A STUDY ON LIQUID BRIDGE BASED MICROSTEREOLITHOGRAPHY (LBMSL) SYSTEM

A Dissertation

Presented to

The Graduate Faculty of The University of Akron

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

Yanfeng Lu

August, 2016
A STUDY ON LIQUID BRIDGE BASED MICROSTEREOLITHOGRAPHY (LBMSL) SYSTEM

Yanfeng Lu

Dissertation

Approved:  

________________________________________  Accepted:

Advisor  
Dr. Jae-Won Choi

________________________________________

Department Chair  
Dr. Sergio Felicelli

Committee Member  
Dr. Abraham Joy

________________________________________

Dean of the College  
Dr. Eric Amis

Committee Member  
Dr. Chang Ye

________________________________________

Dean of the Graduate School  
Dr. Chand Midha

Committee Member  
Dr. Gary Doll

________________________________________

Date

Committee Member  
Dr. Nicholas Garafolo

________________________________________

Committee Member  
Dr. Xiaosheng Gao
ABSTRACT

Although additive manufacturing emerged about 30 years ago, a large number of researchers have been still working on its processes, materials, and applications due to the unique advantages of low cost, high degree of customization, high complexity, fast lead time, less waste material, and integrated assembly. Additive manufacturing has been widely used in a lot of fields, including aerospace, bioengineering, tissue engineering, optics, medical, and electronics.

A vat-based projection microstereolithography (MSL) has been studied for multi-material fabrication with various applications including drug loaded microneedle array and tissue engineering scaffolds. These studies indicate that MSL is an attracting microfabrication process that can create intricate and complex small structures with a high resolution. However, fabrication limitations exist due to the inherent system configuration and fabrication process. These limitations include the difficulty in using highly viscous materials, considerable material consumption, low fabrication speed, and high oxygen inhibition. This thesis sought a method to improve the fabrication capabilities of the existing MSL process by introducing a liquid bridge (a liquid drop formed between two parallel disks) to replace the vat which is a key element in conventional MSL to hold the liquid polymer.
In this thesis, a novel liquid bridge based microstereolithography (LBMSL) was proposed and developed. The liquid bridge was first introduced into the MSL process by replacing the vat, allowing the entire fabrication process to occur within the liquid bridge. The liquid bridge was studied theoretically and experimentally in order to obtain the stable equilibrium shape and the relationship between the height and the volume of the liquid bridge. The adhesion force between the fabricated part and the top disk as well as the oxygen inhibition during the fabrication process were investigated.

Using the LBMSL process, the fabrication layer thickness of 0.5 µm was reached. This could not be achieved in the vat-based MSL due to the oxygen inhibition to the photopolymer. A highly viscous material with the viscosity of more than 3000 cp, which is hard to be used in the conventional MSL, was tested and promising results were obtained. Compared with the vat-based MSL, the material consumption in LBMSL was reduced at least 2 times and the fabrication speed was improved greatly, especially when using a higher viscous material. In addition, the LBMSL showed a potential for multi-material fabrication and continuous fabrication due to this unique fabrication process.

In summary, improvements of fabrication capabilities with the suggested LBMSL process was proved with various experimental results. The suggested process presented many advantages in terms of the layer thickness, the fabrication speed, oxygen inhibition, and highly viscous material fabrication, which can open a route to develop a new additive manufacturing process.
DEDICATIONS

I dedicate my dissertation work to my family and many friends. A special feeling of gratitude to my loving wife, whose words of encouragement and caring during my Ph. D. period. My parents, parents-in-law and my brother have supported me throughout the process although they are half of the earth distance away from me. I especially dedicate my dissertation to my newborn son. Although he has never gave me any word, I always can feel him. He gave me the feeling to be a father and to take more responsibilities. I also dedicate my friends Mrs. Louanne Jenkins and Mrs. Amanda C Worthington, for their kind help of proofreading.
ACKNOWLEDGEMENTS

This dissertation would not have been possible without so much support from so many people.

First of all, I would like to express my deepest gratitude to my advisor, Dr. Jae-Won Choi, for his excellent guidance, patience, and providing me with the great opportunity to work in additive manufacturing area for my Ph. D. study and research. I learned a lot from him, not only in research, but also in life. He was an advisor for four years: he guided and motivated me when I met difficulties in my research. He is also a friend for a life time: he encouraged and supported me when my life was in challenges. For everything you have done for me, Dr. Choi, I thank you.

Second, I would like to thank my committee members (alphabetically): Dr. Gary L. Doll, Dr. Xiaosheng Gao, Dr. Nicholas Garafolo, Dr. Abraham Joy, and Dr. Chang Ye, for your precious time and patience to guide my dissertation.

I would like to acknowledge and thank all the members of the Additive Manufacturing Laboratory for their help and supports and discussion during my graduate studies. I would like to acknowledge Mr. Tanmay Jain, who is Dr. Joy’s student, and Mr. Cale Crowder, for providing me help for polymer synthesis and drug release analysis, respectively.

In addition, I would like to thank Dr. Yang H. Yun from Biomedical Department for his suggestion in the material synthesize. I would like to thank Dr. Todd Blackedge from Biology Department, for helping the microneedle compression test.
TABLE OF CONTENTS

LIST OF FIGURES.............................................................................................................x

LIST OF TABLES............................................................................................................xiv

CHAPTER

I. INTRODUCTION AND RESEARCH OBJECTIVES.................................................1
  1.1 Introduction ........................................................................................................... 1
  1.2 Research objective................................................................................................ 3

II. BACKGROUND AND LITERATURE REVIEW.......................................................5
  2.1 3D printing overview............................................................................................ 5
  2.2 The development of microstereolithography (MSL)............................................. 8
  2.3 Liquid bridge theory............................................................................................. 16
  2.4 Photopolymerization materials in microstereolithography (MSL)....................... 20
    2.4.1 UV curable photopolymers ................................................................. 20
    2.4.2 Photoinitiator.............................................................................................. 23
    2.4.3 Oxygen inhibition in photopolymerization ............................................... 27
  2.5 Microneedles and applications .......................................................................... 28
    2.5.1 Manufacturing methods for microneedles............................................... 29
    2.5.2 Applications of microneedles .................................................................... 33

III. BIOMATERIAL DRUG-LOADED MICRONEEDLE ARRAYS FABRICATED
    FROM VAT-BASED MSL.........................................................................................35
  3.1 Materials and characterization............................................................................. 35
    3.1.1 Synthesis of poly(propylene fumarate)...................................................... 36
    3.1.2 Nuclear Magnetic Resonance (NMR) spectrum and molecular weight of PPF .... 36
3.1.3 Measurement of viscosity of PPF................................................................. 39
3.1.4 Materials preparation for microneedles and the substrate.......................... 40
3.2 Multi-material manufacturing system and microneedle arrays fabrication........ 41
  3.2.1 Cure depth experiment ........................................................................... 41
  3.2.2 The design of the microneedle arrays.................................................... 43
  3.2.3 Fabrication of the PPF-based dacarbazine-loaded microneedle arrays using MSL system.................................................................................................................. 45
3.3 The characterization of the microneedle arrays........................................... 50
  3.3.1 Mechanical testing................................................................................... 51
  3.3.2 The in vitro drug release of dacarbazine from the PPF matrix............... 54
3.4 Conclusion..................................................................................................... 56

IV. LIQUID BRIDGE THEORY AND LIQUID BRIDGE MSL (LBMSL) SYSTEM STUDY ................................................................................................................................. 60
  4.1 Liquid bridge model ................................................................................... 61
    4.1.1 Mathematical model for liquid bridge..................................................... 61
    4.1.2 Experiments for liquid bridge................................................................. 71
  4.2 LBMSL system and fabrication demonstration............................................. 77
    4.2.1 The developed system and fabrication process introduction................ 77
    4.2.2 The adhesion force between the built layer and the top disk............... 82
  4.3 Conclusion..................................................................................................... 90

V. EXPLORATION OF THE FABRICATION CAPACITY AND COMPARISON WITH VAT-BASED MSL ............................................................................................................................. 92
  5.1 The fabrication capacity study..................................................................... 92
    5.1.1 Oxygen inhibition.................................................................................. 92
    5.1.2 The minimum layer thickness investigation in LBMSL and vat-based MSL ...... 94
    5.1.3 The highly viscous material fabrication................................................ 97
    5.1.4 The material consumption.................................................................... 102
5.1.5 Fabrication examples using the LBMSL system ........................................................ 104
5.2 Feasibility tests for LBMSL .......................................................................................... 107
  5.2.1 Multi-material fabrication process ............................................................................. 108
  5.2.2 Continuous fabrication in vertical (z) direction .......................................................... 110
5.3 Conclusion ......................................................................................................................... 112
VI. CONCLUSIONS ........................................................................................................ 115
REFERENCES .................................................................................................................. 118
### LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>CAD image of a teacup and the effects of building using different layer thickness [1]. ........ 7</td>
</tr>
<tr>
<td>2.2</td>
<td>A general additive manufacturing process [40]. .................................................................. 7</td>
</tr>
<tr>
<td>2.3</td>
<td>The number of publications in microstereolithography by years [43]. ............................ 10</td>
</tr>
<tr>
<td>2.4</td>
<td>Schematic diagram of scanning based fabrication apparatus [42]. ..................................... 12</td>
</tr>
<tr>
<td>2.5</td>
<td>MSL device using a dynamic mask-generator [45]. ............................................................ 12</td>
</tr>
<tr>
<td>2.6</td>
<td>A crossbeam two-photon scanning laser microscopic system [46-49]. ................................. 13</td>
</tr>
<tr>
<td>2.7</td>
<td>An illustration for top-down projection SL process [50]. .............................................. 14</td>
</tr>
<tr>
<td>2.8</td>
<td>An illustration for bottom-up projection SL process [50]. ............................................... 15</td>
</tr>
<tr>
<td>2.9</td>
<td>Schematic of CLIP process [51]. .......................................................................................... 16</td>
</tr>
<tr>
<td>2.10</td>
<td>A liquid bridge created between two leaves (a); and in soldering process (b). ..................... 17</td>
</tr>
<tr>
<td>2.11</td>
<td>Liquid bridge of phase 1 surrounded by phase 2 [62]. ........................................................ 18</td>
</tr>
<tr>
<td>2.12</td>
<td>Minimum volume for a liquid floating zone of length ( L ), held by surface tension between two equal disks of diameter ( D ). ( 0A ) is the limit due to detachment from the disk edge, ( AB ) corresponds to a local minimum liquid volume, ( BC ) to nonsymmetric rupture (but still axisymmetric), and ( 0D ) corresponds to a contact angle of 180° at the edge [63]. ................. 19</td>
</tr>
<tr>
<td>2.13</td>
<td>Sketch of the experimental setup [63]. .................................................................................. 20</td>
</tr>
<tr>
<td>2.14</td>
<td>Molecular structures of SL monomers [1]. ............................................................................ 22</td>
</tr>
<tr>
<td>2.15</td>
<td>Free-radical polymerization process [1]. ............................................................................... 23</td>
</tr>
<tr>
<td>2.16</td>
<td>The schematic of excited photoinitiator - energy and time [86]. ........................................ 24</td>
</tr>
<tr>
<td>2.17</td>
<td>The Type I unimolecular scission process (a), and Type II bimolecular hydrogen abstraction process (b) [86-88]. .......................................................... 25</td>
</tr>
<tr>
<td>2.18</td>
<td>Mechanism of radical polymerization affecting by oxygen inhibition [125]. ......................... 28</td>
</tr>
</tbody>
</table>
2.19 Solid microneedles fabricated from silicon, polymer, and metal. (A) Silicon microneedle; (B) Silicon microneedle array; (C) Metal microneedle; (D), (E) and (F) Polymer microneedles with different shapes [129]. ................................................................. 29

3.1 1H NMR spectrum of synthesized PPF. .................................................................................................. 38

3.2 Variation of viscosity with temperature for pure PPF. ........................................................................... 40

3.3 The cure depth versus the exposure energy for PPF/DEF (50:50) and PPF/drug. ....................... 43

3.4 The design of microneedle array. (a) The microneedle array including a 5×5 microneedles pattern, and (b) a single microneedle with substrate. ................................................................. 45

3.5 The slicing process for the microneedle arrays model. (a) The model from CAD software, (b) .STL file transferred from the model, and (c) sliced model by the slicing software. ...... 46

3.6 The multi-material fabrication process for the microneedle arrays: (a) substrate fabrication with the material 1 in the vat 1, (b) rinsing and drying process for the substrate, (c) microneedles fabrication on the substrate with material 2 in the vat 2, and (d) rinsing and drying process for the microneedles. ............................................................................. 48

3.7 Confocal microscopy results for PPF/fluorescence microneedles. The photo was captured from 0 to 1000 µm with intervals of 50 µm. ................................................................. 50

3.8 Microneedle arrays with different drug-loaded ratios: (a) 0 % drug, (b) 1 w% drug, and (c) 2 w% drug. ................................................................. 51

3.9 The SEM image of microneedle arrays with different drug-loaded ratios: (a) 0 % drug, (b) 1 w% drug, (c) 2 w% drug. ................................................................. 51

3.10 Variation of elastic modulus for PPF/DEF (50w/50w) and PPF/drug. ........................................... 52

3.11 The schematic of the compression test for a single microneedle.................................................. 53

3.12 The compression test for the microneedles of 1 % and 2 % drug-loaded ratio. The maximum pre-set loading of the tester was 300 mN. ................................................................. 54

3.13 The pictures for the compression test: (a), (b) are pre-compression and post-compression test for PPF/1w% drug microneedle; and (c), (d) are pre-compression and post-compression test for PPF/2w% drug microneedle. ................................................................. 55

3.14 Dacarbazine release profiles from PPF microneedle arrays. ....................................................... 56

4.11 The schematic of experiment setup for liquid bridge................................................................. 72

4.12 The equilibrium shapes of liquid bridge for water from the experiments and mathematical model with different $\beta_1$. For each figure, the top was from the mathematical model and the bottom was from the experiment. ................................................................. 73
4.13 The error discrepancy between the left liquid bridge profile obtained by the mathematical model and the experimental results for water. The initial angle $\beta_1$ is 55.8°~107.5°. ....... 74

4.14 The equilibrium shapes of liquid bridge for CD9021/HDDA (70w/30w) from the experiments and mathematical model with different $\beta_1$. For each figure, the top was from the mathematical model and the bottom was from the experiment. ................................. 75

4.15 The error discrepancy between the left liquid bridge profiles obtained from the mathematical model and the experimental results for CD9021/HDDA (70w/30w). The initial angle $\beta_1$ is 102°~128.2°. The top two lines in each plot were the left liquid bridge profile obtained by mathematical model (green color) and the experiment (red color). ......................... 76

4.16 Schematic of liquid bridge based MSL system................................................................. 78

4.17 Configuration of the bottom disk in terms of the fabrication area and the material fill channel. The circle was the bottom disk profile and the gray square area was the maximum fabrication area for the system. ....................................................... 79

4.18 Schematic of fabrication process using LBMSL method. .................................................. 81

4.19 The working curve for LBMSL system.................................................................................. 81

4.21 The schematic setup for adhesion force test. ..................................................................... 81

5.1 The oxygen inhibition to vat-based fabrication system (a), and liquid bridge fabrication system (b). ................................................................................................................................. 93

5.2 A stent with a layer thickness of 20 µm, with light absorber. (a) The stent, and (b) overhanging structure in stent. ..................................................................................................................... 94

5.3 A stent structure with a layer thickness of 20 µm, without light absorber. (a) The stent, (b) overhanging structure in stent. ..................................................................................................................... 95

5.4 Posts with the layer thickness of 1 µm. (a) The post array on a substrate, (b) a single post, and (c) the surface of the post. ..................................................................................................................... 95

5.5 Posts with the layer thickness of 0.5 µm. (a) The post array on a substrate, (b) a single post, and (c) the surface of the post. ..................................................................................................................... 95

5.6 Posts with a varying layer thickness from 0.5 to 20 µm. (a) The post array on a substrate, (b) single post with varying layer thickness (LT), and (c) ~ (f), surfaces for 0.5, 1, 10, and 20 µm layer thickness post section................................................................. 96

5.7 Fabrication process using vat-based MSL [161]. In (b) and (c) position, a dwell time and a settling time were needed, respectively................................................................. 97

5.8 A spring structure fabricated by SR150, with a layer thickness of 20 µm by vat-based MSL. (a) The spring structure, (b) part of spring wire, and (c) the surface of the spring wire. ...... 98
5.9 A spring structure fabricated by SR150, with a varying layer thickness of 20 µm by LBMSL. (a) The spring structure, (b) part of spring wire, and (d) the surface of the spring wire. ...........................................................................................................................................99

5.10 A spring structure fabricated by CN293/HDDA (90w/10w), with a layer thickness of 20 µm by vat-based MSL. (a) The spring structure, and (b) part of spring wire. ..............................100

5.11 A spring structure fabricated by CN293/HDDA (90w/10w), with a layer thickness of 20 µm by LBMSL. (a) The spring structure, (b) part of spring wire, and (d) the surface of the spring wire. .....................................................................................................................................101

