of the foregoing embodiments of the present methods, the plurality of openings including at least a portion of two openings tapered from the first side to the second side and positioned between two neighboring microneedles, each of the two openings occupied by the hydrophilic material. In some such embodiments, the hydrophilic material comprises a hydrogel or material configured to form a hydrogel in the presence of water. Additionally, or alternatively, the hydrophilic material includes a material that is selected from the group consisting of poly(meth)acrylate, polyhydroxyethylmethacrylate ,polyacrylamide (PAM), poly(ethylene glycol) (PEG), and polyvinylalcohol (PVA).

[0016] In some of the foregoing embodiments of the present methods, at least one of the pressing device(s) comprises a second tool and the polymer is in a molten state as it is disposed between the tool and the pressing device. In some such embodiments, a cross-sectional shape of the base of each of the cavities is a circle, the microneedles are solid, or both.

[0017] Some embodiments of the present systems (*e.g.*, for manufacturing a microneedle array from one or more sheets of polymer) comprise: a frame; a tool rotatably coupled to the frame around a rotational axis, the tool having a radial surface and defining a plurality of cavities, each of the cavities extending from a base at the radial surface to a distal end within the tool to define a negative mold of a microneedle, the base of each of the cavities having a cross-sectional area larger than that of the respective distal end; a first roller disposed at a first angular position relative to the rotational axis of the tool, the first roller having a radial surface configured to press a layer of polymer against the radial surface of the tool to cause the polymer to flow into the cavities in the radial surface of the tool to define a plurality of microneedles on a first side of the layer, each microneedle having a distal end and a base between the distal end and the second side of the layer, the base of each of the microneedles having a cross-sectional

area larger than that of the respective distal end; and a second roller disposed at a second angular position relative to the rotational axis of the tool, the second roller having a radial surface and a plurality of radial projections each having a base at the radial surface and a distal end extending outward from the radial surface, the projections configured to extend through and between a second side of the layer and the first side of the layer to form openings through the sheet between the bases of the microneedles, the plurality of openings including one or more characteristics (including combinations of the characteristics) selected from the group of characteristics consisting of: at least one opening tapered from the first side to the second side, at least one opening occupied by a hydrophilic material, and at least a portion of multiple openings positioned between two neighboring microneedles. In some such embodiments, the base of each of the projections has a cross-sectional area larger than that of the respective distal end.

[0018] In some of the foregoing embodiments of the present systems, the layer of polymer comprises a first layer, and the present systems further comprising: a third roller disposed at a third angular position relative to the rotational axis of the tool, the third roller configured to press a second layer of the hydrophilic material against the second side of the first layer such that the hydrophilic material flows into the openings in the first layer. In some such embodiments, the tool includes a heat element configured to regulate a temperature of a surface of the tool to above a glass transition temperature of the polymer.

[0019] Some embodiments of the present sets of molds systems (*e.g.*, for injection molding a microneedle array polymer) comprise: a first mold having a proximal surface and defining a plurality of cavities, each of the cavities extending from a base at the proximal surface to a distal end within the tool to define a negative mold of a microneedle, the base of each of the cavities having a cross-sectional area larger than that of the respective distal end; and a second mold having a distal surface and a plurality of projections each having a base at the distal surface and a distal end extending away from the distal surface; where the second mold is configured to be coupled to the first mold with the distal ends of the projections facing the proximal surface of the first mold to define a space between the first and second molds into which space molten polymer can be disposed to cause the polymer to flow into the cavities and around the projections to define a layer: having a first side, a second side, a plurality of microneedles on the first side of the layer, each microneedle having a distal end and a base between the distal end and the second side of the layer, the base of each of the microneedles having a cross-sectional area larger than that of the respective distal end; and defining a

plurality of openings extending between and through the first and second sides of the layer outside the bases of the microneedles, the plurality of openings including one or more characteristics (including combinations of the characteristics) selected from the group of characteristics consisting of: at least one opening tapered from the first side to the second side, at least one opening occupied by a hydrophilic material, and at least a portion of multiple openings positioned between two neighboring microneedles.

[0020] In some of the foregoing embodiments of the present sets of molds, where the base of each of the projections has a cross-sectional area larger than that of the respective distal end. further comprising: a third mold having a distal surface and configured to be coupled, after a first layer of polymer is formed between the first and second molds and the second mold is decoupled from the first mold, to the first mold to define a space between the first layer of polymer and the distal surface of the third mold into which space molten hydrophilic material can be disposed to cause the molten hydrophilic material to flow into at least some of the openings in the polymer layer.

[0021] As used herein, various terminology is for the purpose of describing particular implementations only and is not intended to be limiting of implementations. For example, as used herein, an ordinal term (*e.g.*, "first," "second," "third," etc.) used to modify an element, such as a structure, a component, an operation, etc., does not by itself indicate any priority or order of the element with respect to another element, but rather merely distinguishes the element from another element having a same name (but for use of the ordinal term). The term "coupled" is defined as connected, although not necessarily directly, and not necessarily mechanically; two items that are "coupled" may be unitary with each other. The terms "a" and "an" are defined as one or more unless this disclosure explicitly requires otherwise. The term "substantially" is defined as largely but not necessarily wholly what is specified (and includes what is specified; *e.g.*, substantially 90 degrees includes 90 degrees and substantially parallel includes parallel), as understood by a person of ordinary skill in the art. In any disclosed embodiment, the term "substantially" may be substituted with "within [a percentage] of" what is specified, where the percentage includes .1, 1, or 5 percent; and the term "approximately" may be substituted with "within 10 percent of" what is specified. The phrase "and/or" means and or or. To illustrate, A, B, and/or C includes: A alone, B alone, C alone, a combination of A and B, a combination of A and C, a combination of B and C, or a combination of A, B, and C. In other words, "and/or" operates as an inclusive or.

[0022] The terms "comprise" (and any form of comprise, such as "comprises" and

"comprising"), "have" (and any form of have, such as "has" and "having"), and "include" (and any form of include, such as "includes" and "including"). As a result, an apparatus that "comprises," "has," or "includes" one or more elements possesses those one or more elements, but is not limited to possessing only those one or more elements. Likewise, a method that "comprises," "has," or "includes" one or more steps possesses those one or more steps, but is not limited to possessing only those one or more steps. Any embodiment of any of the systems, methods, and article of manufacture can consist of or consist essentially of – rather than comprise/have/include – any of the described steps, elements, and/or features. Thus, in any of the claims, the term "consisting of" or "consisting essentially of" can be substituted for any of the open-ended linking verbs recited above, in order to change the scope of a given claim from what it would otherwise be using the open-ended linking verb. Additionally, it will be understood that the term "wherein" may be used interchangeably with "where."

[0023] Further, a device or system that is configured in a certain way is configured in at least that way, but it can also be configured in other ways than those specifically described. The feature or features of one embodiment may be applied to other embodiments, even though not described or illustrated, unless expressly prohibited by this disclosure or the nature of the embodiments.

[0024] Some details associated with the embodiments are described above, and others are described below. Other implementations, advantages, and features of the present disclosure will become apparent after review of the entire application, including the following sections: Brief Description of the Drawings, Detailed Description, and the Claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] The following drawings illustrate by way of example and not limitation. For the sake of brevity and clarity, every feature of a given structure is not always labeled in every figure in which that structure appears. Identical reference numbers do not necessarily indicate an identical structure. Rather, the same reference number may be used to indicate a similar feature or a feature with similar functionality, as may non-identical reference numbers. The figures are drawn to scale (unless otherwise noted), meaning the sizes of the depicted elements are accurate relative to each other for at least the embodiment depicted in the figures. Views identified as schematics are not drawn to scale.

[0026] **FIG. 1** is a perspective view of a first example of a microneedle array.

[0027] **FIG. 2A** is a top view of the microneedle array of FIG. 1.

[0028] **FIG. 2B** is a cross-sectional view of the microneedle array of FIG. 1 taken along the line A-A of FIG. 2A.

[0029] **FIGs. 3-14** are cross-sectional views of additional examples of microneedle arrays.

[0030] **FIGs. 15-16** are a top views of examples of a microneedle array.

[0031] **FIG. 17A** is a top view of another example of a microneedle array.

[0032] **FIG. 17B** is a perspective view of the microneedle array of FIG. 17A.

[0033] **FIG. 18** is a diagram that illustrates an example of a set of molds for forming a microneedle array.

[0034] **FIG. 19** is a diagram that illustrates another example of a set of molds for forming a microneedle array.

[0035] **FIG. 20** is a schematic view of an example of a system for manufacturing a microneedle array.

[0036] **FIG. 21** is a schematic view of another example of a system for manufacturing a microneedle array.

[0037] **FIG. 22A** is a diagram that illustrates a cross-sectional view of another example of the present microneedle arrays.

[0038] **FIG. 22B** is a diagram that illustrates an example a cross-sectional view of a set of molds for forming the microneedle array of **FIG. 22A**.

[0039] **FIG. 22C** is a diagram that illustrates an example of stages of an injection molding process to form the microneedle array of **FIG. 22A** using the set of molds of **FIG. 22B**.

[0040] **FIG. 23** is a flowchart illustrating an example of a method of manufacturing a microneedle array.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0041] Referring to FIGS. 1 and 2A-B, FIG. 1 shows a perspective view of a first microneedle array 110, FIG. 2A shows a top view of microneedle array 110, and FIG. 2B shows a cross-sectional view of microneedle array 110.

[0042] Referring to FIG. 1, microneedle array 110 includes a plurality of microneedles 120 extending from a layer 162 having a first side 114 (*e.g.*, a first surface) and a second side 116 (*e.g.*, a second surface). As shown, microneedles 120 extend from side 114 of layer 162.

Although microneedle array 110 is illustrated as including two microneedles 120, in other implementations, microneedle array 110 can include a single microneedle or more than two microneedles, such as tens, hundreds, or thousands of microneedles. Additional examples (e.g., 110a-110p) of microneedle array 110 are described below with reference to FIGS. 3-17 and 22.

[0043] Layer 162 defines a plurality of openings 122 (which may also be referred to as channels or vias). Each opening 122 extends between and through sides 114, 116 to permit fluid flow between sides 114, 116. For example, each opening 112 can be configured to encourage fluid to flow from first side 114 toward second side 116.

[0044] Microneedle array 110 defines two or more openings 122 positioned between two neighboring microneedles 120. Referring to FIG. 2A, at least a portion of multiple openings 122 is positioned between two neighboring microneedles 120. As shown, an entirety of each of two openings 122 is positioned between two neighboring microneedles. Other examples where at least a portion of each of multiple openings 122 is positioned between two neighboring microneedles 120 are described further herein at least with reference to FIGS. 4, 6, and 8-19.

[0045] The present microneedles may, for example, have a maximum transverse dimension ranging from 75 micrometers (μm) to 350 μm. For example, and as shown in top view of FIG. 2A, a diameter or width (W) of microneedle 120 may range from 75 μm to 350 μm. In other implementations, width (W) may be less than or equal to 75 μm, or is greater than or equal to 350 μm. Spacing or distance (S) between two adjacent or closest microneedles may be different than or the same as width (W). To illustrate, spacing (S) may be less than width (W). In a particular implementation, spacing (S) may be within a range from 75 μm to 2 millimeters (mm). In other implementations, spacing (S) is greater than 2 mm.

[0046] A set of openings 122 are arranged about a particular microneedle 120 (*e.g.*, a right depicted microneedle 120) such that openings 122 of the set of openings are radially spaced with respect to a longitudinal axis (associated with a tip 124) of particular microneedle. As illustrated in top view 130, the set of openings includes 4 opens that are evenly distributed about a circumference (indicated by dashed line 132) having a center relative to tip 124. In other implementations, the set of opening may not be evenly distributed about the circumference or may be distributed in another manner, such as linearly or randomly. Examples of additional distributions or placements of openings 122 within microneedle array 110 are described below with reference to FIGS. 15 and 16. Although the set of openings as shown

includes 4 openings, in other implementations, the set of opening may include fewer than or more than 4 openings.

[0047] Referring to FIG. 2B, cross-sectional view is illustrated from the perspective indicated by line A-A illustrated in top view of FIG. 2A. Microneedle array 110 includes a layer 158 (*e.g.*, a polymer layer) having a needle portion 161 and layer 162. Microneedle 120 includes a base 154 and a distal end 152. Base 154 of a particular microneedle has a cross-sectional area larger than that of the respective distal end 152 of the particular microneedle. Tip 124 is positioned at end 152. Sharpness of tip 124 may be expressed by a radius of curvatures of tip 124. In a particular implementation, sharpness of tip 124 is less than 10 μm. In another implementation, sharpness of tip 124 is less than 20 μm. Alternatively, sharpness of tip 124 may be greater than or equal to 20 μm. Although microneedle 120 is illustrated as having a single tip, in other implementations, microneedle 120 may include multiple tips, a blade, or a combination thereof.

