2010

Design and fabrication of micronozzles for drug delivery applications

Yuxuan Zhou

Louisiana State University and Agricultural and Mechanical College, yzhou6@tigers.lsu.edu

Follow this and additional works at: https://digitalcommons.lsu.edu/gradschool_theses

Part of the Mechanical Engineering Commons

Recommended Citation

https://digitalcommons.lsu.edu/gradschool_theses/2805

This Thesis is brought to you for free and open access by the Graduate School at LSU Digital Commons. It has been accepted for inclusion in LSU Master's Theses by an authorized graduate school editor of LSU Digital Commons. For more information, please contact gradetd@lsu.edu.
DESIGN AND FABRICATION OF MICRONOZZLES FOR DRUG DELIVERY APPLICATIONS

A Thesis

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Master of Science in Mechanical Engineering

In

The Department of Mechanical Engineering

By
Yuxuan Zhou
B.E., Tsinghua University, P. R. China, 2006
August 2010
ACKNOWLEDGEMENTS

I would like to express my sincerest appreciation to Dr. Wanjun Wang, my major professor, for sharing with me his extensive knowledge in microelectromechanical systems (MEMS) and microfabrication technology. His guidance, patience, and encouragement made this thesis possible.

I am also indebted to Drs. Wenjin Meng and Jin-Woo Choi for their time and assistance. I would also like to thank my fellow graduate students for their support and advice on all things scientific and nonscientific.

Finally, I am grateful to my parents for encouraging me to pursue a Master’s degree at LSU. Their blessings, guidance and love have brought me a long way in my life.
# TABLE OF CONTENTS

ACKNOWLEDGEMENTS ........................................................................................................ ii

LIST OF TABLES .................................................................................................................... iv

LIST OF FIGURES .................................................................................................................. v

ABSTRACT .............................................................................................................................. vii

CHAPTER 1 INTRODUCTION ................................................................................................. 1

CHAPTER 2 THE FIRST METHOD TO FABRICATE MICRONEEDLES ........................................ 10
  2.1 Introduction to machine .................................................................................................. 10
  2.1.1 Machining principle ................................................................................................. 10
  2.1.2 Machine operate steps ............................................................................................ 11
  2.2 Etching procedure ....................................................................................................... 13
  2.3 Pressing ....................................................................................................................... 14
  2.4 Polishing and etching ................................................................................................. 15
  2.5 Electric plating ........................................................................................................... 19

CHAPTER 3 THE SECOND METHOD TO FABRICATE MICRONEEDLES ..................................... 25
  3.1 Seed layer preparation ............................................................................................... 26
  3.2 Lithography ................................................................................................................ 27
  3.3 Electroplating .............................................................................................................. 33
  3.4 Heat ............................................................................................................................ 37
  3.5 Insert wires in the sample and use it in EDM .............................................................. 37

CHAPTER 4 CONCLUSION ..................................................................................................... 44

REFERENCES ......................................................................................................................... 46

VITA ......................................................................................................................................... 47
LIST OF TABLES

Table 1.1 Comparing of oral needle and inhaled aerosol drugs delivery routes [1] .........................2
Table 1.2 Comparison of aerosol generation methods [2] .............................................................4
Table 2.1 Comparison of polishing, chemical etching, and electric etching processes ..............16
Table 3.1 Three different seed layer wafer parameter .................................................................27
Table 3.2 Prebake temperature control .....................................................................................30
Table 3.3 Postbake temperature control ....................................................................................31
LIST OF FIGURES

Fig. 1.1 Model of airway in human lung [2] .................................................................5
Fig. 1.2 One example of vibrating orifice [5] ...............................................................8
Fig. 1.3 Structural diagram of a drug delivery system ....................................................9
Fig. 2.1 Schematic diagram showing the electric discharge machining (EDM) process ........12
Fig. 2.2 Schematic diagram of parallel grooves on substrate ........................................13
Fig. 2.3 Schematic diagram of array of posts formed by EDM cutting in two perpendicular directions ..................................................................................................................14
Fig. 2.4 Schematic diagram of the press-molding operation ............................................15
Fig. 2.5 Cross-sectional diagrams showing the flatness errors after polishing .................17
Fig. 2.6 The schematic diagram of the Electric etching system .......................................18
Fig. 2.7 An SEM image of a sample polished using electric etching process .....................18
Fig. 2.8 Schematic diagram of the electroplating system ................................................20
Fig. 2.9 SEM image of a sample after 24 hours’ electric plating in solution 1 ....................21
Fig. 2.10 SEM image of a sample after 72 hours’ electric plating in solution 2 .................21
Fig. 2.11 Photograph of a hole after stirring electroplating, the hole is about 30µm in diameter.22
Fig. 2.12 The electric circuit used to supply voltage to the piezoelectric actuator .............23
Fig. 2.13 Photograph of a sample obtained after 6 hours’ electroplating with no mechanical stirring ...............................................................................................................................24
Fig. 3.1. The schematic flow chart of LIGA process .......................................................26
Fig. 3.2 Lithography diagram .........................................................................................31
Fig. 3.3 Su-8 cylinders on 50µm Al seed layer ..................................................................32
Fig. 3.4 Su-8 cylinders on 100µm Al seed layer ..............................................................32
Fig. 3.5 Su-8 cylinders on gold seed layer .................................................................33
Fig. 3.6 Su-8 cylinders on Su-8 sacrifice layer...........................................................33
Fig. 3.7 Schematic diagram showing the fabrication of the nickel plate with micro-holes using LIGA method.................................................................................................35
Fig. 3.8 SEM image of the sample fabricated on 50µm Al seed layer .........................36
Fig. 3.9 SEM image of the sample fabricated on 100µm Al seed layer .......................36
Fig. 3.10 Schematic diagram showing wires being inserted into the LIGA fabricated nickel plate with array of micro-holes ..................................................................................38
Fig. 3.11 Copper wires inserted through the LIGA fabricated substrate with micro-holes ....40
Fig. 3.12 Tungsten wires inserted through the LIGA fabricated substrate with micro-holes ....41
Fig. 3.13 Top image for one of the holes made using EDM, the diameter of the hole is about 60µm .................................................................................................................................42
Fig. 3.14 Image focusing on the bottom view of the hole, the diameter is about 15µm........43
ABSTRACT

Inhaled drug is an important drug delivery route. It is widely used in medications for respiratory disorders. However, it has some significant limitations, for example, concentration of drug, output, and particles size, are not accurately controlled in most of the available drug delivery systems today. Various new devices and technologies continue to be developed and introduced. Vibrating orifice is one of them. The critical issue of vibrating orifice technology is the fabrication of micro-nozzles. Traditional technique to fabricate these nozzles is to use dry etching method, which tends to be expensive and inconvenient for mass production. Other two optional fabrication methods are presented in this thesis. The first one was to fabricate grooves using electro-spark etching to make array of micro-needles. This array of needles was then used as pressing mold to make nozzles. The size of these nozzles could be further reduced using electroplating method. The second approach was to microfabricate a substrate with array of micro-holes. Very thin wires were then inserted through these micro-holes and used in electric discharge machining (EDM) process to make arrays of micro-holes on substrate of copper or other metal plates. This method could be used to fabricate large arrays of nozzles matching the pattern of the mold. The experimental results showed that both two methods are feasible. Further work is required to improve the technology.
CHAPTER 1  INTRODUCTION

There is a long history of using inhaled drug. Ancient civilizations began using it several thousand years ago. A good example of inhaled delivery is smoking. In addition to inhaled drug delivery, there are several other more traditional drug delivery routes. The most familiar one is probably the oral route, for example swallowing a pill, tablet or elixir. Another commonly used one is needle injection, which includes subcutaneous injection, intramuscular injection and intravenous administration. Other less familiar delivery routes are also used, for example transdermal, buccal, and nasal, but these routes are just used in very particular cases. There are advantages and disadvantages to each route of administration [1]. A comparison of the three most common drug delivery routes is presented in Table 1.1, which helps to explain why inhaled delivery route is preferred for many specific treatments.