5.12 The fabrication time comparison with the vat-based MSL and LBMSL using the material SR150 and CN293/HDDA (90w/10w). The time used for the vat-based MSL was 3.8 times and 5 times than that using LBMSL for the material of SR150 and CN293/HDDA (90w/10w), respectively. .....................................................................................................102

5.13 Schematics for material consumption in the vat-based MSL system. (a) The platform and the vat; (b) the size of the platform when the maximum fabrication area is 3×3 mm; and (c) the schematic for fabrication process [170]. ..................................................................................................103

5.14 Schematics for material consumption in the vat-based MSL system. (a) Side view of a liquid bridge, and (b) fabrication area on bottom disk ..............................................................................................104

5.15 Microneedle array fabricated by the LBMSL process with a layer thickness of 30 µm. The model (a) and the SEM image of the microneedle array [30]. .................................................105

5.16 A screw structure fabricated by the LBMSL system with the layer thickness of 20 µm. The model (a) and the SEM image of the screw. .....................................................................................105

5.17 Part of a stent structure fabricated by the LBMSL system with the layer thickness of 20 µm. The model (a) and the SEM image of the stent. ...............................................................106

5.18 Microneedles fabricated using the LBMSL process with different fabrication parameters. (a) the model of the microneedle, (b) intensity: 80, exposure time: 0.2 s for cylinder and 0.2 s for cone tip, (c) intensity: 80, exposure time: 0.2 s for cylinder and 0.3 s for cone tip, (d) intensity: 70, exposure time: 0.2 s for cylinder and 0.3 s for cone tip, (e) intensity: 65, exposure time: 0.2 s for cylinder and 0.4 s for cone tip, (f) intensity: 65, exposure time: 0.2 s for cylinder and 0.5 s for cone tip. ......................................................................................107

5.19 The multi-material fabrication LBMSL system ..........................................................................................................................109

5.20 Multi-material fabrication using LBMSL. (a) Post and (b) stent .................................................................110

5.21 The stent structure fabricated by the LBMSL process. (a) The stent structure and (b) overhanging structure in stent. ........................................................................................................111
**LIST OF TABLES**

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 $E_c$ and $D_p$ values for PPF with different drug-loaded ratios</td>
<td>44</td>
</tr>
<tr>
<td>4.1 Typical physical and chemical properties for CD9021 and HDDA</td>
<td>69</td>
</tr>
<tr>
<td>4.2 The basic properties of PMP material</td>
<td>89</td>
</tr>
</tbody>
</table>
CHAPTER I
INTRODUCTION AND RESEARCH OBJECTIVES

1.1 Introduction

Before the terminology Additive Manufacturing was adopted by the F42 Technical Committee within ASTM, “Rapid Prototyping (RP) was widely used to describe a process for rapidly creating a system or part before final release or commercialization.” [1] Currently, 3D (three-dimensional) printing is alternately used instead of additive manufacturing. 3D printing or additive manufacturing is a process of making three dimensional solid objects from a digital file. After more than 30 years of development, there are several 3D processes, such as Fused Deposition Modeling (FDM), Polyjet printing, and StereoLithography (SL). Although the processes vary, the basic principles for 3D printing are similar. In an additive process, an object is created by laying down successive layers of a material until the desired object is created [1-4].

Along with the fast development of 3D printing, especially in the past ten years, some debates are emerging. It has been suggested that in the future 3D printing will replace the traditional manufacturing technique, such as CNC machining, injection molding, or plastic forming. To the best of the author’s knowledge, 3D printing and traditional manufacturing technology will be the two main manufacturing methods. One will not be replaced by another, as both processes have inherent advantages and disadvantages based on different
manufacturing concepts. In 3D printing processes, lead time, product complexity, customizability, and integrated assembly are predominant factors. In traditional methods, material selection, quantity, product tolerance, and surface finish are principle considerations.

Each 3D printing process has its own unique benefits and advantages created by various fabrication methods and materials. Some processes are suite of liquid materials (e.g. SL or Polyjet printing). In other processes, filaments are needed (e.g. FDM). Direct-print [5-7] as an extrusion based process with materials of aerosol, paste, or viscous compounds has attracted researchers’ interest in a broad application field. Examples include electronics [8-13], bioengineering [14,15], and tissue engineering [16-19]. With the rapid development of material science, more materials can be used in direct-print technology leading to the broadening of applications. These materials include graphene composites [13,20], carbon nanotube composites [21,22], ceramics [23,24] or metal [25] powder composites, and biomaterials [14, 16]. In direct-print process, the material dispensed from a syringe or dispenser, would be solidified immediately or in post processes. Most common curing methods included chemical evaporation [7], in which some chemical solution was mixed with the target materials and would be evaporated after the dispensing leading to the solidification of the target material. The energy sources of UV light [26] or laser [27] were also utilized to make the solidification occur.

The Microstereolithography (MSL) process is an interesting technique that uses liquid composites as materials. MSL is widely adopted in biomedical [28-31], tissue engineering [32-33] and MEMS [34,35] applications. Since the digital micromirror device (DMD) (Texas Instruments) emerged, the projection based MSL has reached a high resolution of
~5 μm, which is an advantage over other 3D printing processes. In addition, the material for this technique is flexible, allowing customers to synthesize their own function materials to realize customized objectives. Researchers have used MSL to fabricate microneedles for drug delivery [30,36], cell scaffolds [37], and bone structures [38].

1.2 Research objective

Vat-based microstereolithography (MSL) is an attractive freeform 3D microfabrication technology, capable of producing complex 3D microstructures in a layer-by-layer fashion. Using the vat-based MSL process, microneedle arrays were fabricated with degradable and biocompatible polymer loaded with a small amount of drug. Previous research results indicate that vat-based MSL is a good process to create complex 3D structures with a high resolution. However, limitations emerged during the fabrication process in terms of high viscous material fabrication, considerable material consumption, low fabrication speed, oxygen inhibition, and the multi-material fabrication process. Therefore, a liquid bridge based MSL (LBMSL) was proposed and studied to improve the fabrication capabilities of the MSL technique.

In this novel liquid bridge based MSL (LBMSL) system, a liquid bridge was adopted to replace the vat, a necessary element to fill the material in a vat-based MSL system. The liquid bridge was formed between two parallel coaxial disks with the same diameter. And the layer-by-layer fabrication process occurred within this liquid bridge. Less material was needed and the fabrication time was reduced. Furthermore, multi-material fabrication and continuous fabrication processes would be realized by the LBMSL.

The research objective was accomplished through the following tasks:
(1) Study of vat-based MSL for microneedle arrays fabrication loaded.

- Biodegradable and biocompatible material, Poly(propylene fumarate) (PPF) was synthesized.
- Microneedle arrays were fabricated by the vat-based MSL process, with the material of PPF with some amount of drug for the transdermal drug delivery.
- The compression test was conducted for the single microneedle and the dynamic drug release profile was obtained.

(2) Foundational effort to obtain the stable equilibrium of liquid bridge formed between two parallel coaxial disks for the LBMSL.

- A mathematical model was developed to obtain the stable equilibrium shape for the liquid bridge.
- A validation and verification of the mathematical model was performed, accomplished through experimental analysis.

(3) Development of LBMSL system and investigation for the adhesion force between the built layer and the top disk, which was to form the liquid bridge.

- The LBMSL system was set up and the working principle of the liquid bridge was described.
- The adhesion force between the built layer and the top disk was tested for different top disks in order to choose a proper material for top disk.

(4) Exploration of the fabrication capacity and comparison with vat-based MSL.

- The key factors that influence the layer thickness was studied.
• The fabrication ability was compared with high viscous material for both vat-based MSL and LBMSL.

• The material amount comparison was conducted in LBMSL and vat-based MSL.

• Oxygen inhibition was analyzed and compared for LBMSL and vat-based MSL.

(5) Feasibility tests for the LBMSL system.

• Multi-material fabrication was attempted by feeding materials from top and bottom disk.

• Continuous fabrication process was tried and the results showed the potential to fabricate continuously.
2.1 3D printing overview

3D printing (also known as additive manufacturing, AM) is one of many various manufacturing methods to create a three-dimensional object. The basic concept for 3D printing is to obtain a 3D object by adding material in layers controlled by computer. Each layer is a thin cross-section of the part produced from CAD data [1,2]. The thinner each layer is, the higher resolution of the part could be fabricated. In other word, the layer thickness determines the resolution of the 3D printer system. Figure 2.1 showed a teacup fabricated from a 3D printing process with different layer thickness. Obviously, the right part with the thinner layer thickness had a better surface [1].

Generally, the first step in a product development process is to come up with some idea regarding to how the product will look and function. The design idea then will be transferred to a CAD model using a 3D software. Once the desired CAD model is obtained, the model will be translated to stereolithography (.STL) file [1,39]. .STL approximates the surfaces of a solid model with triangles. The more complex the surface, the more triangles produced. In this step, users can check the .STL file and fix the errors if found.
Several 3D printing processes have been developed since the first concept proposed in 1993. Some common commercial printing processes include photopolymerization process, powder bed fusion process, extrusion-based process, and beam deposition process. The basic manufacturing principle and process of additive manufacturing is similar [1,39]. Figure 2.2 shows typical steps to achieve a part from the conceptualization to the application.
In 3D printing, the orientation of the part is of an importance because it affects the fabrication time, material consumption, and even the surface property. One should consider the orientation carefully according to the customer’s requirement in real application, like the load direction and surface roughness. Usually, the software along with the 3D printer will generate the support material program and the fabrication toolpath automatically. Before printing, some parameters are set, typically including the layer thickness, surface properties, material selections, and building speed [39]. Normally, an incorrect parameter setup will still result in a part being built, while maybe with bad features. Therefore, proper parameters should be taken into account in order to avoid the fabrication failure. A slicing software will then slice the model into many layers as required. Tool path also will be generated in this step. Typically, the model slicing and tool path generation are integrated in the software along with the 3D printer. Next, the fabrication can start from the first layer and finally, the 3D part will be produced by stacking all the layers. Some 3D printing processes have special requirement to the environment. For example, ambient light should be tried to reduced when using a MSL process due to the UV light or visible light are commonly selected as the energy source. For most of the 3D printing processes, post processing are necessary, including support material removing, surface polish, and residual stress relieving. Support structures will be generated with the model structure for some printing processes. Otherwise a model with overhanging structure cannot be printed. For instance, some fused deposition modeling printers use Acrylonitrile Butadiene Styrene (ABS) as the model material and Polylactic Acid (PLA) as the support material. The support structure should be easily removed without damage to the model structure. A common support structures removing method is to put the 3D printed structure into a
chemical solution, which can dissolve the support material while is inert to the model material. Eventually, a 3D part can be achieved successfully.

Comparing with the conventional manufacturing methods, such as computer numerically controlled (CNC) machine or casting, 3D printing has a large number of advantages in terms of low cost, zero lead time, less material waste, high degree of customization, high complexity, and sustainable/environmentally friendly. The manufacturing time is reduced dramatically in 3D printing process. 3D process maximizes the use of computer aided design from the conceptualization to slicing to start building. Furthermore, products and components can be designed specifically to avoid assembly requirements with intricate geometry and complex features. This eliminates the labor and costs associated with assembly processes. Also, it is very easy to modify the model if any deficiency found in the final product. 3D printing processes allow for mass customization - the ability to personalize products according to individual needs and requirements. Based on unique manufacturing process, 3D printing can build parts with any complexity, which, to some extent, is impossible for the CNC machine.

2.2 The development of microstereolithography (MSL)

Microstereolithography (usually abbreviated as µSL or MSL) technology has been developed over 20 years since the first demonstration presented by two groups [41,42] at the end of last century and still is attracting a growing number of researchers due to its well-known fabrication capabilities, such as free design for 3D complex structure, high resolution and aspect ratio as well as multi-material and multi-scale fabrication. As the fast development of the electronics, optics, and materials, MSL technology was improved rapidly since the first advent and widely used in different areas including optics, sensors
and actuators, biomedical, and tissue engineering. According to a statistical data [43], the number of publications (including journal papers and proceeding) increased rapidly, especially in the last ten years, as shown in figure 2.3. The growing number of publications indicates the increasing tendency of research activities.

![Figure 2.3](image)

**Figure 2.3** The number of publications in microstereolithography by years [43].

Typically, based on a means to create one layer, MSL was sorted to scanning MSL, projection MSL, and two-photon MSL. The first MSL system was a scanning method developed by Takgi *et al.* in 1993 [41,42], in which a focused UV light spot as an energy source was focused on the resin surface through a transparent window. Figure 2.4 showed a scanning-based MSL system widely used in conventional SL technique. A vector-by-vector tracing of each layer was adopted to obtain the final 3D structure. In the cross-sectional fabrication process, the UV laser beam focused on a diameter of a few microns irradiated on the surface of the photopolymers with a UV photoinitiator blended. The photons of the UV light triggered the photoinitiator to produce free radicals and reactive
cations, which initiate the crosslinking of the photopolymer leading to the solidification. After a two-dimensional cross-sectional shape was cured along the laser scanning path, the already built part would be immersed into the liquid material leaving one layer thickness material on the top. Then the next layer fabrication could be started. Consequently, a complex 3D microstructure was generated through stacking up all of the cross-sectional parts. The most disadvantages of the scanning MSL were the consuming of the time and the relatively low resolution. To overcome these disadvantages, the projection MSL was developed based on the projection of an image created by a dynamic mask on the surface of the photocrosslinkable material [44,45]. Using this advanced method, the cross sectional image for each layer can be projected on the surface of the liquid material inducing the solidification for the entire layer (Figure 2.5). The projection MSL process was faster with a higher resolution compared with the scanning technique due to the single exposure to solidify a layer, regardless of its complexity. In order to fabricate the object directly inside the liquid material instead of scanning or projecting layer by layer and to achieve a higher resolution, the two-photon MSL [46-49] was developed, which can reach a submicron resolution. In this process, the built part was inside of the liquid material during all the fabrication process, and no material spreading was needed as happened in the scanning and projection processes. Figure 2.6 showed a typical two-photon MSL fabrication system. However, this technique was limited to fabricate tiny structure at the micro-scale due to the inherent properties of photons.
Figure 2.4 Schematic diagram of scanning based fabrication apparatus [42].

Figure 2.5 MSL device using a dynamic mask-generator [45].
Figure 2.6 A crossbeam two-photon scanning laser microscopic system [46-49].

Recently, projection MSL was developed fast and used widely in different fields based on its distinct advantages compared to the scanning and two-photo technique. The projection MSL process was either top-down or bottom-up depending on the projection direction.

The system in figure 2.7 was a typical top-down projection process, where the patterns generated by DMD were projected from the top onto the resin surface. After a layer fabrication, the built part was moved down with the platform and covered by a fresh layer material. In some systems, a sweeper was used to help the material cover the built part fast and smoothly [50]. In this process, oxygen inhibition was significant when using a very thin fabrication layer thickness (~1 μm) because oxygen in the air can affect the photopolymerization process. In addition, it was difficult to have multi-material process since the material changeover could result in material waste [50].

The bottom-up projection based MSL process was derived from SL process [50,51]. In this process, the bottom window of the vat was transparent and the light patterns
generated by DMD passed the bottom window to solidify the photopolymer. After one layer fabrication, the built part was moved up with the platform allowing the fresh photopolymer to fill the gap between the built part and the bottom window, followed by the next layer fabrication.

Figure 2.8 showed a schematic for the bottom-up projection process. The biggest challenge for this method was to obtain a small adhesion force between the built part and the bottom window of the vat when the platform was moved up. In order to solve this problem, Zhou et al. [50] coated a very thin layer of polydimethylsiloxane (PDMS) on the inside window of the vat. PDMS film can form a thin oxygen inhibition layer (~2.5 µm) that prevented the photopolymerization process. A thin uncured polymer between the built part and the bottom window of the vat reduced the adhesion force and made the separation of the built part from the bottom window easily. However, the amount of oxygen attached on the PDMS film was limited and the adhesion force cannot be eliminated completely.

Figure 2.7 An illustration for top-down projection SL process [50].
Using the bottom-up projection technique, Tumbleston et al. [51] developed a continuous liquid interface production (CLIP) process. In CLIP process, an oxygen-permeable transparent window was utilized as the bottom of the vat. During the printing process, pure oxygen was kept providing to penetrate the bottom window and a thin layer dead zone was formed near the window. With the dead zone, oxygen can either quench the photoexcited photoinitiator or create peroxides by combining with the free radical from the photocleaved photoinitiator [51]. Thus, the photopolymer was prevented to be crosslinked. The dead zone thickness can be adjusted by changing the photo flux, photoinitiator absorption coefficient, and resin curing dosage. With the fresh liquid material exiting between the built part and the bottom window of the vat, the built part can be separated from the bottom window with a very small adhesion force (Figure 2.9).

Figure 2.8 An illustration for bottom-up projection SL process [50].
By providing the pure oxygen, the adhesion force between the built part and the window of the vat was eliminated greatly. However, the fabrication cost and the complexity were increased dramatically.

2.3 Liquid bridge theory

Liquid bridge is a common natural phenomenon which can be formed between two or more solid objects due to the surface tension forces. Figure 2.10(a) is a liquid bridge formed between two leaves by the raindrops. Actually, liquid bridge is also very common in industrial area, like in soldering process. When soldering, the melting solder will form a liquid bridge between the tip of the welding gun and the work piece, as shown in figure 2.10(b).

