## MULTIMATERIAL MULTILAYER FABRICATION OF MICROFLUIDIC DEVICES

#### MULTIMATERIAL MULTILAYER FABRICATION OF MICROFLUIDIC DEVICES

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A Thesis Submitted to the School of Graduate Studies in Partial Fulfilment of the Requirements for the Degree

Doctor of Philosophy

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## McMaster University DOCTOR OF PHILOSOPHY(2019) Hamilton, Ontario, Canada

TITLE:	Multimaterial Multilayer Fabrication of
	Microfluidic Devices
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NUMBER OF PAGES: xiii, 121

### Abstract

Microfluidics technology enables miniaturization, integration and automation of chemical and biochemical assays. Compared to conventional analytical tools, a microfluidic device requires small volume of samples and performs assays faster making it a suitable candidate for pointof-care diagnostic devices. Various fabrication techniques for microfluidic systems have been developed over past three decades to construct microchannels and microfluidics components such as valves, pumps and electrodes. However, most of these methods are either expensive and requiring cleanroom environment or limited to use of single or a few materials primarily due to differences in process conditions of various materials. Therefore, an easy and robust fabrication technique that is able to integrate different microfluidic components into a single device is highly sought. Xurography as a rapid prototyping tool was introduced over a decade ago for construction of microchannel. Although this technique has significant capability to pattern variety of materials, it has not been applied for important microfluidic components such as valves and electrodes. In this thesis, combination of xurography with lamination has been developed to integrate microfluidic components. Use of commercially available film in variety of materials such as thermoplastics, elastomers and metals significantly reduces the cost of fabrication. Also, these materials have different properties such as insulating, conductive, elastic, hard, soft, hydrophobic and hydrophilic providing unique functionality in microfluidic devices. Therefore, various applications such as fluid flow controll by active and passive valves, DNA electrophoresis, electrochemical sensing, electrokinetic mixing and heating are presented.

### Acknowledgement

This thesis would not have been possible without the help and support of many people. First, I would like to express my sincere gratitude to my supervisor, Prof. P. Ravi Selvaganapathy, for his constant encouragement, support, advice and patience. During our course of interaction during the last four and half years, I have learnt extensively from him, including how to raise new possibilities, how to regard an old question from a new perspective and how to approach a problem. I will never forget the lessons learned under his guidance, both professional and personal.

My special thanks also go to Prof. Matiar Howlader who has generously shared his knowledge and laboratory space and research facilities. Without this precious support it would not be possible to conduct this research. I am also thankful to Prof. Mohammed Tauhiduzzaman for agreeing to be on my research committee and for his insightful comments and invaluable advice. A special thanks to Prof. Alison E. Fox-Robichaud our collaborator from the department of Medicine at McMaster University for her valuable input and feedback on my research. I would like to thank Prof. Chan Ching, for his insightful comments and encouragement during my studies. I also would like to thank Dorris Stevanoic for her help with cleanroom facility, Marcia Reid for her help in SEM imaging and Dr. Zeynel Bayindir for his help in XPS measurements. I am also thankful to the technicians in the department of Mechanical Engineering, Mark Mackenzie, Ron Lodewyks, John Colenbrander and Michael Lee for their help in my research.

Next, I would like to thank all past and present members of the CAMEF group, Dr. Hsu, Dr. Dabaghi, Dr. Ghaemi, Dr. Attalla, Dr. Shahid, Nidhi, Alireza, Sreekant, Parker, Juncong, Celine, Devon, Monika, Islam, Vinay, Shayan, Shubham, Pankaj, Shady, Rong, Shadi and Mohammed. Each and every one of you made my experience as a graduate student an enjoyable one. Thank you for all your help, friendship and unforgettable memories both in and outside of the laboratory.

Lastly, I would also like to express my appreciation to my family without whom none of this would have been possible. I am deeply thankful to my parents for their love, support, and sacrifices. Thanks to my caring sisters, Hoda and Hadis, for their endless support and encouragement throughout the years. A special thanks to my loving wife, Sepideh, who has supported me in every dream, every endeavour, every practice, and every commitment.

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## List of Abbreviations

CAD	Computer aided design
CD	Compact disk
cfDNA	Cell-free DNA
$\rm CO_2$	Carbon dioxide
COC	Cyclic olefin copolymer
COP	Cyclic olefin polymer
CV	Cyclic voltammetry
DC	Direct current
DFR	Dry film photoresist
DI water	Deionized water
DNA	Deoxyribonucleic acid
DRIE	Deep reactive ion etching
FDM	Fused deposition modeling
hCG	Human chorionic gonadotropin
HF	Hydrofluoric
i3DP	Inkjet 3D printing
ICEO	Induced charge electro-osmosis
LoC	Lab on chip
NIL	Nanoimprint lithography
PC	Polycarbonate

PCB	Printed circuit board
PCR	Polymerase chain reaction
PDMS	Polydimethylsiloxane
PET	Polyester
PI	Polyimide
$\mathbf{PS}$	Polystyrene
PSA	Pressure sensitive adhesive
PVC	Polyvinyl chloride
PVD	Physical vapor deposition
RT-PCR	Real time polymerase chain reaction
SEM	Scanning electron microscopy
SLA	Stereolithography
SMA	Shape memory alloy
stdev	Standard deviation
TAS	Total analysis system
UV	Ultra violet
XPS	X-ray photoelectron spectroscopy

## Chapter 1 Introduction

#### 1.1 Microfluidics

Microfluidics is a technology for manipulating and controlling fluids in range of microliters to nanoliters by using network of channels or chambers with dimensions in micrometer scale [1]. In contrast to macroscale in which gravity or momentum is important, other effects such as surface energy, diffusion, electric and magnetic fields become dominant in microscale [2]. By applying these effects in microfluidics, variety of components such as pumps, valves, mixers have been developed over the past five decades [3]. Integration of these components into a single chip can facilitate chemical and biochemical assays in faster and more accurate ways. Such a device capable of performing series of chemical analysis in automated way is called a Total Analysis System (TAS) or Lab-on-Chip (LoC) device [4].