There are obvious advantages of using inhaled drug delivery for the treatment of the lung diseases because of its highly efficient and low side effect. Asthma is one of familiar example which is treated by taking medication from an inhaler or nebulizer. However, it is possible that inhaled pharmaceutical aerosols (IPAs) can be used to deliver drugs to the blood by depositing the drug in the alveolar regions and entering the blood in the capillaries in this region [1]. This means that it is possible for the inhaled treatment to take place of traditionally entire body drug injection. It not only can do the job by deliver drug through capillaries but also have several advantages, such as no painful, uniform drugs density in blood etc. The inhaled pharmaceutical aerosol field has broad prospects for development.
### Table 1.1 Comparing of oral needle and inhaled aerosol drugs delivery routes [1]

<table>
<thead>
<tr>
<th>Route</th>
<th>Advantages</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Safe, convenient, and inexpensive.</td>
<td>Unpredictable and slow absorption (e.g. foods ingested with drug can affect drug)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For lung disease: drug not localized to the lung (systemic side effects may occur)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Large drug molecules may be inactivated</td>
</tr>
<tr>
<td>Needle</td>
<td>Predictable and rapid absorption (particularly with i.v.).</td>
<td>Requires special equipment and trained personnel (e.g. sterile solutions)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improper i.v. can cause fatal embolism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For lung disease: drug not localized to the lung (systemic side effects may occur)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infection</td>
</tr>
<tr>
<td>Inhaled aerosol</td>
<td>Safe, convenient, rapid and predictable onset of action, decreased adverse reactions, smaller amounts of drug needed (particularly for topical treatment of lung diseases).</td>
<td>May have decreased therapeutic effect, e.g. in severe asthma other routes may be more beneficial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unpredictable and variable dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For systemic delivery: some drugs poorly absorbed or inactivated</td>
</tr>
</tbody>
</table>

Aerosols, either as solution or suspensions of liquid or solid particles, are commonly used to delivering therapeutic drugs to the lung for the lung diseases treatment. It is very essential to develop an appropriate aerosol delivery system if the aerosol route is chosen as the delivery method for the new drug under development. Because of different inhalation patterns and lung geometries among different individuals, it is difficult to efficiently produce small aerosol particles, and difficult to consistently deliver a reliable dose to the appropriate parts of the respiratory tract. In addition, ergonomics is the other important consideration that eliminates
many possible designs. There are many important issues that can dramatically affect marketability and patient compliance (i.e., whether patients take the prescribed dose at the prescribed frequency), such as cost, portability, delivery times and ease-of-use. However, the advantages of the aerosol route given in Table 1.1 are often enough to overcome its disadvantage and warrant its use for a particular medication. It is therefore imperative that an understanding of inhaled pharmaceutical aerosol mechanics be invoked in designing and using the delivery system, because otherwise a suboptimal delivery system usually results, reducing the effectiveness and marked potential of the drug. [1]

There are many successful inhaled pharmaceutical aerosol delivery systems available on market. Traditional systems include propellant metered dose inhalers, dry powder inhalers and nebulizers. The familiar portable inhaled devices for asthma are propellant metered dose inhalers based on aerosol container technology. Dry powder inhalers can disperse powders into a breath and nebulizers have mouthpiece or mask, the drug is dispersed in mist and inhaled. New devices and technologies continue to be developed and introduced. Some of them are summarized in Table 2. Some of them are suitable for liquid, some of them are suitable for solid, and the others are suitable for both. In many cases, solids can be converted to liquid state by the use of solvents or to powders by grinding. Each method has certain characteristics that may be suited for a particular application. The generators listed in Table 2 offer methods of producing polydisperse and monodisperse aerosols. Polydisperse means the particles have a broad range of size and shape. Polydisperse particles are generated by nebulizers and evaporation-condensation generators. The electrostatic classifier and the vibrating-orifice and spinning-disk generators produce monodisperse aerosols. The evaporation-condensation generator can also produce monodisperse aerosols under controlled conditions. The vibrating-orifice and spinning-disk
generators are usually used for producing micrometer-size particles. The vibrating-orifice has its advantage of producing monodisperse particles in particular sizes and condensations. [2]

<table>
<thead>
<tr>
<th>parameter</th>
<th>Evaporation-condensation</th>
<th>Nebulizer</th>
<th>Electrostatic classifier</th>
<th>Vibrating orifice</th>
<th>Spinning disc</th>
<th>Fluidized bed</th>
<th>Rotating brush</th>
<th>Wright dust feeder</th>
<th>NBS dust generator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerosol output (g/min)</td>
<td>1-10</td>
<td>1-10</td>
<td>1-5</td>
<td>&gt;20</td>
<td>&gt;10</td>
<td>5-15</td>
<td>10-50</td>
<td>10-40</td>
<td>50-85</td>
</tr>
<tr>
<td>Particle concentration loading</td>
<td>$10^3$ - $10^6$</td>
<td>$10^7$ - $10^8$</td>
<td>$&lt;10^3$</td>
<td>10-100</td>
<td>0.01-0.1 g/m</td>
<td>0.07-100</td>
<td>0.01-25</td>
<td>10-200</td>
<td></td>
</tr>
<tr>
<td>Particle size (μm)</td>
<td>0.005-5</td>
<td>0.01-5</td>
<td>0.002-0.3</td>
<td>0.5-100</td>
<td>0.3-100</td>
<td>0.5-40</td>
<td>1-100</td>
<td>0.5-10</td>
<td>1-100</td>
</tr>
<tr>
<td>Size distribution</td>
<td>1.1-1.5</td>
<td>-2</td>
<td>&lt;1.1</td>
<td>1.05</td>
<td>1.05</td>
<td>Determined by powder used</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Output stability (%)</td>
<td>5</td>
<td>&lt;5</td>
<td>&lt;5</td>
<td>&lt;5</td>
<td>5</td>
<td>10-30</td>
<td>7</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Equilibration time after startup (min)</td>
<td>30-100</td>
<td>~1</td>
<td>~1</td>
<td>~1</td>
<td>&lt;5</td>
<td>100-200</td>
<td>100</td>
<td>~</td>
<td>~1</td>
</tr>
</tbody>
</table>

As shown in Figure 1.1, the overall of the airways usually take a form similar to a tree, is therefore called the pulmonary tree. The trunk bifurcates to main bronchi, and the bronchi bifurcate to smaller bronchi. In the classic model of the airways [3], each airway divides to form two smaller next generation airways. As a result, the number of airways at the following generation doubles that of the previous generation. And then some of them have next generation and the others don’t. In the model, the airway has 24 generations in total. Different names were used for different generations and size levers, for example, “trachea” for generation 0, “bronchi” for generation 1, followed by “bronchioles”. All of these three levels are mainly for conducting. Only the small size generation levels respiratory bronchioles, alveolar ducts and alveolar sacs are for exchanging. [2]
In passing from the trachea to the alveolar sacs, two physical changes occur in the airways that are important in influencing airway function. Firstly, the airway caliber decreases with increasing generations. This permits adequate penetration of air to the lower airways.