![Image of a liquid bridge](image)

Figure 2.9 Schematic of CLIP process [51].

The liquid bridge study has a history over 100 years and the basic research can be back even more earlier to the classic experiments of Plateau [52]. In Plateau’s work, the
stability of an infinite vertical falling water jet was investigated experimentally and the observation that the maximum ratio of the stable length to the jet diameter is about a constant $\pi$ was obtained [53]. Young [54] and Laplace [55] developed the capillary pressure theory using Young-Laplace equation. Slobozhanin [56] studied the stability of liquid bridges between two equal disks in an axial gravity field. Mathematical formulation and numerical algorithm were developed to achieve the stability relationships between the maximum volume and maximum height between the two equal disks. Luo et al. [57] explored the behavior of the liquid bridge formed between two nonparallel plates theoretically and experimentally.

Figure 2.10 A liquid bridge created between two leaves (a); and in soldering process (b).

The liquid bridge technique has been used in the 2D and 3D printing industry. In direct-write/print process, a liquid meniscus was formed between the dispenser tip and the substrate [58]. Hasan et al. [59] studied the phenomenon of a liquid droplet impact on a liquid film during the manufacturing processes with jetting technology like a direct-print process and inkjet printing. The analysis of interface tracking and change of shape for an impacted droplet of a dispensed material was investigated. Deladi et al. [60] introduced a
fluidic channel to transport the fluid from the reservoir to the AFM tip, and a liquid bridge was created between the tip and the substrate. The microfluidic nanoprobe developed by Moldovan *et al.* [61] used the liquid bridge principle to have the dip-pen nanolithography approach.

Gillette and Dyson [62] studied the stability of fluid interfaces of revolution between equal solid circular plates without the effect from the gravity. According to their theory, there were two limiting configurations when forming a liquid bridge between two equal parallel coaxial circular plates (figure 2.11).

Suppose the fluid was slowly removed through the valve, the interface gradually shrank down and approached a limiting configuration: curve A. If keep reducing the volume, the bridge ruptured. To be opposite, if the fluid was slowly filled through the valve, the interface would gradually expand and another limiting configuration-curve B would be reached. Further addition of fluid would lead to an unstable interface. From this theory, a
static liquid bridge could be created if the volume of fluid 1 was either less than $V_B$ corresponding to curve $B$ or greater than $V_A$ corresponding to curve $A$. In other word, a stable liquid bridge always can be obtained for any $V \in (V_A, V_B)$. For the ratio of the plate separation to the plate diameter ($l/d$) was less than $\pi$, there would be a bulged outward limiting interface and a constricted one. For $l/d > \pi$, both limiting interfaces were bulged outward.

Sanz and Martinez [63] investigated the minimum volume for a liquid bridge between equal disks experimentally and the results were matched with the theoretical prediction. The bond number used in their experiment was very small and the gravity effects were kept out of the analysis the same with Gillette’s work. The theoretical results about the minimum volume for a liquid floating zone of length $L$, held by the surface tension between two equal disks of diameter $D$ was shown in figure 2.12.

![Figure 2.12](image)

Figure 2.12 Minimum volume for a liquid floating zone of length $L$, held by surface tension between two equal disks of diameter $D$. $0A$ is the limit due to detachment from the disk edge, $AB$ corresponds to a local minimum liquid volume, $BC$ to nonsymmetric rupture (but still axisymmetric), and $0D$ corresponds to a contact angle of 180° at the edge [63].
In their experiment (Figure 2.13), two liquids were used: a 1:2 mixture of water-methanol as the outer liquid, and a dimethyl-silicone oil with a viscosity of 20 times that of water as the working liquid. Then density of both the mixture and the working liquid was measured to be $\rho=954\pm0.5$ kg/m$^3$.

2.4 Photopolymerization materials in microstereolithography (MSL)

Photocrosslinkable liquid materials called photopolymers are needed for microstereolithography. In MSL fabrication process, a solidification process from the liquid to solid has to occur [64 - 67]. Principally, any commercially available photocrosslinkable resins can be used in MSL systems [68,69]. However, materials with a high viscosity are very difficult to be used due to a long refreshing time is required for the highly viscous material, typically if the viscosity is higher than 200 cp.
2.4.1 UV curable photopolymers

Various types of radiation can be used to cure crosslinkable photopolymers, including X-rays, electron beams, UV, and visible light, although UV light is the most prevalent [70-72]. Commonly, two kinds of resins, acrylate-based and epoxy-based resins are widely used in MSL. The first SL resins were reported in 1989 and 1990 [73,74], which was from acrylates, and the first epoxide resins for SL appeared in 1988 [75,76]. Both types of resins own advantages and disadvantages. Acrylate-based resins have a high reactivity but typically produced weak parts due to the high shrinkage of 5-20% and curling leading to low accuracy. Epoxy-based resins only have an approximate 1-2% shrinkage due to the ring opening polymerization. In addition, the polymerization process of the epoxy-based resins is not limited by the atmospheric oxygen. However, the epoxy resins have a relatively slow curing speed and brittleness of the cured parts. Another disadvantage of epoxy resins is the high sensitivity to humidity, which can inhibit polymerization as well. A common way to have good resins for SL is to combine the acrylate-based and epoxy-based resins. In this way, the acrylate-based part will contribute to reduce the brittleness and speed up the reaction rate. The epoxy-based part can decrease the shrinkage level [77] greatly. Therefore, most resins for SL commercially available today are the hybrid of the epoxy-based with some acrylate content [78].

Basically, there are two types of chemical processes for UV curing [79,80]: free-radical-acrylate, and cationic-epoxy and vinyl ether, as shown in figure 2.14 [1]. Free radical chemistry, in which radicals are produced by photoinitiators excited by UV light energy [81-83], is by far the most common system for commercial applications due to the inherently more expensive process of cationic.
Two types of radical generation process occurred when UV light is applied to the photoinitators: type I scission process, and type II abstraction process. In type I, photoinitiators produce free radicals from the excited triplet state in the process [84-86]:

\[ \text{PI (ground state)} + \text{UV} \rightarrow \text{P}^* \text{ (singlet state)} \rightarrow \text{P}^* \text{ (triplet state)} \rightarrow \text{R}^* \text{ (radical)} \]

In type II, a hydrogen donor such as tertiary amines, ethers, and thiols, is needed to provide hydrogen atom, which will form a radical with triplet state photoinitiator [86,87].

\[ \text{P}^* \text{ (triplet state)} + \text{HD (donor)} \rightarrow \text{P} \cdot \text{H} \text{ (radical)} + \text{D} \cdot \text{ (donor radical)} \]

Free radical photopolymerization consists of four processes: initiation, propagation, chain transfer, and termination [88,89]. To be simple, the UV radiation providing photons will be absorbed by photoinitiators. The photoinitiators will form an excited species [90,91]. Radicals will be generated in this step. Then the reaction of a radical with monomers will occur to form monomer radicals, which will start a chain reaction with the monomer and oligomer in the formulation. Cross-linking will occur if multifunctional monomers are used. The step “chain transfer” mentioned above refers to the reaction of the polymer radical with a hydrogen donor [92]. In this process, a hydrogen atom will be transferred to the
polymer chain, and create a new donor radical that can generate a new polymer chain by reacting with more monomers [93].

Schematically, the polymerization process can be illustrated by figure 2.15, where the PI term indicates a photoinitiator, the $P\cdot$ symbol is a free radical, and $M$ is a monomer. The polymerization will be terminated when either of the three phenomenon occurs: recombination, disproportionation, or occlusion.

![Reaction Scheme](image)

Figure 2.15 Free-radical polymerization process [1].

The chemical process occurred for cationic photopolymerization is very similar as the free-radical polymerization [94-96]. First, a photoinitiator generates a cation after absorbing the light energy, and then the cation will react with a monomer to start the propagation to form a polymer, with the same termination conditions [97-99].

2.4.2 Photoinitiator

In the photopolymerization process, the light source is needed to provide the energy. Actually, the light is applied to the photoinitiator which will produce radicals or cations to trigger the photopolymerization [100,101]. When a photoinitiator absorbs light energy, a high-energy singlet state will be produced that may convert to a more stable, but less
energetic, triplet state by intersystem crossing, as shown in figure 2.16. Most of radicals are produced from the triplet state but a few can interact from the excited singlet state directly [86,102].

![Diagram of excited photoinitiator - energy and time](image)

**Figure 2.16** The schematic of excited photoinitiator - energy and time [86].

There are also several decay processes that may occur from the excited states and figure 2.16 shows some common ones [103,104]. The singlet state may decay to the ground state by a fluorescence decay process or convert to the triplet state by an interstate crossing process. And the triplet state may decay to the ground state by a phosphorescence decay or quenching by monomers or oxygen.
Figure 2.17 The Type I unimolecular scission process (a), and Type II bimolecular hydrogen abstraction process (b) [86-88].

It is obvious from the above description that a photoinitiator is essential for the polymerization process [105,106]. There are a large number of different types of commercial photoinitiators in both type I and type II [86]. For some common photoinitiators, hydroxyacetophenones, alkylaminoacetophenones, benzyl ketals and dialkoxyacetophenones, benzoin ethers, and phosphine oxides are belonged to type I, and benzophenones, substituted benzophenones, thioxanthones, anthraquinones, benzoylformate esters, and camphorquinone are in the category of type II [107]. Figure 2.17 (a) and (b) are examples of type I and type II photoinitiators. Besides, a large number of blends of photoinitiators are available commercially [108-110]. Visible light curing
photoinitiators also have been developed for some specific applications both in the industrial and academic areas. Some common visible light photoinitiators include titanocenes, dibenzylidene ketones, 1,2-Diketones, and H-Nu series [111-113].

Some factors should be taken into account when using photoinitiators in terms of the hardness, yellowing, and the primary cure speed [114,115]. According to some research results, a higher concentration of the photoinitiator will lead to a poor cure depth, because most of the energy will be absorbed near the surface leading to a rapid surface cure but poor through cure, which inevitably will result in shrinkage and poor adhesion to the substrate [116]. High levels of photoinitiator, despite offering a higher cure speeds, will lead to reduced hardness, reduced solvent resistance, and increased yellowing. This can be explained that high concentration of photoinitiator provides a large amount of radicals. These radicals will start polymer chains with a low molecular weight distribution and correspondingly softer films [117]. Low concentration, in contrast, produces a low radical count resulting in fewer, high molecular weight polymer with a narrow molecular weight distribution and good hardness.

Cationic curing, although not widely used in industrial area, is growing fast based on some advantages of insensitive to oxygen inhibition, low shrinkage, excellent adhesion, and chemical resistance. The photopolymerization process conducted by cationic photoinitiator is completely different from that by free radical-based photoinitiator. Taking epoxy polymerization process as an example, the Bronsted or Lewis acid generated from the sulphonium or iodonium salt will open an epoxy ring to form a carbonium cation. The cation then triggers the next polymerization to form a polymer chain.
Another way to use photoinitiator is to hybrid cationic/free radical curing using a mixture of the epoxy and acrylate resin [118], which provides additional advantages for some specific applications [119]. In this way, advantages from both types can compensate each other and a better results may be presented [120].

2.4.3 Oxygen inhibition in photopolymerization

One obstacle when using resins in MSL process is the oxygen inhibition [121,122], especially for acrylate-based resins. The oxygen molecular in atmosphere can react with the photoinitiator and weak the activity [123,124].

The mechanism of photoinduced radical polymerization affecting by oxygen can be illustrated by figure 2.18. Ideally, photoinitiators (PI in figure 2.18) absorb energy from the incident UV light and produce radicals (symbol ‘P•’ in figure 2.18). The radicals can start the polymerization to form P-M• and eventually polymers will be obtained (the green-arrow path in figure 2.18) [82,84,86]. However, the excited state of the photoinitiator may be quenched (step a) to the inactive state - ground state by oxygen molecules in the air. This is more likely to happen with Type II photoinitiators that have longer triplet lifetime. The energy quenching is less affecting the Type I photoinitiators due to its short lifetime [86].

In addition, the oxygen molecules may scavenge radicals by reacting with P• or P-M• to form peroxyl radicals (POO•) which have low reactivity toward the acrylate function (step b and c). These peroxyl radicals tend to terminate polymerization through radical-radical recombination (step e) to form peroxide bridges, POOP or by abstracting hydrogen from an adjacent molecule (RH) to form POOH and R• (step f). All these reactions induced by oxygen will weak or terminate the polymerization process [125].
Figure 2.18 Mechanism of radical polymerization affecting by oxygen inhibition [125].

There are a bunch of methods to reduce the oxygen inhibition. The common methods include physical approaches of the use of inerting gas, wax barriers, solid cover film, and high concentration photoinitiator and light intensity in step a, or chemical methods applied to POOH or POOP [126], where to reinitiate polymerization by decomposing the hydroperoxides or alkyl peroxides to generate potentially more reactive alkoxy or hydroxyl radicals [86,87,90]. Or to introduce hydrogen donors (DH) and reduce agents (RA) to form more reactive radicals (D• or PO•). The use of excess tertiary amine is another way to scavenge peroxy radicals [127,128].

2.5 Microneedles and applications

Microneedles have been regarded as an alternative drug delivery device that could deliver drugs, insulin, protein and vaccine. Several research groups have used various materials, designs and fabrication processes to manufacture microneedles. Microneedles can typically be classified into the following categories: solid/hollow, and metallic/polymeric structures.
2.5.1 Manufacturing methods for microneedles

McAllister et al. [129] fabricated solid and hollow microneedles using silicon, metal, and biodegradable polymer, either by etching into silicon or polymer substrates or by filling molds with metal or polymer (Figure 2.19 and Figure 2.20).

![Figure 2.19](image-url)

Figure 2.19 Solid microneedles fabricated from silicon, polymer, and metal. (A) Silicon microneedle; (B) Silicon microneedle array; (C) Metal microneedle; (D), (E) and (F) Polymer microneedles with different shapes [129].

Kuo et al. [130] developed a novel method combining the photolithography and molding processes to fabricate polymeric hollow microneedles, with a dimension of bore diameter of 50 µm and length of 600 µm. Through the multiple exposure and coating process, a three layers structure was fabricated without the bonding process. The material was a mixture of PDMS prepolymer with the commercial prepolymer and catalyzer (Sylgard 184 kit, Dow Corning).

Martanto et al. [131] fabricated solid microneedles by cutting needle structures from stainless steel sheets using an infrared laser (Figure 2.21) as an application of delivering insulin. The laser beam traced the desired shape of needle and created the needles in the plane of the metal sheet. Each needle was bent at 90° out of the plane of the sheet.
The electropolishing process was introduced to remove the debris, and the needle thickness was reduced to 50 µm after this process.

![Figure 2.20 Hollow microneedles fabricated from silicon, metal, and glass. (A) Metal microneedle; (B) Glass microneedle; (C) Tapered metal microneedle; (D) Array of tapered metal microneedles [129].](image)

Matriano et al. [132] manufactured microneedle arrays (i.e. micro-projections) by acid etching from a titanium sheet. The sizes of the microneedle arrays were either 1 or 2 cm², with a density of 190 needles per cm². The length of the needles was 330 µm. A model protein antigen, ovalbumin was coated on the microneedles to produce a dry-film coating and eventually, delivered into the skin.

![Figure 2.21 Cross section of an array of microneedles inserted into rat skin in vivo [131].](image)
Park et al. [133] fabricated biodegradable polymer-based microneedles using poly-glycolic acid (PGA) with base diameters of 250 µm, tip diameters of 10 µm, and lengths of 1500 µm as well as polylactic acid (PLA) microneedles with base diameters of 150 µm, tip diameters of 5 µm, and lengths of 750 µm (Figure 2.22). First, microlenses structures were created by etching, lithography and UV exposure processes with the material of SU-8 negative epoxy photoresist (SU-8 100, MicroChem, Newton, MA). Then, PDMS was poured over the master structures and cured to make molds. Using these molds, biodegradable polymer microneedles were mass fabricated.

![Figure 2.22 Microneedle master structure (a), and biodegradable polymer microneedles produced by micromolding microneedle master structures (b) [133].](image)

Chandrasekaran et al. [134] fabricated hollow microneedles using electroplated metals, such as palladium, palladium-cobalt alloys, and nickel, as the structural materials. The microneedles were 200 µm to approximately 2 cm in length with cross-sectional
widths of 70-200 µm, heights of 75-120 µm, and wall thicknesses of 30-35 µm. The microneedle arrays were typically 9 mm in width and 3 mm in height with 3 to 17 needles per array.

Ji et al. [135] investigated the dry and wet etching technologies for fabricating microneedles. The figure 2.23 was the microneedle array fabricated in isotropic etch. In order to get high aspect ratio microneedle structure, a more complex process, combined the isotropic etching and anisotropic etching was developed. With this technique, a microneedle with ~300 µm in height was achieved (Figure 2.24).

Figure 2.23 Microneedle array fabricated in isotropic etching process [135].

Figure 2.24 Microneedle arrays fabricated in combined process of isotropic and anisotropic [135].
Moreover, microneedles with macroporous tips were manufactured by the developed process [135]. The silicon microneedle was fabricated first and porous tip was then fabricated using coating and etching process. Finally, a silicon microneedle with a porous tip could be obtained, which can serve as drugs loading tool.

