APPLICATION NOTE

HOLLOW SILICON-BASED MICRONEEDLE ARRAY FOR DERMAL INTERSTITIAL FLUID EXTRACTION FABRICATED BY ONLY DRY ETCHING IN WAFER SCALE

by

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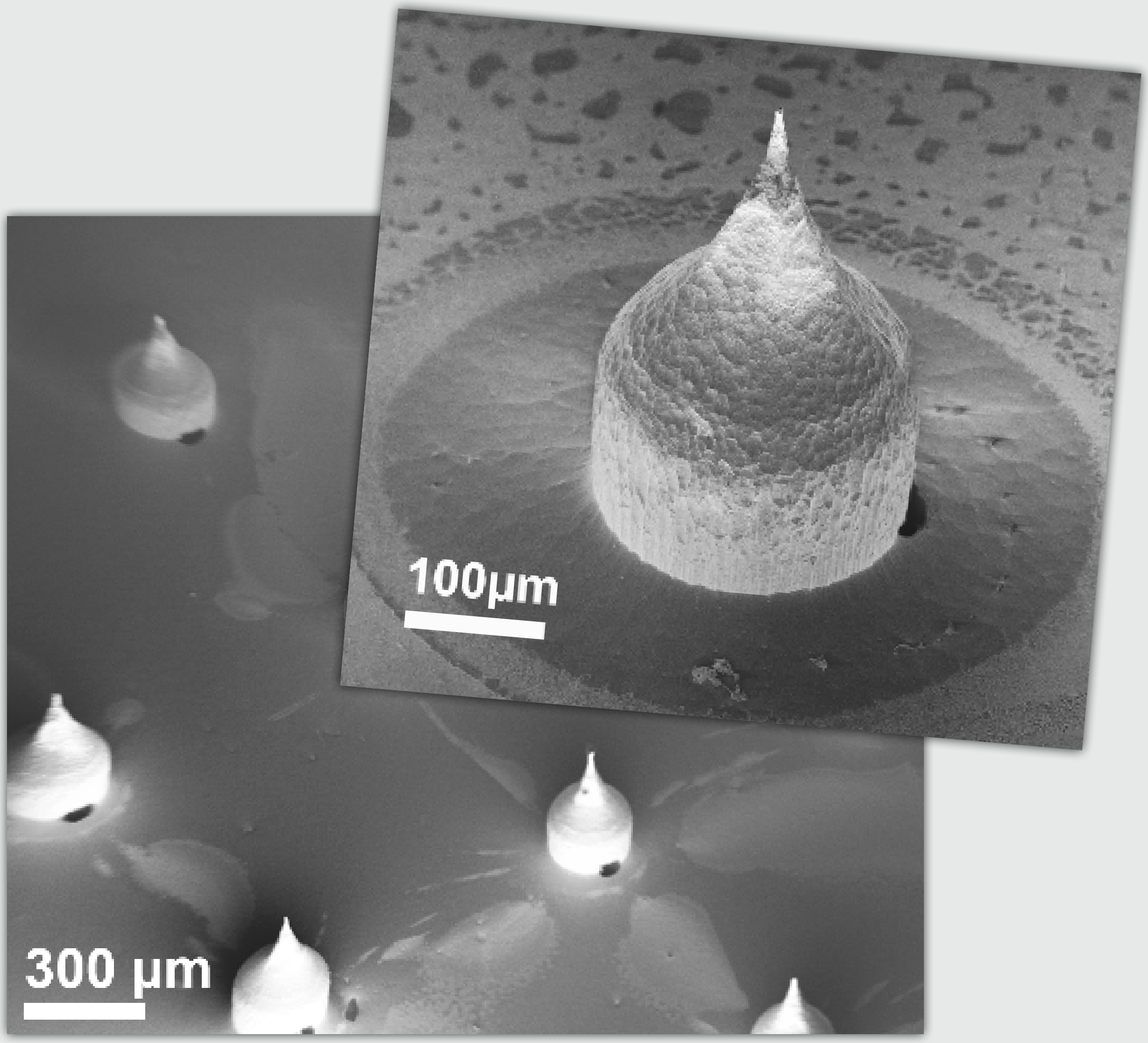

INTRODUCTION

The interstitial fluid (ISF) within the dermal layer serves as a rich source of biomarkers, offering valuable insights into a patient's health [1]. Despite its significance, the extraction of pristine ISF has long posed a challenge. Meanwhile, silicon has emerged as a dominant material in the microfabrication industry due to its accessibility, ease of fabrication, and outstanding mechanical and electrical characteristics. The high Young's modulus of silicon makes it an ideal choice for the fabrication of microneedles (MN), ensuring sharpness for painless penetration. The advantages of silicon-based microneedles include mass production compatibility and seamless integration with sensing and readout systems [2].