![Figure 1.1 Model of airway in human lung](image)

Secondly, the surface area of the airways increases with each generation, to the extent that the total area at the level of the human alveolus is on the order of 140m². [2] Thus only if the particles are small enough, small amount of them can be distributed across large area of the patient’s alveolus to achieve the expected the effect.

The nose and mouth is the first line of defense against the intrusion of particles. Because the nasal passages have small cross sections and sharp turns in some positions. These two ports of entry block off nearly half of the particles larger than 50 μm in diameters. Only the particles that pass through an upstream region have a chance to reach the downstream regions. As a
consequence, the amount of particles deposited in target region depends not only on the size in the region itself but also on those sizes and sharp turns in the upstream regions passages. [3]

Therefore, the size of the inhaled aerosol particles is one of the most important mechanical parameters in determining the effectiveness of an IPA, because it determines if the drug deposit in the target region in the lung or not. If the inhaled particles are too big, they would be blocked by the mouth, nose, and throat as mentioned previously. On the other hand, if the particles are too small, they will be inhaled and the exhaled right back out with little deposition to the target region in lung, which means medication wasting and low efficient using of drug. The density of the particles is another important parameter. In most cases, the concentration is expected high to maximize the efficiency of drug, but if the concentration is too high, it may induce coughing and prevent proper inhalation. Other parameters influencing the final effect include particle surface properties and the geometry. Respiratory tract geometry is different for different person is also a problem. Understanding how these various factors can affect an IPA requires combining aspects of a wide range of traditional science and engineering areas, including aerosol mechanics, single-phase and multiphase fluid mechanics, interfacial science, pharmaceutics, respiratory physiology and anatomy, and pulmonologist [4]. Thus generally as advised by “Guidance for Industry Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products” published by the food and drug administration of the USA, the best distribution size of particles is around 5 \( \mu \text{m} \).

For vibrating orifice method, the size of droplets is related to the orifice size, flow velocity and frequency. Perçin and Khuri-Yakub [5] suggested that a critical balance exists between the size of the ejector orifice and the frequency at which the capillary waves are driven. The criterion governing this balance was presented as a dimensionless surface tension parameter
S based upon the Kelvin equation that defines the wavelength $\lambda_l$ of linear capillary waves driven at a particular frequency $f$, where $r_0$ is the radius of the orifice, $\sigma_l$ and $\rho_l$ are the surface tension and density of the ejected liquid, respectively, the theory can be expressed using the following equation:

$$S = \frac{2\sigma_l}{\rho_lr_0f^2}$$  \hspace{1cm} (1)

However, many examples contradictory to this theory have been reported [5]. Many experiments can also be found in open literature. Berggren et al. reported generation individual droplets of 27 µm or continuous streams of smaller droplets by increasing the amplitude of the pulse sent to the piezoelectric sleeve [6]. Kung et al. reported generation of 3–4 µm diameter droplets from a 1µm orifice [7]. Chen and Basaran used a glass capillary with a much larger orifice diameter of 70 µm to produce droplets as small as 32 µm [8]. Heij et al. and Yuan et al. are able to produce 5 µm diameter droplets by actuating arrays of 5 µm diameter micromachined nozzles [10, 11]. Perçin et al. presented the generation of 2–3 µm diameter from a 10 µm orifice when the driving frequency was as high as 1-2MHZ [5]. It is reasonable to expect nozzles of 15-25µm sizes suitable for generating about 5µm droplets.

The principle of vibrating orifice is as shown in the Figure 1.2 and Figure 1.3. Ceramic piezoelectric element bonded to an insulated shim vibrates in response to an alternating voltage applied across its electrodes on the top and bottom surfaces. The drug fluid enters the chamber from the entrance when the device is in operation. An input voltage is applied to drive the piezoelectric element vibrating, which causes a fluctuating pressure in the fluid chamber. The fluid inside the chamber is therefore pumped out through the micro nozzle to generate the micro droplets.
From the foregoing discussion, it can be seen that the fabrication of micro-nozzles is obviously the most critical part of the fabrication of an inhaled delivery device. Up to date, the state of the art choice is the one based on Deep Reactive Ion Etching (DRIE) fabrication [5]. Deep reactive-ion etching (DRIE) is a highly anisotropic process used to create deep, steep-sided holes and trenches in wafers, with aspect ratios of 20:1 or more. It uses chemically reactive plasma to remove material, silicon in this case. The plasma is generated under low pressure by an electromagnetic field. High-energy ions from the plasma attack the silicon surface and react with it. Obviously it is a good technology that fit the fabrication requirement well, but it is too expensive, especially take too long time. Thus it is not good for mass-production in commercial applications. Our device structure is shown in figure 1.3; two new fabrication methods which are cheaper and more repeatable are presented in this thesis.

Fig. 1.2 One example of vibrating orifice [5]
Fig. 1.3 Structural diagram of a drug delivery system
CHAPTER 2  THE FIRST METHOD TO FABRICATE MICRONOZZLES

2.1  Introduction to machine

2.1.1  Machining principle

The electric discharge machining (EDM) process is one of the most commonly used machining methods. It is normally used for high precision machining. Its principle is schematically shown in Figure 2.1. A very high voltage is charged on a conductive cutting tool and the object to be cut. When the cutting tool moves close to the electrically conductive substrate, similar to high voltage capacitor electric breakdown, an electric spark is generated. Significant amount of heat is generated at the gap between cutting tool and substrate. Because of usually high thermal conductivity of the substrate, very high temperature only exists in a very small area around tip of the cutting tool. When the temperature in this area becomes higher than the melting point of the substrate material, the material at this small area melts and is etched away as the cutting tool moves. With the cutting tool is controlled to move across the substrate, material is removed at the desired location on the substrate, and the work piece (the substrate here) is fabricated into the designed geometry. This fabrication technology is called the electric discharge machining process. The process is also commonly referred as “spark machining”, “spark eroding”, “burning”, “die sinking”, or “wire erosion”.

We targeted to use the EDM technology to fabricate large array of micro-nozzles for inhaled drug delivery applications. In ideal case, we would like to have the work piece cut during the EDM process and no “wearing down” of the cutting tool. However, like in any other
conventional machining processes, “wearing down” of the cutting tool, which is one of the electrodes in the EDM operation, is inevitable. In the EDM fabrication process, if the localized temperature is higher than the melting point of cutting tool, the erosion happens at the cutting tool too. In practical operation, the temperature in the gap may be higher than the melting temperatures for the materials of both of cutting tool and substrate. Therefore erosions of both electrodes, the cutting tool and the substrate, are inevitable in an EDM process. While erosion of the substrate (work piece) is desired (it is the part to be machined), the process also leads to constant consumption and the requirement for replacement of the cutting tool (wires used as electrodes in our case). The consuming ratio, which is defined as the ratio between the consumed lengths of the cutting tool to that of eroding depth of the sample work piece, depends on the materials and the geometries of both the cutting tool and the sample work piece. It is therefore necessary to run some tests to calibrate the consuming rate of cutting tool each time when a new cutting tool and substrate of different material are used for preparation of after steps.