A simple example of LoC system in the market is pregnancy test strips [5]. In these devices, urine passively wicks into porous materials by capillary forces. A hormone in pregnant women called human chorionic gonadotropin (hCG) binds to its antibody linked to an enzyme [6]. After binding, the hCG hormones is transported to the test zone in which other hCG antibodies are immobilized to the strip. In this zone, the linked enzyme catalyzed a reaction with dye molecules and trigger a color showing pregnancy. All of these operation such as transportation of samples, mixing with antibodies and dyes and chemical reactions are carried out in an automated way inside the test strips. Although there were macroscale devices to perform such as an assay, the portability and speed of microscale devices have a significant advantage for use by end-users. Also, these miniaturized devices do not require electrodes or other complicated detection system to perform the analysis.

Fabrication and integration of electrodes for LoC devices have enabled the development of accurate testing systems such as glucometer that require smaller sample volumes and perform analysis rapidly. In glucometer, a droplet of whole blood sample is mixed with dried glucose oxidase on test strips and subsequently coupling with the redox compounds produces electrochemical signals [7]. Accordingly, the detected electrical signal is used to measure glucose concentration.

Recently, incorporating electrodes in LoC systems has gain great attention in development of point-of-care devices [8]. In one example, a microfluidic device for early diagnosis of septic conditions was developed in 2015 [9, 10]. In this prototype, the whole blood sample was obtained from patients, injected into a microchannel without sample preparation. Hydrogels inside the device were used as mobility trap to concentrate and collect cell free DNA (cf-DNA) in blood using electrophoretic methods. Fluorescent imaging methods were used as a quantification method. Although collection and quantification of cf-DNA in this protype was autonomous, further development of this prototype regarding sample injection, integration of hydrogels and electrodes was required to perform the assay in fully automated way. In order to address that, a fabrication method capable of integrating different materials into a single chip is needed.

#### **1.2** Microfabrication of microfluidic devices

Various techniques for fabrication of microfluidics systems has been developed since 1970s to construct microchannels and microfluidics components [11]. At the beginning, silicon and glass micromachining techniques were the most common used technique to fabricate microfluidics due to their well-development and mature fabrication processes. Although precise and scalable, different requirements for biological assays such as disposability, flexibility and biocompatibility have been resulted in development of microfabrication of polymeric materials. Therefore, various fabrication methods have been developed over past three decades for a range of polymeric materials such as thermoplastics, thermosets and elastomers.

#### 1.2.1 Silicon and glass micromachining

Historically, microfluidic devices were initially fabricated on silicon and glass by photolithography and micromachining techniques used in semiconductor industry [12]. Silicon is the most common element in the Earth's crust that makes it affordable to be used as the basis material for memory chips, transistors and computer processers [13]]. For fabrication of silicon in microfluidics, bulk and surface micromachining have been developed [14].

In bulk micromachining, silicon is removed by etching methods either in wet (liquid) or dry(gas) modes to shape microstructures on the substrate [15]. In deep reactive ion etching (DRIE) as a dry method, silicon etching rate (below 1  $\mu$ m/min) is much lower than wet etching modes (about 2-3  $\mu$ m/min) and structures with aspect ratio of 100:1 is achievable [16]. In surface micromachining, silicon based materials like as polysilicon are deposited on the substrate to form microfluidic structures [17]. In both bulk and surface micromachining, photolithographic methods are utilized to pattern the structures on the substrate. Photolithography processes typically start with spin-coating of a photosensitive resist material followed by exposing to ultra violet light through a photomask. Feature size as small as 80 nm can be achieved by photolithography [18]. The process flow of typical photolithography for surface micromachining is shown in Fig.1.1.

In 1979, a miniaturized gas chromatography analyzer with integrated thermal conductivity sensor was fabricated on silicon [12]. Since then, silicon micromachining has been used to fabricate microfluidic devices for different applications such as microreactors



Figure 1.1: Pattern transferring by photolithography in surface micromachining [19]

[20], cell culture chambers [21] and micropumps [22].

Although fabrication techniques for silicon-based microfluidics are well-established and smooth side walls are obtained, there are main disadvantages associated with that. Compared to electronics industry, cost of the material and fabrication is high for biomedical and lab-on-chip applications. Also, electrical and thermal conductivity of silicon requires addition insulation layer that increases the cost of fabrication. In addition, silicon is opaque to visible and ultra violet light and cannot be used with optical detection methods. To address the optical limitations, glass-based devices have been introduced in microfluidics technology [23].

Microfabrication methods developed for glass micromachining are belongs to bulk micromachining techniques including mechanical, wet or dry etching processes [24]. For example, glass substrates glass can be mechanically machined by ultra-sonic manufacturing using abrasive grains hitting surface of the substrate [25]. This technique specially developed for hard and brittle materials such as glass, silicon and ceramics. In wet etching approaches, hydrofluoric (HF) acid solutions are mostly used to selectively etch glass substrates [26]. In DRIE, ionized gas etchants like as sulfur hexafluoride have been applied to etch the surface of glass workpieces [27]. In bulk micromachining, depth of channels can be controlled by etch rate of etchants and the duration of etching. Because of isotropic nature of glass substrates, aspect ratio of 1 or less is achievable for microchannel structures.

Glass microfluidic devices have been extensively used for many application. For example, a glass microfluidic device was developed for DNA amplification and capillary electrophoresis systems [28]. In another work, hemi-spherical channels were fabricated within glass substrates for gas chromatography [29].

Similar to silicon micromachining, cost of fabrication is high for glass substrates. In addition, neither glass nor silicon is not permeable to gases which is crucial for work with living mammalian cells. Although glass and silicon micromachining techniques have very high resolution, they are slow and tedious, expensive, requiring cleanroom facilities and limited in the number of materials that can be used. Therefore, polymer fabrication methods have been developed to overcome these limitation.

#### **1.2.2** Polymer fabrication techniques for microfluidic systems

#### 1.2.2.1 Soft lithography

Among polymeric fabrication methods, soft lithography was introduced in 1990s as a rapid prototyping technique. In this method, an elastomer is casted on a silicon master mold fabricated by photolithography. As a result, structures of master molds are replicated on elastomer substrates. The most common used material in this method is polydimethylsiloxane (PDMS), where the base elastomer is mixed with the curing agent in ratio of 10:1, then casted over a master mold and cured at 65° for one hour. The resolution of replica for PDMS is very high, where structures in 10-nm size have been reported [30]. Also, PDMS has significant properties such as high optical transparency, electrically insulating, chemically inert and biocompatibility that make it a commonly used material in microfluidic devices for chemical and biochemical assays [31]. In 1998, PDMS based microfluidic devices were introduced that they were capable of performing capillary electrophoresis separation [32]]. Since then, many microfluidics devices for DNA amplification [33], diagnostics [34] and environmental monitoring [35] have been developed.