Boehm et al. [136] used a commercial Perfactory III SXGA+ visible light MSL system (Envision TEC GmbH, Gladbeck, Germany) to fabricate master structures of microneedle arrays. The manufacturing process using the commercial machine was similar with the process described in the MSL review. The master structure then was used to create molds with PDMS with a coating and curing procedure. Finally, microneedle arrays with material of Gantrez® AN-139 were achieved using the PDMS molds (Figure 2.25).

![Microneedle arrays with: (a) unmodified and (b) quantum dot-coated Gantrez® AN-139 [136].](image)

Figure 2.25 Microneedle arrays with: (a) unmodified and (b) quantum dot-coated Gantrez® AN-139 [136].

2.5.2 Applications of microneedles

The applications of microneedles have been extended to a broad fields, including intracellular, transdermal, and ocular delivery. Among these fields, the transdermal
delivery is the dominant research area. Drug delivery into the skin is difficult due to the barrier properties of the skin’s stratum corneum. Microneedles have been verified to be a promising approach to deliver an increasing number of drugs, including low molecular weight drugs, vaccines, and biotherapeutics [137,138]. Some researchers also used coated microneedles and hollow microneedles to deliver lidocaine [139,140]. Biotherapeutic drugs, like proteins, peptides, DNA and RNA, are large molecules that have big challenges to be administered orally or transdermally. Therefore, utilizing coated microneedles or encapsulated within dissolving microneedles would be a considerable alternative. Insulin and vaccine are another common drugs that can be delivered successfully by the microneedles, both coated and encapsulated [141-145]. Some other drugs, like EPO [146,147], low molecular weight heparin [148], leuprolide acetate [149], desmopressin [150], hormone [150-152], and salmon calcitonin [153], were delivered by dissolving or coated microneedles.

Currently, microneedles are not limited to delivery drugs into the skin. Some researchers have applied the microneedles to deliver drugs to eyes. Coated microneedles were firstly used to administer model compounds into the sclera and corneal stroma [154]. Then, hollow microneedles were attempted to make invasive injections of soluble molecules, as well as nano- and micro-particles, into the sclera [155].
Yuen et al. [156] used microneedle coated with silver to realize Surface-Enhanced Raman Scattering (SERS) measurements to detect Rhodamine 6G and glucose test molecules buried deeper than 700 µm inside phantoms with elastic scatterers and absorbers to mimic the human skin (Figure 2.6). In their work, a 750 nm thick silver film was coated onto the surface of the microneedle patches (AdminPatch 1200 [157], AdminMed, California, US) by using the Tollen’s method.
CHAPTER III

BIOMATERIAL DRUG-LOADED MICRONEEDLE ARRAYS FABRICATED FROM VAT-BASED MSL

MSL is an attractive manufacturing technique for biomedical applications, especially for micron-scale manufacturing. In this chapter, biodegradable and biocompatible material, poly(propylene fumarate) (PPF) was synthesized and prepared with loading a cancer treated drug, dacarbazine. Microneedle arrays using the composite as the material for transdermal delivery of a chemotherapeutic drug were fabricated by the developed multi-material vat-based MSL system. Compression test and characterization of the elastic moduli of the PPF/diethyl fumarate (DEF) (50:50) and PPF/drug mixtures were carried out. Five weeks drug release kinetics was obtained to study the drug release control.

3.1 Materials and characterization

Additive manufacturing technology has been widely used in biomedical and tissue engineering areas based on the unique advantages [158]. A large number of research has been conducted on biomaterials, which can be used to fabricate tissue, scaffolds, and bones. Kang et al. [159] utilized aminoethyl methacrylated hyaluronic acid (HA-AEMA) and trimethylene carbonate-trimethylolpropane (TMC-TMP) to fabricate scaffolds. Gauvin et al. [160] synthesized collagen-based gelatin methacrylate (GelMA) hydrogels to generate
scaffolds for cell seeding. Among these biomaterials, poly(propylene fumarate) (PPF) attracted a lot of researchers in scaffolds and microneedles areas [158, 161-163].

3.1.1 Synthesis of poly(propylene fumarate)

PPF has been widely used in tissue engineering and biomedical applications as a biocompatible material based on its crosslinkable and biodegradable properties. To date, a number of synthetic techniques for PPF have been reported with a variety of polymer properties. A common method for synthesizing PPF follows a two-step procedure, beginning with diethyl fumarate (DEF) and propylene glycol (PG, Sigma-Aldrich, St. Louis, MO, US), and involving bis(hydroxypropyl) fumarate as an intermediate[164]. Briefly, in the first step, DEF and PG reacted in a heated vessel with zinc chloride and hydroquinone as the catalyst and the crosslinking inhibitor, respectively. The reaction occurred at a temperature gradually increasing from 110°C to 140°C under a continuous flow of nitrogen gas. In the second step, bis(hydroxypropyl) fumarate produced in the first step was transformed into PPF through a transesterification reaction. This stage of reaction was conducted under vacuum with mechanical stirring and with a gradual increase in temperature from 100 °C to 140 °C. The reaction proceeded until the desired molecular weight of PPF was obtained. After these two steps, several purification agents were used to purify the PPF solution [164].

3.1.2 Nuclear Magnetic Resonance (NMR) spectrum and molecular weight of PPF

The NMR spectrum was achieved in this work and compared with the spectrum reported by Fisher et al. [164] to verify the purity of the PPF. The NMR was carried out with a NMR spectrometer (300MHz NMR, Varian, USA) operated at ambient temperature. Approximately 0.6 g PPF was dissolved in 1.8 g of CDCl₃ to prepare the sample. The 1H
NMR (Figure 3.1) spectrum demonstrated the characteristics peaks for each of the PPF’s functional groups and indicated that PPF was successfully synthesized without significant impurities [164].

Figure 3.1 1H NMR spectrum of synthesized PPF.

The molecular weight of the PPF was a significant index that can affect the degradation rate directly, according to others’ reports [162, 163]. Gel permeation chromatography (GPC) was carried out (Tosoh EcoSEC HLC-8320, Tosoh Bioscience LLC, and King of Prussia, PA, USA) to test the molecular weight of synthesized PPF, with a packing material of crosslinked polystyrene as columns and chloroform (High-performance liquid chromatography (HPLC) grade) as eluent. The whole modular system was thermo-regulated at 40°C. The flow rate of the eluent was 0.4 ml/min and each sample was run for approximately 50 min. The estimated molecular weights of the samples were
used to make solutions of approximate concentrations. The samples were dissolved completely by leaving for 12 h on a shaker at a low speed. The dissolved samples were then injected into the GPC autosampler vials after filtering through 0.45 µm polytetrafluorethylene (PTFE) filters. Next, the samples were loaded into the GPC, and 20 µl solution from each sample was injected into the sample columns for analysis using both refractive index (RI) and ultraviolet (UV) modes of detection. Polystyrene standards were used to analyze the molecular weight of the PPF samples. EcoSEC analysis software provided by Tosoh was used for analysis and characterization of the GPC results (i.e. to obtain the molecular weight of the PPF). The number average molecular weight (Mn) and weight average molecular weight (Mw) of the synthesized PPF obtained from GPC using the RI method were 1,183 Da and 1,268 Da, respectively. Mn and Mw of the synthesized PPF obtained from GPC using the UV method was 1,510 Da and 1,592 Da, respectively. It was observed that the difference of the molecular weight of PPF obtained from UV and RI method was in an acceptable range, which means both methods can be used for finding the molecular weights of PPF.

3.1.3 Measurement of viscosity of PPF

Besides the molecular weight, another important index for PPF was the viscosity, which determined fabricability using the MSL process, because the recommended viscosity of polymer for MSL was ~200 cP [165,166]. In order to measure the viscosity of uncured PPF, a rheometer (ARES-G2, TA Instruments, New Castle, DE, USA) was conducted at a 10 Pa shear stress from 25 °C to 100 °C with a ramp rate of 5 °C/min. Variation of viscosity with temperature for pure PPF was obtained, as shown in figure 3.2.
Figure 3.2 Variation of viscosity with temperature for pure PPF.

It was observed that the viscosity of PPF at room temperature was ~8,400 cP, which was too high to be used in the MSL system directly. When the temperature was increased to 100 ºC, however, the viscosity of PPF dropped down to ~101 cP. With this low viscosity, theoretically, the material could be utilized in MSL fabrication process. Two issues, however, should be considered regarding the high temperature. Firstly, the PPF with a photoinitiator solution at 100 ºC would be partly crosslinked by the heat and become a gel-like solid, which can not be used for MSL anymore. Secondly, the chemical reactivity of the PPF may be changed at high temperature about 100 ºC. Based on these two considerations, DEF and DMSO were introduced to decrease the viscosity of the PPF at the room temperature for manufacturing the substrate and microneedle bodies, respectively [167].
3.1.4 Materials preparation for microneedles and the substrate

A model drug, dacarbazine, which is used in the treatment of various cancers, especially skin cancer, was loaded in the PPF matrix at different ratios. Bis(2,4,6-trimethylbenzoyl)-phenylphosphineoxide (BAPO) was introduced as the ultraviolet-activated photoinitiator. Dimethyl sulfoxide (DMSO), a low viscous liquid solution with the solubility of 2.5 mg/ml to dacarbazine at 25°C, was chosen to dissolve the dacarbazine completely and decrease the viscosity of the PPF. A PPF/quantum dot mixture was also prepared to have the confocal images using a confocal microscope. First, dacarbazine or quantum dot solutions were made by dissolving the dacarbazine or quantum dots into DMSO or distilled water, respectively. Afterward, 1% BAPO by weight of the PPF was dissolved in the dacarbazine/DMSO or quantum dot solutions. Finally, the resulting solutions were obtained through mixing the PPF with dacarbazine/DMSO/BAPO or quantum dot/BAPO solution. The theoretical drug loading was 1 or 2% by weight of the PPF. Also, control solutions that were devoid of dacarbazine and quantum dots were prepared. The prepared solutions were light sensitive and were covered with aluminum foil and refrigerated at 4°C.

Because the viscosity of the PPF prohibits its solo use in MSL, DEF was added to the PPF solution to decrease the viscosity of the PPF [167], making it fabricable via MSL. DEF also contains crosslinkable carbon-carbon double bonds, which can facilitate crosslinking with PPF, resulting in an increase in the elastic modulus and fracture strength of crosslinked PPF/DEF biomaterials [167]. A ratio of 50:50 (w/w) of PPF: DEF was prepared for the fabrication of the substrate in this work.
3.2 Multi-material manufacturing system and microneedle arrays fabrication

In this application, two materials were prepared for the microneedle body and the substrate, respectively. Correspondingly, a multi-material manufacturing process was developed and microneedle arrays with drug loading in the microneedle body and no drug in the substrate were manufactured.

3.2.1 Cure depth experiment

The critical energy \( (E_c) \) and the penetration depth \( (D_p) \) of the light were considered as two important parameters that must be studied and controlled carefully in order to achieve a high resolution in the MSL process. \( E_c \) is the energy at that point the polymer starts to crosslink, and \( D_p \) is a measure of how deep a light radiation can penetrate into a liquid material. It is defined as a depth at which the intensity of the radian inside the material falls to \( 1/e \) (\( e \) is Euler’s number). Generally, the minimum condition for polymerization is the energy to which the resin is exposed has to be greater than the critical energy [215].

To examine the penetration depth and the critical energy, curing depth experiments were conducted using the PPF/DEF prepolymer (50:50 (w/w)), PPF/1 w% dacarbazine and PPF/2 w% dacarbazine solutions.

A square light pattern was projected onto the surface of the resin. The irradiance in the developed MSL system was 31.37 mW/cm\(^2\), and the exposure energy was controlled by opening the shutter for 1-7 seconds in 1 second interval. For each exposure time, three samples were created and rinsed using alcohol and dried in the air before the measurement. Curing depths were measured using a microscope (Stereo discovery V12, Carl Zeiss Micro Imaging, LLC, Thornwood, NY, USA) at the center of the cross section, and the mean was
obtained to get the cure depth and exposure energy plot, called working curve. From the curing experiment, a cure depth versus exposure energy plot was obtained, as shown in figure 3.3. The energy delivered on the solution surface ($E_{\text{max}}$) penetrates into the solution as depth ‘z’ ($E(z)$), which was defined by Beer-Lambert law as described in Equation (1), where $D_p$ was the penetration depth of the solution. By introducing the critical energy ($E_c$) into Equation (1), the curing depth ($C_d$) can be defined as in Equation (2), where $E_c$ was the energy at the gel point. The gel point was the point at which solidification begins. Therefore, two important characteristics of the photocurable solution, $E_c$ and $D_p$ can be experimentally determined through measuring the curing depth according to the exposure energy where the exposure energy and stacking thickness can be chosen. Based on the Beer-Lambert law (Eqs. (1) and (2)), $E_c$ and $D_p$ were calculated as shown in Table 3.1.

\[ E(z) = E_{\text{max}} \cdot e^{\left(\frac{z}{D_p}\right)} \quad (1) \]

\[ C_d = z(E_{\text{max}}) = D_p \ln\left(\frac{E_{\text{max}}}{E_c}\right) \quad (2) \]

![Figure 3.3](image-url)  
Figure 3.3 The cure depth versus the exposure energy for PPF/DEF (50:50) and PPF/drug.
Table 3.1 $E_c$ and $D_p$ values for PPF with different drug-loaded ratios.

<table>
<thead>
<tr>
<th>Material</th>
<th>Critical Energy ($E_c$) (mJ/cm$^2$)</th>
<th>Penetration Depth ($D_p$) (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPF/DEF (50:50)</td>
<td>18.91</td>
<td>157.65</td>
</tr>
<tr>
<td>PPF with 1% drug</td>
<td>24.47</td>
<td>133.34</td>
</tr>
<tr>
<td>PPF with 2% drug</td>
<td>26.28</td>
<td>120.68</td>
</tr>
</tbody>
</table>

From the table 3.1, it was observed that the critical energy was increased as the drug-loaded ratio increases, while the penetration depth had the opposite trend, which may be ascribed to the drug, which affected the light penetration. Therefore, the light intensity or the exposure time may need to be adjusted during the fabrication process when using different drug loading concentration.

3.2.2 The design of the microneedle arrays

The microneedle arrays were designed using 3D CAD software (SolidWorks, SolidWorks Corp., Waltham, MA, USA). A single microneedle body was composed of a cylindrical base and a conical tip, with the length of 700 μm and 300 μm, respectively. The diameter of the apex of the cone was 20 μm, whereas the base diameter for cylinder base design was 200 μm. The surface area of each microneedle was 0.58 mm$^2$, and the volume was 0.33 mm$^3$. A microneedle array with 25 individual microneedles (5 × 5) were patterned on a 2 mm × 2 mm substrate with a thickness of 300 μm, as shown in figure 3.4.
Figure 3.4 The design of microneedle array. (a) The microneedle array including a 5×5 microneedles pattern, and (b) a single microneedle with substrate.

This design was for the experiments in lab. Actually, the shape of the microneedle arrays was customized depending on the real clinical requirements. Furthermore, the length and the diameter of each microneedle could be various to meet the local skin conditions.

The microneedle array model designed by 3D CAD software (figure 3.5 a) was saved as a .STL file, which was consist of triangles (figure 3.5 b). The .STL file was then sliced by a slicing software to obtain cross sectional bitmap images, which would be delivered to the DMD to generate light patterns. The number of the slicing layers depended on the resolution requirement. More layers sliced, higher resolution would be achieved for the fabricated part. In this work, the microneedle array model was sliced into 65 layers with a layer thickness of 20 µm, as shown in figure 3.5(c). Cross sectional image for each layer was obtained and was imported to the DMD sequentially during the fabrication process. The surface property of the part depends on the layer thickness, especially for inclined surface, where stair features was obvious for a big layer thickness. Generally, a thinner layer thickness means a smoother surface, but needs a longer fabrication time leading to the increase of the fabrication cost. One may need to choose a proper layer thickness
considering the application requirement to balance the fabrication cost and the surface property.

Figure 3.5 The slicing process for the microneedle arrays model. (a) The model from CAD software, (b) .STL file transferred from the model, and (c) sliced model by the slicing software.

3.2.3 Fabrication of the PPF-based dacarbazine-loaded microneedle arrays using MSL system

The microneedle array consisted of two parts, the microneedle bodies and the substrate with different materials. In order to fabricate the microneedle arrays with two materials, a multi-material process was designed and developed [166, 168, 169]. A microneedle array model with a total height of 1300 µm of the microneedle body and substrate was sliced into 65 layers with a layer thickness of 20 µm. Two glass vats, glass vat 1 and glass vat 2 were prepared and filled with two types of materials, PPF/DMSO/drug and PPF/DEF for the microneedles and the substrate, respectively [216]. Two Z stages (moving up and down vertically) were installed in the multi-material fabrication system with the stainless steel platform on the Z1 and the vat holder on the Z2, as shown in figure 3.6.