2.1.2 Machine operate steps

The EDM machine can operate in the horizontal plane along two directions (x, y) and vertical direction (z) precisely to micrometer.

The operation procedures can be explained as follow:

1. Start the machine, turn on the pump to supply oil to the operating position to protect both cutting tool and substrate from oxidizing at high temperature;

2. After each cutting movement, while the cutting tool is in the groove, move the cutting tool up over the substrate. Clean up the cutting tool because there would be scrap during etching procedure.

3. Enter the (x, y) coordinates of the next cutting position and bring the cutting tool to this
position, then set it as (0, 0).

4. Bring the cutting tool slowly down to contact with the substrate surface, z value on this position should be equal to how much the cutting tool consumed in last operation. Record this position and set it as $z=0$. For each cutting movement, the machine can only control the displacement of the cutting tool. The depth of the groove to be cut is therefore equal to the difference of travelled distance of the cutting tool minus the consuming length of cutting tool.

5. Set how far the machine delivers the cutting tool in z direction in this cutting movement.

Moves the cutting tool slightly from contacting substrate.

6. Start etching, the machine will do the etching automatically.

As shown in figure 2.1, because the top part of the groove is maintained at high temperature longer than at the bottom, the top width of the groove is always wider than that at the bottom. Its width depends on the materials and shapes of the cutting tool and substrate.

![Fig. 2.1 Schematic diagram showing the electric discharge machining (EDM) process](image)

Fig. 2.1 Schematic diagram showing the electric discharge machining (EDM) process
2.2 Etching procedure

As mentioned in Section 2.1.2, the depth of the groove cut by an EDM depends on how far the cutting tool goes and the width depends on the width of the cutting tool. So the size of the groove can be roughly controlled.

A permenorm alloy foil of 2.5 cm by 2.5 cm with a thickness of 0.8mm was used. Its surface was polished, and cleaned up to make sure the surface is flat and smooth. The permenorm alloy is chosen because of the high hardness requirement of next pressing step. However, because the high melting point of permenorm alloy, the material of cutting tool needs to have a higher melting point. Molybdenum was chosen for its high melting point. As shown in Figure 2.2, a series of grooves can be cut on the substrate surface. The depth of each groove is around 0.5mm with a width of 0.5mm. The gap between grooves is about 0.1mm.

Fig. 2.2 Schematic diagram of parallel grooves on substrate

If we repeat the same procedure in the perpendicular direction, an array of square columns can be created on the surface of the substrate as shown in Figure 2.3. Each column is about 0.1mm on each side and with a height of 0.5 mm. It can be used as a pressing mould for fabricating array of holes. As mentioned in Section 2.1, for each groove, top width is wider than
at the bottom, tips of the column obtained this way are always smaller than the bottoms as shown in Figure 2.4.

![Fig. 2.3 Schematic diagram of array of posts formed by EDM cutting in two perpendicular directions](image)

2.3 Pressing

The array of columns as shown in Fig. 2.3 may then be used as pressing mould to fabricate micro-holes as shown in Figure 2.4. Copper was selected as the substrate because it is softer than permenorm alloy. The length of each column is about 0.5mm. To avoid using too large pressing force, the pressing mould was only pressed about 0.2 mm into the substrate, therefore the holes on the substrate are at about 0.2mm deep. Because the topside of the micro-columns is smaller than at bottom as mentioned in Section 2.2, the openings of the holes created on the substrate are therefore bigger than their bottoms. The separation of the press mould is another critical issue. A thin layer of crystal bond from Buehler Company is deposited on the mould surface to reduce sticking force in demolding process. Even with the addition of stick-reducing layer on the press mould, the demolding force was still significant enough to bend the substrate and cause deformation in the final product. To increase the thickness of the substrate
would help. Substrates with thicknesses of 0.2 mm, 0.5 mm and 0.8 mm thickness were tested. The copper substrate with a thickness of 0.2 mm copper bent so severely that it was almost broken. The copper substrate with a thickness of 0.5 mm was bent and stretched so much that it change the shape of the hole from circle to a narrow strip. Only the sample with a thickness of 0.8 mm did not suffer with significant damage and was acceptable.

**Pressing mould**

![Pressing mould diagram]

*Fig. 2.4 Schematic diagram of the press-molding operation*

### 2.4 Polishing and etching

From the discussion in Section 2.3, the substrate thickness needs to be 0.8 mm, and the depth of the holes on the substrate will be at 0.2 mm. This means that at least material of at least 0.6 mm thick needs to be removed from the substrate in order to make the through-holes on the substrate. Usually there are three ways to do it: to polish, chemically etch, and electrical etch. The advantages and disadvantage of for all three approaches are listed in Table 2.1 for comparison.

Both the chemical etching and electric etching methods were tried. The experimental results have proved that because the holes is so small that the solution in the hole hardly
exchange with the solution outside, both ways almost do no damage to the holes. But to keep a
good surface quality, the reaction rate is very slow. Comparing three ways as shown in the table,
we decide to polish the foil thin enough the electric etch it though.

**Table 2.1 Comparison of polishing, chemical etching, and electric etching processes**

<table>
<thead>
<tr>
<th></th>
<th>Advantage</th>
<th>disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polishing</td>
<td>Fast, cheap</td>
<td>May stuff up the holes when the holes get though, and the substrate may not be evenly polished</td>
</tr>
<tr>
<td>Chemical etching</td>
<td>No damage to the holes</td>
<td>Slow, consuming chemicals</td>
</tr>
<tr>
<td>Electric etching</td>
<td>No damage to the holes</td>
<td>Slow</td>
</tr>
</tbody>
</table>

To polish the substrate mechanically is fast, cheap and convenient. We tried to polish the
substrate thinner first to make the bottom of holes thinner so that through-holes could be obtained. However, because the substrate could easily be bent as shown in Figure 2.5, the central part of the foil would be thicker than at the edge after polishing. It is therefore difficult to obtain through-holes by polishing only, some chemical etching is always necessary even if mechanical polishing is used. Because the openings of the micro-holes are always bigger than the their bottoms, the bottom sizes of the though-holes were different when chemical etching was done following the mechanical polishing process because of flatness errors caused by mechanical polishing. The sizes of holes near the edge of the substrate were observed to be bigger than at the central area. It was also noted that the holes in the central part of the sample had almost the same sizes. We therefore tried over-etch the sample and controlled the etching time to make the through-holes in the central part of the sample at about 0.15 mm in diameter.

The electric etching was used to reduce the thickness of the sample substrate to obtain through-holes. Electric etching is the inverse process of electroplating in principle. As shown in the schematic diagram of electrical etching system in Figure 2.6, the sample was used as the
anode, and a copper piece was used as the cathode. With a controlled voltage supplied between the anode and the cathode, the sample would be electrically etched. To avoid etching the holes and making them bigger or damaging them, a piece of polymer membrane was used to cover the holes and to have only the opposite side of the sample exposed to electrical etching. The polymer used for this purpose, called crystal bond, was a commercial product from Buehler Company. The melting temperature of the polymer is 150°C. It was heated to the melting temperature and then coated on the sample to seal the holes on the sample to prevent etching on the side with holes. After the etching process was completed, the polymer coating was easily removed using acetone. To prevent possible etching at the edge of the sample, the sample was also typed around the edge.

