THREE-DIMENSIONAL HOLLOW MICRONEEDLE AND MICROTUBE ARRAYS

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ABSTRACT

Three-dimensional arrays of hollow microneedles (hollow tapered-shaft structures) and microtubes (hollow straight-shaft structures) were fabricated from both silicon and electrodeposited metals. The hollow silicon structures were fabricated using deep reactive ion etching combined with a modified black silicon process in a conventional reactive ion etcher. The hollow metal structures were fabricated from epoxy (SU-8) micromolds and electroplating. Microneedles and microtubes have been tested for their suitability in two diverse application areas: transdermal drug delivery and microcombustion. The hollow metal and silicon microneedles have been inserted across skin with no apparent clogging of the needle bores, which is significant to transdermal drug delivery. In addition, a propane-air mixture has been combusted through hollow silicon microneedles and metal microtubes, which act to confine small-scale flames to geometrically controllable areas.

INTRODUCTION

Previously we reported that micromachined three-dimensional arrays of solid silicon microneedles (150 μm in length) increased the permeability of human skin by up to four orders of magnitude *in vitro* [1]. Preliminary tests on human subjects indicated that microneedles can be inserted into skin painlessly due to their short length. However, to increase rates of transport further and achieve better control over the drug delivery profile, hollow needles are desirable. These structures are of interest in biomedical applications such as transdermal drug delivery and transdermal sampling of interstitial fluid to monitor blood analyte concentration (e.g. glucose). In addition to biomedical applications, other microfluidic processes such as controlled microcombustion, which takes advantage of geometrically-defined microflameholders, are of interest.

Lin et al. and Talbot and Pisano have fabricated hollow silicon and polysilicon microneedles as hypodermic needles which are less invasive (i.e. reduction of insertion pain and tissue damage) than conventional needles [2,3]. These single silicon needles range in length from 1 mm - 7 mm and are 30 μm - 200 μm in diameter. Chun et al. fabricated arrays of SiO_2 hollow microcapillaries for controlled injection of genetic materials into cells [4]. These tubes are 30 μm in height, 5 μm in diameter, and have a wall thickness of 1 μm. However, to make hollow microneedles that can be inserted across the skin without either breaking or causing pain, optimal needle dimensions should fall between those of the previously fabricated polysilicon microneedles and micro-capillaries. In particular, the desired hollow needle sizes are heights of approximately 150 μm and wall thicknesses sufficient to provide the mechanical strength to pierce skin. Needles which are oriented perpendicular to the surface are also desirable so that a large needle density per unit area can be achieved.

A second application of hollow microneedles is in the field of combustion on the MEMS scale. Recently, there has been much interest in MEMS-scale combustion processes and the use of energy released by these processes to drive actuators such as electrical power generators [5]. Microgenerators based on MEMS-scale combustion may provide a suitable replacement for batteries in some applications. However, one important issue in combustion on the small scale is the minimization of quenching and unwanted heat transfer, e.g., to the walls of the combustor. These issues become particularly severe on the small scale, as surface-to-volume ratios increase. Hollow microneedles may provide a method of addressing these issues by creating defined 'microflameholders' which isolate MEMS-scale flames from the combustor walls.

This paper describes a variety of fabrication sequences for three-dimensional arrays of hollow microneedles (hollow tapered-shaft structures) and microtubes (hollow straight-shaft structures). These structures are fabricated using combinations of dry etching processes [6,7]; micromold creation in lithographically-defined polymers and selective sidewall electroplating; or direct micromolding techniques using epoxy mold transfers.

FABRICATION TECHNIQUES

Bulk Silicon Methods for Needles and Tubes

Hollow silicon microtubes are fabricated as shown in Figure 1. First, arrays of 40 μm diameter holes are patterned into a 1 μm thick SiO_2 layer on a two inch silicon wafer (Fig. 1a). The wafer is then etched using deep reactive ion etching (DRIE) [6] in an inductively coupled plasma (ICP) reactor to etch deep vertical holes (Fig. 1b). The deep silicon etch is stopped after the holes are approximately 200 μm deep into the silicon substrate (Fig. 1b) and the photoresist is removed. A second photolithography step patterns the remaining SiO_2 layer into circles concentric to the holes, thus leaving ring shaped oxide masks surrounding the holes (Fig. 1c). The photoresist is then removed and the wafer is again deep silicon etched, where simultaneously the holes are etched completely through the wafer (inside the SiO_2 ring) and the silicon is etched around the SiO_2 ring leaving a cylinder (Fig. 1d). A section of a 10 x 10 hollow silicon microtube array is shown in Figure 2. The tubes are 150 μm in height, with an outer diameter of 80 μm, an inner diameter of 40 μm, and a tube center to center spacing of 300 μm.