Although soft lithography is a relatively fast and cost-effective fabrication approach, it is limited to PDMS. This method relies basically on the bonding of PDMS to silicones or glass by plasma activation that limits the number of materials can be used in a single device [36]. In addition, PDMS's ability in absorbing proteins and easily fouling does not often meet requirements for many biomedical applications.

#### 1.2.2.2 Hot embossing

Hot embossing that is more suitable for industrial production and commercial applications has been developed over the past twenty years for fabrication of microfluidic devices [37]. In this method, thermoplastic materials such as poly(methyl methacrylate) (PMMA), polycarbonate (PC) or polystyrene (PS), are heated up above their glass transition and conformed to topography of a master mold by applying pressure. Afterwards, the mold and the substrate are cooled down and separated away. This method has significant resolution that is reported as small as 25 nm and often named thermal nanoimprint lithography (NIL) [38]. In NIL, as it has been shown in Fig.1.2, a thin layer of imprint resist is spin coated on substrate. After heating up the polymer above its glass temperature to be a viscous fluid, a mold with nanostructures on its surface is pressed into the thin resist. So, the nanostructures can be duplicated into the imprint resist. After being cooled down, the mold is separated, and the imprint resist is left with the nanostructures pattern. Finally, a pattern transfer process, such as DRIE can be used to remove the residue resist [39]. Hot embossing is a suitable process for replicating high aspect ratio microstructures (more than 2) that has been used for fabrication of microfluidic devices made of PMMA and PC [40]. Cycle time for hot embossing including heating, pressing and cooling depends on the material and feature sizes and it is about 10 minutes or above [41]. Important parameters for the replication process are uniform temperature distribution, vacuum condition to prevent air trapping and chemical compatibility to prevent sticking of the mold and the substrate [42].



Figure 1.2: Process flow for thermal nanoimprint lithography [43]

Hot embossing has been extensively used over the past twenty years as a suitable method for the fabrication of microfluidic devices both in industry and academia [44]. For example, microfluidic devices made of PMMA were fabricated by hot embossing for DNA separation and detection [45]. Additionally, microfluidic devices for cell studies [46], biosensing [47], environmental monitoring [48], etc. have been fabricated by this technique.

Although hot embossing is simple and compatible with industrial equipments, it is limited to thermoplastics and integration of other polymers such as thermosets and elastomers is not possible. In addition, integration of multiple thermoplastic materials with different glass transition temperatures is even complicated. Also, this method relies on a master mold that makes the entire process longer and not suitable for rapid prototyping.

#### 1.2.2.3 Micro injection molding

Micro injection molding is another mold based fabrication technique that melts thermoplastic polymers and injects them into microstructured mold inserts [49]. In this system melted polymer flows through small size nozzle with high speed and high pressure. Afterward, the substrate with the mold is cooled down and demolded. This technique that has been used for many years for production of polymeric parts is suitable for large scale production [49]. While hot embossing technique exhibits very high resolution for imprinting parts, micro injection molding shows slightly lower precisions in the range of hundreds of nanometer [50]. However, compared to hotembossing, it has shorter cycle time about 2 minutes or above [51].

Many microfluidic devices have been fabricated by injection molding. For instance, a microvalve system consists of two molded parts and a polyimide membrane was fabricated in 1995 [52]. In another work, a microfluidic chip with integrated interconnects was fabricated on cyclic olefin copolymer (COC) [53]. Also, a real-time PCR microfluidic device for pathogen detection was fabricated on cyclic olefin polymer (COP) [54].

The main advantage of injection molding is the ability to form 3D structures that is crucial for fluidic interconnections [53]. Also, the process cycle time is very short, and it typically does not need additional process steps. However, the same as hot embossing, main disadvantage of this technique is limitation of using only thermoplastic polymers. Thus, integration of different materials is not possible. Also, using microinjection molding requires high speed injection of melted polymers through small nozzles that promotes high shear stress resulting polymer degradation [55].

#### 1.2.2.4 Micro milling and laser micromachining

In recent years, there is an increasing attention in the development of direct manufacturing techniques that are based on removal of the material such as micro milling and laser micromachining. These direct fabrication technique do not require clean room facilities and are suitable for rapid prototyping. In particular, using masks and molds that adds additional steps for photolithography and replication methods is eliminated.

In micro milling approach, microstructures are created by a rotating cutting tool that

removes material from a workpiece [56]. Microfluidic channels were fabricated on metals and polymers by micro end milling and micro electrical discharge milling [57]. Micro milling can also be used to fabricate molds. For instance, nickel molds were fabricated for hot embossing prototyping of thermoplastic microfluidic devices [58].

In this method, features size as small as 10  $\mu$ m was fabricated on a graphite substrate [59]. Also, an array of posts with aspect ratio of 10:1 and size of 50  $\mu$ m was fabricated on a master for injection molding [60]. In addition, surface roughness of about 100-200 nm on metals and 80-120 nm for polymers was reported [57]. For cutting stainless steel, tool wear after 100 mm length cut was observed [61].

Although this technique is fast and flexible for creation of a single micro structure, it becomes limited and complicated for large batch size production. Also, considering tool wear besides slow machining speeds makes this approach less cost-effective. In addition, rough finished surface of devices fabricated by this method puts another limitation of using this method.

Laser micro machining is a contactless fabrication method in which focused laser beam removes material by energizing and thus evaporating at the focal point of the beam [62]. Although there have been some works using masks as a patterning tool, the laser beam can be moved eliminating needs of any pattern transfer step. Depending on the material to be removed, excimer lasers in varying wavelength in the range of 200 nm to 10  $\mu$ m have been used to fabricate microfluidic devices .

In laser machining, microfluidic channels can be created by partially ablation of the substrate defining height of the channel and sealing on top with another layer by thermal and solvent bonding [63]. In another approach, the substrate can be ablated all through the layer and sealed on top and bottom by intermediate adhesive layers [64]. In this approach, assembly of chip with multi layers showing 3D structured channels has been demonstrated [65].