In electrical etching process, the reaction formula in anode is

\[ \text{Cu} = \text{Cu}^{2+} + 2e^- \]

and the reaction formula in cathode is

\[ \text{Cu}^{2+} + 2e^- = \text{Cu} \]

Fig. 2.5 Cross-sectional diagrams showing the flatness errors after polishing
Fig. 2.6 The schematic diagram of the Electric etching system

Fig. 2.7 An SEM image of a sample polished using electric etching process.

If the supplied voltage is too high, electrolysis may generate oxygen and hydrogen bubbles which may affect the surface quality. For a square sample of 2.5 cm by 2.5 cm, the direct current was set at 0.1 A with the voltage at about 12.54V. It took 6 hours to etch backside of the sample substrate to make obtain through-holes, and took another 2 hours to over-etch the sample
slightly. After etching process was completed, the protective layer of polymer was removed using acetone. An SEM image of the array of through-holes is shown in Figure 2.7.

2.5 Electric plating

As can be seen from the SEM image in Figure 2.7, the size of the holes is about 0.1mm by 0.1mm. This size is still larger than what is needed for effective inhaled drug delivery, and is limited by the minimum size of the EDM fabrication process. It is very difficult to make holes smaller than this size. It is therefore necessary to find a suitable technology to make these through-holes smaller.

The well-known electroplating technique, the inverse process of electric etching, was used to achieve this goal. In an electroplating process as shown schematically in Figure 2.8, the sample was used as the cathode and a copper piece as the anode. The surface quality of electroplating is more sensitive to the process parameters than that for electric etching, the requirement of the electric plating environment is therefore stricter. Any particles stuck on the sample surface may become significantly larger in size. The electroplating tank was completely covered, and the anode pocket was used to prevent crumb dropping from anode copper piece. Similar to the case for electric etching, higher than needed voltage supplied between the cathode and anode may lead to production of hydrogen bubbles and oxygen bubbles and negatively impact the surface quality of electroplating in the sample. The electroplating voltage is therefore carefully controlled so that it is low enough that few no bubbles were observed on both anode and cathode. The copper sample used has a size of 2.5cm by 2.5cm with a thickness of 0.15mm. The electroplating current was controlled to be 0.05A with the voltage at 5.65V.

The reaction formula at the anode is

\[ \text{Cu}^{2+} + 2e^- = \text{Cu}. \]
The reaction formula in cathode is

\[ \text{Cu} = \text{Cu}^{2+} + 2e^- \]

![Diagram of electroplating system](image)

**Fig. 2.8 Schematic diagram of the electroplating system**

The electroplating bath is a copper sulfate solution (CuSO₄·5H₂O 60-100g/liter, sulfuric acid, H₂SO₄ 180-270 mg/liter, Chloride 50-100mg/liter). [13]

The SEM image shown in Figure 2.9 was the sample after 24 hours electroplating. It can be observed that the surface of the sample becomes quite rough.

We then tried a commercial electroplating solution OttoFrei Company. With this solution, the electroplating time was much longer and took 72 hours. The resulted sample had a much better quality. Figure 2.10 shows an SEM image of the sample obtained using this solution. As can be observed from the SEM image, the surface quality was improved significantly. However, similar to the etching process, the electroplating solution did not get circulated inside the micro-
sized holes. This significantly limited the available ions in the holes. As the consequence, after 72 hours of electric plating, no significant changes in the size were observed.

Fig. 2.9 SEM image of a sample after 24 hours’ electric plating in solution 1

Fig. 2.10 SEM image of a sample after 72 hours’ electric plating in solution 2

To help to improve the solution circulation in and out the micro-holes, the two methods were tried.
First, mechanical stirring was use to improve the circulation of plating solution in these holes. A close-in image of a micro-hole on the sample (after 6 hours of electroplating) was shown in Figure 2.11. The size of the hole shown in the image is about 30µm in diameter but with an irregular shape though its size was obviously reduced. Because of the non-uniformity of the solution circulation, these holes tend to have different sizes.

![Image](image.png)

**Fig. 2.11 Photograph of a hole after stirring electroplating, the hole is about 30µm in diameter.**

The second method is to package the device as show in Figure 1.3, the up part of the device is made by SU-8 polymer using a lithograph process, a piezoelectric actuator (from Omega Comerica Company) was used to actuate the membrane to vibrate and deliver the electroplating solution in through these holes. The piezoelectric actuator used in the test is a 2cm diameter cylinder with a thickness of 100µm. The membrane is about 100µm thick. The actuator is supplied with a voltage by specially designed circuit as shown in Figure 2.12, which can be used to adjust the frequency from 5000 Hz to 500000 Hz and with a voltage between 0 and 24V. The entire device was placed into the electroplating solution. Because the air was trapped inside
the device, the solution cannot fill the entire chamber, but at least some could get into it and contact the bottom of the nozzles. Apply voltage to drive the piezoelectric actuator to vibrate. The solution on the bottom of the nozzles would be pushed out and then pulled in to achieve the circulation of the solution. Theoretically, if the electroplating is conducted this way, copper can be electroplated on the sidewalls of the holes and therefore reduce their sizes.

![Electric Circuit Diagram](image)

Fig. 2.12 The electric circuit used to supply voltage to the piezoelectric actuator

However, before the entire device was placed into the solution, a layer of polymer had to be coated on the piezoelectric actuator to prevent circuit short. This layer of polymer will negatively affect the swing of the piezoelectric actuator. In addition, the vibration of the membrane would strip the polymer gradually, this means that the voltage on the piezoelectric actuator will leak to the solution gradually, leading to the continuous decreasing of the membrane motion. In practical operation, the polymer layer could not last over 6 hours. Because the membrane’s motion becomes so small, electroplating in these 6 hours almost had no effect to the size of the nozzles. To solve this problem, many methods had been tried.
For example, if the vibrating membrane and piezoelectric actuator were kept above the plating solution and only the copper membrane was kept under the solution, the protection polymer on the piezoelectric actuator would not be needed. The only problem for this approach is whether the fluid entrance should be kept above or below the level of electroplating solution. If we kept it above the solution, electroplating solution would not be pumped through the micro-holes and therefore cannot be plated. Experimental results proved that it had almost no effect on the size reduction of nozzles. If the entrance is coated with polymer for electrical insulation, the air pressure inside the chamber may become too high and the solution also could not be pumped in. The thickness of the upper part of the sample device is about 500μm thickness. A plastic tube was inserted into the fluid entrance to prevent electroplating on the fluid entrance. To prevent electroplating solution from getting onto the piezoelectric actuator and causing electricity leakage, mechanical stirring was not used. Without stirring, the electroplating process was very slow. An image of the sample after 6 hour electroplating was shown in Figure 2.13. There is almost no shrinkage to the holes.
CHAPTER 3  THE SECOND METHOD TO FABRICATE MICRONOZZLES

Because the results obtained using the first method mentioned were not satisfactory as discussed in detail in chapter 2, a new method was used to fabricate the array of micro-holes and presented in this chapter.