Firstly, the substrate was built. A 2D cross sectional image for the substrate was transferred to the DMD, and the pattern was projected onto the surface of the liquid material
to solidify the first layer on the stainless steel platform, with a curing time of 3 s (equivalent to 94.11 mJ/cm²) and a layer thickness of 20 µm. After photopolymerization for the first layer, the platform with the already built layer was moved down for 2 mm along the vertical direction with the Z1 stage to immerse the fabricated portion in the liquid solution completely. A dwell time of 2 s was given to let the material cover the built part thoroughly. Then, the platform was moved up for 1.98 mm leaving an exact 20 µm thickness of the liquid material on the surface of the built layer. A settling time of 40 s was used to ensure that the solution surface was even. By stacking all of the layers, theoretically, a 3D substrate was created. Within these previous steps, the Z2 stage holding the glass vat was maintained at a specific position. Afterwards, the Z2 stage was moved down to allow the platform getting out of the glass vat 1, which would be replaced by the glass vat 2 in the following fabrication process. The substrate on the stainless steel platform was then rinsed with ethanol and autoclaved water three times to remove all of the residual material and then completely dried using compressed air [170].
Figure 3.6 The multi-material fabrication process for the microneedle arrays: (a) substrate fabrication with the material 1 in the vat 1, (b) rinsing and drying process for the substrate, (c) microneedles fabrication on the substrate with material 2 in the vat 2, and (d) rinsing and drying process for the microneedles.

The microneedles were fabricated after the substrate was finished. The glass vat 1 was removed and the glass vat 2 filled with the material for the microneedle bodies was positioned under the stainless steel platform. Then, the Z2 stage was lifted and remained in a specific position to start the manufacturing of the first layer of the microneedle bodies. The remaining fabrication process was exactly the same as that described for the fabrication of the substrate, including the rinsing and drying steps.

In order to have the same weight of the substrate and microneedle bodies for each of the microneedle arrays, the weights of the liquid materials for both the substrate and microneedle bodies were maintained at a constant value in this work. After each fabrication of the substrate and microneedle bodies, the glass vat was filled back to the original weight and put back to the initial position using the Z2 stage. In other words, for each fabrication iteration of the substrate and microneedle bodies, the platform and the vat were always started from the same position, with the material started from the same weight. Thus, the repeatability for all of the microneedle arrays was maintained. With this method, all of the
substrates and microneedle bodies can be considered to have the same weight within an acceptable error range. In this work, the average weight of the substrate was 1.4 mg, and that of the entire microneedle array (including the substrate and the microneedle body) was 3.7 mg.

To verify that the drug was only dispersed in the microneedle bodies using this multi-material fabrication process, quantum dots were first encapsulated into PPF/DEF microneedle bodies and no quantum dots in the substrate. A Confocal microscopy was used to optically section the microneedle array at intervals of 50 µm and the micrographs were shown in figure 3.7. The presence of red fluorescence clearly showed the presence of quantum dots, which were dispersed within the bodies of the microneedles. In general, the quantum dots were uniformly distributed within the tips (0-700 µm), but phase separation could be observed near the base (750-1000 µm). Since the quantum dots were hydrophilic, some degree of phase separation was expected. However, dacarbazine is a hydrophobic drug and was expected to uniformly distribute within the body of the microneedles.
Figure 3.7 Confocal microscopy results for PPF/fluorescence microneedles. The photo was captured from 0 to 1000 µm with intervals of 50 µm.

After verification of the manufacturing process from fluorescent confocal images, microneedle arrays with different drug-loading ratios were fabricated using the multi-material MSL process. The microneedle arrays were viewed under the optical microscope to verify the features and dimensions, as shown in figure 3.8. To have a clear 3D view, these microneedle arrays were viewed in a scanning electron microscope (SEM) also as shown in figure 3.9.
3.3 The characterization of the microneedle arrays

The microneedle arrays would be used to treat skin carcinomas through penetrating the microneedles into epidermis of the skin. Therefore, a certain level of mechanical strength of the microneedles was needed to prevent from breaking or bending. Mechanical tests were conducted to demonstrate the microneedle arrays strength in this section.

3.3.1 Mechanical testing

Compressive testing of the PPF/DEF prepolymer and PPF/drug prepolymer specimens was conducted using a mechanical testing system (UTS 5582, INSTRON, Norwood, MA, US). Cylindrical samples were prepared by pouring the prepolymer
solutions into cylindrical glass tube and curing using UV light for 30 min. The cylindrical samples were then cut to the desired length of approximate 25.4 mm and a diameter of 12.4 mm. The whole compressive testing specimen dimensions and procedure were guided by ASTM D695-10 standards. The samples were compressed at a rate of 1.3 mm/min, and the experiment was halted after sample fractured. For each prepolymer combination, five samples were tested to obtain the elastic moduli.

The elastic modulus of the solidified PPF was determined using the compressive testing. The elastic moduli of PPF/DEF (50w/50w), PPF/1w% and PPF/2w% drug-loading combinations were calculated and plotted (Figure 3.10). Compared to the other two formulations, the PPF/DEF (50w/50w) has a relatively higher elastic modulus. From the figure 3.10, the elastic modulus of 1 w% drug-loaded material was reduced 3.4 times compared to the PPF/DEF matrix, while 2 w% drug-loaded compounds reduced by almost 5 times.

![Figure 3.10 Variation of elastic modulus for PPF/DEF (50w/50w) and PPF/drug.](image)

52
When a microneedles was penetrated into the skin, two forces should be taken into account: the failure force and the insertion force. Generally, the failure force should be greater than the insertion force so that the microneedles can puncture the skin without being broken.

The insertion force can be calculated by an experimental equation according to the tip dimension of the microneedle (equation (3)) [171,172].

\[ F_i(N) = 0.00012 \times A(\mu m^2) \]  

where \( F_i \) is the insertion force in Newtons and \( A \) is the cross sectional area of the microneedle tips in units of \( \mu m^2 \). The insertion force for the designed microneedle with the tip diameter of 20 \( \mu m \) was 37.6 mN based on the equation (3).

Single microneedle compression was conducted in order to get the failure force using a Nano Bionix tensile tester (Aglien Technologies, Oakridge, TN, US). A single
microneedle was fabricated on a substrate and compressed between two compression pads with a loading rate of 0.05 mm/s, as shown in figure 3.11. The max pre-set load was 300 mN. Five samples were tested for each formulation.

Figure 3.12 The compression test for the microneedles of 1 % and 2 % drug-loaded ratio. The maximum pre-set loading of the tester was 300 mN.

The deformation varying with the compression force was obtained (Figure 3.12). Before 100 mN compression force, only less than 0.03 mm deformation occurred for both 1 w% and 2 w% drug. And no fractures were observed even though the compression force reached to the pre-set loading of 300 mN. Therefore, the failure force can be considered higher than 300 mN, which was much larger than the theoretical insertion force of 37.6 mN calculated before.

Figure 3.13 showed microscope images before and after compression test for 1 w% and 2 w% drug-loaded microneedle tips. Comparing the tips before and after compression,
the shapes of the tips changed slightly, but there was no fracture observed. Therefore, the microneedles can penetrate into the skin without failure. The slight deformation might be ascribed to two reasons. One was the elastic and plastic of the material and the other possible reason leading to the deformation could be from the alignment error when installed the microneedle between the two compression pads. Even though a slight angle between the microneedle axis and the force loading direction may lead to a bending easily.

Figure 3.13 The pictures for the compression test: (a), (b) are pre-compression and post-compression test for PPF/1w% drug microneedle; and (c), (d) are pre-compression and post-compression test for PPF/2w% drug microneedle.

3.3.2 The in vitro drug release of dacarbazine from the PPF matrix

   Ideally, the drug should be released gradually within an anticipated time frame from the microneedle arrays in order to treat the skin disease. To obtain the in vitro drug release kinetics, drug-loaded microneedle arrays were submerged in 100 μl of phosphate-buffered saline (PBS) in microcentrifuge tubes at 37°C with agitation [162, 163, 173]. Three groups
including 1 w% drug, 2 w% drug and an unloaded control group were prepared. Each group contained 12 microneedle arrays divided into 3 sub-groups with an average weight of 15 mg in each sub-group. At the predetermined time points (1, 2, 4, and 7 days and weekly afterward), the PBS solutions were collected and refrigerated at -20°C, and fresh PBS was added to the tubes. A spectramax M2 (Molecular Devices, CA, US) was used to analyze the collected samples at a wavelength of 400 nm.

A five-week in vitro drug release study was conducted for microneedle arrays containing 1 w% and 2 w% dacarbazine. From the figure 3.14, 285.6 ± 82.8 and 534.1 ± 82.8 µM (1 and 2 w% loading, respectively) of dacarbazine was released after the first day, and a burst release was observed during the first week in which 451.3 ± 83.2 and 782.2 ± 84.9 µM (5.48 ± 0.20% and 4.74 ± 1.17% of the drug loading) of dacarbazine was released, respectively. The release rate afterwards became linear (R² = 0.89 and 0.99 for 1 and 2 w% loading, respectively), low (1.3 and 2.4 µM/day for 1 w% and 2 w% loading, respectively), and continuous. The total amount of dacarbazine release after five weeks was 490.2 ± 82.8 and 855.5 ± 82.9 µM, respectively. As expected, the higher drug loading resulted in more drug release, 2 w% drug-loaded microneedles resulted in approximately twice the amount of drug release as compared to the 1 w% drug-loaded formulation.

![Figure 3.14 Dacarbazine release profiles from PPF microneedle arrays.](image-url)
3.4 Conclusion

The molecular weight (Mn) of synthesized PPF was a significant parameter that can vary in a large range from 400 to 5000 Da depending on the synthesis process [162, 163]. A relatively longer transesterification reaction produced a higher Mn [162, 163], which potentially could affect the release kinetics of the PPF matrix. The PPF matrix with a higher Mn would have a faster release rate within the diffusion release phase, which was the dominant release before approximately 150 days [162,174]. The release rate can be controlled by varying the Mn of the synthesized PPF.

The therapeutic dosages for dacarbazine range from 300 to 600 mg/m² for a single injection or infusion [175]. Assuming an average adult has a surface area of 1.7 m² and six liters of blood, the systemic dosages range from 274.5 to 548.9 µM, respectively. Thus, the release rates of dacarbazine from the microneedles are well matched with the therapeutic requirements. Diffusion is likely the primary mechanism of the drug-release kinetics, but the degradation of PPF could contribute to the zero-order kinetics observed after the burst release phase. A first-ordered kinetics is typically observed for non-biodegradable polymer, but PPF degrades slowly by hydrolysis. Approximately 10% of mass loss is expected for PPF during a five week time point in PBS solution [176]. However, PPF in this study could degrade even slower because the low Mn [162].

In the substrate of the microneedle array, DEF was introduced to decrease the viscosity and improve the mechanical properties of the PPF. DEF contains a crosslinkable carbon-carbon double bond, which can participate in the crosslinking when the PPF/DEF compound was induced by the photoinitiator with UV irradiation. Within a proper percentage range of DEF, the mechanical strength of PPF/DEF can be improved [167],
which is advantageous because all of the microneedle bodies were fabricated on the substrate. Some level of mechanical strength was needed to prevent the microneedles from being fractured upon insertion, which may lead to the detachment of the microneedle bodies. However, in the fabrication process of the microneedle bodies, instead of DEF, DMSO was used to dissolve dacarbazine, which was insoluble in DEF at room temperature. Different from DEF, DMSO can not contribute to the mechanical stability of the PPF. When DMSO was mixed with the PPF, a balance between the ratio of drug loading and the fabricability should be taken into account. In this work, only 1 w% and 2 w% drug loading were adopted, considering the solubility of dacarbazine and the ability to fabricate the microneedles when introducing more DMSO. For the PPF matrices with a higher ratio of DMSO, a longer exposure time would be needed to obtain a completely crosslinking. But the increasing exposure time would result in fabrication issues, such as decreases in the manufacturing tolerances and the geometric accuracy of the microneedles. Furthermore, DMSO also reduced the elastic modulus of the matrix compared to the PPF/DEF matrix. That was why there was a large difference of elastic modulus between the PPF/DEF and PPF/drug observed from figure 3.10. It was necessary to seek an alternative with a higher solubility to dacarbazine. The concentration of the drug could be increased without affecting the fabrication accuracy and the mechanical properties.

The PPF was synthesized with a two-step procedure and the chemical properties were analyzed. The NMR and GPC spectrums showed the successful synthesis of PPF without significant impurities. As expected, the resulting PPF had a high viscosity at room temperature, which would impede the fabrication process using the MSL process. Thus, DEF was introduced into the PPF solution to decrease the viscosity when to fabricate the
substrate. This addition resulted in the ability to manufacture the PPF using MSL. For the microneedle bodies, DMSO was chosen to dissolve the dacarbazine and decrease the viscosity of the composite. The microneedle arrays with two different drug loadings were successfully fabricated. The confocal microscopy images showed the drug dispersing into the microneedle bodies and no drug in the substrate. The single microneedle compression results indicated that the microneedles had high mechanical strengths and the failure force was much greater than the calculated insertion force. Finally, the drug release kinetics was obtained through a drug release test for 5 weeks. The amount of the drug released could be altered by increasing the drug loading, but changing the molecular weight of PPF was needed to alter the release profile. These results showed that MSL could be a valuable technique to fabricate the drug release devices that required high structural stabilities.

In this project, the MSL was a vat-based projection system, with two vats were used. Disadvantages were emerged during the fabrication process. First, for a vat-based system, the material consumption was considerable. The platform, on which the target part was built, would move up and down freely to ensure the built layer was covered by the liquid material completely and evenly. A large amount of material was needed to fill the vat. Second, a vat-based MSL was not convenient to realize the multi-material fabrication. The cleaning and reloading process would lead to the material waste and time consuming. Third, the layer thickness about 1 µm or less was difficult to reach due to the oxygen inhibition on the surface of the photopolymer. In addition, the fabrication speed was limited, especially for the material with a high viscosity (typically, higher than 200 cp).
As discussed in chapter 3, in order to overcome the disadvantages presented in vat-based projection MSL, a liquid bridge MSL (LBMSL) system was proposed and developed. In the suggested system, instead of using a vat, the liquid photopolymer was put between two parallel coaxial circular disks with the same diameter. This formed a liquid bridge, in which the entire fabrication process happened. The transparent top disk allowed the light pattern to pass through with the least energy loss. The size and the shape of the liquid bridge could be customized by changing the diameter and the shape of the disks.

Figure 4.1 The schematic of vat-based MSL (a) and LBMSL (b). The vat was replaced by forming a liquid bridge between two disks and the fabrication will be processed in the liquid bridge.
A liquid bridge could be easily formed between two objects if they approached each other within a certain distance with liquid material inside [55]. It was beneficial to introduce the liquid bridge replacing the vat in the conventional MSL system in order to improve the fabrication capabilities, as shown in figure 4.1. In LBMSL process, the amount of material consumption was reduced since no vat was used. Due to a very small settling time and no needed dwell time, the fabrication speed was dramatically improved. A top disk was adopted to form the liquid bridge, eliminating contact between the top surface of the liquid material and oxygen from the air, significantly reducing the oxygen inhibition. In addition, the easy material changeover facilitated the operation of the multi-material fabrication. The continuous fabrication process was possible using the developed LBMSL technique.

4.1 Liquid bridge model

As mentioned in the literature review, liquid bridge theory has been developing for more than 100 years [52,54,55,177]. Most of the research focused on a small liquid bridge, in which the surface tension was dominant and the acceleration force was neglected [62,178,179]. In this work, based on the requirement of fabrication, a relatively large liquid bridge was needed. In order to generate the liquid bridge, both the surface tension and gravity were taken into account. A mathematical model involved the surface tension and gravity were necessary to describe the equilibrium liquid bridge profile.

4.1.1 Mathematical model for liquid bridge

In LBMSL system, a liquid bridge was used as an alternative of the vat that was necessary for the conventional MSL system. Two circular disks with the same diameter were installed parallel and coaxial with an adjustable separation distance. The stable liquid
bridge can be formed by applying the proper amount of liquid material between two disks for MSL manufacturing, as shown in figure 4.1(b). As in the conventional MSL system the liquid bridge functioned as the ‘vat’, allowing the 3D microstructures to be fabricated within the liquid bridge. During the fabrication process, the top disk was fixed and the bottom disk was installed on a stage permitting free movement up and down according to the fabrication program. After each layer was fabricated, the bottom disk was moved down one layer thickness allowing liquid polymer to be injected, maintaining the stable liquid bridge shape for the next fabrication.

An equilibrium shape of the stable liquid bridge could be slim or bulged, as shown in figure 4.2 (a)-(e) [54, 58]. A liquid bridge like figure 4.2(a) provided small effective fabrication space, even affecting the fabrication process because the built part may touch the edge of the liquid bridge. In opposite, if a liquid bridge shape was near figure 4.2 (e), the material out of the disk had no contribution to the fabrication and increased the instability. Assume the cylinder boundary formed by the two disks is Γ (the dashed line in figure 4.2(c)), the liquid bridge boundary should be near Γ, because the fabrication process only can happen between two disks and the material out of Γ is useless but leading to instable. Perturbation and vibration were inevitable, demonstrating the stability and effective volume should be maintained around figure 4.2(c) during the entire fabrication process. This stability was important for the surface quality of the 3D structure [180-182]. Therefore, in the real fabrication process, how to maintain a stable and effective liquid bridge is essential.
Figure 4.2 Schematic of the liquid bridge between two disks. In (c), the dashed line stands for the assumed cylinder boundary shape $\Gamma$.