Laser machining is a flexible technology that does not require expensive and time

consuming equipment. However, interaction of laser light with the substrate change the chemistry of the surface which is not often desirable. In addition, this technique has only been used to create microchannels and not developed for integration of different materials and other microfluidic components such as valves, pumps and electrodes.

#### 1.2.2.5 3D printing

Printing has recently become popular as an additive manufacturing method to fabricate microfluidic devices because of its 3D fabrication, cost-effectiveness and automated assembly [66]. Mostly there are three forms of 3D printing including stereolithography (SLA), inkjet 3D printing (i3DP) and fused deposition modeling (FDM).

In SLA, a focused laser is exposed to a tank of photoresin precursor and a 3D structure is fabricated by layer-by-layer building of those photopolymerized resins [67]. Microfluidics channels with resolution of 150  $\mu$ m with surface roughness of 0.35  $\mu$ m can be printed by SLA printers [68]. One of the main major limitation of this type of 3D printers is the restriction to print of a single material at a time. Using this approach, microfluidic devices for wide range of application such as glucose sensing [69], cell culturing [70] and water monitoring [71] have been fabricated.

In i3DP, liquid photopolymers are printed by inkjet heads onto a tray and immediately polymerized by UV light [72]. As a result, a 3D object is built by layer-by-layer stacking of cured polymers. In this method, support material is printed along with build material and is removed by high pressure water jetting. As a result, one of the main disadvantages of this method for microfluidic constructions is that support material needs to be removed which is impossible for enclosed structures. However, this type of 3D printers can print different materials simultaneously by multiple nozzles. Using this method, microfluidics channels with resolution of 200  $\mu$ m with surface roughness of 1  $\mu$ m can be printed [73]. Also, different types of microfluidic devices for applications such as gel electrophoresis [74], diagnostics [75] and cell lysis [76] have been fabricated by 3D inkjet printers. In FDM, thermoplastic materials are melted and extruded via a high temperature nozzle head and rapidly cooled down on a tray [77]. Thus, a 3D object is fabricated by layer-bylayer printing of extruded thermoplastics. Due to printing conditions, this type of printers has lower precision compared to the other 3D printing techniques. For example, channels with minimum feature size of about 300  $\mu$ m with accuracy of 5  $\mu$ m and surface roughness of about 11  $\mu$ m can be fabricated [68]. However, FDM has a lower purchase price compared to the other ones that makes it a suitable choice for rapid prototyping of microfluidic devices. For example, FDM has been used to fabricate microfluidic devices in applications such as chemical synthesis [78], electrochemical sensing [79] and pathogen detection [80].

Although FDM is limited to thermoplastic materials, i3DP is able to print wider range of materials such as elastomers[81], hydrogels[82], [83], hard and soft plastics[84]. However, most of these materials are expensive with poor surface properties [85]. Also, materials for SLA and i3DP are proprietary that require biocompatibility studies. As a result, 3D printing is a newly emerging technology that is in its infancy and requires further studies to be able to become dominant fabrication process for microfluidic devices.

# **1.3** Fabrication and integration of microelectrodes in microfluidics

In fabrication of microfluidic devices, integration of metals is crucial. Metals as electrode components have been used for variety of applications in microfluidics as sensors for electrochemical detection, actuators for fluid transportation or heaters for temperature control [86]. Historically, electrodes were fabricated and integrated into microfluidic devices by conventional methods originated from semiconductor industry such as physical vapor deposition.

Although this method is well-established and precise, it requires expensive equipment and clean-room facilities. Since then, other techniques have been developed to fabricate electrodes in microfluidics such as electroplating, inkjet printing and microwire integration. However, a robust technique to fabricate electrodes easily and cost-effectively while capable of incorporating a variety of high quality materials is still needed.

#### 1.3.1 Physical vapor deposition (PVD)

PVD refers to a set of process to deposit thin layer of materials in vacuum conditions without chemical or composition change. In this method, solid metal is evaporated by heating or bombardment of a beam of electrons/ions and then is deposited on a substrate forming a thin layer [87]. PVD is mostly combined with photolithography to pattern a desired structure on substrates that make the process high precise able to create sub-micrometer features [88]. Also, the thickness of the deposited film can be as thin as tens of nanometer to tens of micrometers [88]. Mostly metals such as gold, platinum, chromium, silver, copper and their alloys are deposited by PVD.

Since development of early microfluidics until now, PVD is the most commonly used method for fabrication of electrodes [89, 90, 91]. Integration of electrodes into microfluidic devices was demonstrated as early as 1979 by deposition of 100 nanometer thick layer of nickel on silicon wafer as thermal conductivity detector for gas chromatography [92]. Since then, PVD has been used to fabricate electrodes in microfluidics for wide range of applications such as DNA amplification [93], electrochemical immunosensing [8], environmental monitoring [94] and fluid transportation [95].

Although this technique is precise and scale, the fabrication process needs vacuum conditions and cleaning room facilities, experienced level operation and multiple process step, that is more suitable for semiconductor industry. While in microfluidic devices, high density electrodes with sub-micrometer resolution in not often required.

#### 1.3.2 Electroplating

Electrochemical deposition has gained increasing attention in fabrication of microelectrodes in microfluidics because of its advantages such as high degree of control, deposition speed, reliability and relatively inexpensive equipments [96]. As it has been shown in Fig.1.3, this method involves a conductive coated substrate and a patterning photoresist in which metals are galvanically deposited by external direct current [97]. After deposition, the photoresist is removed by a developer.



Figure 1.3: Process flow for electroplating technique [97]

Using photolithography for pattern transferring, microelectrodes with feature size down to 1  $\mu$ m and aspect ratio up to 500 can be fabricated by electroplating techniques [98]. By controlling the electroplating parameters, metal films with thickness from tens of nm to hundreds of  $\mu$ m can be plated [96]. Variety of metals and their alloys such as gold, silver, platinum, nickel, chromium, etc. can be electroplated on conductive substrates [99].

Electroplated electrodes become crucial in microfluidics where vertical and 3D electrodes are necessary. For instance, gold was electroplated as side wall electrodes with thickness of 50  $\mu$ m to provide uniform electric field in a microfluidic electroporation device for cell lysis [100]. In another work, electroplated gold micropillars generating dielectrophoresis force were used in a cell trapping microfluidic device [101]. Also, 1  $\mu$ m thin layer of permalloy was electroplated in form of arrays for magnetic bead-based immunoassay with fully on-chip sampling for disposable point of care testing in clinical diagnostics [102]. In addition, to eliminate the problems associated with the wet photoresist such as long processing time and liquid handling, dry film resists were used to electroplate silver as referce electrodes for electrochemical sensing in microfluidics [103, 104].