In this fabrication method, a plate with array of micro-holes was made first, micro-wires were then inserted into these holes to form a special tool which was then used as cutting tool to make array of through-holes on a substrate in EDM process. In this method, it is potentially possible to make injecting holes for drug delivery in batch production and relatively low cost. The first step in this fabrication method is therefore the fabrication of a plate with micro-holes. It can be done either using LIGA (German acronym for Lithographie, Galvanoformung, Abformung), which is based on x-lithography of PMMA, or using its lower cost alternative, so-called UV-LIGA, which is based on ultra violet (UV) lithography of thick resist such as the negative photoresist SU-8. In the research reported in this thesis, UV-LIGA process was used. A typical LIGA fabrication flow chart is schematically shown in Figure 9. A thin layer of metal film is coated on the substrate (silicon, ceramic or any other material) (1). A layer of photoresist (SU-8) is then spin-coated on the substrate (2). After prebaking, the sample is then exposed in UV or x-ray source (3) and developed to produce the plating mold (4). Selected metal or alloy can then be electroplated into the exposed regions on the substrate as shown in (5). The polymer plating mold is then stripped to obtain the metal structures which will be used as mold insert (6). The insert mold is then used to replicate plastic patterns in batch production (7). Finally the
plastic mold is glued on a substrate coated with metal film that can then be electroplated again for replication of the metal structures.

3.1 Seed layer preparation

A 2” silicon wafer was used as substrate for fabrication. A thin layer of metal is required to be coated on the silicon wafer first. The purpose of this metal layer is:

1. To serve as the seed layer for electroplating, which means it is required to be electrically conductive so that the metal can be deposited on it during the electroplating process;

2. To also serve as sacrificial layer so that the plated structure can be released layer
in a lifting-off process at later stage.

For these two purposes, three different seed layers were prepared:

1. A 5µm thick chrome was coated on the wafer first, followed by 10µm gold on the nickel (because gold cannot stick to the silicon, chrome is the bonding layer);

2. A layer of aluminium is sputtered on the wafer as seed layer. Sputtering method cannot be precisely controlled to make highly uniform thin layer. The thickness of the seed layer cannot be either too thin because some part may not completely covered, or too thick because sputtering would make the centre of the layer thicker than the edge. Two samples were prepared, one is 5µm thick and the other is 10µm thick;

3. For easy to remove, a layer of exposed SU-8 was also used as sacrificial layer, and a layer of aluminium was then sputtered on it for electrical conductivity. When heated up over 150°C after electroplating, the SU-8 layer would melt and the electroplated structure can then be taken off easily from the wafer. The detail is present in Section 3.2.

### 3.2 Lithography

#### Table 3.1 Three different seed layer wafer parameter

<table>
<thead>
<tr>
<th></th>
<th>50µm Al seed layer wafer</th>
<th>100µm Al seed layer wafer</th>
<th>Au seed layer wafer</th>
<th>Su-8 sacrifice layer wafer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wafer weight without Su-8 (g)</td>
<td>9.70</td>
<td>9.05</td>
<td>9.42</td>
<td>11.61</td>
</tr>
<tr>
<td>Wafer weight with Su-8 (g)</td>
<td>15.02</td>
<td>14.28</td>
<td>15.56</td>
<td>17.72</td>
</tr>
<tr>
<td>Estimating thickness (µm)</td>
<td>198</td>
<td>194</td>
<td>228</td>
<td>227</td>
</tr>
</tbody>
</table>
After the seed layer was prepared, an ultraviolet lithography of SU-8 was conducted to make an array of columns on the seed layer. SU-8 is a negative resist that can be used to make high aspect ratio microstructures. It has very good lithography property. The main disadvantage is it cannot easily strip once cured by UV light. The basic procedures followed in the lithography are as shown below:

1. Wafer cleaning. The wafer was cleaned with water and acetone. Because SU-8 and seed layer bonding is not as good as between SU-8 and silicon, surface cleaning is very critical. And after cleaning, heat up wafer to 80°C for 1 hour for dehydration purpose;

2. Coating SU-8 resist. To create a thick layer of resist, the SU-8 100 was used. This particular resist has very high viscosity. Unexposed SU-8 resist can be easily removed by acetone. The thickness of SU-8 is proportional to the viscosity of SU-8, spinning time, and speed. The spinning speed and time are 1000r/s and 30s respectively. The thickness of the resist was about 200µm. The average thickness can be also estimate using the total weight of the SU-8 on the wafer (see Table 3.1);

3. Prebaking. The purpose of prebake is to evaporate the solvent in the resist. The prebaking temperature is shown in Table 3.2. It should be noted that care must be taken to clean up the backside of the wafer because any possible SU-8 on the backside of the wafer may lead to the wafer being glued onto the hotplate after prebaking. Efforts also need to be made to clean up any obvious bubbles in the resist, otherwise they might be trapped in the resist after baking. Existence of smaller bubbles is not a critical issue because they would be eliminated during
4. Mask design and preparation. The mask is obviously the key part that determines the accuracy of the lithography. It is piece of glass on it a thin layer of chrome was deposited and patterned. A thin layer of chrome was first coated on the glass wafer. A thin layer of AZ, a positive resist, was first coated on a glass wafer. The pattern of the mask was first design using AUTOCAD, the date file was then entered into the PG (pattern generator) machine. Pattern generator was then used to expose the AZ layer according to the pattern. After the exposure, the mask was then placed in AZ developer for several minutes to remove the exposed part. The patterned glass plate was then placed in the chrome etching solution for several minutes to etch the chrome not covered with AZ resist. And finally the remaining AZ was stripped to obtain the completed optical mask;

5. Exposing. The prebaked silicon wafer (coated with seed layer and covered with SU-8 resist) was then exposed using the mask in the UV station. As shown in Figure 3.2, UV light passes through the pattern on the mask and selectively exposed the SU-8 on the silicon wafer. For the 200µm thick SU-8 resist, an exposure dosage of about 500mj/cm² was used. The intensity of the ultraviolet light was measured to be at 9.1mj/cm³s, the exposure time was therefore set at 55s;

6. Postbake. When SU-8 is exposed to ultraviolet light, an acid is generated and it reacts with the resin in the resist to complete the cross-link process. The purpose of the post bake is to promote the cross-link. The postbaking temperature was designed for fast reaction and also avoids residual stress and distortion of the final
features. It was first ramped up, dwelled for some time, and then ramped down.

The detailed set of the postbaking temperatures was shown in Table 3.3.