Figure 4.3 Geometry and coordinate system for the liquid bridge model. $g$ is the gravity acceleration, $s$ is the arch length, and $\beta_1$ and $\beta_2$ are angles between the radius axis and the tangent of the liquid bridge interface.

In order to develop the mathematical model, the configuration of the liquid bridge was considered to be subject to a constant, axial gravity field, as shown in figure 4.3.

The top and bottom disks were made from different materials, with a small surface energy for the top and a large surface energy for the bottom. Both disks have sharp edges and therefore, the configuration can be uniquely characterized by the following dimensionless parameters [56,183]:

\[ \ldots \]
The slenderness, which was the ratio of the gap distance to disks diameter, \( \Lambda = L/(2R) \), where \( L \) was the gap distance between two disks and \( R \) was the disks diameter;

The dimensionless volume of liquid, \( V = V/(\pi R^2) \), which means the ratio of the physical volume \( V \) to the volume of a cylinder of the same \( L \) and \( R \);

The Bond number \( Bo = |\Delta \rho g| 2RL/\sigma \), where \( \Delta \rho \) was the difference between the liquid density and the surrounding medium density, \( g \) was the axial acceleration (negative when it has the direction of the \( z \) axis), and \( \sigma \) was the surface tension (both \( \Delta \rho \) and \( \sigma \) were assumed to be constant). The Bond number is a dimensionless number measuring the importance of surface tension forces compared to gravity. A high Bond number indicates the system is relatively unaffected by surface tension effects and a low value means the surface tension is dominant in the system.

In the following, all lengths were made dimensionless with \( L_C = \sqrt{\sigma/|\Delta \rho \cdot g|} \), a dimensionless radius \( r_0 = R/L_C \), and disk separation \( h = L/L_C \).

In this work, the axial acceleration was the gravity. The arc length \( s \) was measured from the point where \( z=0 \). The equilibrium shape of the liquid bridge can be characterized by \( r(s), z(s), \) and \( \beta(s) \), which were functions of the arc length \( s \). \( r(s) \) was the radius of the liquid bridge, \( z(s) \) was the vertical distance from the bottom disk, and \( \beta(s) \) was the angle between the radius axis and the tangent of the interface. The equilibrium shape of the liquid bridge can be computed by numerically integrating the differential equations [54-56]:

\[
\begin{align*}
    r''(s) &= -z'(s)\beta''(s) \\
    z''(s) &= r'(s)\beta'(s) \\
    \beta'(s) &= -z(s) + C - \frac{z'(s)}{r(s)}
\end{align*}
\]  

The boundary conditions:
\[ r(0) = r_0 \quad (7) \]
\[ r'(0) = \cos \beta_1 \quad (8) \]
\[ z(0) = 0 \quad (9) \]
\[ z'(0) = \sin \beta_1 \quad (10) \]

Where \( C = \frac{\Delta P}{\sqrt{\rho g y}} \), and \( \Delta P \) was the pressure difference between the reference pressure inside the liquid bridge at \( z=0 \) and that of the surrounding medium.

MATLAB was adopted to integrate the equations. For a given \( r_0 \) (\( Bo=r_0^2 \)), the equilibrium shapes can be obtained for different disks separation \( h \). For \( h^{(1)} \), a value for \( \beta_1^{(1)} \) was assumed in the interval \( 0 \leq \beta_1 \leq \pi \). In order to integrate the systems of equations (4)-(6), \( C \) was adjusted until an \( s=s^* \), at which \( |z(s^*)-h|<\delta \) (usually \( \delta \) can be given as the constant step length in the MATLAB program), and then adjusted \( C \) to satisfy \( |r(s^*)-r_0|<\delta \). During this process, if when \( |z(s^*)-h|<\delta \), while \( |r(s^*)-r_0|>\delta \), and \( r(s^*)>r_0 \), \( C \) should be increased. In opposite, if when \( |z(s^*)-h|<\delta \), while \( |r(s^*)-r_0|>\delta \), and \( r(s^*)<r_0 \), \( C \) should be decreased. The process will be repeated for a value of \( \beta_1^{(2)} \) with a desired interval for \( h^{(1)} \).

In this way, a series of equilibrium shapes with a various \( \beta_1^{(1)} \) will be obtained according to the requirement [53, 56]. Figure 4.4 showed the flowchart for the integrating process. By repeating the above process, equilibrium shapes for different \( h \) can be completed. The volume of the liquid corresponding to each \( \beta_1 \) can be calculated by:

\[ V = \pi \int_{0}^{z^*} r^2(s)z'(s) \text{d}s \quad (11) \]
In order to verify the mathematical model, water was used to obtain the equilibrium shape and the volume for each $\beta_1$ of the liquid bridge. The parameters needed in this integration were: $\rho=1\times10^3$ kg/m$^3$, $\sigma=0.072$ N/m, and $g=9.8$ m/s$^2$. Different disks separation $h$ of 3mm, 4mm, and 5 mm were computed for the $\beta_1$ from 60° to 110° with intervals of 10°, as shown in figure 4.5, figure 4.6 and figure 4.7.
Figure 4.5 The equilibrium shape of water liquid bridge and the corresponding volume with the height of 3 mm.

Figure 4.6 The equilibrium shape of water liquid bridge and the corresponding volume with the height of 4 mm.
Based on the LBMSL process, some amount of liquid material was filled as the separation distance increased during the fabrication process in order to maintain the same liquid bridge shape [184]. Therefore, the volume and height relationship was necessary for the pump system to fill material. Using the mathematical model, the volume for different disks separation $h$ of 1~5 mm, with intervals of 0.5 mm, for the water was calculated with $\beta_1$ of 70°, 80°, and 90° and a volume and height relationship plot was obtained, as shown in figure 4.8. From the plot, a linear relationship was observed, which indicated that a constant feeding rate can be applied to the pump.
The equilibrium shapes for a combination material of propoxylated glyceryl tracrylate (CD9021) and 1,6-hexanediol diacrylate (HDDA) (70w/30w) were obtained as well with the mathematical model. The table 4.1 showed the typical physical and chemical properties for CD9021 and HDDA [185,186].

![Graph](image.png)

Figure 4.8 The volume vs height for water with h from 1~5 mm, and β1 of 70°, 80°, and 90°.

Table 4.1 Typical physical and chemical properties for CD9021 and HDDA.

<table>
<thead>
<tr>
<th>Properties</th>
<th>CD9021</th>
<th>HDDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific Gravity @25°C</td>
<td>1.064</td>
<td>1.020</td>
</tr>
<tr>
<td>Viscosity, cps @25°C</td>
<td>95</td>
<td>9</td>
</tr>
<tr>
<td>Surface Tension, dynes/cm</td>
<td>35.6</td>
<td>35.7</td>
</tr>
<tr>
<td>Tg, °C</td>
<td>-11</td>
<td>43</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>573</td>
<td>226</td>
</tr>
</tbody>
</table>

The surface tension of CD9021/HDDA (70w/30w) was calculated based on equations 12-14 [187-190].
\[ \gamma_s \approx \gamma_l \left( \frac{(1+\cos \theta)^2}{4\phi^2} \right) \]  

(12)

\[ \phi = \frac{4(\gamma_5 \gamma_l)^{1/3}}{\left(\gamma_s^{1/3} + \gamma_l^{1/3}\right)^2} \]  

(13)

\[ V = \frac{M}{\rho} \]  

(14)

Molecular weight \( M = 392.54 \text{ g/mol} \), density \( \rho = 1 \times 1.16^3 \text{ kg/m}^3 \), and the contact angle \( \theta = 6.5^\circ \) was measured for CD9021/HDDA (70w/30w) on poly(methyl methacrylate) (PMMA) substrate. The surface tension of PMMA is \( \gamma_s = 38 \text{ mJ/m}^2 \), which is known. And the calculated surface tension of CD9021/HDDA (70w/30w) was 34.5 mJ/m².

Figure 4.9 showed the equilibrium shape and the volume with the height of 3 mm and different \( \beta_1 \) of 70°-120°. As the same for water, the volume and height relationship was...
obtained by calculating the volume for different disks separation $h$ of 1-3 mm, in which the intervals was 0.5 mm, and $\beta_1$ was 100°, 110°, and 120°, as shown in figure 4.10.

Figure 4.10 The volume vs height for CD9201/HDDA (70w/30w) with $\beta_1$ of 100°, 110°, and 120°.

4.1.2 Experiments for liquid bridge

The quasi-static liquid bridge experiment was carried out to observe the equilibrium shape and verify the mathematical model in this work [191,192]. The liquid used was water with the viscosity of 0.894 cP at 25 °C, density $\rho$ of $1\times10^3$ kg/m$^3$ and surface tension $\sigma$ of 0.072 N/m. The bottom and top disks were Poly(methyl methacrylate) (PMMA) with a liquid feeding hole in the bottom disk, as shown in figure 4.11. The top disk was fixed and the bottom disk was installed on a stage with a resolution of 0.5 µm and travel range of 75 mm. The material was fed by an automatic pump NE-1000 (New Era Pump System Inc. NY US) with the minimum pumping rate of 0.73 µL/hr. The disks were cleaned by ethanol

71
before conducting the experiment to minimize the possible contamination and surfactant absorption which may lead to Marangoni stresses [53,193-195].

Figure 4.1 The schematic of experiment setup for liquid bridge.

The disks separation \( h \) was increased from 0 to 4 mm with intervals of 0.1 mm. At each \( h \), liquid material was injected using the automatic pump with the feeding amount of 0.001 ml/pulse to ensure the liquid just touching the edge of the top disk. After the \( h \) reached to 4 mm, the disks were fixed but the material kept filling with the feeding amount of 0.001 ml/pulse until the liquid bridge collapsed [196,197]. A high speed camera was used to capture an image of the liquid bridge for each volume. The equilibrium shape was extracted by image analysis software (ImageJ, by National Institutes of Health). Figure 4.12 compared the equilibrium shape of the liquid bridge obtained from the mathematical model and experiment for water with \( \beta_1 \) of 58.5°, 68.9°, 78.1°, 88.4°, 97.8°, and 107.5°. Figure 4.13 showed the discrepancy of the liquid bridge shape obtained from the mathematical model and the experiment.
Figure 4.22 The equilibrium shapes of liquid bridge for water from the experiments and mathematical model with different $\beta_1$. For each figure, the top was from the mathematical model and the bottom was from the experiment.
From the figure 4.13, the error percentage was less than 5%, which may be caused by the measurements or the vibration of the liquid bridge during the experiment.

Figure 4.33 The error discrepancy between the left liquid bridge profile obtained by the mathematical model and the experimental results for water. The initial angle $\beta_1$ is $55.8^\circ$~$107.5^\circ$. 

74
Figure 4.14 was the mathematical model and experiments for CD9021/HDDA (70w/30w) for different $\beta_1$.

![Image 1](image1.png)

![Image 2](image2.png)

![Image 3](image3.png)

![Image 4](image4.png)

Figure 4.44 The equilibrium shapes of liquid bridge for CD9021/HDDA (70w/30w) from the experiments and mathematical model with different $\beta_1$. For each figure, the top was from the mathematical model and the bottom was from the experiment.

From the error discrepancy plot (figure 4.15), the error percentage was less than 5%. [198-200]. The good agreement of the mathematical results and the experimental results for different materials, water and prepolymer, indicated that the mathematical model successfully predicted the equilibrium profile and the relationship between the height and the volume [201,202]. For any new liquid material, the mathematical model can be applied.
to obtain the equilibrium profile and the relationship between the height and the volume
instead of conducting the complex liquid bridge experiments.

Figure 4.55 The error discrepancy between the left liquid bridge profiles obtained from the
mathematical model and the experimental results for CD9021/HDDA (70w/30w). The
initial angle β1 is 102°~128.2°. The top two lines in each plot were the left liquid bridge
profile obtained by mathematical model (green color) and the experiment (red color).
4.2 LBMSL system and fabrication demonstration

An improved system was developed based on the liquid bridge theory [203]. The configuration was similar to the vat-based MSL, and the difference was that the vat was replaced with a liquid bridge formed between two parallel disks.

4.2.1 The developed system and fabrication process introduction

The entire system consisted of five major subsystems [170,204]: the Light Emission Subsystem, Light Delivery Subsystem, Pattern Generation Subsystem, Movement Subsystem, and Liquid Bridge Subsystem.

The Light Emission Subsystem included a mercury lamp (OmniCure™S2000, Lumen Dynamics, Canada), with an output of 200 W, a filtered wavelength of 365 nm, and an optical fiber (Lumen dynamics) to deliver the light from the lamp to a collimating lens set.

The Light Delivery Subsystem was composed of a light gate prism, which compacted the light path and projected the incident light onto a DMD™ surface. A relay lens (achromatic doublet lens, Melles Griot CO., US) with a focal length of 120 mm and a diameter of 40 mm was adopted to pass the light pattern generated by DMD. A reflecting mirror was used to change the light path from horizontal to vertical down towards an objective lens (IM-4, Nikon Co., Japan). The lens has a focal length of 20 mm and numerical aperture (N. A.) of 0.13.

The Pattern Generation Subsystem included a DMD (Texas Instruments, US), which consisted of ~786,000 micromirrors. Each micromirror, which was a 13.68 µm square, can independently tilt ±12° according to the black or white color of each pixel.
The Movement Subsystem was composed of a Z stage (Aerotech, PA, US) with a resolution of 500 nm. The function of the Z stage was to move the bottom disk up and down according to the fabrication program.

The Liquid Bridge Subsystem included two parallel coaxial disks with the same diameter, a top disk holder, a bottom disk holder, and a pump (NE-1000, New Era Pump System Inc. NY US) (figure 4.16).

In this system, the top disk was the key element to form the liquid bridge and provide reliable fabrication capability. It exhibited excellent UV transparency and very low surface tension which reduced the adhesion force between the top disk and the built layer. A top
disk holder which was fabricated by a commercial 3D printer was installed on a height adjustable post. A channel was created through the bottom disk allowing the syringe tip to inject the material. The bottom disk holder along with the bottom disk were mounted on the Z stage, allowing freedom of movement up and down.

![Diagram](image)

Figure 4.77 Configuration of the bottom disk in terms of the fabrication area and the material fill channel. The circle was the bottom disk profile and the gray square area was the maximum fabrication area for the system.

The top and bottom disks were customized and the size could be varied according to the system maximum manufacturing size and fabrication requirement. Both top and bottom disks were positioned under the objective lens and aligned concentrically. The image patterns coming from the objective lens could pass through the top disk and project on the center of the bottom disk. In this work, the maximum fabrication size was 3 mm by 3 mm, therefore, theoretically, disks with the diameter of 3.24 mm (diagonal line of a 3×3 mm square) were needed. After considering the operability, including the alignment of the pattern image area with the disks and easy detachment of the fabricated part from the
bottom disk once fabrication was completed, some tolerance was given according to the fabrication experience. The disks with the 6 mm diameter were adopted, as shown in figure 4.17.

The fabrication principle and process were similar to the vat-based MSL, including the model and cross sectional images preparation. The difference was that a liquid bridge was adopted to replace the real vat in the vat-based MSL. Figure 4.18 depicted the entire fabrication process. Before fabrication, the top and bottom disks were touching each other, and then the bottom disk was moved down for an exact one layer thickness distance. Liquid material was fed between the two disks by the automatic syringe pump using a predetermined volume to form a proper liquid bridge. After the liquid bridge was formed, a short settling time, dependent on the viscosity of the material, was given to allow the liquid bridge to stabilize. The stabilization time was allowed because any perturbation during the crosslinking process could lead to an unsmooth surface. At this point, the first layer fabrication could start. Since the surface tension of the top disk was higher than the bottom disk, the adhesion force between the bottom disk and the built layer was much greater than that between the top disk and the built layer. Therefore, the built layer was detached from the top disk and moved down with the bottom disk for one layer thickness distance. As the built layer was detached from the top disk, a vacuum area was generated. The suction force produced by the vacuum pulled the material in filling the gap rapidly, even though it was a high viscous material. After the settling time, the next layer fabrication was started. By repeating this process, a 3D structure can be fabricated by stacking all the layers. After fabrication, the remaining material would be drawn back by the syringe pump and recycled. Cleaning and post-processing are necessary in this fabrication method.
As the same with section 3.2.1, the working curve for the LBMSL system was obtained. The energy of the light was 31.37 mJ/cm$^2$. The curing depth was measured with the exposure time of 1-7 s, with an interval of 1 s. From the figure 4.19, the $E_c$ was 1.15 mJ/ cm$^2$ and $D_p$ was 302.95 µm.