[0048] Layer 158 may include one or more polymers, such as liquid-crystal polymer (LCP), polyether ether ketone (PEEK), fluorinated ethylene propylene (FEP), polysulfone (PSU), polyethylenimine (PEI), polyimide (PI), polycarbonate (PC), polycarbonate copolymer (PC COPO), cyclic olefin copolymer (COC), cyclo olefin polymer (COP), polyamide (PA), acrylonitrile butadiene styrene (ABS), polyphenylene ether (PPE), or a combination thereof. In a particular implementation, needle portion 161 includes a first polymer and layer 162 includes a second polymer not included needle portion 161 and that is distinct from the first polymer.

[0049] As shown, microneedle 120 is shaped as a cone having a circular cross-sectional base 154. In other implementations, base 154 may have a different cross-sectional shape, such as ellipsoid, triangular, square, rectangular, star, or other shape. In other configurations, however, the present microneedles can have any suitable outer surface profile or shape. For example, outer surfaces may be curved or curvilinear (*e.g.*, concave) to result in a relatively sharper tip 124, or one or more blades along the vertices along which the outer surfaces of the microneedle meet one another may be curved or curvilinear (*e.g.*, concave). In yet further configurations, the present microneedles can have any suitable shape that permits the microneedle to puncture a patient's skin as contemplated by this disclosure.

[0050] Microneedle 120 has a height (H), which may range from 250 μm to 1,100 μm (*e.g.*, from 400 μm to 1,000 μm, or from 400 μm to 800 μm). In a particular implementation, height (H) is 250 μm. In other implementations, height (H) is less than 250 μm or is greater

than 1,000 μm.

[0051] As shown, microneedle 120 is a "solid" microneedle that does not include a channel extending through the microneedle. In other implementations, microneedle 120 may be a "hollow" microneedle with an internal channel extending through at least a portion of the microneedle 120.

[0052] Opening 122 extends between a first aperture 160 (*e.g.*, a first end of the opening) defined by layer 158 on side 114 and a second aperture 159 (*e.g.*, a second end of the opening) defined by layer 158 on side 116. As shown, the first and second ends of each of the openings have a circular cross-sectional shape. In other implementations, the first and second ends of each of the openings can have a different cross-sectional shape.

[0053] Microneedle array 110 is configured such that, when layer 158 (*e.g.*, second side 116) is disposed flat against a planar supporting surface, at least a portion of opening 122 extends through a portion of the first side 114 of the layer 158 that is substantially planar and parallel to a planar portion of the second side 116. In such a configuration, microneedle array 110 includes two openings 122 each having at least a portion of their first aperture 160 interposed between bases 154 of two neighboring microneedles 120. In other implementations, one or both of the first end and the second end has a cross-sectional shape other than circular.

[0054] As shown, opening 122 is illustrated as cylindrical with a circular cross-sectional shape in which a diameter (D1) of first aperture 160 is the same as a diameter (D2) of second aperture 159. In other implementations, diameter (D1) and diameter (D2) may be different. To illustrate, diameter (D2) may be greater than diameter (D1) or, alternatively, diameter (D1) may be greater than diameter (D2). It is noted that the sizes of diameters (D1, D2) may be selected (*e.g.*, during design of the microneedle array) to facility transportation of liquid from side 114 towards side 116 through opening 122. For example, diameter (D2) may be greater than diameter (D1) to create or increase a capillary effect of liquid through aperture 160. To illustrate, in a particular implementation, opening 122 is tapered from a first end (*e.g.*, first aperture 160) at side 114 having a first cross-sectional area to a second end (*e.g.*, second aperture 159) at side 116 having a second cross-sectional area that is larger than the first cross-sectional area. In some implementations, the size of each of diameters (D1 and D2) may be within a range of 25 to 1000 μm. In a particular implementation, a size of one of diameter (D1) or diameter (D2) is less than or equal to 25 μm. In another implementation, a size of one of diameter (D1) or diameter (D2) is greater than or equal to 1000 μm. A ratio of microneedle

120 (*e.g.*, width (W)) to opening 122 (*e.g.*, diameter (D1) or diameter (D2)) may range from 0.25 to 50. In some implementations, the openings 122 are sized so as to maintain the structural and mechanical integrity of array 110. It is noted that in some implementations, to facility manufacturing of the array 110 using a mold, openings 122 may have a draft angle to facility release of microneedle array 110 from the mold.

[0055] In some implementations, openings 122 may at least partially be occupied by a hydrophilic material, such as a hydrogel or material configured to form a hydrogel in the presence of water. Additionally or alternatively, the hydrophilic material may be used as a backing material coupled to second side 116. To illustrate, the microneedle array 110 may include a first layer (*e.g.*, layer 158) and a second layer of hydrophilic material coupled to second side 116 with the hydrophilic material extending into at least a portion of opening 122.

[0056] The shape of the present microneedles and openings are not particularly limited, but certain considerations may guide selection and design of different shapes. For example, the shape of the openings may impact the ability to manufacture molds. Additionally, the shape of the openings may impact the ease with which a microneedle array can be separated from a tool or mold after the polymer solidifies (*e.g.*, the ease or lack thereof with which the microneedles can be removed from the cavities). For example, draft angles in the mold greater than 0.5 degrees may facilitate removal of a molded array from a mold. Additionally, the shape of the microneedle can impact the ability of the microneedle to puncture a patient's skin, the ability of fluids to be extracted from a patient, or both. For example, a microneedle may be designed to be strong enough to pierce the patient's skin and, while a broader base may result in a stronger microneedle, the increased angles of the sides of such a microneedle (with a broader base) may cause relatively greater trauma to the patient's skin.

[0057] In a particular implementation, microneedle array 110 includes layer 158 of polymer that defines a plurality of microneedles 120 on side 114 and defines openings 122 (outside the bases 154 of the microneedles 120) extending between and through sides 114, 116. Array 110 includes one or more characteristics selected from the group of characteristics consisting of: layer 158 defining at least one tapered opening 122, at least one opening 122 occupied by a hydrophilic material, and two or more openings positioned between two neighboring microneedles 120.

[0058] As described with reference to FIGS. 1 and 2A-B, the microneedle array 110 includes at least one tapered opening 122, at least one opening 122 partially occupied by a

hydrophilic material, at least a portion of multiple openings positioned between two neighboring microneedles 120, or a combination thereof. Relative to a cylindrical opening, a tapered opening improves a capillary effect to cause fluid to enter or pass through the opening, and improves manufacturability of array 110 by facilitating removal of microneedle array 110 from a mold or tool. Openings 122 that are partially occupied by a hydrophilic material benefit from improved collection and storage of fluid relative to openings that are not at least partially occupied by a hydrophilic material. Microneedle array 110 that includes at least a portion of multiple openings positioned between two neighboring microneedles 120 has faster collection of fluid relative to a microneedle array in which a portion of a single opening is positioned between two neighboring needles.

[0059] FIGS. 3-14 depict additional examples of microneedle arrays 110a-110p. Microneedle arrays 110a-110p are shown in cross sectional views to illustrate certain internal features of the respective microneedle arrays. The examples of FIGS. 3-14 are each described as separate examples for illustration purposes, but aspects of one example may be combined with another aspect of a different example (and/or with the example described with reference to FIGS. 1 and 2A-2B). Additionally, each of the examples of FIGS. 3-14 describe arrays 110a-110p with two microneedles 120 for illustration purposes, but arrays 110a-110p can include more than two microneedles 120.

[0060] FIG. 3 shows an example 110a of the present microneedle arrays in which each of the plurality of openings 122 have a tapered configuration in which diameter (D2) is greater than diameter (D1). As shown, microneedle array 110a includes at least one opening 122 that is tapered from first side 114 to second side 116. Relative to an implementation of a microneedle array having a single cylindrical opening positioned between two neighboring microneedles, the tapered openings 122 of example 110a improve a capillary effect to cause fluid to enter or pass through opening 122, and improve manufacturability of microneedle array 110a by facilitating removal of microneedle array 110a from a mold or tool.

[0061] FIG. 4 shows another example 110b of the present microneedle arrays with openings 122 have a tapered configuration in which D2 is greater than D1. As shown, array 110b includes at least one opening that is tapered from side 114 to side 116 and includes at least a portion of multiple openings (*e.g.*, two or more openings) positioned between two neighboring microneedles 120. Relative to an implementation of a microneedle array having a single cylindrical opening positioned between two neighboring microneedles, the tapered openings of example 110b improve flow of fluid through array 110b, improve a capillary effect to cause

fluid to enter or pass through openings 122, and improve manufacturability of array 110b by facilitating removal of array 110b from a mold or tool.

[0062] FIG. 5 shows another example 110c of the present arrays in which two different configurations of openings are present. Opening 122 (depicted on the right side of example 110c) includes a first configuration, such as a cylindrical configuration in which diameter (D1) and diameter (D2) are the same size. As shown, at least one opening 122 has a second configuration (a tapered configuration) in which opening 122 is tapered from side 114 to side 116 (e.g., diameter (D3) is less than diameter (D4)). In some implementations, each of D1 and D2 is less than or equal to D3. Relative to an implementation of a microneedle array having a single cylindrical opening positioned between two neighboring microneedles, the tapered opening of example 110c improves a capillary effect to cause fluid to enter or pass through openings 122. Additionally, by having two different configurations of openings, tapered configuration openings can be positioned where fluid between neighboring microneedles is likely to collect and cylindrical configuration openings can be positioned at other locations throughout the microneedle array 110c. Having openings 122 with the first configuration (*e.g.*, the cylindrical configuration) may increase a rate of flow of fluid through the openings while maintain (and not degrading) a structural integrity of the array 110c.

[0063] FIG. 6 shows another example 110d of the present microneedle arrays, that is similar to example 110b, in which array 110d includes at least one opening 122 that is tapered from side 114 to side 116 and includes at least a portion of multiple openings 122 (*e.g.*, two or more openings) positioned between two neighboring microneedles. Additionally, example 110d includes a "hollow" microneedle having an opening 620 (*e.g.*, a channel). Opening 620 includes a first aperture 660 (*e.g.*, a first end) associated with a diameter (D5) and includes a second aperture 662 (*e.g.*, a second end) associated with a diameter (D6). As shown, D5 is the same as D6, however, in other implementations, D5 and D5 may be different. To illustrate, D6 may be greater than D5. Relative to example 110b, example 110d enables fluid to flow though the hollow microneedle 120, thereby increasing a rate of flow of example 110d.

[0064] FIG. 7 shows another example 110e of the present microneedle arrays, that is similar to example 110a, in which array 110a includes at least one opening 122 that is tapered from side 114 to side 116. Relative to example 110a, example 110e includes openings 122 with a different taper configuration from example 110a. Example 110e has a tiered tapered configuration in which a diameter (D7) is less than a diameter (D8), D8 is less than a diameter (D9), and D9 is less than a diameter (D10). Relative to an implementation of a microneedle

array having a single cylindrical opening positioned between two neighboring microneedles, the tiered tapered openings 122 (of 110e) improve a capillary effect to cause fluid to enter or pass through opening 122, and improve manufacturability of array 110e by facilitating removal of array 110e from a mold or tool.

[0065] FIG. 8 shows another example 110f of the present microneedle arrays, that is similar to example 110b, in which the array includes at least one opening 122 that is tapered from side 114 to side 116 and includes at least a portion of multiple openings 122 positioned between two neighboring microneedles 120. As shown, layer 158 includes multiple layers, such as a first layer 852 and a second layer 854. Layer 852 can include a first polymer and layer 854 can include a second polymer different from the first polymer. In some implementations, the first polymer is not include in layer 854, the second polymer is not included in layer 852, or both. Layer 852 can be harder than layer 854, such that microneedles 120 are formed of layer 852 and layer 162 is formed of layer 854. Such a difference can be beneficial in providing microneedles with relatively harder and more-durable outer surfaces, while potentially reducing costs by avoiding the need to provide harder (and potentially more-expensive) polymer materials in other layers (*e.g.*, second layer 854).

[0066] FIG. 9 shows another example 110g of the present microneedle arrays that is similar to example 110f of FIG. 8. Relative to example 110f, a portion of the first layer 852 is included in layer 162. When layer 852 is harder than layer 854, having the portion of the first layer 852 included in the base portion can improve the structural integrity of microneedle array 110g relative to example 110f.

[0067] FIG. 10 shows another example 110h of the present microneedle arrays that is similar to example 110b of FIG. 4. Relative to example 110b, microneedle array 110h includes at least one opening 122 occupied by a hydrophilic material 1010, such as a hydrogel or material configured to form a hydrogel in the presence of water. For example, the hydrophilic material can include polyhydroxyethylmethacrylate. Additionally, or alternatively, the hydrophilic material can include Eudragit ® (registered trademark of Evonik Röhm GmbH, Darmstadt, Germany), Soluplus ® (registered trademark of BASF SE, Ludwigshafen am Rhein, Germany), Kollidon (registered trademark of BASF SE, Ludwigshafen am Rhein, Germany), Tensistat (available from Jonnin Innovation ApS, Denmark), poly(meth)acrylate, polyacrylamide (PAM) and copolymers, poly(ethylene glycol) (PEG), polyvinylalcohol (PVA), or a combination thereof. Openings 122 that are partially occupied by material 1010

benefit from improved collection and storage of fluid relative to openings that are not occupied by material 1010. Material 1010 can, for example, be configured for analysis or sensing of one or more properties of a bodily fluid of a patient.