Electroplating is a precise, low cost and high speed method that does not require expensive facilities such as PVD. However, electrodeposition can be performed only on conductive substrates resulting limited choice of materials or use of PVD as a coating step. Also, for case of electroplating of multiple materials, conventional methods use a sequential process of coating one material at a time that requires significant amount of time and steps. In addition, they use large volume of electrolytes which is suitable for large production level and coating of large areas, but it is wasteful and unnecessary for prototyping or coating of small area electrodes.

#### **1.3.3** Chemical etching of printed circuit boards

A printed circuit board (PCB) is composed of non-conductive layers such as polyimide and laminated layers of copper as conductive substrate [105]. The main fabrication process involves photolithography for pattern transferring and use of etchants such as acid tanks to form the copper electrodes in desired design. Insulating layer of the composites are commercially available in variety of materials such as polyimide, polystyrene, glass or ceramic substrates and are in form of flexible or rigid boards [106]. For photolithography, dry film photoresists (DFR) have been widely used in PCB microfluidics due to its process simplicity and low raw material cost. Using DFR, electrodes with feature size as small as 20  $\mu$ m can fabricated on PCBs [107]. Copper layers are mostly etched by immersion in a tank of chemical wet etchants such ammonium persulfate or ferric chloride for about 20 minutes and more depends on copper thickness [108]. PCBs with copper layers with thickness in range of between 2  $\mu$ m to 200  $\mu$ m are commercially available. In 1997, PCB technology has been introduced to integrate electrodes in microfluidic systems [109]. In this work, PCB was used as a platform hosting conductive pads and interconnection lines. Since then, PCB technology has been used extensively for rapid prototyping of microfluidic devices [110]. In one study, a three-layered composite foil of polyimide coated with copper in both sides was used for fabrication of a microfluidic device [111]. In this work, an aqueous solution of  $CuCl_2$  and  $H_2O_2$  was used for selective etching of copper for fabrication of electrodes. Afterward, plasma etching was used to create liquid channel into the polyimide layer. In another study, rapid prototyping of digital microfluidic platforms was introduced by using printed circuit boards [112].

Although this technique is rapid and scalable because of using printed circuit boards, it still needs photolithographic approach which requires a number of steps. In addition, chemical etchants might not be compatible with other polymers when integration of them is needed. Also, copper laminates are the only material that is available in this technology, while other electrode materials such as platinum, gold and silver are required for many applications such as electrochemical sensing. In order to address that, an additional coating approach such as PVD [113] or electroplating [114] is required.

#### **1.3.4** Microwire integration

Using wires as electrodes is a simple and easy approach for rapid prototyping of microfluidics. In this method, wires can be easily used by placing directly at the reservoir of a microchannel after assembly or permanently and precisely in microchannels during assembly and before device bonding. Fig.1.4 shows an electrode wire inserted precisely into a glass chip grooved by a chemical etchant.

Since microwires have been used in semiconductor industry to interconnect integrated circuits, they have high quality properties such as high tensile strength [116]. Also, variety of materials such as gold, silver, platinum, Ni-Cr alloy with diameter size as small as 10  $\mu$ m are commercially available. Regarding integration of electrodes in microfluidic devices, the



Figure 1.4: A detector electrode placed into a glass chip [115].

position of electrode is mostly controlled manually by placing into the prefabricated channels or grooves.

Microwires as electrodes have been used for variety of applications in microfluidic devices. In one study, carbon fiber electrodes were placed into specified channels created in a PDMS device by aide of a light microscope[117]. This device used for capillary electrophoresis with electrochemical detection of nitrite oxide [118]. In another work, platinum wires were inserted into hot-embossed grooves in PMMA [119]. Other materials such as Ni-Cr wires have been integrated into a PDMS device in a complex shape before curing [120]. Also, insertion of gold and copper wires into a glass chip grooved by chemical etching using HF have been demonstrated [115].

Although this method is suitable for rapid prototyping as it is rapid, fast and uses commercially available wires, the choice of material is limited to wires and fabrication of planar electrodes which is necessary in some applications is not feasible. Also, because of integration difficulties, these methods are not cost effective for mid to large volume production. Although there have been some efforts for scalable integration of microwires in elastomer microfluidic devices [121], further studies are still required for more implementation of wires in microfluidics.

#### 1.3.5 Screen and inkjet printing

Screen and inkjet printing are non-vacuum, low cost and direct patterning techniques for deposition of thin conductive films [122]. In these methods, conductive nanoparticles are dissolved in solvents in form of inks/pastes and printed on a substrate by an inkjet or a screen printer. After deposition, the printed ink/paste is dried and sintered using hotplates [123] or other methods such as lasers [124], plasma [125], microwave [126], etc. Conductive inks/pastes are commercially available in form of low to high viscous materials such as platinum, gold, copper, carbon nanotube, etc. Printing of small feature size is limited by size of nozzle heads and jetting conditions such as viscosity of inks and surface energy of substrates [72]. Therefore, electrodes with feature size over 20  $\mu$ m can be fabricated in these methods [127]. Also, the thickness of the printed structures is in the range of several micrometers to hundreds of micrometers [128]. The conductivity of the printed electrodes is typically less than the conductivity of bulk materials and is about 40%-60% of it [122, 126].

Variety of microfluidic devices have been developed using nanoparticle sintering techniques. Carbon paste was used as a self-regulating heater for microfluidic reactors [129]. In another work, screen printed electrodes were used for cell trapping in a dielectrophoresis chip [130]. Despite of easily operation and cost-effectiveness of this technique, there are main disadvantages associated with that. Clogging of inkjet printer nozzles due to viscosity of inks is a frequent problem. Also, quality of electrodes is significantly lower than ones fabricated by PVD or electroplating. Electrodes printed on polymeric substrate are easily cracked by thermal expansion or mechanical bending.

### 1.4 Xurography-lamination: A technique for fabrication and integration of microfluidic components

Xurography was introduced in 2005 by Bartholmoeusz et al. as a rapid prototyping

method for fabrication of microfluidic devices [131]. In this method, a cutter plotter is used to pattern adhesive films. After cutting, the unwanted regions are peeled off and subsequently an application tape is used to transfer the remaining patterns to the desired substrate. The fabrication process is shown in Fig.1.5.