4.2.2 The adhesion force between the built layer and the top disk

The LBMSL technique was a top-down fabrication process, ideally, after one layer fabrication, the built part should be separated from the top disk and moved down with the bottom disk, as described above. However, the adhesion force produced during the
polymerization process may make the separation fail. Two cases commonly occurred: the
built layer attached to the top disk tightly, and separated from the bottom disk; or the built
layer attached on both disks. This was a challenging issue in bottom-up SL or MSL
processes. Some solutions have been reported. Chi Zhou’s group [50] developed a two-
channel system using a PDMS film coated on half of the glass vat to reduce the adhesion
force. In the fabrication process, after one layer fabrication, the platform was moved
horizontally to another half of the vat without coating PDMS and shifted back after the
platform moved up for a layer thickness distance. This approach, however, was not suitable
for LBMSL because of the different fabrication process and system setup. John
Tumbleston’s [51] group kept providing oxygen gas passing an oxygen-permeable window
of the bottom vat to form a dead-zone. The dead-zone was formed because a controllable
layer of oxygen inhibited the crosslinking of the polymer and a very thin layer of liquid
material was sandwiched between the built layer and the vat window. This thin liquid
polymer changed the solid-solid adhesion to a solid-liquid adhesion. This method reduced
the adhesion force, but dramatically increased the fabrication cost and system complexity
because the oxygen had to be injected during the entire fabrication process. Therefore,
seeking an ideal top disk material with a low surface tension was essential.

In this work, first a circular glass was tried for the top disk and a microneedle was
fabricated using the glass top disk, as shown in figure 4.20. From the figure 4.20 (a), no
layers were observed on the microneedle body. After one layer fabrication, the bottom disk
moved down, but the built layer failed to detach from the top disk. The bottom disk kept
moving down after each layer of fabrication. Finally, after several layers of fabrication and
the bottom disk moving down, the built layer suddenly separated from the top disk. A big
gap formed between the built layer and the top disk with liquid material filling in. Then a big thickness material was cured in one exposure time.

Figure 4.20 The failure fabrication of microneedle (layer thickness of 30 µm) because of the big adhesion force between the built part and the top disk during the LBMSL fabrication process. (a) Top disk material was glass, and (b) top disk material was glass with PDMS coating.

Next, glass with ~30 µm PDMS coating was used as the top disk. This decision was based on the established property of absorbing a small layer of oxygen to inhibit the crosslinking of the photopolymer and make a thin layer of liquid material between the built layer and the top disk. Using the glass with PDMS coating, the microneedle was fabricated again with the same fabrication parameters, and from the figure 4.20(b), still no layers were observed in some sections (red rectangle area in figure). The experiments indicated that both glass and glass with PDMS coating were not eligible for the LBMSL process due to the bigger adhesion force which occurred during the fabrication process.

In order to select a suitable top disk material for LBMSL, adhesion force between the cured structure and glass, glass-PDMS coating, and TPX®Polymethylpentene (PMP) were tested. In this test, the material for the bottom disk was poly(methyl methacrylate) (PMMA). PMMA had a relatively high surface tension of 42 mJ/m², which can ensure the cured part
be adhered to the bottom disk and separated from the top disk. The top disk was fixed and the bottom disk was installed on the top of a force sensor (DILLON Force Measurement Equipment, Fairmont, MN, US) with a resolution of 0.2 N. The force sensor could move down with a z stage, as showed in figure 4.21.

![Figure 4.101 The schematic setup for adhesion force test.](image)

The material was injected from the bottom disk by a pump syringe. The separation distance between two disks was 100 µm. A 3 mm by 3 mm square was crosslinked by the UV image from the top disk. After the square pattern was solidified, the stage moved down with a speed of 0.01 mm/s until the built structure separated from the top disk. A MATLAB program was used to collect the force with a sampling frequency of 20. The liquid material was CD9021/HDDA (70w:30w).
Figure 4.22 Adhesion force between the top disk and the cured layer with a curing exposure time of 3s. Three different top disks, (a) glass, (b) glass-PDMS coating, and (c) PMP.
Figure 4.22 showed the adhesion force test results for glass, glass-PDMS coating, and PMP, with different exposure time of 3 s. The adhesion force for the glass as the top disk was approximate 2 times higher than that from the glass-PDMS coating and PMP as the top disk. The glass-PDMS coating and PMP when used as the top disks showed a similar adhesion force at the exposure time of 3 s.

From the plots, the adhesion force was proportional to the time indicating that as the bottom disk was moving down gradually, the adhesion force increased with a linear trend. For different top disk, the maximum adhesion force was different with a varying maximum time to reach that force. The maximum adhesion force occurred at the point the built layer detached from the top disk, and then the adhesion force dropped to 0 precipitously.
Figure 4.3 Adhesion force between the top disk and the cured layer with a curing exposure time of 5 s. Three different top disks, (a) glass, (b) glass-PDMS coating, and (c) PMP.

Figure 4.24 showed the comparisons of adhesion force for different top disks with different exposure time. From the testing results, the glass had much higher adhesion force than glass-PDMS coating and PMP for both 3 s and 5 s exposure time. PMP had the lowest adhesion force with a maximum adhesion force less than 1 N and 2 N for 3 s and 5 s exposure time, respectively. In addition, for 3 s exposure time, the adhesion force for glass-
PDMS coating and PMP were close, while the difference was enlarged for 5 s exposure time. The exposure time affected more for glass-PDMS coating than PMP. Based on the test results, PMP was selected as the top disk in this work in order to generate a relatively low adhesion force. Table 4.2 showed the basic chemical and physical properties of PMP material. Also, compared the adhesion force for 3 s and 5 s exposure time, it was obvious that the adhesion force was increasing as the exposure time increased [50]. That result was probably due to longer exposure time providing more energy to produce sufficient radials or cations and better polymerization being conducted. Long polymer chains and strong crosslinking was formed in a large exposure time leading to a bigger adhesion force between the cured layer and the substrate. Another possible reason was that although the material was sandwiched by two disks, still some oxygen can diffuse into the liquid material, and the oxygen inhibition occurred. In a shorter exposure time, less radicals or cations were produced, and the oxygen inhibition, which may scavenge radicals or cations, was significant, resulting in partial crosslinked polymer. There was a gel layer generated between the fully cured part and the substrate. This gel layer decreased the adhesion force.
Figure 4.4 The comparison of adhesion force for glass, glass with PDMS coating, and TPX® Polymethylpentene (PMP) with exposure time 3 s (a), and 5 s (b).

Table 4.2 The basic properties of PMP material

<table>
<thead>
<tr>
<th>Properties</th>
<th>Unit</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density</td>
<td>Kg/m³</td>
<td>833</td>
</tr>
<tr>
<td>Surface Tension</td>
<td>mN/m</td>
<td>24</td>
</tr>
<tr>
<td>Gas Permeability (O₂)</td>
<td>mol·m/(m²·s·Pa)</td>
<td>9.4×10⁻¹⁵</td>
</tr>
<tr>
<td>Melting Point</td>
<td>°C</td>
<td>232</td>
</tr>
<tr>
<td>Yield Stress</td>
<td>MPa</td>
<td>30</td>
</tr>
<tr>
<td>Tensile Modulus</td>
<td>MPa</td>
<td>1900</td>
</tr>
<tr>
<td>Transmittance</td>
<td>%</td>
<td>94</td>
</tr>
<tr>
<td>Refractive Index</td>
<td>—</td>
<td>1.462</td>
</tr>
</tbody>
</table>
4.3 Conclusion

In this chapter, the liquid bridge was studied theoretically and experimentally. A mathematical model was built and the equilibrium profile of the liquid bridge was described by three basic functions: \( r(s) \), \( z(s) \), and \( \beta(s) \) based on the mathematical model. The model was successfully verified by liquid bridge experiments using water and composite polymer. The good agreement of mathematical results and experimental results indicated that the equilibrium stable shape of any liquid material can be predicted using the mathematical model. The mathematical model can guide the material feeding during the fabrication process. However, the phase change from the liquid to solid that happened during the photopolymerization process was ignored. A more precise model could be built when this phase change is considered, especially for a small volume liquid bridge.

The LBMSL system was set up by replacing the vat with the liquid bridge in the vat-based MSL. The fabrication process occurred within the liquid bridge which was formed between two parallel coaxial disks. In this process, the top disk was the most critical element. The top disk required a low surface energy to make the separation between the built part and the top disk easy. Different materials for the top disk were investigated by the adhesion force test between the cured layer and the top disk. Finally, PMP was selected for the LBMSL process in this work based on the unique properties, such as low surface energy, high chemical resistance, and high UV transmittance.
CHAPTER V
EXPLORATION OF THE FABRICATION CAPACITY AND COMPARISON WITH VAT-BASED MSL

Compared with conventional MSL, the fabrication capacity was improved greatly in LBMSL in terms of layer thickness, material viscosity, and material consumption. A submicron layer thickness was reached due to reducing the oxygen inhibition in LBMSL. And because of the unique system configuration and fabrication process, a highly viscous material was used. The material consumption was reduced compared with conventional MSL for fabricating the same size structure. In addition, the LBMSL showed potential for the multi-material fabrication and continuous fabrication.

5.1 The fabrication capacity study

In this section, the advantages of LBMSL, including the oxygen inhibition, the minimum fabrication layer thickness, the highly viscous material fabrication, and the material consumption were explored and compared with conventional MSL process.

5.1.1 Oxygen inhibition

As discussed in chapter 2, oxygen inhibition was a key issue in any type of polymerization process, especially in the SL and MSL processes, where a thin layer of material, typically 1-100 µm, is cured in the air ambient [125,128]. In the top-down vat-
based MSL fabrication process (figure 5.1 a), a very thin layer of material covered the cured layer and was exposed to the air, therefore, the oxygen inhibition affected the polymerization process, making sub-micron fabrication almost impossible [85,121,127].

Different methods have been developed to overcome the oxygen inhibition in polymerization applications [205]:

- Adding amines, which can consume the dissolved O\textsubscript{2} [206].

- Converting the dissolved O\textsubscript{2} into its excited singlet state by introducing a dye sensitizer [207,208].

- Increasing the concentration of the photoinitiator or the light intensity [209,210].

- Coating with wax barrier or performing the radical polymerization under inert conditions, such as using N\textsubscript{2} or CO\textsubscript{2} [211-214].

In order to reduce the oxygen inhibition, in the vat-based top-down MSL process, the most common methods used were to increase the concentration of the photoinitiator or light intensity, and use inert gas during the fabrication process. A high concentration of the photoinitiator or light intensity may have decreased the fabrication resolution due to over curing. Applying inert gas could increase the fabrication cost significantly. In the liquid bridge system, a top disk was used to form a liquid bridge. The top disk can prevent the contact of the top surface of the material with oxygen from the air, as shown in figure 5.1 (b). Even though oxygen intruded into the side of the liquid bridge, the concentration of the oxygen was very low between the built layer and the top disk [51]. Based on a unique
configuration, the LBMSL process can reduce the effect of oxygen inhibition greatly and consequently, a submicron layer thickness can be reached.

Figure 5.1 The oxygen inhibition to vat-based fabrication system (a), and liquid bridge fabrication system (b).

5.1.2 The minimum layer thickness investigation in LBMSL and vat-based MSL

As the oxygen inhibition was reduced greatly, a thin layer thickness around 1 µm or less was achieved using the LBMSL process. In vat-based MSL process, the light absorber was important for structures with overhanging features. Figure 5.2 and 5.3 were stent structures with the layer thickness of 20 µm. The material was CD9021/HDDA (70w/30w), with 1 w% DMPA as the photoinitiator, and 0.15 w% Tinuvin 327® as the light absorber in figure 5.2, and without Tinuvin 327® in figure 5.3 [215]. The light irradiance was 37.4 mJ/cm² and the exposure time was 2 s for both fabrications. Comparing these two figures, the light absorber was important in controlling the curing depth in an overhanging structure. Without the light absorber, a deeper curing depth was observed (figure 5.3), and the material under the overhanging structure was photopolymerized by the latter layer curing. Therefore, the light absorber was critical for high resolution fabrication [204]. One should choose a proper concentration of the light absorber carefully, because a high concentration may lead to the cure depth being thinner than the desired depth, resulting in fabrication
failure [215]. In the following fabrication examples in this chapter, the light absorber, Tinuvin 327® was used.

Figure 5.2 A stent with a layer thickness of 20 µm, with light absorber. (a) The stent, and (b) overhanging structure in stent.

Figure 5.4 and 5.5 were post arrays with the layer thickness of 1 and 0.5 µm, respectively. Layerless surface was achieved for both 1 µm and 0.5 µm posts from the pictures. Some fluctuations on the surface were observed, especially for posts with the layer thickness of 0.5 µm, which might have come from the ambient perturbation. In the LBMSL process, the dominant vibrations were from the stage moving, material feeding, and ambient air flow. Liquid material with a thinner layer thickness was prone to be disturbed. Therefore, for a thinner layer thickness less than 1 µm fabrication process, a relatively longer settling time was needed to remove the vibration generated from the stage moving and the material feeding. A cover was necessary to eliminate the air perturbation to the liquid bridge.
Figure 5.3 A stent structure with a layer thickness of 20 µm, without light absorber. (a) The stent, (b) overhanging structure in stent.

Figure 5.4 Posts with the layer thickness of 1 µm. (a) The post array on a substrate, (b) a single post, and (c) the surface of the post.

Figure 5.5 Posts with the layer thickness of 0.5 µm. (a) The post array on a substrate, (b) a single post, and (c) the surface of the post.
Figure 5.6 was a post array including 4 sections with a varying layer thickness of 0.5 µm, 1 µm, 10 µm, and 20 µm for each section from top to bottom for each single post. The height for each section was 200 µm. The layer numbers for each section was different because of the varying layer thickness (figure 5.6 (b)). The surfaces for each section were shown (c) ~ (f).

Figure 5.6 Posts with a varying layer thickness from 0.5 to 20 µm. (a) The post array on a substrate, (b) single post with varying layer thickness (LT), and (c) ~ (f), surfaces for 0.5, 1, 10, and 20 µm layer thickness post section.

5.1.3 The highly viscous material fabrication

In the vat-based MSL process [161], after one layer was fabricated (figure 5.7 a), the built layer was moved down with the platform by a z stage to a depth that completely covered the built layer, it remained there for a dwell time (figure 5.7 b). Next, the platform was moved up to a predetermined position leaving one layer thickness of material on the top of the built layer. A settling time was needed for material refreshing (figure 5.7 c and d). After the material surface was refreshed, the next layer of fabrication could be started (figure 5.7 e). The dwell time and the settling time depended on the viscosity of the material used. This time could be obtained experimentally. The higher the viscosity of the material, the longer the dwell time and settling time needed. Therefore, the viscosity of the material
was a big limitation for the vat-based MSL and the viscosity for vat-based MSL was recommended to be less than 200 cp [161,216].

Due to the unique system configuration of the LBMSL process, a vacuum was generated between the top disk and the built layer. The suction force drew the material filling the vacuum area rapidly, even for a relatively high viscous material. Thus, the refreshing time for the LBMSL was greatly reduced compared to the vat-based MSL.

In this work, different viscous materials were tested to fabricate complex structures using the vat-based MSL and LBMSL systems. These tests were conducted in order to explore the fabrication capability of highly viscous material. All the spring structures bellow were based on the same model. Figure 5.8 showed a spring fabricated from the material of SR150 with 1 w% DMPA and 0.15 w% Tinuvin327® as the photoinitiator and light absorber, respectively.

Figure 5.7 Fabrication process using vat-based MSL [161]. In (b) and (c) position, a dwell time and a settling time were needed, respectively.

The viscosity of SR150 was 700 cp at 25 °C. The layer thickness was 20 µm and the layer number was 175. The light irradiance was 37.4 mJ/cm² and the exposure time was 2
s. After one layer of fabrication, the platform was moved down for 2 mm and stayed for a dwell time of 5 s and then moved up for 1.98 mm with a settling time of 30 s for the material refreshing with the moving speed of 0.1 mm/s. The time for each layer fabrication was 77 s, and for the entire structure of 175 layer was 3.74 h, including the stage moving time, the exposure time, the dwell time, and the settling time.

Figure 5.8 A spring structure fabricated by SR150, with a layer thickness of 20 µm by vat-based MSL. (a) The spring structure, (b) part of spring wire, and (c) the surface of the spring wire.

The spring structure in figure 5.9 was fabricated by the LBMSL system using the same material and fabrication parameters. After one layer was fabricated, the bottom disk was moved down for 0.4 mm with the speed of 0.1 mm/s in order to make the built layer separate from the top disk completely, and then moved up for 0.38 mm with a settling time of 8 s to let the liquid bridge static, followed by the next layer of fabrication. The time for each layer was 20 s and the entire fabrication time was 0.87 h, which was 3.8 times less than the vat-based MSL.
A higher viscous material, CN293/HDDA (90w/10w) was tried to fabricate the spring using the vat-based MSL (figure 5.10) and LBMSL (figure 5.11) [217,218]. The viscosity of the matrix material was 3200 cp at 25 °C, and the same concentration of DMPA and Tinuvin327® were added. The dwell time and the settling time for the vat-based MSL fabrication was 10 s and 60s, respectively. The light irradiance was 37.4 mJ/cm² and the exposure time was 2 s. The time for each layer fabrication was 112 s and the entire fabrication time was 5.4 h. In addition, the diameter of the spring wire in figure 5.10 was approximate 700 µm, which was higher than the model of 500 µm. This was attributed to the settling time not being long enough, leading to the polymer surface being uneven, which may make the curing spot above the focus level. Since the light pattern from the objective lens was convergent, the curing spot above the focus level could result in a bigger curing area than on the focus level.
When using LBMSL with the same material, the settling time was 12 s with other parameters the same with that in figure 5.9. The time for each layer was 22 s and the entire fabrication time was 1.07 h, which was 5 times less than that using the vat-based MSL.