[0068] FIG. 11 shows another example 110i of the present microneedle arrays that is similar to example 110h; however, example 110i further includes a hydrophilic layer 1110 coupled to side 116 of array 110i. As shown, array 110i includes layer 158 (*e.g.*, a first layer) of polymer and layer 1110 (*e.g.*, a second layer) coupled to side 116. Hydrophilic material 1010 of layer 1110 extends into at least a portion of openings 122 of layer 158. Hydrophilic layer 1110 includes hydrophilic material 1010 and example 110i may have a greater fluid storage capacity than example 110h.

[0069] FIG. 12 shows another example 110j of the present microneedle arrays that is similar to example 110f of FIG. 8 and that includes layer 1110 of example 110i of FIG. 11. Example 110j advantageously incorporates the benefits described above with respect to examples 110f and 110i.

[0070] FIG. 13 shows another example 110k of the present microneedle arrays that is similar to example 110g and that includes layer 1110 of example 110i. Example 110k advantageously incorporates benefits described above with respect to examples 110g, 110i.

[0071] FIG. 14 shows another example 110l of the present microneedle arrays that is similar to example 110g. Openings 122 of example 110l include the tiered tapered configuration of example 110e and includes layer 1110 of example 110i. Layer 1110 includes hydrophilic material 1010 that extends into at least a portion of the tiered tapered configuration openings. Example 110l advantageously incorporates benefits described with respect to examples 110e, 110g, 110i.

[0072] FIGS. 15-16 show top views of other examples (110m, 110n) of the present microneedle arrays. The top views are similar to top view of FIG. 2A; however, the top views of FIGS. 15-16 illustrates layouts having at least 4 microneedles. Referring to the top view of FIG. 15, when used to sample fluid from tissue, array 110m having 4 microneedles, relative to a microneedle array having a fewer number of microneedles, may result in an more fluid being released from tissue in a shorter amount of time, which may shorten a fluid collection process and reduce patient discomfort. The top view of FIG. 16 is similar to top view of FIG. 15; however, top view of FIG. 16 illustrates a different layout of openings 122 of microneedle array 110n having 4 microneedles 120. Relative to top view of FIG. 15, microneedle array 110n of

FIG. 16 includes a greater number of openings 122, which increases a rate at which fluid may be collected when microneedle array is used to collect a fluid sample from tissue.

[0073] FIG. 17 shows a top view and a perspective view of another example 110o of microneedle arrays that is similar to the top views of FIG. 2A and 15; however, the top view (FIG. 17) illustrates a layout of microneedle array having 8 microneedles 120. When used to sample fluid from tissue, microneedle array 110o have 8 microneedles 120, relative to an array having a fewer number of microneedles, may result in an more fluid being released from tissue in a shorter amount of time, which may shorten a fluid collection process and reduce patient discomfort.

[0074] Referring to FIGS. 18 and 19, sets of molds for forming a microneedle array are illustrated. For example, FIG. 18 depicts a diagram that illustrates a cross-sectional view of an example of a set of molds 1802, and FIG. 19 depicts a diagram that illustrates a cross-sectional view of another example of a set of molds 1902. The molds 1802, 1902 may be configured to be used to form the microneedle array of FIGS. 1-17. As used herein, a mold may also be referred to as a tool. In some implementations, the molds 1802, 1902 may be configured to be used in an embossing process, such as a roll embossing process, as described with reference to FIGS. 20-21.

[0075] Referring to FIG. 18, the molds 1802 includes a first mold (M1) 1810 and a second mold (M2) 1820 that is configured to be coupled to mold (M1) 1810. Mold (M1) 1810 includes a proximate surface 1818 that corresponds to side 114 of array 110. Mold (M1) defines multiple cavities 1812 that correspond to microneedles 120 of array 110. Each of the cavities extends from a corresponding base 1814 at proximal surface 1818 to a distal end 1816 within mold (M1) (*e.g.*, a first tool) to define a negative mold of a microneedle. Base 1814 of each of the cavities 1812 has a cross-sectional area larger than that of respective distal end 1816. In a particular implementation, a cross-sectional shape of base 1814 of each of the cavities 1812 includes a circle. In other implementations, the cross-sectional shape of base 1814 includes a shape other than a circle.

[0076] Mold (M2) (*e.g.*, a second tool) includes a distal surface 1828 and a plurality of projections 1822. Surface 1828 may correspond to side 16 of array 110 and the projections 1822 may correspond to opening 122 of the array. Each projection 1822 includes a base 1826 at surface 1828 and a distal end 1824 that extends away from surface 1828. In a particular implementation, base 1826 of each of the projections 1822 has a cross-sectional area larger

than that of respective distal end 1824. Mold 1820 is configured to be coupled to mold 1810 with distal ends 1824 of projections 1822 facing proximal surface 1818 of mold (M1) to define a space between molds (M1) and (M2). To form array 110, molten polymer can be disposed into the space to cause the polymer to flow into the cavities 1812 and around the projections 1822 to define layer 158.

[0077] Although each proximate surface 1818 and distal surface 1828 are illustrated as planar, in some implementations, each of the surfaces 1818, 1828 may have a curved surface. For example, each of the surfaces 1818, 1828 may have a convex surface. In a particular implementation, each of mold (M1) and mold (M2) is incorporated into a surface of a corresponding cylinder that rotates about an axis for use in a roll embossing process to form array 110.

[0078] In an alternative implementation, the projections 1822 may be included in mold (M1). To illustrate, distal end 1824 may be coupled to surface 1818 and the projections 1822 may extend from distal end 1824 at proximate surface 1818 to base 1826. When mold (M2) is coupled to mold (M1), distal surface 1828 of mold (M2) contacts base 1826 of the projections of mold (M1). In some implementations, the set of molds 1802 can be configured to form any of the present microneedle arrays 110-110o.

[0079] Referring to FIG. 19, the set of molds 1902 includes molds (M1) and (M2), as described above, and a third mold (M3) 1950. Mold (M3) includes a distal surface 1958 and is configured to be coupled, after a first layer of polymer is formed between molds (M1) and (M2) and after mold (M2) is decoupled from mold (M1), to mold (M1) to define a space between the first layer of polymer and surface 1958 of mold (M3) into which space molten hydrophilic material can be disposed. The molten hydrophilic material may include to material 1010.

[0080] Although distal surface 1958 is illustrated as planar, distal surface 1958 may be a curved surface (*e.g.*, such as a convex surface). In a particular implementation, mold (M3) is incorporated into a surface of a cylinder that rotates about an axis for use in a roll embossing process to form array 110 including hydrophilic material included at least partially within one or more openings 122 or included in a hydrophilic layer 1110 coupled to side 116 of array 110. In some implementations, the molds 1902 can be configured to form any of the present arrays 110-110o.

[0081] Referring to FIG. 20, a schematic view of an example of a system 2000 for manufacturing a microneedle array from one or more polymer sheets is depicted. For example,

system 2000 may be configured for use in an embossing process to form microneedle array 110.

[0082] System 2000 includes an apparatus 2002 having a frame 2012 configured to support one or more components of system 2000. System 2000 includes spindles 2016 and pulleys 2018 rotatably coupled to frame 2012. A dispenser roll 2030 is coupled to frame 2012 by a corresponding spindle 2016 and includes a sheet 2032 (*e.g.*, a sheet of softened or molten polymer film). Sheet 2032 includes a first side 2034 and a second side 2036. Roll 2030 is configured to rotate about the first spindle to provide sheet 2032 in a direction indicated by arrow 2070. A dispenser roll 2040 is coupled to frame 2012 by a corresponding spindle 2016 and includes a sheet 2042 (e.g., a sheet of hydrophilic material). Sheet 2042 includes a first side 2044 and a second side 2046. Roll 2040 is configured to rotate about the second spindle to provide sheet 2042 in a direction indicated by arrow 2072.

[0083] A tool 2050 having a rotational axis 2052 is rotatably coupled to frame 2012. Tool 2050 is configured to rotate about rotational axis 2052 in a direction indicated by arrow 2076. Tool 2050 is associated with a negative image, similar to mold (M1) 1810, of a microneedle shape. For example, tool 2052 has a radial surface that defines a plurality of cavities. Each of the cavities extends from a base at the radial surface to a distal end within tool 2050 to define a negative mold of a microneedle. The base of each of the cavities has a cross-sectional area larger than that of the respective distal end.

[0084] A first roller 2031 is rotatably coupled to frame 2012 by a spindle 2016 and disposed at a first angular position relative to rotational axis 2052 of tool 2050. Roller 2031 includes a radial surface configured to press sheet 2032 (*e.g.*, a layer of polymer) against the radial surface of tool 2050 to cause the polymer to flow into the cavities in the radial surface of tool 2050 to define a plurality of microneedles (*e.g.*, 120) relative to first side 2034. Each such microneedle has a distal end and a base between the distal end and second side 2036. The base of each of the microneedles has a cross-sectional area larger than that of the respective distal end.

[0085] A second roller 2082 is rotatably coupled to frame 2012 by a spindle 2016 and disposed at a second angular position relative to rotational axis 2052 of tool 2050. Second roller 2082 has a radial surface including a surface patter similar to mold (M2) 1820. For example, the radial surface of roller 2082 has a plurality of radial projections that each have a base at the radial surface and a distal end extending outward from the radial surface. The projections are configured to extend through and between sheet 2032 (*e.g.*, through sides 2036 and 2034) to

form openings through sheet 2032 between the bases of the microneedles.

[0086] One or more third rollers 2084, 2086 are disposed at a corresponding angular position relative to rotational axis 2052 of tool 2050. For example, roller 2084 is disposed at a third angular position relative to rotational axis 2052 and roller 2086 is disposed at a fourth angular position relative to rotational axis 2052. Each of the one or more third rollers 2084 is configured to press the hydrophilic material of sheet 2042 against second side 2036 such that the hydrophilic material flows into the openings formed by second roller 2082.

[0087] A receiver roll 2060 is coupled to frame 2012 by a corresponding spindle 2016 and is configured to receive sheet 2062 formed from sheet 2032 and sheet 2042. Sheet 2062 includes one or more portions 2071 that each includes a microneedle array (*e.g.*, array 110) that includes microneedles 120. The microneedle array can include a plurality of openings including at least one opening tapered from the first side to the second side, at least one opening occupied by a hydrophilic material, at least a portion of multiple openings positioned between two neighboring microneedles, or a combination thereof. In other implementations, dispenser roll 2040 and third rollers 2084, 2086 may be omitted such that a microneedle array formed by the system does not include a hydrophilic material coupled to the layer of polymer.

[0088] During operation of system 2000, sheet 2032 is provided from roll 2030 to tool 2050. Sheet 2032 is provided between roller 2031 and tool 2050 and pressed into the negative mold of tool 2050 to form microneedles. In a particular implementation, roller 2031, a portion of tool 2050, or both may be at a temperature sufficient to heat sheet 2032 above the polymer's glass transition temperature. After being pressed between roller 2031 and tool 2050, the pressed sheet is provided between roller 2082 and tool 2050 to form openings (*e.g.*, openings 122) in the pressed sheet. In a particular implementation, roller 2082, a portion of tool 2050, or both may be at a temperature sufficient to heat sheet 2032 above the polymer's glass transition temperature. After formation of the openings, the pressed sheet reaches a temperature zone (*e.g.*, a lower temperature) and solidifies or hardens. Sheet 2042 is provided from roll 2040 to tool 2050 in a direction indicated by arrow 2074. For example, sheet 2042 is provided between one or more third rollers 2084, 2086 and pressed against the pressed sheet that includes openings formed by second roller 2082. To illustrate, third rollers 2084, 2086 exert pressure on sheet 2042 to cause the hydrophilic material to fill the openings in the pressed sheet and to form sheet 2062. Sheet 2062 is provided to receiver roll 2060 in a direction indicated by arrow 2074.

[0089] Thus, FIG. 20 depicts system 2000 configured to manufacture one or more of the present microneedle arrays 110-110o. System 2000 enable arrays (*e.g.*, large arrays) of microneedles to be manufactured more rapidly than prior art methods. Additionally, system 2000 can produce one or more arrays extending along an elongated sheet or layer of polymer rather than being limited to producing one singular discrete array at a time. For example, a sheet of polymer with a length that is five or more times its width can have one or more microneedle arrays extending along a majority of its length. The ability to produce multiple microneedle arrays reduces time and cost of manufacturing microneedle arrays.