Figure 1.5: Fabrication process in xurography technique [131].

Xurography is a rapid and low cost fabrication technique that makes it a suitable approach for rapid prototyping. Compared to other fabrication techniques, cost of equipment (below \$2000 USD), materials (tens of cents (USD) per square feet), and maintenance (blades and matts are in \$10s (USD)) are significantly lower. The smallest feature size that can be achieved in xurography is over 100  $\mu$ m [131, 132]. One of the main advantage of the technique is that thick structures (>100  $\mu$ m) can be fabricated by xurography easily and rapidly while it is long, cumbersome and sometimes impossible in photolithography and soft lithography approaches. One the other hand, one of the main disadvantages of this technique is the roughness of the channel walls.

Various film materials such as vinyl adhesive, polyimide and polyolefin shrinkable films have been used to construct microchannels in microfluidics. In one study, multi layers of polystyrene were cut and stacked by double sided tape using xurography to fabricate a gradient generator [133]. Also, a spinning disk platform consisting three thin film for polymerase chain reaction (PCR) applications was fabricated by xurography [134]. Also, adhesive film with thickness of 100  $\mu$ m patterned by xurography to be used as channels in a centrifugal microfluidic device for pollutant monitoring [135].

Beside use of xurography to fabricate microchannels in microfluidics, it has been used to fabricate master molds or mask. For example, xurography was used to fabricate a master mold for soft lithography of PDMS for cell culture devices [136]. In another work, a mask made of vinyl adhesive patterned with xurography was incorporated in chemical etching of glass for a electrophoresis microfluidic device [137].

For fabrication of electrodes, xurography has been used as a combinative method to facilitate the fabrication process. For example, it was used to pattern a mask for physical vapor deposition of gold for electrochemical sensors [138]. In another study, it was used to fabricate masks made of vinyl adhesive for electroplating of gold on Compact Disks (CDs). Recently, Liu *et al.* demonstrated using xurography to insert microwires into PDMS microfluidic devices [121].

The use of xurography has been significant for fabrication of microfluidics due to its rapid production without the need for a cleanroom or expensive facilities. Although its resolution is significantly lower than photolithographic methods, it is sufficient enough for microfluidics applications.

#### 1.5 Thesis motivation

As discussed above, state-of-the-art techniques for fabrication of microfluidic devices were reviewed. Semiconductor based techniques, such as silicon and glass micromachining, PVD and chemical etching are highly precise methods which rely on expensive clean-room facilities and photolithography. Other fabrication techniques have been introduced such as soft lithography, hot embossing and micro injection molding, that are suitable for polymeric devices. Although these methods lower the cost of fabrication, they still require a master mold to replicate patterns. Also, it is difficult to integrate multiple materials based on these methods. In addition, direct fabrication methods such as milling, laser machining and 3D printing have been introduced in recent years. Some of these methods are in early stages and require considerable research to enable multimaterial integration into a single device. Also, these methods are not cost effective for mid to large volume production. With respect to electrode fabrication and integration, methods such as inkjet and screen printing are fast and cost effective. However, quality of printed materials and operation of printers are of their limitations. Alternatively, wire integration is a simple method for rapid prototyping of microfluidic devices, but it can only be used in elastomeric devices. Electroplating has been attracted many research work due to its high degree of control and cost-effectiveness. However, need of a conductive substrate for deposition or use of combined methods for pattern transferring are among its limitation.

Xurography is a method that has been developed over a decade ago for rapid prototyping of microfluidics. Although this technique has large capability to pattern variety of materials, it has been mainly used to fabricate microchannels in microfluidics. Combination of xurography with lamination have potential to integrate different materials with different properties to integrate essential microfluidic components such as pumps, valves and electrodes. There are variety of commercially available materials such as thermoplastics, elastomers and metals that use of them as films can reduce the cost of fabrication. Also, these materials have different properties such as insulating, conductive, elastic, hard, soft, hydrophobic and hydrophilic that can provide unique functionality in microfluidic devices.

In particular, this technique has potential to be adapted for fabrication of diagnostic microfluidic devices cost effectively in mid-large volume production. A typical diagnostic device requires microchannel for sample transportation, electrodes for sensing or electrophoresis detection and gels and biomarkers for DNA separation and detection. Meanwhile this device needs to be easy to use and inexpensive. To address all these points, a robust and comprehensive fabrication method is required.

#### 1.6 Thesis outline

The thesis is organized in five chapters as following:

**Chapter 1:** As discussed above, this chapter reviews current techniques for fabrication of microfluidic devices. Most of these techniques are only able to use single or two materials in construction of microfluidic devices due to mismatch in processing conditions. Also, methods for fabrication and integration of electrodes are reviewed. These methods mostly originate from electronic industry and depend on photolithography and sputtering processes. As a result, a robust, low cost, rapid fabrication technique is required that can integrate different materials and fabricate essential microfluidic components such as electrodes in minimum steps.

**Chapter 2:** In this chapter, development of a rapid and inexpensive fabrication technique is described in which xurography and cold lamination methods are combined to build microfluidic devices incorporating multi materials. It is shown that materials with different surface energy and properties provides unique functionality in microfluidic devices. These functionalities include controlling rate of capillary wicking in micro channels, stopping capillary filling in passive valves and integration of elastomer membranes in active valves. Also, utilizing these functionalities, a device capable of autonomous wicking of gel and samples are developed. This device can concentrate DNA from samples in a confined region by electrophoresis. Then, the concentrated DNA is quantified for diagnostic purposes.

**Chapter 3:** In this chapter, the xurography-lamination technique is used to fabricate and integrate micro electrodes in microfluidic devices. This novel method does not need any step for pattern transferring, thus it is fast and inexpensive. This technique uses thin commercially available metal foils as electrode material and patterns them by xurography. This method is capable of creating electrode sizes down to 66  $\mu$ m and pitch sizes as small as 25  $\mu$ m. It is demonstrated that adhesive films can be used to integrate these foils in a microfluidic devices. Finally, different applications such as heating, mixing and electrochemical sensing in microfluidic devices are demonstrated.

