Polymer-based disposable microneedle array with insertion assisted by vibrating motion

F.-W. Lee, W.-H. Hung, C.-W. Ma, and Y.-J. Yang^{a)}

Department of Mechanical Engineering, National Taiwan University, Taipei 10617, Taiwan

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This work presents a disposable polymer-based microneedle array that carries out insertions by mimicking the vibrating motion of a mosquito's proboscis. The proposed device, which comprises a 10:1 high-aspect-ratio parylene microneedle array and a chamber structure, was monolithically realized using a novel fabrication process. The vibrating motion of the microneedles was generated using a piezoelectric actuator. This device can be potentially applied to extract and collect blood by puncturing the dermis layer of human skin. The fabricated device is advantageous because of its biocompatibility, simple fabrication process, and low associated costs. Additionally, the graph of the measured extraction flow rate versus the pressure drop that is presented shows an agreement with the results predicted by analytical models. A 40% reduction of insertion force was demonstrated when the microneedle insertion was assisted by actuator-induced vibratory motions. Buckling analyses for estimating the maximum loads that the microneedle can sustain before failure occurs were also evaluated. Finally, the relationship between the insertion force and the vibration frequency was demonstrated in this study. © 2016 AIP Publishing LLC. [<http://dx.doi.org/10.1063/1.4939948>]

I. INTRODUCTION

Blood analysis, which is used to acquire essential biological information, is critical to the diagnosis of many human diseases.¹ The parameters or levels in blood analysis include glucose, proteins, blood fats, electrolytes, minerals, urinalysis, waste products, enzymes, hormones, and risk factors. In general, blood is extracted using hypodermic needles or finger-pricks.² However, hypodermic needles have to be used by professionals in hospitals and are not suitable for personal use. Additionally, the blood volume extracted by the finger-prick method is usually insufficient for a typical comprehensive blood test.

In recent years, various research teams have developed minimally invasive microneedles to replace traditional hypodermic needles.^{3–13} Li *et al.* reported a microsystem for automated blood sampling from laboratory mice.¹⁴ The proposed device, which consists of a microneedle, a reservoir, and an actuator, was designed to instantaneously prick the animal for a time-point sample. Khumpuang *et al.* reported a blood-extraction device integrated with an electrolyte-monitoring system.¹⁵ This device can precisely control the dosage of extracted blood. A novel blood-extraction system realized by assembling a high-aspect-ratio microneedle in a polydimethylsiloxane elastic self-recovery actuator was proposed.¹⁶ The elastic self-recovery actuator converts finger force into elastic energy to power blood extraction and transport blood without requiring an external power source. Wang *et al.* developed a polymer-based process for fabricating microneedles using UV lithography.¹⁷ A hollow microneedle array and baseplate, in which needle lumens extend through the thickness of the baseplate, were demonstrated. Izumi *et al.* proposed a biodegradable polymer needle with a sharp tip using a micromolding technique was proposed.¹⁸ The proposed device imitates a mosquito's blood-sucking motion and is

^{a)} Author to whom correspondence should be addressed. Electronic mail: yjy@ntu.edu.tw. Tel.: +886-2-3366-4941. Fax: +886-2-23646491.

intended for medial application. These aforementioned devices comprise separate extraction units (microneedles) and storage units (chambers).

For designing and fabricating microneedles, it is crucial to ensure that the structural rigidity of the microneedles is sufficient for needle insertion into the intended medium. The microneedles are also required to tolerate anticipated forces caused by normal human movements. It has been demonstrated that the cutting forces of powered surgical devices with ultrasonic vibrating motion have been dramatically reduced by about one order of magnitude.^{19,20} In addition, Yang and Zahn investigated the effect of vibratory actuation on microneedle insertion force.²¹ A vibratory actuator was integrated with hypodermic microneedles. About a 70% reduction in microneedle insertion force was observed when vibratory actuation was employed.