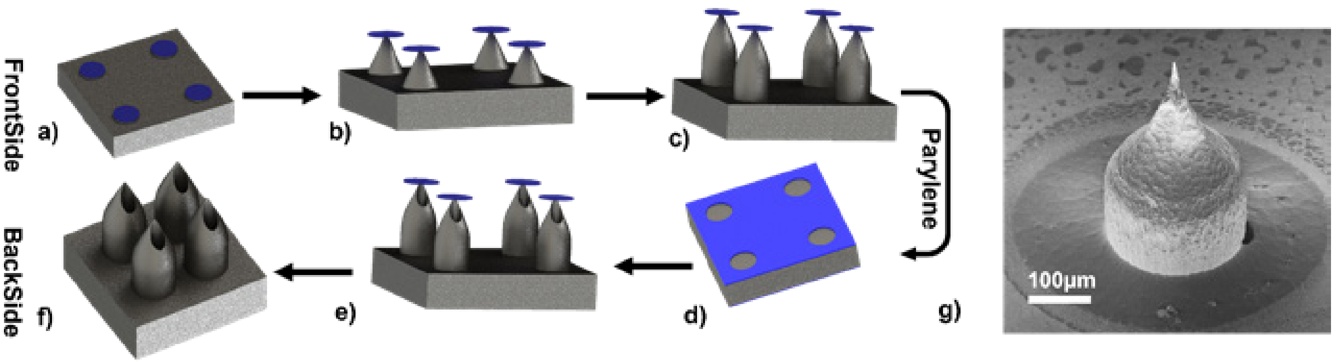

Figure 1. HMNA fabrication process flow: a) Circle SiO_2 Mask Pattern: Initiation of the process involves creating a circular SiO_2 mask pattern. This step is crucial in defining the initial structure for subsequent fabrication. b) RIE Dry Etching: The fabrication process then proceeds to Reactive Ion Etching (RIE), a dry etching technique. This step involves the precise removal of material from the silicon wafer, guided by the SiO_2 mask pattern. c) DRIE for Needle Elongation: Deep Reactive Ion Etching (DRIE) is employed to elongate the microneedles. This specialized technique allows for controlled and deep penetration, shaping the microneedles to the desired length. d) Backside SiO_2 Patterning for Holes: To create the hollow structure, backside SiO_2 patterning is introduced. This step is performed after the topside is covered with parylene, a protective material, ensuring the integrity of the needles during subsequent processes. e) Continuing DRIE Till Revealing Holes: The DRIE process continues until the holes are fully revealed. This meticulous step ensures the formation of hollow microneedles with the desired dimensions. f) BHF Bath to Remove SiO_2 from Both Sides: Subsequent to the fabrication steps, a Buffered Hydrofluoric Acid (BHF) bath is utilized. This step is essential for removing the SiO_2 material from both the front and back sides of the silicon wafer, leaving behind the completed microneedle array. g) Single Fabricated Needle: The cumulative effect of these fabrication steps results in the successful creation of a single fabricated needle. This final product represents the culmination of the intricate processes involved in developing the Hollow Microneedle Array.