**Chapter 4:** In this chapter, a new method for electroplating of high quality electrodes in electroanalytical systems is introduced. In this study, gold and silver electrolytes are mixed with agarose and printed in form of gel droplets. Gel as immobilizing environment reduces the amount of plating electrolytes and enables simultaneous electroplating of gold and silver in a single step without cross deposition. Using this method, , the amount of plating electrolytes is significantly reduced which is crucial for prototyping fabrication. Subsequently, different electrodeposited patterns are shown by printing array of spots or using microfluidic flows on a mask created by xurography. Also, the functionality of the method is demonstrated by fabrication of a three electrode sensor integrated in a microfluidic device.

**Chapter 5:** In this chapter, a summary of the works is presented. Also, the main points of my research contribution to knowledge is summarized. Finally, a few recommendations for future work in this field of study are discussed.
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# Chapter 2

# Rapid and inexpensive method for fabrication of multi-material multi-layer microfluidic devices

## Complete citation:

Mohammadzadeh, Aliakbar, Alison E. Fox-Robichaud, and P. Ravi Selvaganapathy. "Rapid and inexpensive method for fabrication of multi-material multi-layer microfluidic devices." Journal of Micromechanics and Microengineering 29.1 (2019): 015013

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## Contribution:

*Mohammadzadeh A*: Designed and perfomed all experiments, interpretation and analysis of data and wrote drafts of the manuscript including all figures and text.

Selvaganapathy P.R.: Supervised A. Mohammadzadeh and provided guidance with the research focus, idea development, analysis of the results, manuscript revision, and was responsible for the final manuscript submitted to the journal.

*Fox-Robichaud, Alison E.*: Provided advice with analysis of the results and manuscript revision.

# Abstract

The vast majority of polymeric microfluidic devices that have been developed so far feature the use of a single or two material of construction. This is mainly due to the difficulty in integrating multiple materials into these devices using conventional microfabrication techniques such as photolithography, soft lithography or hot embossing either due to mismatch in the processing conditions or due to poor bonding between the materials. Nevertheless, integration of multiple materials into microfluidic devices can enable new and interesting functionalities. In this study, a rapid and inexpensive fabrication technique has been developed in which xurography and cold lamination methods were combined to create microfluidic devices integrating different materials. Materials with different surface energy and properties were used to provide unique functionality. This functionality was shown by fabricating channels that can have varying capillary filling rates from 33 mm s<sup>-1</sup> to 24 mm  $s^{-1}$  by changing the surface energy of the materials that constitute the top and bottom of the microchannels. Similarly, highly robust and integrated passive values that were able to stop capillary filling was also demonstrated by combining patterned features of hydrophobic and hydrophilic surfaces. Integration of thin elastomeric membrane with thermoplastic materials was also demonstrated by fabrication an active pneumatic valve that was capable of stopping capillary flow. Finally, this method of integration of multiple materials, was also used to integrate hydrogels into microfluidic devices in a parallel manner and to confine it locally in specific regions.

**Keywords**: xurography, lamination, microvalves, gel integration, multimaterial, additive manufacturing

# 2.1 Introduction

Microfluidics and lab-on-a-chip technology enable miniaturization, integration and automation of chemical and biochemical assays. This technique has emerged as an alternative to conventional biomedical assays as a result of small volume of sample required and its ability to automate and perform assays faster. A number of microfabrication methods have been developed over the past three decades for the manufacture of these microfluidic devices for scientific, industrial, and biomedical applications [1, 2, 3, 4]. However, most of these methods are confined to the use of single or a few materials primarily due to differences in process conditions and physical properties (such as melting temperatures) of various materials [5]. An easy and robust fabrication technique that is able to integrate different materials into a single device can potentially extend the capabilities of these microfluidic devices into several new application areas.

Historically, microfluidic devices were initially fabricated in either glass or silicon by photolithographic method [5, 6]. Although this technique is highly precise, it is expensive, sophisticated and is limited in the number of materials that can be used. In 1990s, soft lithography was introduced as a rapid prototyping method. In this method, polydimethylsiloxane (PDMS) is casted on a mold fabricated by photolithography [7]. Although soft lithography is relatively fast and inexpensive, it is limited to PDMS which is not often the most suitable material for many biomedical applications due to its ability to adsorb proteins and foul easily. In addition, the method relies entirely on the ability of PDMS to form effective bonding with other surfaces by plasma activation, limiting the number of other materials that can be integrated.

Meanwhile, some other methods that are more suitable for industrial production and commercial applications, including hot embossing [8], injection molding [9] and hot lamination [10], have also been used to produce microfluidic devices. For instance, lamination has been utilized to fabricate masters for microfluidics sturcture using a dry film photoresist [11]. These methods take advantage of glass transition or melting point of thermoplastic materials to structure, reshape and bond multiple layers together. However, using other materials other than thermoplastics, such as thermoset polymers or elastomers, is not possible in these techniques. Even integrating multiple thermoplastic materials that have widely different glass transition temperatures is complex.

Newly emerging methods such as the use of laser machining [12] or 3D printing [13] have been recently used to fabricate microfluidic devices. Although, low cost and promising, they have so far been only used to fabricate devices with limited materials and effective scalable approaches to fabricate multimaterial combinations have not been developed. For instance, mylar films were cut with  $CO_2$  laser and laminated together with pressure sensitive adhesive to fabricate a microfluidic mixer [14]. Also, hydrogels have been fabricated using 3D printing approaches such as stereolithography [15].

Xurography is an alternative direct method that does not need any mold to fabricate microfluidic devices [16, 17, 18]. It uses a cutting blade and its precise motion on a polymer substrate to cut patterns in them. Hence, it is low cost and rapid for prototyping. However, it has so far been used to fabricate single channel microfludic devices. For example, double sided adhesive tapes were cut by a razor blade and sandwiched between two glass slide to detect algal for environmental monitoring [19].

Here, we combine xurography with cold lamination to create multimaterial microfluidic devices where the materials and properties of the individual surfaces of the channels can be made different. Using this technique, we are able to integrate wide variety of materials, like as elastomers and thermoplastics into a single materials. This capability provides unique functionality that may not be possible otherwise. We demonstrate examples of new functionalities by controlling the speed of capillary wicking through the integration of passive and active valves. Finally, we also demonstrate the ability to integrate hydrogels into microfluidic devices in a parallel manner and to confine it locally in specific regions regions that enabled us to quantificaty cell free DNA (cfDNA) in whole blood sample for early diagnosis of septic conditions. These functional components have not been integrated into xurographically defined microfluidic devices before and demonstrated the capabilities that are possible by being able to integrate a diverse set of materials.