A variation to the silicon microtube fabrication sequence yields hollow silicon microneedles. An array of holes is first fabricated as described above. The photoresist and SiO_2 layers are replaced with conformal DC sputtered chromium rings. The second ICP etch is replaced with a SF_6/O_2 plasma etch in a reactive ion etcher (RIE), which results in positively sloping outer sidewalls [1] (needles not shown here).

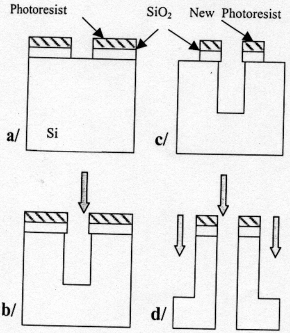

Figure 1 – Fabrication sequence for silicon microtubes: (a) circular holes are patterned through photoresist and SiO_2; (b) holes are partially etched through the wafer with DRIE; (c) rings of SiO_2 are patterned around the holes; and (d) areas not protected by the SiO_2 ring are etched.

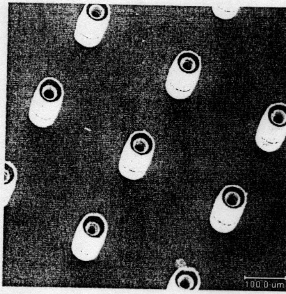

Figure 2 – A scanning electron micrograph of a section of 10 x 10 silicon microtube array.

Micromold Plating Method for Tubes

Unlike the previous fabrication sequences, the creatio of hollow metal tubes does not require dry silicc etching. The process relies on a thick photo-define mold of epoxy (SU-8). A thick layer of SU-8 is spi cast onto a substrate (see below) that has been coate with 30 nm of titanium (Fig. 3). Arrays of cylindrica holes are photolithographically defined through an SU- layer of typical thickness 150 μm [7] (Fig. 3a). Th diameter of these cylindrical holes defines the oute diameter of the tubes.

The upper surface of the substrate is then partiall removed at the bottom of the cylindrical holes in the SU 8 photoresist. The exact method chosen depends on th choice of substrate. The process has been successfull performed on silicon and glass substrates (in which th upper surface is etched using isotropic wet or dr etching techniques), and copper-clad printed wirin board substrates. In the latter case, the copper laminat is selectively removed using wet etching (Fig. 3b). A seed layer (Ti/Cu/Ti – 30 nm/200 nm/30 nm) is then conformally DC sputter-deposited onto the upper surface of the epoxy mold and onto the sidewalls of the cylindrical holes (Fig. 3c). As shown in Figure 3c, the seed layer is electrically isolated from the substrate. Ni, NiFe, Au, Cu, or other electroplatable metals or alloys of interest are then electroplated onto the seed layer (Fig. 3c). The rate and duration of electroplating is controlled in order to define the wall thickness and inner diameter of the microtubes. A photomicrograph of a section of a 40 x 40 array of NiFe microtubes is shown in Figure 4. The microtubes are 200 μm in height with an outer diameter of 80 μm, an inner diameter of 60 μm, and a tube center to center spacing of 150 μm.

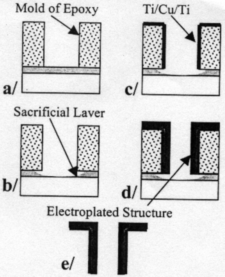

Figure 3 – Fabrication sequence for hollow metal microtubes: (a) cylindrical holes in SU-8 are defined; (b) the sacrificial layer is partially removed; (c) a seed layer (Ti/Cu/Ti) is conformally sputtered; (d) metal is plated; and (e) the surrounding epoxy is removed.

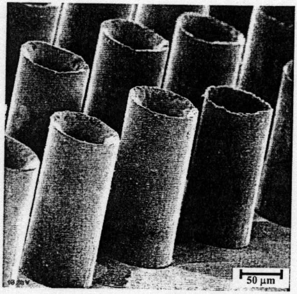

Figure 4 – A scanning electron micrograph of NiFe microtubes. The tubes are 200 µm in height, with an 80 µm outer diameter, a 40 µm inner diameter, and a tube center to center spacing of 150 µm. The holes in the interior of the microtubes protrude through the base metal supporting the tubes.