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramp to 25</td>
<td>10 min</td>
</tr>
<tr>
<td>25</td>
<td>2 hour</td>
</tr>
<tr>
<td>Ramp to 75</td>
<td>15 min</td>
</tr>
<tr>
<td>75</td>
<td>30 min</td>
</tr>
<tr>
<td>Ramp to 110</td>
<td>30 min</td>
</tr>
<tr>
<td>110</td>
<td>4.5 hour</td>
</tr>
<tr>
<td>Ramp to 75</td>
<td>40 min</td>
</tr>
<tr>
<td>75</td>
<td>15 min</td>
</tr>
<tr>
<td>Ramp to 55</td>
<td>40 min</td>
</tr>
<tr>
<td>55</td>
<td>4 hour</td>
</tr>
<tr>
<td>Ramp to 25</td>
<td>3 hour</td>
</tr>
<tr>
<td>25</td>
<td>2 hour</td>
</tr>
</tbody>
</table>

7. Developing. After postbake, SU-8 developer can only remove the unexposed part but not the exposed part. When the wafer was placed in SU-8 developer, it would take very long time if the wafer was facing up. It is generally suggested that the wafer is placed in a facing down orientation to speed up the development process because gravity effect would help to enhance the development process. A facing down development of the sample would take about 40 minutes. Because the microstructures on the wafer are array of columns with diameters of 30µm and 40µm and height of 200µm, they tend to be very easy to break. The sample was slowly removed from the developer to prevent mechanical damage by surface tension of fluid. Figures 3.3, 3.4, 3.5 and 3.6 show arrays of columns on different seed layers. One of the wafers still shows a thin layer of SU-8 that was supposed to be the sacrificial layer as mentioned in Section 3.1. During prebake and post bake, the temperature was ramped up to 110°C. This might have caused the small
cracks on the sacrifice layer. Because the electroplating process requires the plating base to be free of cracks, this sample was therefore not used.

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramp to 25</td>
<td>10 min</td>
</tr>
<tr>
<td>25</td>
<td>10 min</td>
</tr>
<tr>
<td>Ramp to 75</td>
<td>30 min</td>
</tr>
<tr>
<td>75</td>
<td>15 min</td>
</tr>
<tr>
<td>Ramp to 110</td>
<td>30 min</td>
</tr>
<tr>
<td>110</td>
<td>45 min</td>
</tr>
<tr>
<td>Ramp to 75</td>
<td>40 min</td>
</tr>
<tr>
<td>75</td>
<td>15 min</td>
</tr>
<tr>
<td>Ramp to 55</td>
<td>40 min</td>
</tr>
<tr>
<td>55</td>
<td>1 hour</td>
</tr>
<tr>
<td>Ramp to 25</td>
<td>30 min</td>
</tr>
<tr>
<td>25</td>
<td>10 min</td>
</tr>
</tbody>
</table>

Fig. 3.2 Lithography diagram
Fig. 3.3 Su-8 cylinders on 50µm Al seed layer

Fig. 3.4 Su-8 cylinders on 100µm Al seed layer
3.3 Electroplating

The electroplating equipment used was the same as mentioned in Section 2.5 with only the plating solution changed to nickel electroplating solution from OttoFray Company. The
principle is as shown in Figure 2.8. The electrically conductive seed layer was directly connected
to the cathode of the plating station. With a controlled current supplied, the nickel ions would
move to the cathode and receive free electrons there and deposit on the surface of the exposed
area of the sample. After the electroplating was completed, the remaining plating mold of SU-8
was stripped and the sacrificial layer was chemically etched to release the plated microstructures
from the silicon wafer.

The surface quality is very important for uniformity of the electroplated structures. There
were four arrays of cylinders on one silicon wafer, each represents one sample. Each wafer was
cut four pieces with one array of cylinders on each quarter. The electroplating was done
separately for each of them. The sample (1/4 of the wafer) was immersed in acetone for sever
minutes to remove oil, fingerprint and other dirty first; it was then taped at the edges to prevent
nickel deposition along the edges of the sample. The cleaned sample was then immersed into 10%
diluted sulphuric acid to active the plate surface for about 20 seconds. It should be noted that the
sample can only be taped after it was cleaned using acetone because it may be damaged by
acetone.

The electroplating current needs to be carefully controlled as mentioned in Section 2.5 to
prevent bubble generation. The voltage was set at 5.37V and the current was at about 0.07A. In
general, larger plating current may lead to faster deposition rate, larger residual stress in the
sample, more bubble generation, and therefore lower plating quality.

The reaction formula in anode is,

\[ \text{Ni}^{2+} + 2e^- = \text{Ni} \]

and the reaction formula in cathode is,

\[ \text{Ni} = \text{Ni}^{2+} + 2e^- . \]
To consistently monitor the electroplating quality, a small piece of nickel was also connected to the cathode. This small piece of nickel was periodically taken out the plating bath to check the stress condition of electroplating part. If it bends because of stress, this means that the plating current was too high, and needs to be reduced. Because ashes may stick to the surface of the sample and grow to larger grain on the surface of the sample during electroplating process, the plating tank needs to be covered and efforts need to be taken to make sure no dusts can get into the tank.

The experimental results are shown in Figure 3.8 and Figure 3.9. As can be seen from the image, there were some cracks on the gold seed layer. This was primarily caused by the stress generated in electroplating.

![Fig. 3.7 Schematic diagram showing the fabrication of the nickel plate with micro-holes using LIGA method](image)

Su-8 cylinders

Nickle

seed layer

Wafer

Fig. 3.7 Schematic diagram showing the fabrication of the nickel plate with micro-holes using LIGA method
Fig. 3.8 SEM image of the sample fabricated on 50µm Al seed layer

Fig. 3.9 SEM image of the sample fabricated on 100µm Al seed layer
3.4 Heat

For the sample with aluminum seed layer, the bonding between the aluminum and the wafer was quite weak. The electroplated structures were therefore easily peeled off by hand. The bond between the aluminum seed layer and the electroplated nickel structure was also quite weak, it is therefore possible to simply wipe off the seed layer from the nickel structure after it was mechanically removed from the silicon wafer.

Very often, the micro-columns of exposed SU-8 were very strong and difficult to remove by using chemicals. However, the remaining SU-8 structures can be easily removed by burning. When the temperature reaches above 600°C, the SU-8 structures can be completely burned and removed. The samples were therefore burned at 700°C to remove the SU-8 columns imbedded in electroplated nickel structure. After kept at 700°C for 7 hours, all the SU-8 had been burned. A sample of 2 cm by 2 cm square nickel plate with 10×10 array of holes was obtained. Each of the holes is 40µm in diameter and the distance between them is 500µm.

3.5 Insert wires in the sample and use it in EDM

As shown schematically in Figure 3.10, micro-wires can then be inserted into these holes on the sample. After these wires are inserted, it can then be used in EDM machine to fabricate array of holes on work piece for batch fabrication of thin membranes with precisely controlled array of through-holes and used in construction of inhaled drug delivery system as discussed in Section 2.1. When charge voltage to the foil, because the wires are contacted with the wires, the wires are charged voltage.

After these wires were inserted, another piece of conductive substrate was then attached on the opposite side of the sample to help to hold these wires. After installed in the EDM system and moves close to the work piece, the electro sparks were generated between the tips of these
wires and work piece and generated highly localized heating spots on the work piece. Because
the melting temperature of the wires is much higher than that of the work piece, theoretically
material on the work piece was removed and the wires kept intact. An aluminum plate of 250µm
thick was used as work piece on which micro-holes would be fabricated to form elastic
membrane with array of through-hole for drug delivery purpose as mentioned in Section 1.3.

metal wire

foil

substrate

Fig. 3.10 Schematic diagram showing wires being inserted into the LIGA fabricated nickel plate
with array of micro-holes

The melting temperature of aluminum is 660 °C, lower than that for copper (melting
temperature at 1083 °C). Copper wires were therefore tried first. A total of nine wires in a 3×3
array were inserted into the nickel plate as shown in Figure 3.11.

During the electric spark etching, oil is consistently supplied to the wires for cooling
purpose. To understand the effect of this supplied flow on the wires and to determine how long
the wires can be made without being bent by this cooling flow, a simple calculation was conducted as shown below.