In this study, we proposed a miniaturized blood extraction device that consists of a parylene microneedles array and a microchamber that are monolithically integrated using the embedded parylene channel fabrication process.²² The device is designed as an alternative hypodermic needle for personal use. The primary purpose of the device is to extract and collect blood by puncturing the dermis layer of human skin. In addition, the insertion process is proposed to be carried out by using a piezoelectric actuator to imitate the motion of a mosquito's proboscis. By imitating the vibrating motion, the puncture force of the microneedles can be effectively decreased without buckling effects. The remainder of the paper is organized as follows: Section II presents the device design, operational principle, materials, and fabrication processes. Section III discusses the measurement results, and finally, the conclusion is presented in Section IV.

II. MATERIALS AND METHODS

A. Working principle and design

Fig. 1(a) shows the schematic of the proposed device, which consists of a microneedle array, a chamber structure, and an outlet. To minimize pain during needle insertion, the dimension of the microneedles was designed to mimic a mosquito's proboscis. The microneedle array and chamber structure of the proposed device can be monolithically fabricated using the quasi-hemi-circular embedded channel fabrication process. Since the diameter of each microneedle is quite small, the effective flow resistance is very large. To maintain a sufficient flow rate in practical applications, a 10×1 linear array of microneedles was proposed. The length of the microneedle is 2 mm, and the chamber dimensions are $5 \text{ mm} \times 5 \text{ mm} \times 30 \mu\text{m}$.

Fig. 1(b) illustrates the schematic of the insertion process using the proposed microneedle array. The proposed device is attached on a piezoelectric actuator, which is fixed onto an XY stage. The actuator produces the vibrating motions, and the XY stage adjusts the position of the device during the insertion process. After the microneedles penetrate the skin, blood is collected in the chamber using the microneedle array when the syringe pump draws in the liquid. The microneedle can be considered as a thin-walled column, and buckling should be the most likely failure mode as the microneedle array is inserted into the surface of a softer material. Therefore, the vibratory motion generated by the actuator, which imitates the motion of the mosquito's blood extraction process, can potentially reduce the resistance force, which ensures the required insertion force is below the critical force, which induces the bulking of microneedles.

B. Materials and fabrication

Parylene C was selected as the structural material for the microneedle array because of its biocompatibility and chemical inertness to organic and inorganic solvents.^{22,23} Furthermore, parylene can be conformally deposited on a substrate, which is essential to embed channels onto a patterned silicon substrate. Parylene films can also be deposited at room temperature, so the process is compatible with other microfabrication technologies. Figure 2 illustrates the sequence of steps that comprise the fabrication process of the proposed device. The top view (the right column) and the A–A' and B–B' cross sectional views are illustrated. The process

FIG. 1. (a) Schematic of the proposed device. (b) Schematic of the insertion of microneedle array with vibratory motion.

begins with a single-side polished silicon wafer that is $525\ \mu\text{m}$ thick. The first $4\ \mu\text{m}$ -thick parylene layer was deposited on the silicon substrate after the A-174 silane adhesion promoter treatment (Fig. 2(a)). Then, the parylene layer was patterned using reactive ion etching (RIE) with oxygen plasma (Fig. 2(b)). The patterned parylene layer served as the etching mask for the subsequent silicon etching process. Isotropic silicon etching was performed with the application of a hydrofluoric nitric acetic solution²⁴ ($\text{HF}:\text{HNO}_3 = 3:20\ \text{ml}$) (Fig. 2(c)). The trenches that were created have an undercut of approximate $30\ \mu\text{m}$ from the edge of the parylene openings. The second parylene layer with a thickness of about $20\ \mu\text{m}$ was then deposited. Since parylene deposition is a very conformal process, the inside surfaces of the trenches were coated with parylene films and the openings of the first parylene layer were sealed.^{22,25} Microneedles were then formed by the parylene film that was deposited inside the trenches, as shown in Fig. 2(d). The parylene structure was then patterned using RIE with a photoresist (AZ P4620) mask (Fig. 2(e)) to remove the parylene between microneedles. As shown in Fig. 2(f), the microneedle array was released by dissolving the silicon substrate in KOH. Finally, the microneedles were sharpened using a razor blade (Fig. 2(g)).