Micromold Plating Method for Needles

Photolithography yields vertical sidewalls through thick layers of SU-8. The vertical sidewall limitation can be overcome by molding a preexisting 3D structure (i.e., mold-insert). The subsequent removal of the mold-insert leaves a mold that can be surface plated in a fashion similar to the hollow metal microtubes.

The mold-insert that enables the fabrication of hollow metal needles using this process is an array of solid silicon microneedles [1]. The fabrication sequence for arrays of hollow metal microneedles proceeds as diagramed in Figure 5. A layer of epoxy (SU-8) is spin cast onto the array of silicon needles (Fig. 5a) to completely blanket the entire array of needles. The epoxy settles during pre-bake to create a planar surface above the silicon needle tips. The epoxy is then fully pre-baked, photolithographically cross-linked, and post-baked.

The upper surface of the epoxy is then etched away with an O_2/CHF_3 plasma until the needle tips are exposed (Figure 5b), preferably about 1 - 2 µm of tip protruding from the epoxy. The silicon is then selectively removed by using a SF_6 plasma or a HNO_3/HF solution (Figure 5c). The remaining epoxy mold is the negative of the microneedles with a small diameter hole where the tip of the silicon needle was. After the removal of the silicon, a seed layer (Ti-Cu-Ti) is conformally sputter-deposited onto the epoxy micromold. Following the same process sequence as described for hollow metal microtubes, NiFe (or Au, Cu, etc.) is then electroplated onto the seed layer (Fig. 5c). Finally, the epoxy is removed using an O_2/CHF_3 plasma leaving an array of hollow metal microneedles (Fig. 5d). A photomicrograph of a section of a 20 x 20 array of NiFe microneedles is shown in Figure 6. The microneedles are 150 µm in height with a base diameter of 80 µm, a tip diameter of 10 µm, and a needle to needle spacing of 150 µm.

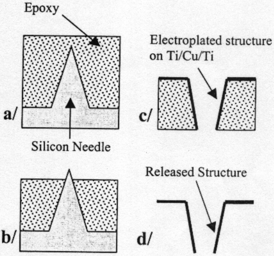

Figure 5 – Fabrication sequence for hollow metal needles: (a) SU-8 is spin cast onto arrays of silicon needles, (b) the SU-8 layer is etched (O2/CHF3 plasma) until silicon needle tips are exposed, (c) a seed layer is deposited; a metal is electroplated, and (d) the SU-8 is removed (O2/CHF3 plasma).

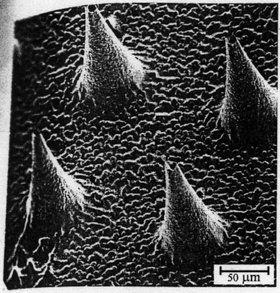

Figure 6 – Hollow NiFe microneedles fabricated using an epoxy (SU-8) mold of a silicon mold-insert.

APPLICATIONS

Both silicon and hollow metal microneedles have been inserted through human skin epidermis. A hollow metal microneedle penetrating up through the underside of epidermis is shown in Figure 7. The needles are still intact and the tips are not clogged with debris. The hollow microneedles have also been shown to permit the flow of water through their bores (data not shown). Minimal clogging and fluid flow are important if fluid is to be transported through the bore of the needle.

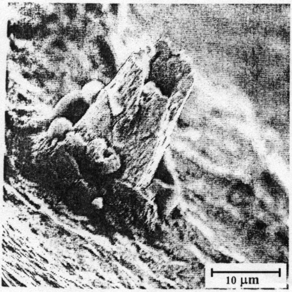

Figure 7 - A scanning electron micrograph of a NiFe microneedle penetrating up through the underside of human epidermis.

Both silicon microneedles and metal microtubes have been used to combust a stoichiometric mixture of propane and air at room temperature. An array of silicon microneedles combusting this gas mixture is shown in Figure 8. This demonstrates the feasibility of using microneedles to create small hydrocarbon-based flames for microcombustion applications.

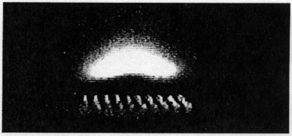

Figure 8 - A photomicrograph of an array of microneedles combusting a mixture of propane and air.

CONCLUSIONS

Three-dimensional microneedles and microtubes have been fabricated from both silicon and metal. Silicon microneedles, metal microneedles, and metal microtubes have been successfully inserted through human skin for transdermal drug delivery. In addition, microneedles and microtubes have been successfully used as flameholders for microcombustion experiments.

ACKNOWLEDGEMENTS

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