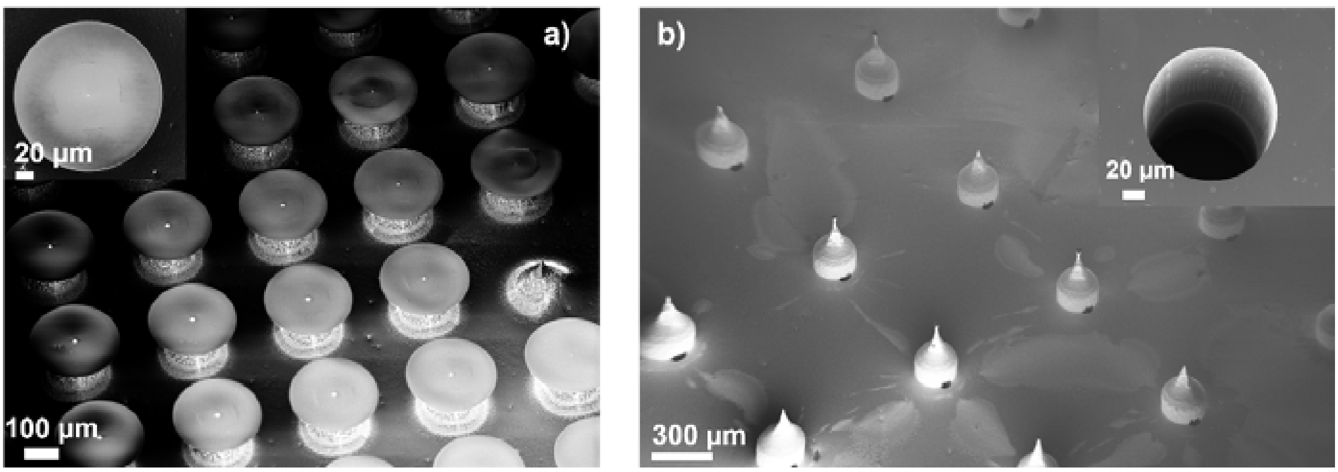

Figure 2. a) Microneedle Array (MNA) Prior to Decapping: Top-view presentation of the Microneedle Array (MNA) in its state before the decapping process, providing an in-situ perspective. b) Hollow Microneedle Array (HMNA) with Backside Hole: In-situ view of the Hollow Microneedle Array (HMNA), showcasing the backside hole, a crucial feature in the array's design and functionality.

SILICON-BASED MICRONEEDLE FABRICATION

Two approaches for silicon-based microneedle fabrication are explored: the in-plane and out-of-plane configurations [3,4]. In the in-plane method, microneedles are shaped by thorough silicon etching within the same plane as the wafer, enabling the creation of very long microneedles. However, fragility becomes a concern, and the technique is limited to a single-row microneedle array (MNA). The out-of-plane approach involves top-to-bottom fabrication, with needle elongation and sharpening as crucial steps. Various methods, such as laser cutting and blades, have been employed for needle sharpening, often necessitating tool switching. Both approaches face challenges in fabricating hollow microneedles [2].

PROPOSED TECHNIQUE

This study introduces a comprehensive dry etching technique, utilizing reactive ion etching (RIE), for the fabrication of silicon-based hollow microneedle arrays (HMNA). The proposed technique is designed to be compatible with wafer-scale fabrication approaches. The needles achieved a length of approximately 500 μm on a 1mm thick wafer, effectively reaching the ISF pool in the dermal layer. The hollow structure, with a hole size of 100 μm, enhances biofluid extraction. Dry etching is advantageous due to its potential for a greater number of needles on small chips compared to wet etching techniques [2].