[0090] FIG. 21 shows a schematic view of another example of a system 2100 for manufacturing a microneedle array from one or more polymer sheets. For example, system 2100 may be configured for use in an embossing process to form one or more of the present arrays (*e.g.*, 110-110o). System 2100 is similar to system 2000 (described above) and further includes a dispenser roll 2180. Roll 2180 is coupled to frame 2012 by a corresponding spindle 2016 and includes a sheet 2182 (e.g., a sheet of polymer). Sheet 2182 includes a first side 2184 and a second side 2186. Roll 2180 is configured to rotate to provide sheet 2182 in a direction indicated by arrow 2070. System 2100 is configured such that sheets 2032, 2182 are provided to tool 2050 and pressed between roller 2031 and tool 2050. In other implementations, sheet 2032 (and not sheet 2182) is provided between roller 2031 and tool 2050, and sheet 2182 and pressed sheet 2032 are provided to between second roller 2082 and tool 2050. It is noted that in some implementations, dispenser roll 2040 and third rollers 2084, 2086 may be omitted. In such implementations, a microneedle array formed by system 2100 does not include a hydrophilic material coupled to a layer of polymer.

[0091] Sheet 2182 may include a different polymer than sheet 2032. The polymer of sheet 2032 can be harder than the polymer of sheet 2182, such that the microneedles are formed of the polymer of sheet 2032 and at least a portion of openings are formed of the polymer of sheet 2182. Such a difference can be beneficial in providing microneedles with relatively harder and more-durable outer surfaces, while potentially reducing costs by avoiding the need to provide harder (and potentially more-expensive) polymer materials in other layers (e.g., formed of sheet 2182).

[0092] Thus, FIG. 21 depicts system 2100 configured to manufacture microneedle array 110 (or any of the microneedle arrays 110a-110o). Similar to system 2000, system 2100 enable arrays (*e.g.*, large arrays) of microneedles, and multiple arrays of microneedles, to be manufactured more rapidly than prior art methods and at a lower cost. Additionally, system

2000 can produce microneedle arrays having two different polymers. Microneedle arrays having two different polymers can be beneficial in providing microneedles with relatively harder and more-durable outer surfaces, while potentially reducing costs by avoiding the need to provide harder (and potentially more-expensive) polymer materials in other layers.

[0093] Referring to FIGS. 22A-C, FIG. 22A depicts a cross-sectional view of an example 110p, FIG. 22B shows a cross-sectional view of an example of a set of molds 2208, and FIG. 22C shows stages of an injection molding process 2240 to form array 110p using set of molds 2208.

[0094] Referring to FIG. 22A, FIG. 22A shows an example of microneedle array 110p formed by injection molding. In such injection molding efforts, polymer (*e.g.*, a polymer 2202) has been melted and forced to flow into a mold that includes a plurality cavities or "negative" (female) molds each defining a microneedle. Stated another way, the mold defines a plurality of "inverse" microneedles. As shown in FIG. 22A, microneedle array 110p includes a layer of polymer 2202 that microneedles and openings defined therein. Layer 2202 may include or correspond to layer 158. Microneedle array 110p also includes hydrophilic layer 2204 including a hydrophilic material. Hydrophilic layer 2204 may include or correspond to layer 1110.

[0095] Referring to FIG. 22B, FIG. 22B shows molds 2208 which includes a first mold (M1) 2210, a second mold (M2) 2220, and a third mold (M1) 2230. In some implementations, molds 2208 includes or corresponds to molds 1802 or molds 1902. Mold (M1) 2220 includes proximate surface 2218 and defines cavities 2212 that each extend from a corresponding base 2214 to a respective distal end 2216. Mold (M2) 2220 includes a distal surface 2228 and projections 2222 that each have a corresponding base 2226 and extend from distal surface 2228 to a distal end 2224. In an alternative implementation, the plurality of projections 2222 may be included in mold (M1). Third mold (M3) 2230 includes a distal surface 2238. In other implementations, the molds 2208 can be configured to form the present microneedle arrays 110-110o.

[0096] Referring to FIG. 22C, FIG. 22C shows injection molding process 2240 in which mold (M1) is coupled to mold (M2) at a first stage 2250. Mold (M2) is coupled to mold (M1) with distal ends 2224 of projections 2222 facing proximal surface 2218 to define a space 2252 between molds 2210, 2220. At a second stage 2260, layer of polymer 2202 has been injected into space 2252. At a third stage 2270, mold (M2) 2220 has been decoupled (*e.g.*, removed)

from mold (M1) 2210. At a fourth stage 2280, mold (M3) has been coupled to mold (M1) to define a space 2282. At a fifth stage 2290, hydrophilic material, such as hydrophilic material 1010, has been injected into space 2282 to form hydrophilic layer 2204. It is noted that at least a portion of the hydrophilic material is injected into and occupies at least a portion of openings 122. After formation of hydrophilic layer 2204, mold (M1) and mold (M3) can be decoupled to reveal the microneedle array 110p.

[0097] Thus, FIG. 22 depicts set of molds 2208 and injection molding process 2240 to form microneedle array 110p. Injection molding process 2240 (and set of molds 2208) enables microneedle arrays to be mass produced faster and at a lower cost than other manufacturing techniques, such as a laser drilling process or a silicon etch process.

[0098] Referring to FIG. 23, a method 2300 of manufacturing a microneedle array is illustrated. The microneedle array includes a plurality of microneedles and may include or correspond to the microneedle arrays as described with reference to FIGS. 1, 2A-2B, 3-17, and 22. In a particular implementation, the plurality of microneedles is disposed on a first side of a layer of polymer that also has an opposing second side. Each microneedle includes a base between its distal end and the second side of the layer. The base of each of the microneedles has a cross-sectional area larger than that of the respective distal end. The layer defines a plurality of openings extending between and through the first and second sides of the layer outside the bases of the microneedles. The plurality of openings including at least one opening tapered from the first side to the second side, at least one opening configured to be occupied by a hydrophilic material, at least a portion of multiple openings positioned between two neighboring microneedles, or a combination thereof.

[0099] Method 2300 may be performed by a manufacturing device or system (*e.g.*, system 2000 or system). Method 2300 includes disposing a polymer between a pressing device and a surface of the tool, at 2302. A temperature of at least a portion of the polymer in contact with the tool is above the polymer's glass transition temperature. The polymer may include or correspond to a material of layer 158, a material of first layer 852, polymer of sheet 2032, polymer 2202, or a combination thereof. The tool may include or correspond to mold (M1) 1810, tool 2050, or a combination thereof. The pressing device may include or correspond to roller 2031, roller 2082 (*e.g.*, another tool), or a combination thereof. In some implementations, the pressing device includes another tool and the polymer is in a molten state as it is disposed between the tool and the pressing device (*i.e.*, the other tool).

[0100] Method 2300 also includes pressurizing at least a portion of the polymer between the pressing device and the tool, at 2304. At least the portion of the polymer may be pressurized such that the polymer defines a layer of polymer between the pressing device and the surface of the tool (the layer having a first side facing the tool and a second side facing the pressing device), and such that the polymer flows into cavities of the tool until the polymer substantially fills the cavities to form a plurality of microneedles on the first side of the layer. In some implementations, the plurality of microneedles are substantially solid. In a particular implementations, the plurality of microneedles are solid. The first side of the layer and the second side of the layer may include or correspond to side 114 and side 116, respectively. At least one of the surface of the tool and a distal side of the pressing device includes a plurality of projections that extend through the layer to define a plurality of openings extending between and through the first and second sides of the layer outside the bases of the microneedles. The projections may include or correspond to projection 1822 or projection 2222. The plurality of openings include at least one opening tapered from the first side to the second side, at least one opening configured to be occupied by a hydrophilic material, at least a portion of multiple opening positioned between two neighboring microneedles, or a combination thereof.

[0101] In a particular implementation, the layer of polymer includes a first layer and the pressing device includes a first pressing device. Method 2300 may further include disposing a hydrophilic material between a second pressing device and the second side of the first layer. The second pressing device may include or correspond to roller 2084, roller 2086, or both. A temperature of at least a portion of the hydrophilic material in contact with the first layer is above the hydrophilic material's glass transition temperature but below the polymer's glass transition temperature. The hydrophilic material may include or correspond to material 1010, a material of layer 1110, hydrophilic material of sheet 2042, a material of hydrophilic layer 2204, or a combination thereof. The hydrophilic material may include a hydrogel or material configured to form a hydrogel in the presence of water. In a particular implementation, the hydrophilic material includes polyhydroxyethylmethacrylate.

[0102] Method 2300 may also include pressurizing at least a portion of the hydrophilic material between the second pressing device and the first layer such that the hydrophilic material defines a layer of hydrophilic material (between the second pressing device and the second side of the first layer) and such that the hydrophilic material flows into the openings in the first layer until the hydrophilic material substantially fills at least a portion of the openings. In some implementations, the second pressing device includes another tool and the polymer is

in a molten state as it is disposed between the tool and the second pressing device (*i.e.*, the other tool).

[0103] One product or article of manufacture that can be formed from method 2300 includes a microneedle array that includes a layer of polymer having a first and a second sides. The layer (*e.g.*, the polymer) defines microneedles on the first side, where each microneedle has a distal end and a base between the distal end and the second side. The base of each microneedle has a cross-sectional area larger than that of the respective distal end. The layer defines a plurality of openings extending between and through the first and second sides outside the bases of the microneedles. The plurality of openings including at least one opening tapered from the first side to the second side, at least one opening configured to be occupied by a hydrophilic material, at least a portion of multiple openings positioned between two neighboring microneedles, or a combination thereof.

[0104] Thus, method 2300 describes manufacturing of an array of microneedles, such as microneedle array 110 (or any of 110a-110p). Method 2300 advantageously enable arrays (*e.g.*, large arrays) of microneedles, and multiple arrays of microneedles, to be manufactured more rapidly than prior art methods and at a lower cost. Additionally, microneedle arrays manufactured according to method 2300 can include a characteristic, such as at least one opening being tapered from a first side (of a layer of polymer) to a second side (of the layer of polymer), at least one opening being occupied by a hydrophilic material, at least a portion of multiple openings (*e.g.*, two or more openings) being positioned between two neighboring microneedles, or a combination thereof. Relative to a cylindrical opening, a tapered opening improves a capillary effect to cause fluid to enter or pass through the opening and improves manufacturability of microneedle array by facilitating removal of microneedle array from a mold or tool. Openings that are partially occupied by a hydrophilic material benefit from improved collection and storage of fluid relative to openings that are not at least partially occupied by a hydrophilic material. Microneedle array that includes at least a portion of multiple openings positioned between two neighboring microneedles has a faster collection of fluid relative to a microneedle array in which a portion of a single opening is positioned between two neighboring needles.

[0105] The above specification and examples provide a complete description of the structure and use of illustrative embodiments. Although certain embodiments have been described above with a certain degree of particularity, or with reference to one or more individual embodiments, those skilled in the art could make numerous alterations to the

disclosed embodiments without departing from the scope of this disclosure. As such, the various illustrative embodiments of the methods and systems are not intended to be limited to the particular forms disclosed. Rather, they include all modifications and alternatives falling within the scope of the claims, and embodiments other than the one shown may include some or all of the features of the depicted embodiments. For example, elements may be omitted or combined as a unitary structure, connections may be substituted, or both. Further, where appropriate, aspects of any of the examples described above may be combined with aspects of any of the other examples described to form further examples having comparable or different properties and/or functions, and addressing the same or different problems. Similarly, it will be understood that the benefits and advantages described above may relate to one embodiment or may relate to several embodiments. Accordingly, no single implementation described herein should be construed as limiting and implementations of the disclosure may be suitably combined without departing from the teachings of the disclosure.

[0106] The claims are not intended to include, and should not be interpreted to include, means-plus- or step-plus-function limitations, unless such a limitation is explicitly recited in a given claim using the phrase(s) “means for” or “step for,” respectively.

CLAIMS

1. A method of manufacturing a microneedle array, the method comprising:

disposing a polymer between a pressing device and a surface of a tool with a temperature of at least a portion of the polymer in contact with the tool above a glass transition temperature of the polymer, the tool defining a plurality of cavities, each of the cavities extending from a base at the surface to a distal end within the tool to define a negative mold of a microneedle, the base of each of the cavities having a cross-sectional area larger than that of the respective distal end; and

pressurizing at least a portion of the polymer between the pressing device and the tool such that the polymer:

defines a layer of polymer between the pressing device and the surface of the tool, the layer having a first side facing the tool and a second side facing the pressing device; and

flows into the cavities until the polymer substantially fills the cavities to form a plurality of microneedles on the first side of the layer;

where at least one of the surface of the tool and a distal side of the pressing device includes a plurality of projections that extend through the layer to define a plurality of openings extending between and through the first and second sides of the layer outside the bases of the microneedles, the plurality of openings including one or more characteristics selected from the group of characteristics consisting of:

at least one opening tapered from the first side to the second side,

at least one opening configured to be occupied by a hydrophilic material, and

at least a portion of multiple openings positioned between two neighboring microneedles.