The force on a wire can be calculated using the following equation,

\[ f = C_D p r L v^2, \]

where \( f \) represents the force, \( C_D \) is the flow resist coefficient, \( r \) is the radius of the wire, \( L \) is the length of wire, \( \rho \) is the density of the fluid, \( v \) is the velocity of oil flow. The diameter of the wire is 25\( \mu \)m; velocity of flow is about 1m/s. The density of oil is about 0.8kg/L. The flow resistance coefficient is dependent on the material of both fluid and wires and the velocity of the flow can be estimated to be 1. Thus,

\[ q \text{ represents force on unit length wire.} \]

\[ q = f / L = C_D \rho rv^2 \]  \hspace{1cm} (2)

The deflection at the tip of the wire is

\[ Y_{\text{max}} = 5ql^4 / (384EI) \]  \hspace{1cm} (3)

where \( Y \) is the deflection of the wire, \( q \) represents force on unit length wire, \( l \) is the length of wire, \( E \) is the young’s modulus of the wire, and \( I \) is the moment of inertia of the wire. Young’s modulus of copper is \( 2.0 \times 10^{11} \text{ N} \cdot \text{m}^{-2} \). The density of copper is \( 8.9 \times 10^3 \text{ kg/m}^3 \). The moment of inertia of the wire is calculated as,

\[ I = mr^2 / 2 = \rho_{\text{copper}} \pi r^4 lgr / 2 \]  \hspace{1cm} (4)

The maximum deflection at the tip of the wire is then calculated as,

\[ Y_{\text{max}} = \frac{5l^3 C_D \rho v^2}{192E \rho_{\text{copper}} \pi r^3} \]  \hspace{1cm} (5)
Using equation, the deflection for a copper wire of 500µm in diameter can be calculated to be 0.075µm, which can be reasonably neglected. We can therefore safely conclude that the oil flow would not have any significant effects on the EDM fabrication quality.

Fig. 3.11 Copper wires inserted through the LIGA fabricated substrate with micro-holes

The experimental results showed that the electric spark etching almost did not have any effect on the work piece. The reason for the failure is that the melting temperature of the copper wire is not high enough in comparison with aluminum. It was obvious that the copper wire was not perpendicular to the substrate because it is too soft.

To overcome this problem, tungsten wires (melting temperature 3340 °C) were inserted into the holes on the substrate as shown in Figure 3.12. The effect of flow in the experiment can be calculated using equation 5. The Young’s modulus of tungsten is $3.8 \times 10^{11} \text{ N}\cdot\text{m}^2$, and mass density is 19.35 kg/m$^3$. The deflection for a wire of 500µm long is calculated to be 0.018µm, which again is small enough to be negligible.

To make sure the wires would not move during the EDM operation, the wires on the backside of substrate were intentionally bent first and then pressed against a back plate. This
would help to eliminate any possible wiggling of the wires in the holes and also help to maintain good electrical contact during the operation of EDM. It was found in experiments that all the wires were broken at the connecting points. One possible reason for this failure is that the electric resistance at the contacting point was much higher than the wires’, and tends to get heated first.

To solve this problem, the backside of the sample was slightly polished while care was taken to avoid the micro-holes. Accidentally polishing the holes may lead to blocking them and make it difficult to insert the wires into them. After the backside of the sample was carefully polished, wires were inserted and bent on the wires on the backside to maintain a good contact and, then taped together with a conductive tape. The resistance between the substrate and wires was measured to be almost zero.

Fig. 3.12 Tungsten wires inserted through the LIGA fabricated substrate with micro-holes

Two images for one of the holes etched using EDM technology are shown in Figure 3.13 and Figure 3.14. In Figure 3.13, it is the version of the top view of a micro-hole, the diameter is about 60µm. In Figure 3.14, it shows the bottom view, the diameter is about 15µm. The depth is measured by focusing a microscope to the top and bottom respectively and then reading the
difference of the records. The depth was estimated to be about 40µm. Considering the fact that the foil was not completely flat because of the residual stress generated in electroplating, the machine was stopped when the spark is generated between substrate and foil. The consumption of the wires is less than the length of the wires out of the foil which is 500µm. The 50µm thickness of aluminum membrane is thick enough for using as membrane with holes for inhaled drug delivery.

However, a 50µm thick aluminum plate is not physically strong enough to stand on the stage of the EDM machine itself, we cannot do EDM etch through 50µm thickness aluminum right now because of this reason. Some type of supporting mechanism needs to be designed in the future to overcome this problem.

Fig. 3.13 Top image for one of the holes made using EDM, the diameter of the hole is about 60µm
Fig. 3.14 Image focusing on the bottom view of the hole, the diameter is about 15µm
CHAPTER 4 CONCLUSION

We have tried two different methods to make arrays of micro-holes on a thin metal membrane. One is to use EDM technique to make holes (50µm ranges) on a metal substrate, then using electroplating technique to make these holes small enough to be used for inhaled drug delivery system. The experimental results have proved that the first method of fabricating nozzles (presented in Chapter 2) has some very challenging technical hurdles to overcome. One of the main challenges is how to obtain uniform electroplating in these micro-holes. Several measures, including stirring and pumping methods were used with no obvious success. However, the membranes with through-holes in size of 50µm still can be used for some applications.

For the second method as presented in Chapter 3, the experimental results prove that it is good to fabricate the nozzles with suitable sizes and uniformity. However, it has very strict requirements for the straightness of the wires through the nickel plates with micro-holes which were used as cutting tool for EDM process. Only for high Young’s modulus metals it is possible to keep these wires straight. To reduce the consumption of the wires, high melting temperature metals need to be selected for wires and low melting temperature metals need to be selected for substrate on which holes will be cut. The experimental results found that tungsten is a good candidate for wires, which has both high young’s modulus and high melting temperature. If it is used as material for wire, most of other metals can be used for membrane.

The advantage of both these two ways in comparison with dry etching method as reported by some other researchers is cheap and repeatable, which make mass producing feasible at low cost. For the first way, it can only fabricate array of square nozzles with designed gap, but the second method is more flexible. For further work, the vibrating mode can be studied, and the
nozzles can be arranged to the vibrating swing peek point, which may help to improve the output flow rate and the efficiency of the input energy. If the fabrication error of the holes can be controlled in 10µm, nozzles of 5-15µm sizes are perfect for most application. However, this would require a very high controlling accuracy for electroplating process. The only disadvantage of the second method comparing with the first one is the cost of wires. If a hole consumes 500µm tungsten wire as mentioned in Section 3.5 and assume 1000 holes need to be made on a membrane, this means that each membrane for an inhaled drug delivery device would consume 0.5m tungsten wire. Only the consuming of tungsten wire for a 1000 nozzle membrane would be about 50 dollars. This is obviously too high for wide applications. Future study may be needed to improve the quality and at the same time to reduce the consumption of tungsten wires.
REFERENCES


VITA

Yuxuan Zhou was born in Jingdezhen, Jiangxi, P. R. China, in 1986. He received his bachelor of engineering degree in mechanical engineering from Tsinghua University in Beijing, P. R. China, in July 2006. And then, he entered the Louisiana State University in fall 2006. He is expected to receive the Master of Science in Mechanical Engineering in August 2010.