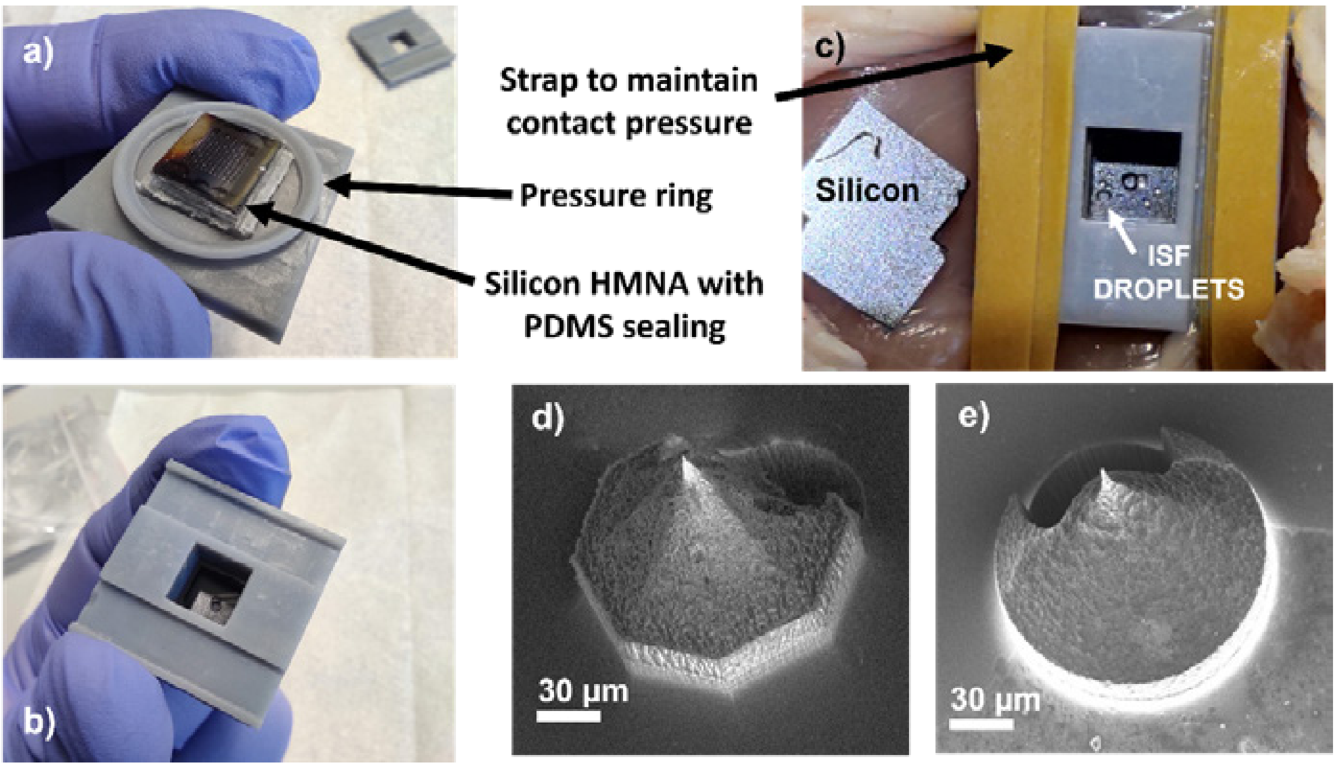

Figure 3. a) Top View from the HMNA Holder: Observation from the upper perspective of the Hollow Microneedle Array (HMNA) holder, providing insights into its configuration and arrangement. b) Bottom View from the HMNA Holder: Examination from the lower perspective of the HMNA holder, offering a view of the underside and additional details about its structure. c) Assembled HMNA on Chicken Skin with Applied Pressure: The HMNA assembly is showcased on chicken skin, emphasizing the application of pressure using straps. Additionally, a dummy silicon substrate is incorporated for condensation control. d) Needle Before Insertion: Visual representation of the microneedle in its original state before undergoing the insertion process. e) Needle After Insertion: Depiction of the microneedle subsequent to the insertion, highlighting no changes or adaptations resulting from the interaction with the target surface.

FABRICATION PROCESS

The fabrication involves both sides of a silicon wafer, utilizing a thick silicon oxide layer as a dry etch mask (4 μm). The process begins with needle formation on the front side and concludes with hole creation from the backside using deep reactive ion etching (DRIE), thanks to the backside alignment capability of the MLA 150 from Heidelberg Instruments, revealing the needles on the other side. The sharpness of the needles is achieved through careful optimization of the undercut etching in the Bosch process, enabling elongation. Perylene is deposited on the front side before backside etching to protect the needles and the tool's vacuum and cooling system. The protective mask is removed by buffered hydrofluoric acid (BHF) etching at the end of the process [2].

MECHANICAL ENDURANCE AND ISF EXTRACTION STUDY

To evaluate the performance of the developed hollow microneedle arrays (HMNA), mechanical endurance and ISF extraction capabilities were studied. The HMNA chip was assembled on a 3D printed setup equipped with straps for applying pressure around the chip holder. Insertion into chicken meat served as a model to simulate skin penetration. The study demonstrated that a 10×10 HMNA was capable of extracting 5 μL of ISF within 10 minutes after insertion, followed by the application of pressure. Figure 3 depicts the needle shapes before and after insertion, showcasing the effectiveness of the HMNA in extracting ISF [3,4].

CONCLUSION

This research presents a significant advancement in silicon-based hollow microneedle array fabrication, introducing a full dry etching technique compatible with wafer-scale production. The resulting HMNA demonstrated mechanical endurance and efficient ISF extraction capabilities, making it a promising tool for various biomedical applications. The potential for mass production and integration with sensing systems positions silicon-based hollow microneedle arrays as a valuable technology in the field of minimally invasive diagnostics and monitoring.

[1] Miller, P.R., Taylor, R.M., Tran, B.Q. et al. Extraction and biomolecular analysis of dermal interstitial fluid collected with hollow microneedles. Commun Biol 1, 173 (2018).

[2] He X, Sun J, Zhuang J, Xu H, Liu Y, Wu D. Microneedle System for Transdermal Drug and Vaccine Delivery: Devices, Safety, and Prospects. Dose-Response. 2019;17(4).

[3] Izumi, Hayato, and Seiji Aoyagi. "Novel fabrication method for long silicon microneedles with three-dimensional sharp tips and complicated shank shapes by isotropic dry etching." IEEJ Transactions on Electrical and Electronic Engineering 2.3 (2007): 328-334.

[4] O'Mahony, Conor, et al. "Hollow silicon microneedles, fabricated using combined wet and dry etching techniques, for transdermal delivery and diagnostics." International Journal of Pharmaceutics 637 (2023): 122888.

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