2. The method of claim 1, where at least a portion of the plurality of openings are each between microneedles.

3. The method of claim 1, where at least a portion of the plurality of openings extend through a portion of the first side of the layer that, when the layer is disposed flat against a planar supporting surface, is substantially planar and parallel to a planar portion of the second side.

4. The method of any of claims 1-3, where each of the plurality of openings is tapered from a first end at the first side having a first cross-sectional area to a second end at the second side having a second cross-sectional area that is larger than a first cross-sectional area.

5. The method of claim 4, where the first and second ends of each of the plurality of openings have a circular cross-sectional shape.

6. The method of claim 1, where the layer of polymer comprises a first layer, the pressing device comprises a first pressing device, and the method further comprises:

disposing a hydrophilic material between a second pressing device and the second side of the first layer with a temperature of at least a portion of the hydrophilic material in contact with the first layer above a glass transition temperature of the hydrophilic material but below the glass transition temperature of the polymer; and

pressurizing at least a portion of the hydrophilic material between the second pressing device and the first layer such that the hydrophilic material:

defines a layer of hydrophilic material between the second pressing device and the second side of the first layer; and

flows into the openings in the first layer until the hydrophilic material substantially fills at least a portion of the openings.

7. The method of claim 6, where the plurality of openings including at least a portion of two openings tapered from the first side to the second side and positioned between two neighboring microneedles, each of the two openings occupied by the hydrophilic material.

8. The method of any of claims 6-7, where the hydrophilic material comprises a hydrogel or material configured to form a hydrogel in the presence of water.

9. The method of any of claims 6-7, where the hydrophilic material comprises polyhydroxyethylmethacrylate.

10. The method of any of claims 6-7, where the hydrophilic material includes a material that is selected from the group consisting of poly(meth)acrylate, polyacrylamide (PAM), poly(ethylene glycol) (PEG), and polyvinylalcohol (PVA).

11. The method of any of claims 1-3 or 5-7, where the microneedles are solid.

12. The method of any of claims 1-3 or 5-7, where at least one of the pressing device(s) comprises a second tool and the polymer is in a molten state as it is disposed between the tool and the pressing device.

13. The method of claim 1, where a cross-sectional shape of the base of each of the cavities is a circle.

14. A system for manufacturing a microneedle array from one or more sheets of polymer, the system comprising:

a frame;

a tool rotatably coupled to the frame around a rotational axis, the tool having a radial surface and defining a plurality of cavities, each of the cavities extending from a base at the radial surface to a distal end within the tool to define a negative mold of a microneedle, the base of each of the cavities having a cross-sectional area larger than that of the respective distal end;

a first roller disposed at a first angular position relative to the rotational axis of the tool, the first roller having a radial surface configured to press a layer of polymer against the radial surface of the tool to cause the polymer to flow into the cavities in the radial surface of the tool to define a plurality of microneedles on a first side of the layer, each microneedle having a distal end and a base between the distal end and the second side of the layer, the base of each of the microneedles having a cross-sectional area larger than that of the respective distal end; and

a second roller disposed at a second angular position relative to the rotational axis of the tool, the second roller having a radial surface and a plurality of radial projections each having a base at the radial surface and a distal end extending outward from the radial surface, the projections configured to extend through and between a second side of the layer and the first side of the layer to form openings through the sheet between the bases of the microneedles, the plurality of openings including one or more characteristics selected from the group of characteristics consisting of:

at least one opening tapered from the first side to the second side,

at least one opening occupied by a hydrophilic material, and

at least a portion of multiple openings positioned between two neighboring microneedles.

15. The system of claim 14, where the base of each of the projections has a cross-sectional area larger than that of the respective distal end.

16. The system of any of claims 14-15, where the layer of polymer comprises a first layer, and further comprising:

a third roller disposed at a third angular position relative to the rotational axis of the tool, the third roller configured to press a second layer of the hydrophilic material against the second side of the first layer such that the hydrophilic material flows into the openings in the first layer.

17. The system of any of claim 14-15, where the tool includes a heat element configured to regulate a temperature of a surface of the tool to above a glass transition temperature of the polymer.

18. A set of molds for injection molding a microneedle array, the set comprising:

a first mold having a proximal surface and defining a plurality of cavities, each of the cavities extending from a base at the proximal surface to a distal end within the tool to define a negative mold of a microneedle, the base of each of the cavities having a cross-sectional area larger than that of the respective distal end; and

a second mold having a distal surface and a plurality of projections each having a base at the distal surface and a distal end extending away from the distal surface;

where the second mold is configured to be coupled to the first mold with the distal ends of the projections facing the proximal surface of the first mold to define a space between the first and second molds into which space molten polymer can be disposed to cause the polymer to flow into the cavities and around the projections to define a layer:

having a first side, a second side, a plurality of microneedles on the first side of the layer, each microneedle having a distal end and a base between the distal end and the second side of the layer, the base of each of the microneedles having a cross-sectional area larger than that of the respective distal end; and

defining a plurality of openings extending between and through the first and second sides of the layer outside the bases of the microneedles, the plurality of openings including one or more characteristics selected from the group of characteristics consisting of:

at least one opening tapered from the first side to the second side,

at least one opening occupied by a hydrophilic material, and

at least a portion of multiple openings positioned between two neighboring microneedles.

19. The set of claim 18, where the base of each of the projections has a cross-sectional area larger than that of the respective distal end.

20. The set of any of claims 18-19, further comprising:

a third mold having a distal surface and configured to be coupled, after a first layer of polymer is formed between the first and second molds and the second mold is decoupled from the first mold, to the first mold to define a space between the first layer of polymer and the distal surface of the third mold into which space molten hydrophilic material can be disposed to cause the molten hydrophilic material to flow into at least some of the openings in the polymer layer.