Figure 5.10 A spring structure fabricated by CN293/HDDA (90w/10w), with a layer thickness of 20 µm by vat-based MSL. (a) The spring structure, and (b) part of spring wire.

From figure 5.10, with the high viscosity of more than 3000 cp, the spring can be fabricated by the vat-based MSL, but with a low resolution. A distorted scale and bad surface feature were observed, which was probably due to the dwell time and settling time not being long enough even though the entire fabrication time was more than 5 h. Compared with the vat-based MSL, the spring fabricated from the LBMSL achieved much better features, in terms of the resolution and the real scale. The stair structures were observed clearly on the spring surface. Comparing the springs with the viscosity of 700 cp and 3200 cp fabricated by the LBMSL, a similar feature was obtained, which indicated that the viscosity had a slight influence on the LBMSL process.
From figure 5.12, when using SR150 with the viscosity of 700 cp at 25 °C, the fabrication time for the vat-based MSL was 3.8 times more than the LBMSL, this value increased to 5 when using a higher viscous material CN293/HDDA (90w/10w). Comparing the fabrication parameters, the settling time was increased greatly when using a higher viscous material in vat-based MSL, while no big change was noticed for settling time for LBMSL. Therefore, LBMSL exhibited a huge potential for highly viscous material fabrication, which can broaden the material selection significantly for the MSL process.
5.1.4 The material consumption

One of the benefits of LBMSL compared to the vat-based MSL was less material consumption during the fabrication process. In the vat-based MSL process, the liquid material was filled into a vat and a platform on which the fabrication occurred moved up and down in the vat. In order to ensure the liquid material covered the built part uniformly, the built part was moved down for a certain distance. This distance depended on the surface tension and the viscosity of the liquid material used to completely immerse the built part. Then the part was moved up to leave exactly one layer of material covering the built part. Hence, there would be a tolerance distance between the platform and the bottom of the vat. For a material with higher viscosity and surface tension, the tolerance would be greater leading to more material being needed. However, higher material viscosity and surface tension would not change the material consumption in LBMSL process [168,170]. Figure 5.13 showed the schematic for the material consumption in the vat-based MSL process.

Figure 5.12 The fabrication time comparison with the vat-based MSL and LBMSL using the material SR150 and CN293/HDDA (90w/10w). The time used for the vat-based MSL was 3.8 times and 5 times than that using LBMSL for the material of SR150 and CN293/HDDA (90w/10w), respectively.
where the maximum fabrication area was 3×3 mm. Theoretically, the platform can have the exact size of 3×3 mm. However, based on fabrication experience, the platform should be bigger than the fabrication area in order to eliminate the surface tension effect from the vertical post of the platform and to avoid damaging the built part when detaching it. Assume there was a 0.5 mm tolerance between the fabrication area and the edge of the platform, and between the edge of the platform and the inside wall of the vat. Assume a cubical structure with the size of 3mm×3mm×3mm was fabricated. The tolerance distance between the platform and the bottom of the vat was 2 mm. In this case, the minimum volume of the material V needed can be calculated by subtracting the volume of the platform (V2) from the inside volume of the vat (V1):

\[ V = V_1 - V_2 = 5\text{mm} \times 6\text{mm} \times 6\text{mm} - 4\text{mm} \times 5\text{mm} \times 1\text{mm} = 160 \text{ mm}^3 = 0.16 \text{ ml} \]

To fabricate the same cubical structure using the LBMSL system, a liquid bridge with a diameter about 5.24 mm was needed (the diagonal of 3×3 mm area plus tolerance), assuming the tolerance between the corner of the fabrication area and the edge of the disks was 0.5 mm as well, as shown in figure 5.14.

![Figure 5.13](image)

Figure 5.13 Schematics for material consumption in the vat-based MSL system. (a) The platform and the vat; (b) the size of the platform when the maximum fabrication area is 3×3 mm; and (c) the schematic for fabrication process [170].
In order to calculate the volume of the liquid bridge easily, a cylinder was assumed for the liquid bridge. The volume of the liquid bridge was:

\[ V' = \pi \times (2.62\text{mm})^2 \times 3\text{mm} = 64.7\text{mm}^3 = 0.065\text{ ml} \]

According to the analysis above, it was obvious that the material consumption in the vat based MSL was about 3 times that in the LBMSL. Especially, in the real fabrication process, considering the easy operation, such as detaching the built part, alignment of the light pattern and the platform, vat-based MSL needed more tolerance between the platform edge and the fabrication area, which lead to more material needed to fill the vat. Therefore, the LBMSL method can save material a great deal of material compared with the vat-based MSL. This was very important when costly materials were involved.

5.1.5 Fabrication examples using the LBMSL system

Microneedle array was fabricated using the LBMSL system with a layer thickness of 30 µm, as showed in figure 5.15. A tiny feature was obtained, like the microneedle tip, with a diameter of 20 µm. In addition, some complex structures were fabricated by the
LBMSL system in order to explore the fabrication capacity, such as the screw shown in figure 5.16 and the stent shown in figure 5.17, with the layer thickness of 20 µm.

![Microneedle array](image1)

Figure 5.15 Microneedle array fabricated by the LBMSL process with a layer thickness of 30 µm. The model (a) and the SEM image of the microneedle array [30].

![Screw structure](image2)

Figure 5.16 A screw structure fabricated by the LBMSL system with the layer thickness of 20 µm. The model (a) and the SEM image of the screw.

The material for both the screw and the stent was CD9021/HDDA(70w/30w) with DMPA and Tinuvin 327® as the photoinitiator and light absorber. The light irradiance was 37.4 mJ/cm², and the exposure time was 2 s. In figure 5.17, the overhanging structure in the stent was achieved successfully due to the light absorber.
When fabricating structures using the LBSML process, the light intensity (light energy) and the exposure time were two fundamental parameters needed to be considered for using different materials [219]. Generally, a high intensity of light can provide a deeper cure, but may decrease the accuracy due to the scattering of the light. In order to balance polymerization and accuracy, the light intensity can be lowered and the exposure time increased relatively. Figure 5.18 showed microneedles fabricated with different combinations of light intensity and exposure time. Figure 5.18(a) was the model for the microneedle, including a substrate and a microneedle body (700 µm height of cylinder and 300 µm height of cone tip). Figure 5.18 (b) and (c) used the same intensity 80, but different exposure time for the cone tip. Compared to (b) and (c), the tip in (c) was blunt, meaning the exposure time can affect the height of the cone tip. For (c) and (d), only the intensity was different, and a more accurate cylinder was obtained with a smaller intensity in (d). When the intensity was decreased to 65 (figure 5.18(e) and (f)), the diameter of the cylinders were close to the model size (200 µm). Compared with (e), the exposure time for the cone tip was longer in (f), and the total height of the microneedle was near 1000 µm.
with a pretty sharp tip. From the analysis above, the light intensity and the exposure time should be balanced to have the desired features. The exposure time had a conspicuous effect on the small feature, because when the spot was small, the energy decreased dramatically. Also, oxygen inhibition may affect the polymerization significantly for a small curing area [220,221].

![Image of microneedles fabricated using the LBMSL process with different fabrication parameters.](image)

<table>
<thead>
<tr>
<th>Intensity</th>
<th>80</th>
<th>80</th>
<th>70</th>
<th>65</th>
<th>65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time for body (s)</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Exposure time for tip (s)</td>
<td>0.2</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Figure 5.18 Microneedles fabricated using the LBMSL process with different fabrication parameters. (a) the model of the microneedle, (b) intensity: 80, exposure time: 0.2 s for cylinder and 0.2 s for cone tip, (c) intensity: 80, exposure time: 0.2 s for cylinder and 0.3 s for cone tip, (d) intensity: 70, exposure time: 0.2 s for cylinder and 0.3 s for cone tip, (e) intensity: 65, exposure time: 0.2 s for cylinder and 0.4 s for cone tip, (f) intensity: 65, exposure time: 0.2 s for cylinder and 0.5 s for cone tip.

5.2 Feasibility tests for LBMSL

In this work, some feasibility tests were conducted for the LBMSL, including multi-material fabrication [168,215] and continuous fabrication. The LBMSL was an open
system, therefore, the operation of material changeover including the clean and dry process was much easier than that in vat-based MSL process. In addition, the LBMSL process has a potential for continuous fabrication with the bottom disk moving down continuously and the images changing fast. This can decrease the fabrication time dramatically and make the surface smooth.

5.2.1 Multi-material fabrication process

The LBMSL system was modified to realize the multi-material fabrication process. The materials were feeding from the bottom and top disks separately, as shown in figure 5.19 [3,222]. Compared to single material fabrication LBMSL, two stages and two pumps were utilized. An x, z stage system was used to move in horizontal and vertical directions. Material 1 was feeding from pump 1 through the channel in the bottom disk and material 2 from the top disk by pump 2. The basic fabrication process was the same with single material fabrication using LBMSL except a material changeover was needed. The bottom part (blue one in the liquid bridge) was built by material 1. After the fabrication was finished, the material was drawn back to the pump 1. The built part was moved along X stage to provide enough space to use ethanol to rinse and air to blow it dry. After the rinsing and drying process, the built part was moved back to the original position and material 2 was injected from pump 2 to form a proper liquid bridge between the two disks. Once a stable liquid bridge was formed, the fabrication for the top part (gray one in the liquid bridge) could be started, again with the rinse and dry processes after fabrication. In this process, the material contamination presented a great challenge during the material changeover. A high resolution stage was needed to move the built part, fabricated from the
first material back to the original position after the material changeover. Otherwise, an unsmooth connection occurred at the boundary of the two materials [223].

![Figure 5.19 The multi-material fabrication LBMSL system](image)

A post and stent structure were fabricated using the modified multi-material fabrication system, as shown in figure 5.20. The material for the bottom part in both structures was CD9021/HDDA (70w/30w), which was clear, with 1 w% DMPA and 0.15 w% Tinuvin327®. The material for the top part was CN293/HDDA (90w/10w), a light yellow monomer, with the same concentration of DMPA and Tinuvin327®. The light irradiance was 37.4 mJ/cm² and the exposure time was 2 s for both material fabrications. From the structures, the connection between the two parts was not smooth. It was possible the stage lost the original position, during the material changeover discussed above. In addition, the rinsing material ethanol may lead to shrinkage due to the temperature dropping abruptly. A more temperate rinsing material may be needed.
Attempting post and stent fabrication showed a potential for multi-material fabrication using the LBMSL process. In addition, it was beneficial to try multi-material in one layer, which broadened the fabrication capacity.

Figure 5.20 Multi-material fabrication using LBMSL. (a) Post and (b) stent.

5.2.2 Continuous fabrication in vertical (z) direction

Using the LBMSL, continuous fabrication process was attempted [51,224]. In this process, the bottom disk was kept moving down with a specific speed, while the liquid material was fed and a continuous sequence of UV images were projected. The essential factor for continuous fabrication was the low surface energy for the top disk. If the surface energy was large, the adhesion force would prevent separating between the cured layer and the top disk. In this work, the top disk was TPX®Polymethylpentene (PMP) with the surface tension of 24 mN/m. In addition, according to the adhesion test results discussed in the previous section, a longer exposure time lead to a higher adhesion force. Therefore,
a proper exposure time should be chosen based on experiments. Using this process, no dwell time and settling time were needed, and the fabrication speed improved dramatically.

A stent was fabricated by the continuous process using the LBMSL system, as shown in figure 5.21. A stent model was sliced with a slicing thickness of 10 µm and saved as a sequence of 2D cross sectional images. During the fabrication process, the UV images were projected on the liquid material without any time delay, and the bottom disk kept moving down at speed of 0.01 mm/s. A 4 mm height stent was built in less than 10 min, which typically would take at least one hour using the regular LBMSL. Also, with the same fabrication speed, slicing thickness can be varied. The various slicing thicknesses only affect the part resolution [51].

![Figure 5.21](image_url) The stent structure fabricated by the LBMSL process. (a) The stent structure and (b) overhanging structure in stent.

5.3 Conclusion

The minimum layer thickness for the LBMSL was studied and compared with vat-based MSL. Using LBMSL, the layer thickness can reach 0.5 µm, which typically is impossible for the vat-based MSL process due to oxygen inhibition. Theoretically, a smaller layer thickness can be reached, which depends on the resolution of the moving stage and the stability of the whole system. Based on the unique fabrication method, low
oxygen inhibition and highly viscous material fabrication were two more benefits from the LBMSL process. The top disk was functional as an insulating cover to prevent oxygen from intruding into the top surface of the polymer. In addition, since the suction force formed between the built layer and the top disk, the material was easily drew in as the built part separated from the top disk after a layer was fabricated. With this suction force, a high viscous material was used without sacrificing the fabrication speed. From this work, a highly viscous material of more than 3000 cp was used in the LBMSL process with a high fabrication speed.

Some structures were fabricated to demonstrate the fabrication capacity of the LBMSL. The influence from the intensity and exposure time were explored by fabricating the same structure with various intensity and exposure time. Generally, a higher intensity and longer exposure time lead to a deep photopolymerization, while a decrease in the resolution could be noticed. The intensity and the exposure time should be balanced to obtain the best fabrication results.

Two feasibility tests were conducted using the LBMSL process, multi-material fabrication test and continuous fabrication test. In LBMSL, material changeover was easy to operate due to the open liquid bridge. However, the material contamination was a big issue in the multi-material fabrication process. In LBMSL, because the materials were fed from the channels through two disks, the material contamination easy occurred when withdrawing the material in order to change to another material. For the continuous fabrication, the biggest challenge was the adhesion force between the built layer and the top disk. Ideally, if the adhesion force could be reduced to 0, the best continuous fabrication
result would be obtained. Therefore, a better top disk or method to reduce the adhesion force was needed to improve the continuous fabrication ability.
CHAPTER VI
CONCLUSIONS

An attractive additive manufacturing technology, Microstereolithography, was investigated in this thesis. A novel liquid bridge MSL (LBMSL) was proposed and developed, in which the conventional vat was replaced by a liquid bridge formed between two parallel coaxial disks with the same diameter.

In this work, a multi-material fabrication process using vat-based MSL was developed, and microneedle arrays were fabricated using synthesized biocompatible material PPF with some amount of drug loading. The compression test and the drug release test results indicated that vat-based MSL was a potential technique for some specific applications, like biofabrication.

Some disadvantages, however, emerged in the conventional vat-based MSL, including the oxygen inhibition, the difficulty of using the high viscous material, big material consumption, and inconvenience of multi-material fabrication. In order to overcome these disadvantages and improve the fabrication capacity, a novel liquid bridge based MSL was developed. In this process, the vat used in the conventional MSL to hold the liquid material, was replaced by the liquid bridge, and the microstructure was fabricated within the liquid bridge.
The liquid bridge technique used in this LBMSL process was studied theoretically and experimentally. The mathematical model was verified by the liquid bridge experiments and a good agreement was obtained compared with the mathematical results and the experimental results. Consequently, the mathematical model can be applied for any new material to achieve the stable equilibrium liquid bridge profile. In addition, the volume and height relationship also can be obtained by the mathematical model, which was useful when using an automatic pump to feed material during the fabrication process.

Using the developed LBMSL system, the material with a viscosity of more than 3000 cp was used to fabricate complex structures successfully with a much less time than that using a vat-based MSL. This can broaden the material selection for MSL, especially for polymer and biomaterial, which typically have a relative high viscosity.

Oxygen inhibition was one of the biggest challenges for the MSL process to reach a thin layer thickness. The oxygen in the air can scavenge the radicals generated by photoinitiator and prevent the polymerization process. In LBMSL system, the top disk played an important role to insulate the top surface of the polymer to the oxygen and decreased the effect from the oxygen inhibition greatly. Therefore, submicron layer thickness was reached by preventing the oxygen inhibition.

Due to the unique configuration of the LBMSL system, the material consumption for fabrication of the same structure was reduced several times compared with vat-based MSL. This was meaningful for high cost material or the material in the lab stage.

The multi-material fabrication was attempted using the LBMSL process with the materials fed from the bottom and top disk, respectively. After one material fabrication was finished, the material was withdrawn and recycled, with the rinsing and drying process
following. Simple recycling reduced material waste in the LBMSL process compared to the vat-based MSL.

The possibility for continuous fabrication was shown using the LBMSL process, which improved the fabrication speed. In this promising process, the top disk was the essential factor because as the bottom disk moved down continuously, the built layer should separate from the top disk easily.

In summary, the novel LBMSL process showed advantages in terms of the fabrication speed, the highly viscous material fabrication, the submicron layer thickness, and multi-material and continuous fabrication. The advanced process improved the fabrication capacity of MSL and could be used for numerous application fields.
REFERENCES


[52] Plateau, Joseph Antoine Ferdinand. Experimental and theoretical researches on the figures of equilibrium of a liquid mass withdrawn from the action of gravity.-Third series.


[185] CD 9021 data sheet, HDDA data sheet, SARTOMER USA, LLC.


[223] R.B. Wicker, and E.W. MacDonald. Multi-material, multi-technology stereolithography: This feature article covers a decade of research into tackling one of the major challenges of the stereolithography technique, which is including multiple materials in one construct. Virtual and Physical Prototyping 7.3 (2012): 181-194.