Figure 3(a) shows the fabricated devices. Fig. 3(b) shows a microneedle array whose outlet was connected to one end of a thin Polyethylene (PE) pipe. The other end of the PE pipe was connected to the outlet of a syringe pump. Additionally, the device was fixed to the top of the surface of a piezoelectric actuator. The length of the microneedle is about $2\ \text{mm}$, and the size of the chamber is about $5\ \text{mm} \times 5\ \text{mm}$. Fig. 4(a) shows the scanning electron microscopy (SEM) image of the fabricated microneedles. The grooves resulting from the sealing of the

FIG. 2. The fabrication process of the proposed device.

FIG. 3. (a) The fabricated device. (b) A zoomed-in view of the device.

FIG. 4. (a) SEM images of the fabricated microneedles array. (b) SEM image of the zoomed-in view of the parylene microneedle.

trench opening can be clearly observed. The zoomed in cross-sectional SEM image of a parylene microneedle is shown in Fig. 4(b). The cross-section of the microneedle channel is comparable to a semi-ellipse with a major radius of $50\ \mu\text{m}$ and a minor radius of $20\ \mu\text{m}$.

III. RESULTS AND DISCUSSION

A. Flow rate measurement

The schematic of the experimental setup for measuring the flow rate of the microneedle array is shown in Fig. 5(a). Fig. 5(b) illustrates the experiment setup. The device was connected to a syringe pump (kd Scientific Inc., KDS 100) using a PE pipe, which controlled the flow rate precisely. A pressure sensor (KEYENCE Inc., MGP01TW) was also connected to the middle of the PE pipe to measure the flow pressure. The flowrate was adjusted manually by using the syringe pump, and the measured steady-state pressure drop was shown on the display of the pressure sensor.

The model of the system can be easily derived using pipe flow models. The system can be divided into three segments: the parallel channels of the microneedles, the microchamber, and the PE pipe. Fig. 6 illustrates the flow resistance model of the system. The flow resistance for each case is defined as the ratio of the pressure drop between the ends of the resistance to the corresponding flow rate.

The microneedle array can be modeled as 10 flow resistors arranged in parallel. Here, we assumed that the microneedle channel is an ideal circular pipe. Due to the low Reynold's

FIG. 5. (a) Schematic for measuring the chamber pressure versus flow rate as the microneedle array draws in DI water. (b) Picture of the experimental setup.

FIG. 6. Equivalent circuit schematic of the fluidic system.

number, the flow inside the microneedles is considered as a fully developed laminar flow in a pipe. Since the flow in the microneedle is very small, we assume the flow to be a fully developed laminar flow in a pipe. Therefore, the flow resistance of the microneedle R_n can be written as follows:²⁶

$$R_n = \frac{\Delta p}{Q} = \frac{8\mu L_n}{\pi r_{eff}^4}, \quad (1)$$

where Δp is the pressure difference in the pipe, Q is the flow rate, μ is the viscosity, L_n is the length of the microneedle, and r_{eff} is the effective radius of the pipe. The cross sectional area of the channel was estimated to be about $500\pi \mu\text{m}^2$ from the SEM images. Consequently, we assumed that the effective radius r_{eff} of the pipe was $22.36 \mu\text{m}$. The length of the pipe L is 2 mm, and the viscosity of deionized (DI) water μ is $1.002 \times 10^{-3} \text{ Pa s}$. The flow resistance of each microneedle was evaluated using Eq. (1) and found to be $2.04 \times 10^{13} \text{ Pa s/m}^3$.