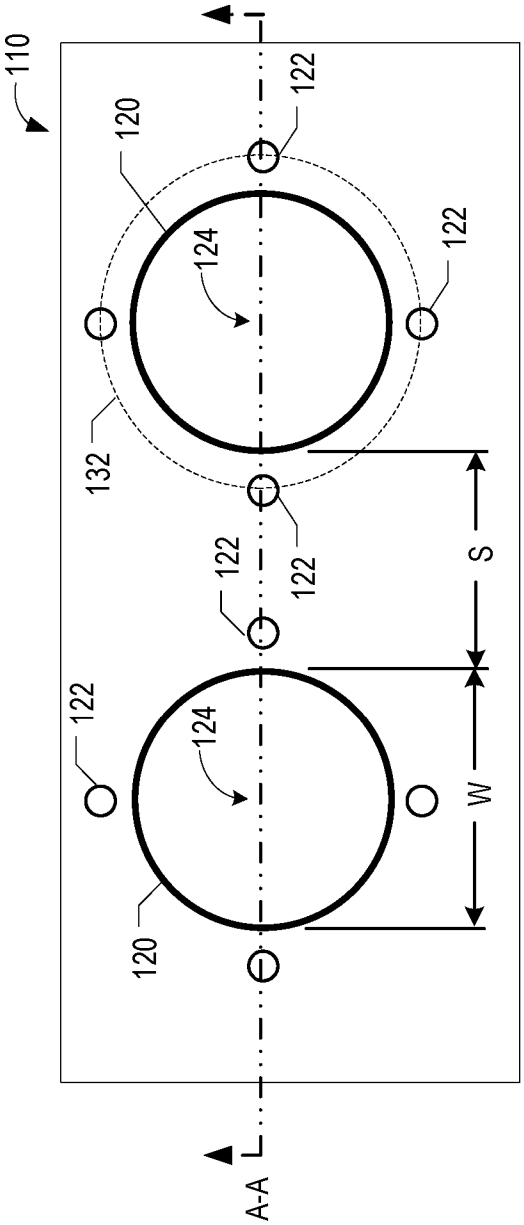


FIG. 2A

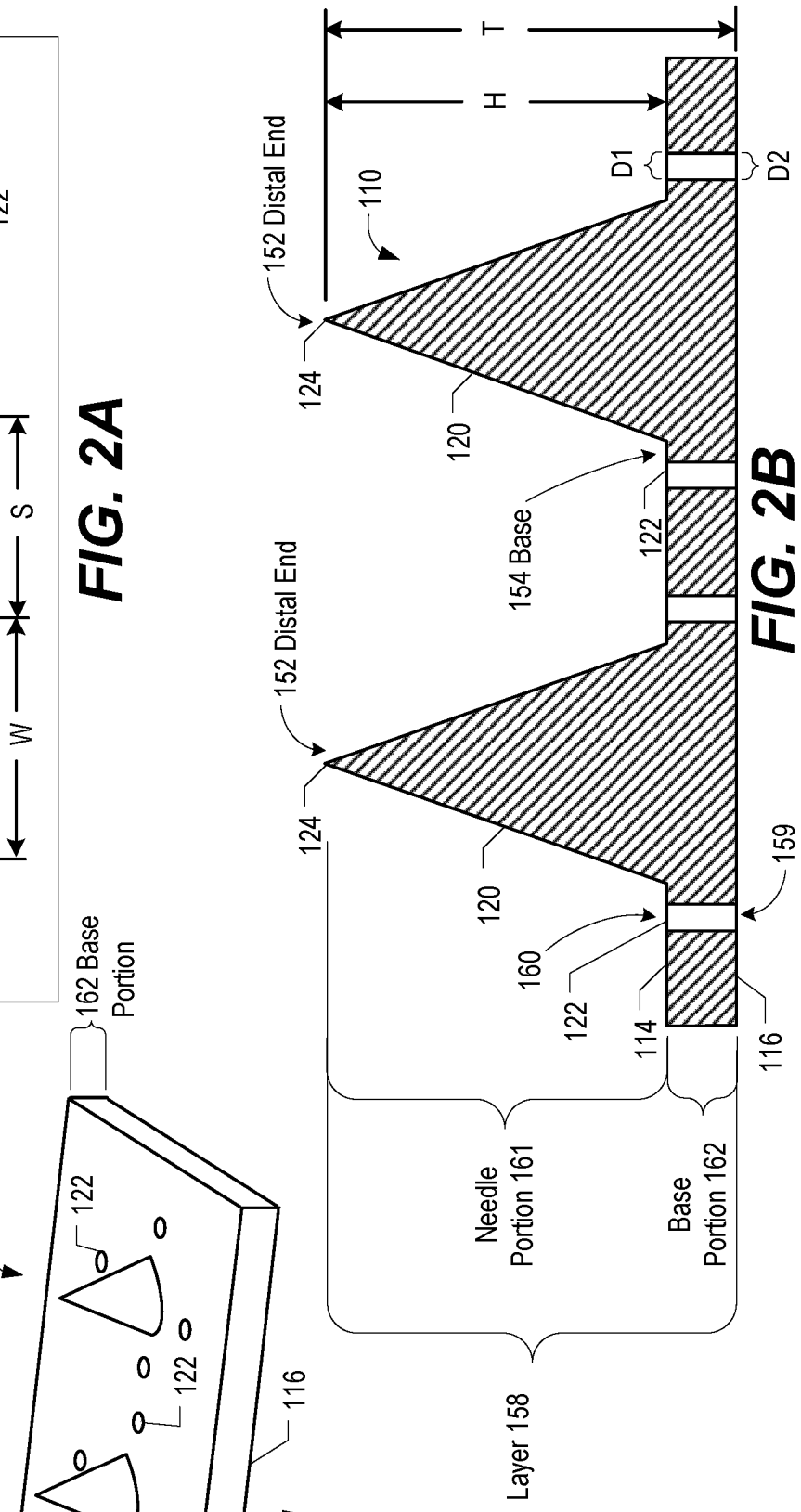


FIG. 2B

FIG. 1

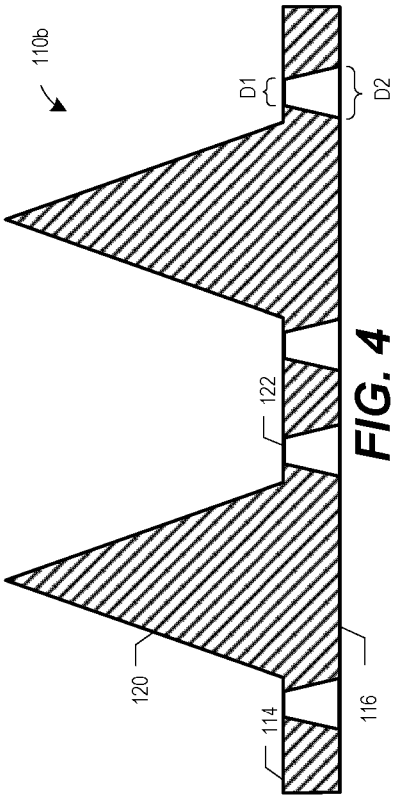


FIG. 4

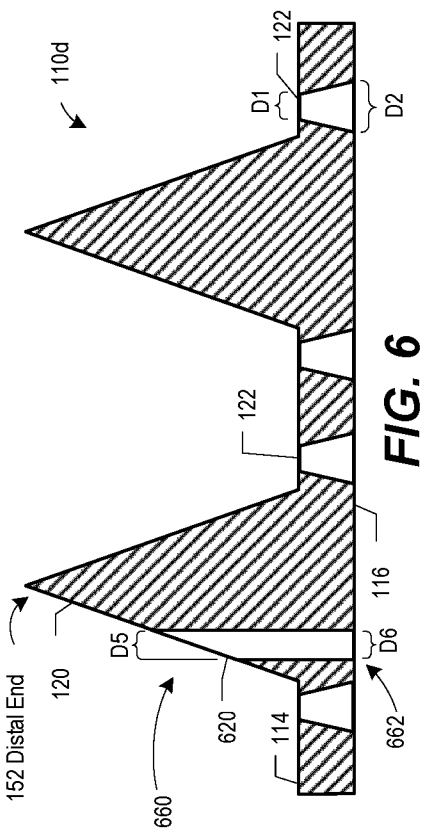


FIG. 6

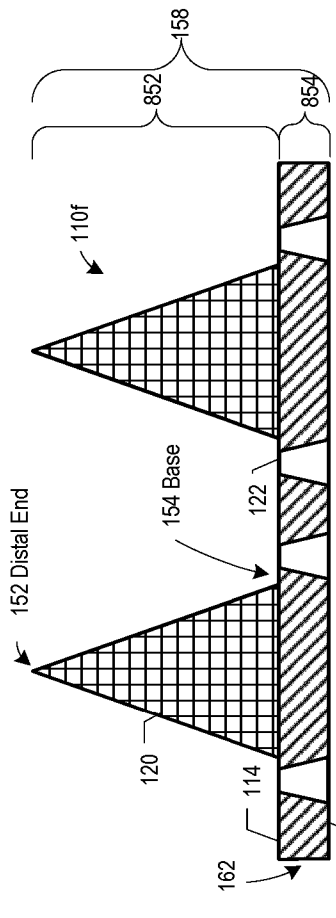


FIG. 8

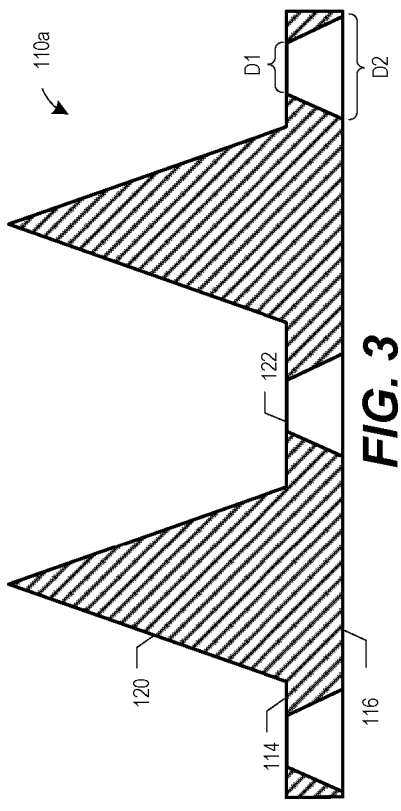


FIG. 3

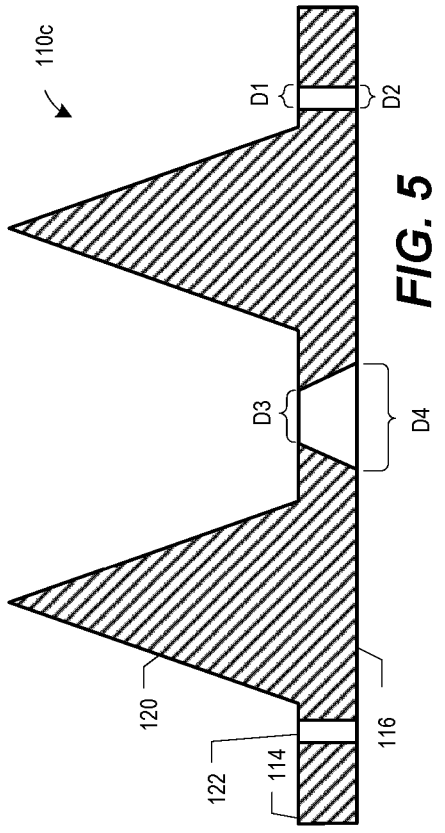


FIG. 5

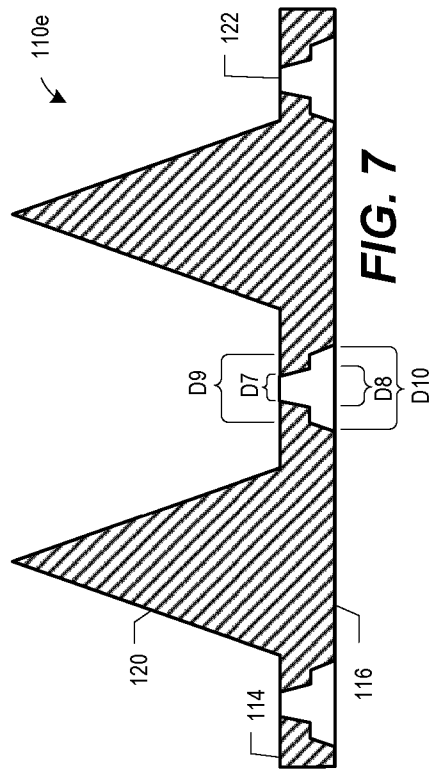


FIG. 7

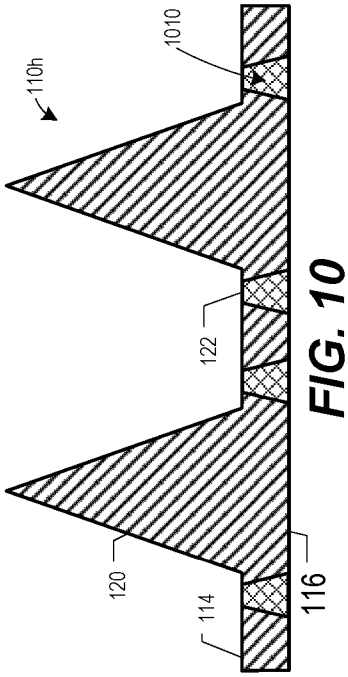


FIG. 10

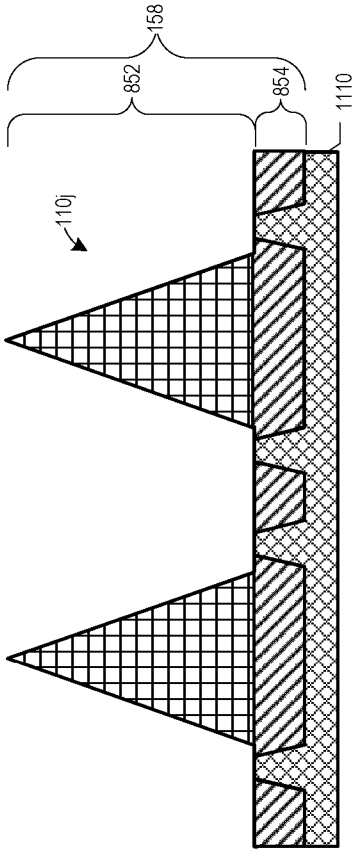


FIG. 12

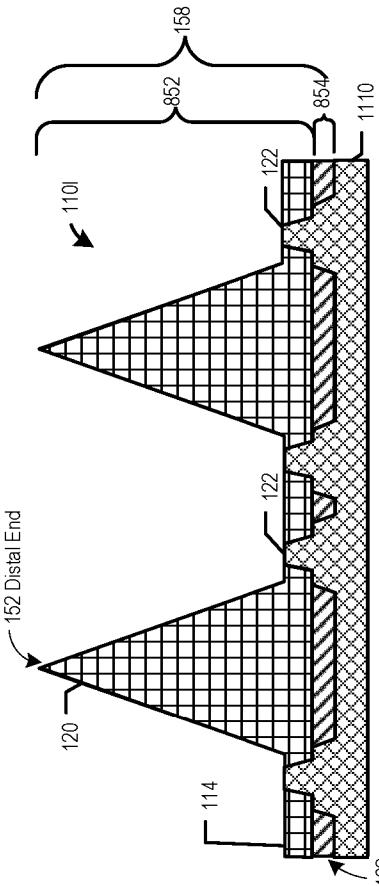


FIG. 14