For the microchamber, given the assumption of a low Reynold's number, the flow resistance of the chamber R_c can be written as follows:²⁶

$$R_c = \frac{\Delta p}{Q} = \frac{12\mu L_c}{g^3 w}, \quad (2)$$

where g is the chamber gap between the top and the bottom of the inner surface, w is the width of the chamber, and L_c is the distance from the microneedle base to the center of the outlet on the chamber (see Fig. 1(a)). L_c , g , and w are designed to be 2.5 mm, $20 \mu\text{m}$, and 5 mm, respectively. The calculated flow resistance of the chamber R_c is $7.52 \times 10^{11} \text{ Pa s/m}^3$.

The PE pipe has a circular cross section. Therefore, Eq. (1) can be used to estimate the corresponding flow resistance. The radius of the pipe is about 1.5 mm, which is two orders of magnitude larger than that of the microneedles. According to Eq. (1), the flow resistance of the PE pipe is much less than the total flow resistance of the microneedles, even though the length of the PE pipe is about a few hundred millimeters long. Thus, the pressure drop along the PE pipe was assumed to be negligible when compared with the pressure drop inside the microneedles. Consequently, the flow resistance of the PE pipe was not considered in the model.

Fig. 6 shows the equivalent flow circuits of the total system. The microneedles array can be modeled as 10 flow resistors R_n in parallel. The total flow resistance R_{Total} can be written as

$$R_{Total} = \frac{R_n}{10} + R_c. \quad (3)$$

Based on the dimensions of the device, the total flow resistance R_{Total} is estimated to be about $2.792 \times 10^{12} \text{ Pa s/m}^3$.

Fig. 7 shows the measured results. The dashed line represents the analytical prediction values, and the solid line represents the measured values. The measured values were reasonably consistent with the values obtained via analytical prediction. The slope of the measured values was relatively greater than that of the analytical prediction values. This discrepancy is mainly

FIG. 7. The measured relationship between the pressure and the flow rate.

due to the under-estimation of the flow resistance of the microneedles. In our model, we assumed that the microneedles have perfectly circular cross-sections. The radius of the circular cross-section was actually estimated from the cross-sectional area of microneedles, which is semi-elliptical in reality.

B. Penetrating capability

During the needle insertion process, an axial load was induced using the XY stage to generate a linear displacement of the microneedle array. This force was resisted by the material under test (MUT), into which the microneedles were inserted. Buckling analyses were conducted to estimate the maximum load that the microneedle could sustain before the occurrence of failure. The results of these analyses were used to provide insight on and to prevent failure conditions during needle insertion.

To calculate the critical buckling load, each microneedle was considered as a hollow cylinder. Based on the buckling theory of a hollow cylinder,²⁷ regardless of its end conditions, the critical load P_{cr} can be expressed in a general form as

$$P_{cr} = \frac{\pi^2 EI}{K^2 L^2}, \quad (4)$$

where E is the Young's modulus of the material, I is the moment of inertia of the cross section²⁸ ($I = 0.5 \cdot m(r_1^2 + r_2^2)$), L is the length of the column, and K is the effective length factor that is dependent on the boundary conditions of the column. The effective length factor will be discussed later.

Based on the SEM images, the outer minor radius of the microneedles is about $40 \mu\text{m}$, and the inner minor radius of the microneedle is about $20 \mu\text{m}$. Therefore, the lower bound of the critical buckling force can be estimated by assuming that the microneedle is a hollow cylinder with an inner diameter of $20 \mu\text{m}$ and an outer diameter of $40 \mu\text{m}$, as shown in Fig. 8.

The theoretical values of K for two possible boundary conditions of our device are shown in Fig. 9.²⁷ Before the microneedle punctures the skin, the end of the needle that comes in contact with the MUT can be considered to be hinged at the surface of the MUT without sliding. These boundary conditions of the needle are shown in Fig. 9(a). Based on the aforementioned information, the effective length factor K is equal to 0.7, L is 2 mm, and the Young's modulus of parylene C is 4 GPa.²⁹ Thus, the critical load P_{cr} of the microneedle is 12.36 mN, using Eq. (4).