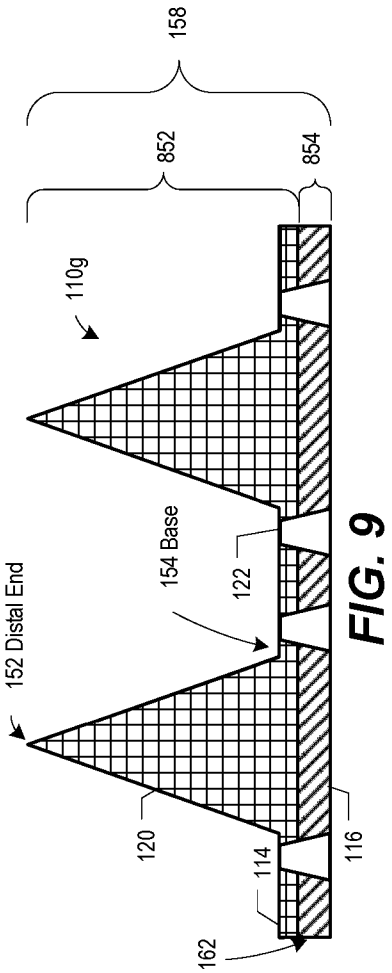


FIG. 9

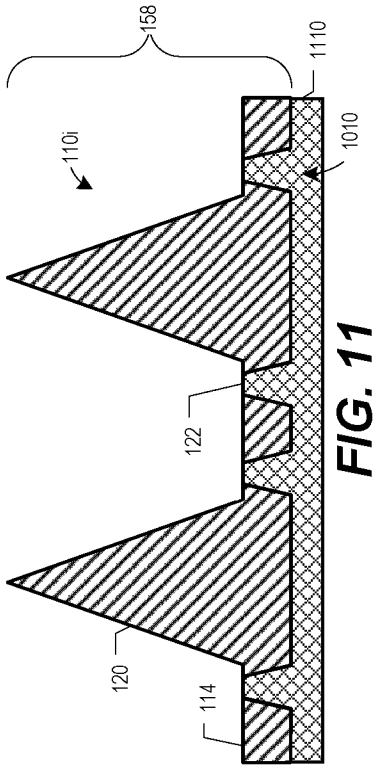


FIG. 11

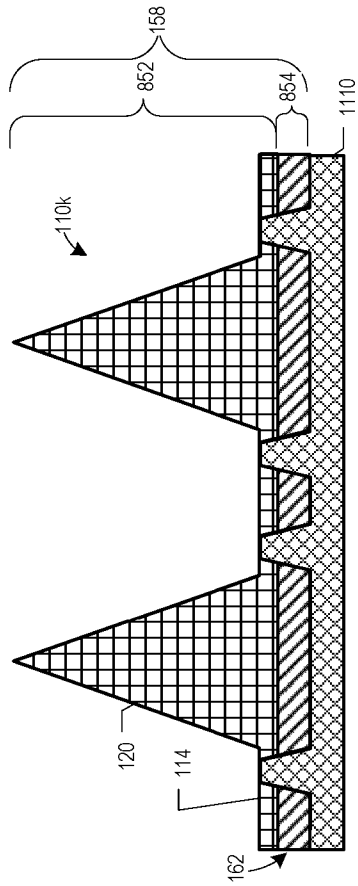


FIG. 13

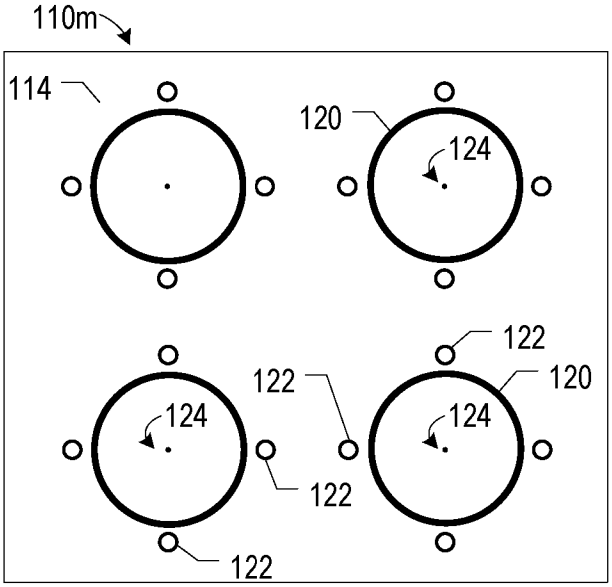


FIG. 15

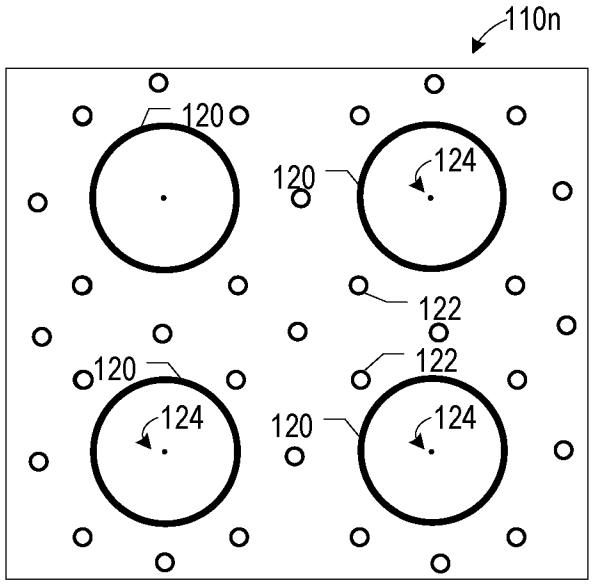


FIG. 16

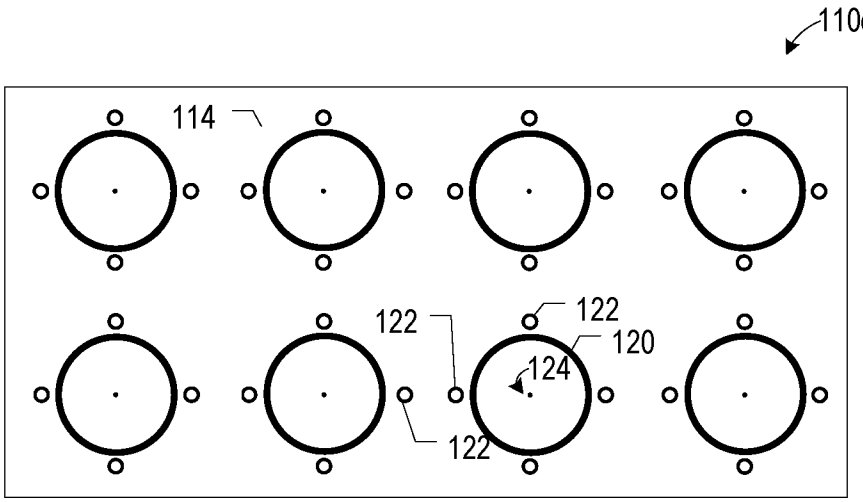


FIG. 17A

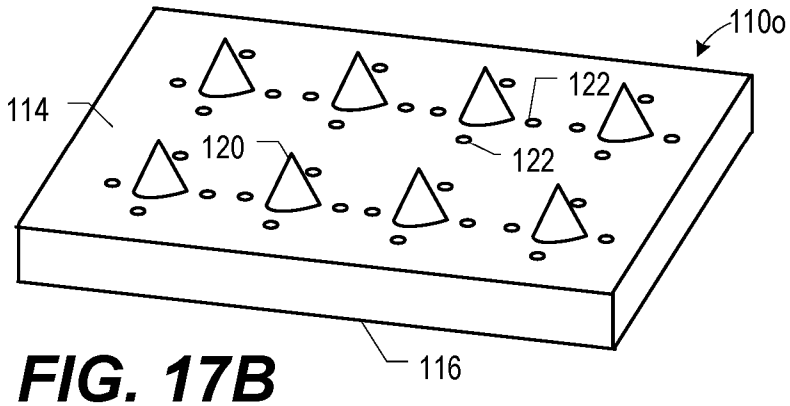


FIG. 17B

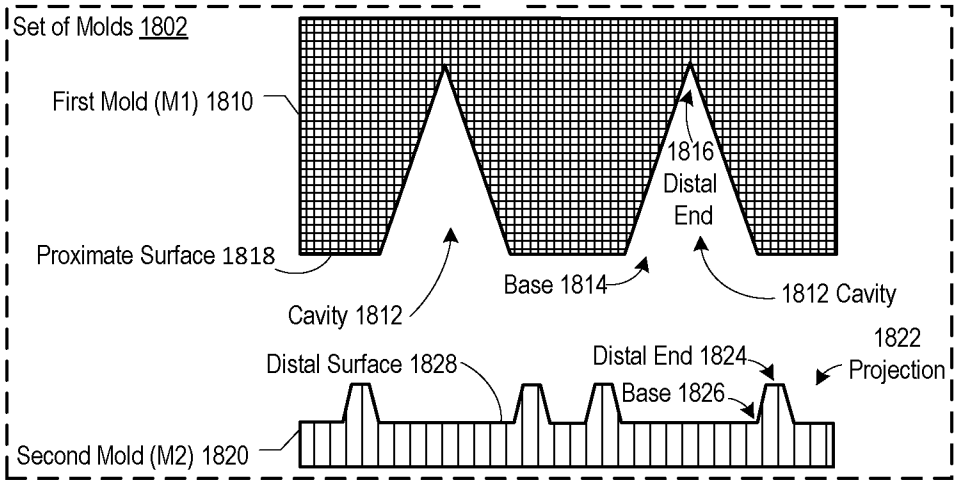


FIG. 18

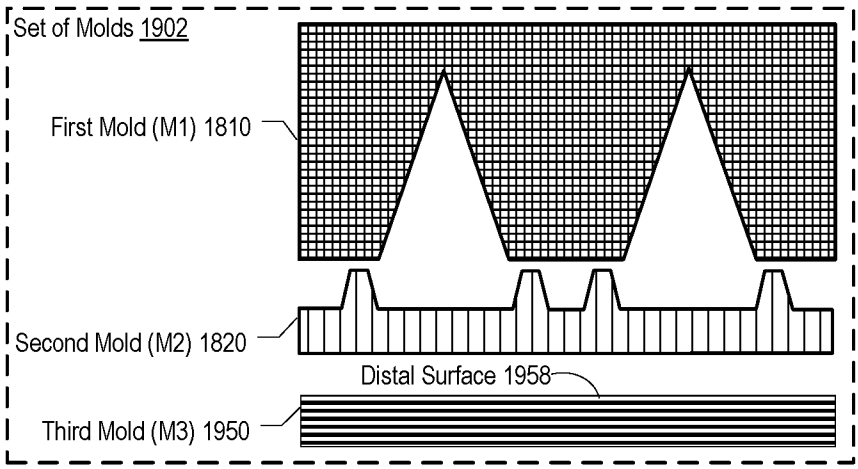


FIG. 19

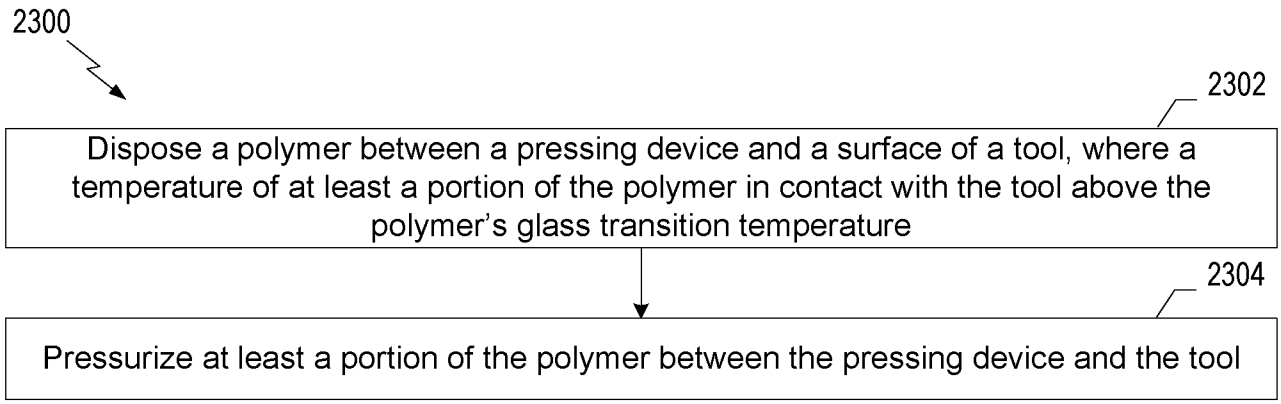


FIG. 23

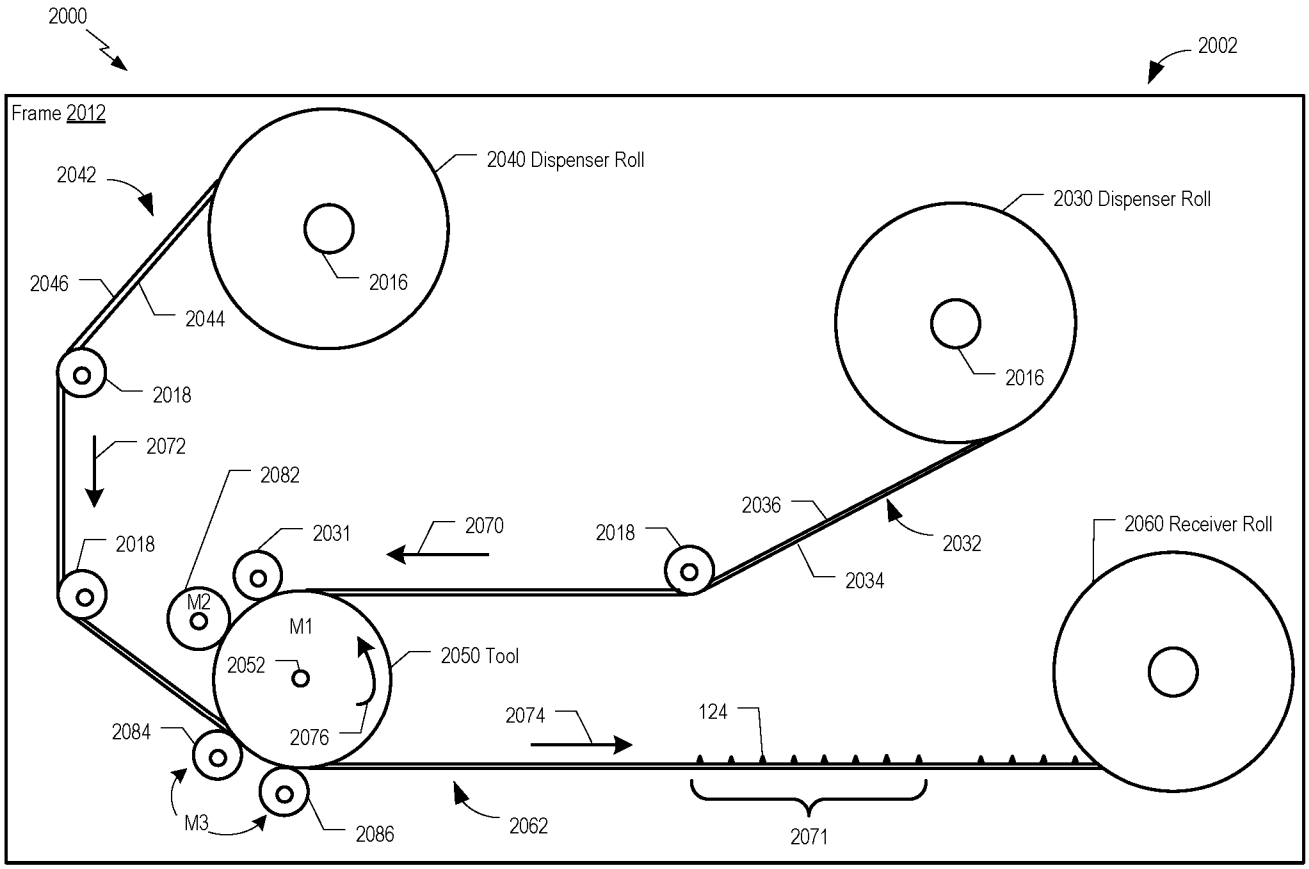
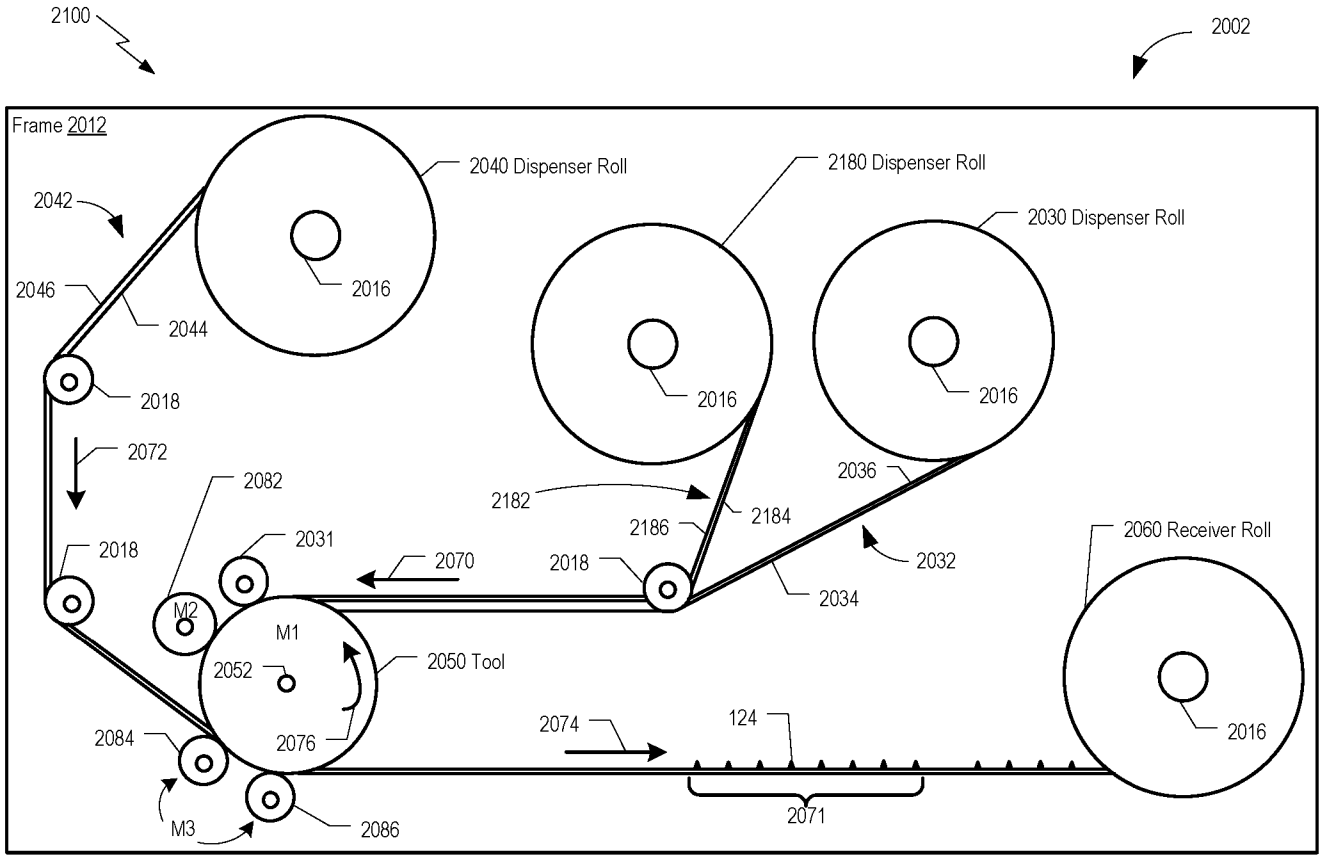

2000
2002
Frame 2012
2042
2040 Dispenser Roll
2030 Dispenser Roll
2046
2044
2016
2018
2072
2082
2031
2070
2036
2032
2060 Receiver Roll
M2
M1
2052
2050 Tool
2034
2074
124
2084
2076
M3
2086
2062
2071

FIG. 20


2100
2002
Frame 2012
2042
2040 Dispenser Roll
2180 Dispenser Roll
2030 Dispenser Roll
2046
2044
2016
2018
2072
2082
2182
2184
2036
2186
2031
2070
2032
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M1
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2050 Tool
2034
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2084
2076
M3
2086
2071

FIG. 21

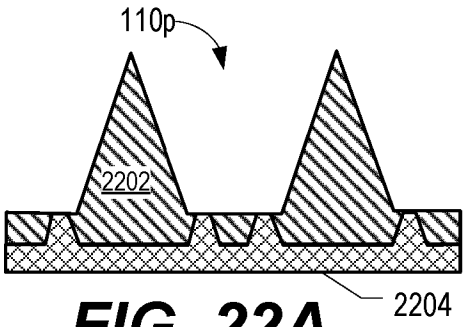

FIG. 22A

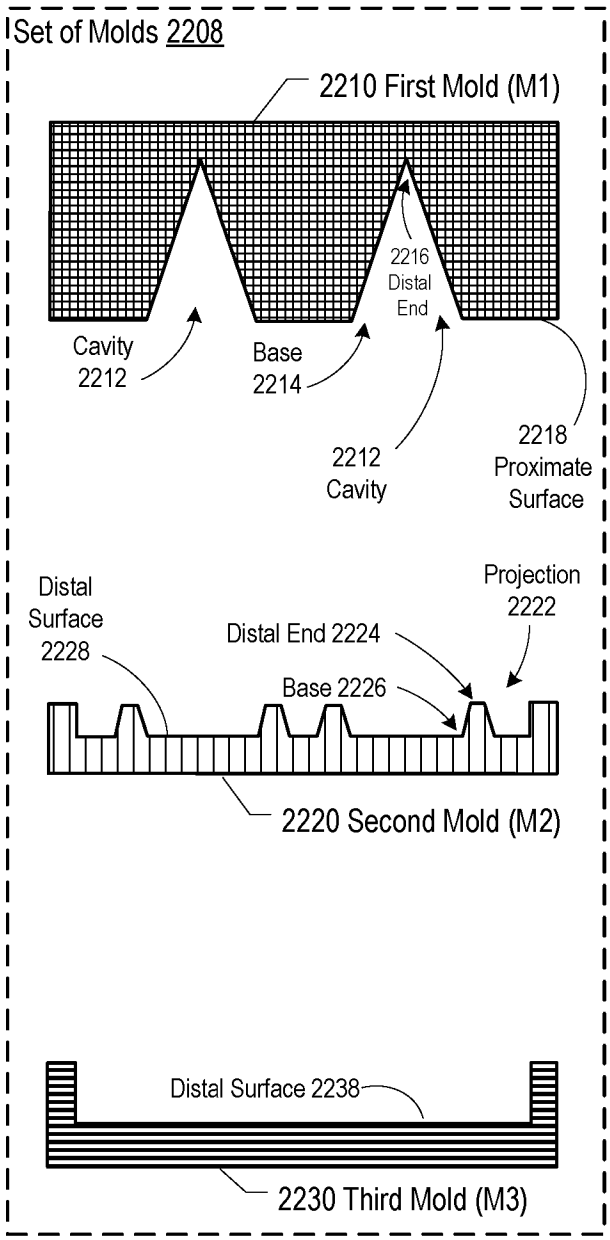

FIG. 22B

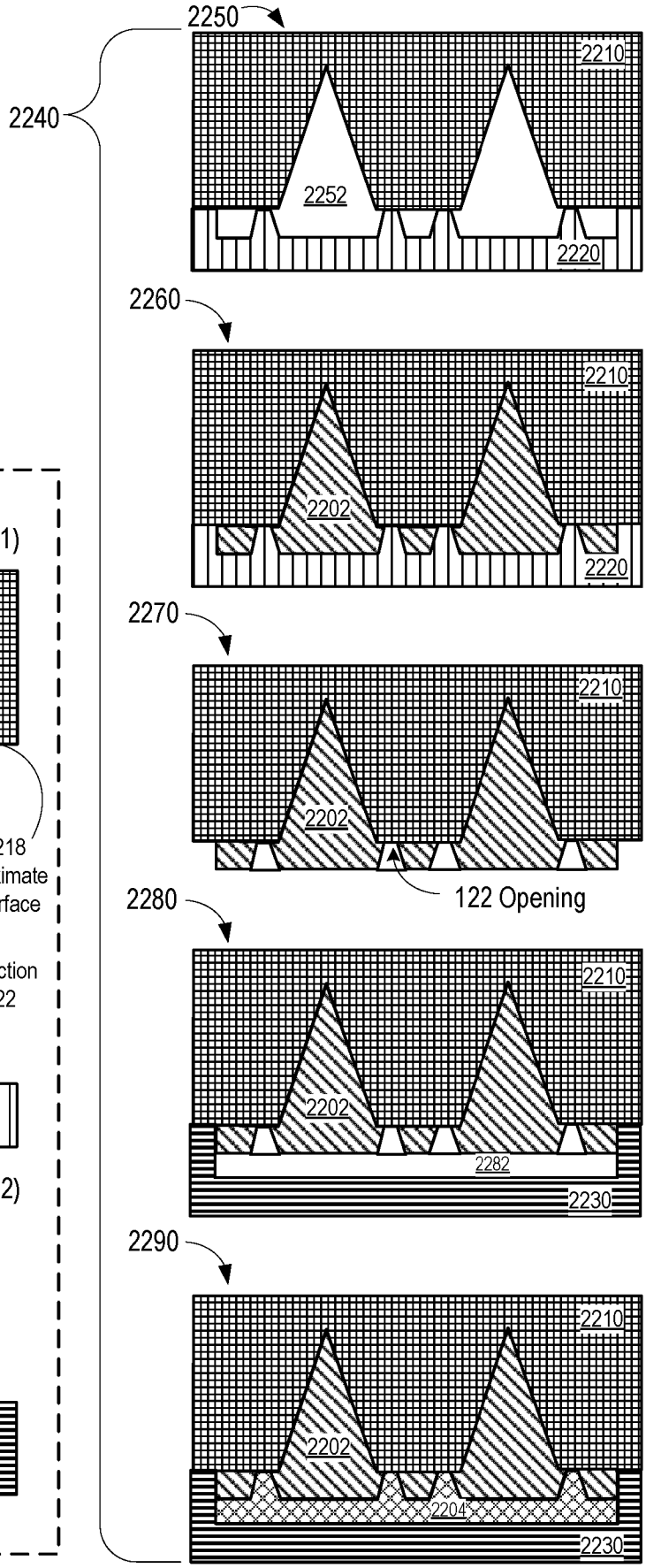

FIG. 22C

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2018/057321

A. CLASSIFICATION OF SUBJECT MATTER
INV. B29C33/00 B29C45/26 A61M37/00 B29C43/22 B29C43/30
ADD.

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)
B29C A61M B29L

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 practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 312 612 B1 (SHERMAN FAIZ FEISAL [US] ET AL) 6 November 2001 (2001-11-06) cited in the application column 3, line 16 - line 20 figures 12-14, 15a column 10, line 48 - column 11, line 65 column 4, line 18 - line 37 column 12, line 32 - line 53 -----	1,4,5, 11-13, 18,19
Y	US 2006/030812 A1 (GOLUBOVIC-LIAKOPOULOS NEVENKA [US] ET AL) 9 February 2006 (2006-02-09) paragraphs [0007], [0009], [0066], [0082] figures 7,14,22, 28-30, 36, 37 ----- -/--	1,4,5, 11-13, 18,19

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

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 January 2019	13/03/2019

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Alink, Maarten

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2018/057321

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

4, 5, 11-13, 15, 17, 19(completely); 1, 14, 18(partially)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2018/057321

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2011/018171 A1 (SEKIHARA KANJI [JP]) 27 January 2011 (2011-01-27)	1,4,5, 11-13, 18,19
A	abstract figures 1a,1b,2a,2b,5a-5c,6a,6b,7a,7b paragraph [0002] - paragraph [0012]	14

Y	WO 01/66065 A2 (NANOPASS LTD [IL]; FRIEDMAN MARK M [IL]; YESHURUN YEHOSHUA [IL]) 13 September 2001 (2001-09-13) figures 7f, 8, 9 page 20, line 14 - page 21, line 16	1,18

Y	DATABASE WPI Week 200620 Thomson Scientific, London, GB; AN 2006-185054 XP002787692, -& CN 1 569 271 A (TECH INST PHYSICS & CHEM CHINESE ACAD) 26 January 2005 (2005-01-26) abstract figures 4, 5l, 5m	1,18

Y	JP 2015 002860 A (TOPPAN PRINTING CO LTD) 8 January 2015 (2015-01-08) figure 1	1,18

Y	WO 00/35530 A1 (MINIMED INC [US]) 22 June 2000 (2000-06-22) figure 8 page 17, line 18 - line 30	1,18

A	US 2011/135539 A1 (SEKIHARA KANJI [JP] ET AL) 9 June 2011 (2011-06-09) abstract figure 3	1

A	US 2012/193840 A1 (KWON SUNG-YUN [US]) 2 August 2012 (2012-08-02) abstract figures 1a, 1b, 2a, 2b paragraph [0030]	14

A	WO 2008/157592 A1 (3M INNOVATIVE PROPERTIES CO [US]; FERGUSON DENNIS E [US]; NAYAR SATIND) 24 December 2008 (2008-12-24) abstract	14

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 4, 5, 11-13, 15, 17, 19(completely); 1, 14, 18(partially)

   Method of manufacturing a microneedle array for forming arrays with a tapered opening from one side to the other side, as well as corresponding system and injection molding set

   ---

2. claims: 6-10, 16, 20(completely); 1, 14, 18(partially)

   Method of manufacturing a microneedle array for forming arrays, whereby the opening is occupied by a hydrophilic material, as well as corresponding system and injection molding set

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3. claims: 2, 3(completely); 1, 14, 18(partially)

   Method of manufacturing a microneedle array for forming arrays whereby multiple openings are positioned between two neighbouring microneedles, as well as corresponding system and injection molding set

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2018/057321

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