After the tip of the microneedle is inserted, the end of the microneedle cannot be considered to be hinged at the MUT. This end is somewhat constrained, not only in terms of translational motions but also with respect to rotational motions, even though the MUT is not a fully rigid material. In addition, part of the microneedle in this case penetrates into the MUT, which

FIG. 8. The inner and outer diameters of the hollow, circular column for estimating the lower bound of the critical force.

FIG. 9. Theoretical K values for idealized columns with two different boundary conditions. The buckled shape of the column is shown with the dashed line.²⁷

FIG. 10. Experimental setup for measuring the puncture force.

in turn decreases the effective L in Eq. (4). Therefore, the critical load P_{cr} will be larger than that in the case when the microneedle is not inserted into the MUT. To simplify the calculation, the boundary condition can be approximated based on the schematic shown in Fig. 9(b), in which the value of K is 0.5, and the calculated critical load increases to be about 24 mN.

The proposed microneedle device consists of 10 microneedles; so the effective critical load before the device is inserted into the MUT is about 123.6 mN, and the effective critical load after insertion into the MUT is about 240 mN.

The experimental setup for measuring the insertion force with different materials is shown in Fig. 10. The fabricated device was attached to a piezoelectric actuator, which was mounted on an XY stage. A power amplifier was used to drive the piezoelectric actuator, which produced the vibrating motion of the microneedles. A function generator fed the waveform into the power amplifier. The force gauge, with a maximum resolution of 1 mN, was used to measure the penetrating force and was fixed on a stage. Chicken skin, chicken heart muscle, and jelly were chosen as sample MUTs to assess the penetrating capability of the parylene microneedles. The MUT was fixed on the probe of the force gauge. The resistance force was measured and recorded using a data acquisition device, which was connected to a computer.

Fig. 11(a) shows the measured resistance forces during the insertion process for three of the aforementioned MUTs (i.e., chicken skin, chicken heart muscle, and jelly). During the

(a)

(b)

FIG. 11. (a) Transition of resistance force during the insertion process for three different MUTs. (b) Effect of vibration frequency on puncture force.

insertion process, the piezoelectric actuator oscillated along the direction of insertion at 30 Hz. For the chicken skin and the chicken heart muscle samples, as the displacement of the micro-needle array increased, the resistance force also increased. The curve then decreased as the microneedle array punctured the material, and the corresponding force, which is the local maximum of the force curve, was identified as the puncture force. The resistance force increased again with displacement, as the base of the microneedles came into contact with the material. For the jelly sample, the puncture force was not observed in the curve because the material was so soft that the needles punctured it easily on contact. Fig. 11(b) shows the insertion forces with respect to the vibrating frequency for the chicken skin and the chicken heart muscle samples. The results show that the longitudinal vibrating motion of the microneedles indeed reduces the required puncture forces. As seen in the figure, there is a reduction of about 40% in puncture force when the piezoelectric actuator operates at 500 Hz, with a lateral vibration amplitude of 0.3 mm during microneedle insertion into chicken skin. Additionally, increasing the vibrating frequency further decreases the puncture force.

IV. CONCLUSIONS

A disposable parylene-based microneedle array for blood extraction is presented in this paper. The insertion of the microneedles into testing materials was assisted by the vibrating motion generated by a piezoelectric actuator. The proposed device consists of a parylene microneedle array and a chamber structure and can be monolithically fabricated using the embedded parylene channel fabrication process. The vibrating motion of the microneedles imitates a mosquito's blood-sucking motion. The measured relationship between the pressure and the flow rate was presented. The measured values were shown to be consistent with the analytical prediction values. Insertion tests with the proposed device were conducted to demonstrate its ability to puncture different materials. The test results showed that the device was able to puncture the chicken skin and chicken heart muscle samples successfully. The relationship between the puncture force and vibration frequency was also illustrated. The measured results showed that by imitating a mosquito's blood-sucking motion, the insertion force can be effectively reduced by about 40%.

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