# 2.2 Experimental details

## 2.2.1 Materials

Pressure sensitive adhesives (PSA) and thin plastic films were extensively used. In general, PSAs that are commercially available are of three types: transfer, one-sided and double-sided tapes with one or two liners on top and/or bottom. Figure 2.1 illustrates the layers consisting of these tapes. The transfer adhesive tapes used were silicone adhesive (ARseal<sup>TM</sup>-8026, 25  $\mu$ m thickness) and acrylic adhesive (7951MP, 50  $\mu$ m thickness) obtained from adhesive research (AR), Glen Rock, PA and 3M<sup>TM</sup>,Maplewood, MI) respectively. The one-sided adhesive tapes used were polyolefin film with acrylic adhesive (9793R-3M<sup>TM</sup>, 81  $\mu$ m), polyolefin film with silicone adhesive (9795R-3M<sup>TM</sup>, 100  $\mu$ m), polyester film with acrylic adhesive (93049-AR, 100  $\mu$ m and 9969-3M<sup>TM</sup>, 100  $\mu$ m) and polyimide film with silicone adhesive coated on polyester film (7535ARclad-AR, 94  $\mu$ m) and acrylic adhesive on poleyester film (90178-AR, 89  $\mu$ m). These adhesive do not elicit any adverse biological response and do not affect cell growth and viability.

Hydrophilic low contact angle Polyester film (9984, 99  $\mu$ m) was from 3M<sup>TM</sup> and polyvinyl chloride (PVC) films (Clear-Lay, 75–250  $\mu$ m), and polyester (PET) films (Duralar, 25–250  $\mu$ m) were from Grafix (Maple Heights, OH). Also, PVC films (3 mm) were obtained from McMaster-Carr (Cleveland, OH). A non-sticky liner was obtained from AR. PDMS Sylgard 184 was from Dow Corning (Midland, MI) and Agarose 1% was from BioShop Canada Inc (Burlington, ON). Superhydrophobic Spray, Neverwet®was from Rust Oleum Corporation (Vernon Hills, IL) and silicon wafers were from University Wafer (Boston, MA).

The surface wettability of the films used here was measured using KRUSS DSA100 goniometer. In this process, 6  $\mu$ l of DI water was dropped on the surface and the software of the equipment analyzed the contact angle. The results are shown in table 2.1 demonstrate that materials that were superhydrophilic to super hydrophobic were included



Figure 2.1: Different types of pressure sensitive adhesive tapes.

Film model	93049- AR	PET	PVC	Polyethylene (backside of 9795R-3M <sup>™</sup> )	9795R- 3M <sup>™</sup>	9984- 3M <sup>™</sup>	8026-AR	7951MP- 3M <sup>™</sup>	PDMS	Kapton tape	Superhydro-phobic coating
Adhesive	Acrylic	_			Silicone		Silicone	Acrylic	NA	Silicone	NA
Contact angle (degree)	80 to 10	70	95	95	105	45	106	107	113	117	160

Table 2.1: Contact angle of various films.

in the range of films and adhesives used. It should be noted that in the case of the hydrophilic adhesive, initially the contact angle was around 80 degrees, but after one second, the droplet spread out on the film and the contact angle was reduced to 10 degrees. The kapton film was the most hydrophobic material among those tested. The superhydrophobic coating (Neverwet®) was sprayed on different films and the contact angle obtained was 160 degrees irrespective of the substrate.

## 2.2.2 Fabrication process

The fabrication process is based on the laminated object manufacturing approach in additive manufacturing. In this approach, 2D layers that are patterned using a variety of methods are aligned and stacked upon each other and laminated to create a 3D structure. In a similar manner, 2D layers constituting the top, bottom and sides of the microfluidic channels are patterned using xurography (supplementary figure S1 (stacks.iop.org/JMM/29/015013/mmedia)), aligned with each other and cold laminated [14] to form a multilayer stack that consitutes a microfluidic network. With the use of cold

lamination a variety of material types can be used to constitute the individual layers and integrated into the final product.

#### 2.2.2.1 Creating 2D patterns on films

Large films and tapes rolls were cut to smaller sizes by a mat cutter, Logan Graphics Product (Wauconda, IL). Then, as shown in figure 2.2(a), a cutting plotter, FC-8600, Graphtec America (Irvine, CA) was used to create patterns on these films. Features that correspond to the channels, inlet and outlets were cut and peeled off. In order to cut PVC and PET films, a backing was required. Hence, a layer of one-sided adhesive tape, (9793R-3M<sup>TM</sup>) was laminated to PVC and PET films by a cold laminating machine (ASC365 LTD, Canada). Since the adhesive tapes already had their releasing liners which could be used as a backing, there was no need for additional backing support. Specific blades were used in the plotter based on the thickness of the films to be cut and the resolution of the patterns. Blade CB09UB for cutting films up to 0.25 mm, CB15U for cutting films up to 0.5 mm, CB15U-K20 for cutting films up to 3.0 mm and CB15UB for cutting ultra-fine patterns (less than 100  $\mu$ m) were used.

#### 2.2.2.2 Alignment stage and assembly

A backing and alignment stage was also fabricated using xurography. A 3 mm PVC film was laminated with backing layer as mentioned above. Two rectangles  $(7.62 \times 15.2 \text{ cm})$  with four holes (diameter 3/8'') on its corners were cut by the cutter plotter. After cutting, the two rectangular PVC pieces were peeled off cleanly leaving behind the backing layer. These rectangular pieces were used as alignment stages for insertion of the alignment pins and for assembly of the subsequent patterned layers.

After cutting and patterning individual films (figure 2.2(a)), each layer was placed on one of the two alignment stages and they were secured by four dowel pins (McMaster Carr, OH) inserted into the alignment holes. A non-sticky liner was inserted between successive cut layers to avoid adhesion of PSA surfaces to the adjacent films during the assembly and alignment process. The top edge of the films that have the two alignment holes do not have the non sticky liner which allowed the two films to be fixed after alignment. Next, the dowel pins and the alignment stages were removed and stacked layers placed under the cold laminator. As the stacked layers moved into the laminator, the non-sticky liner was slowly removed and the entire area of PSA was activated (figure 2.2(b)). By repeating the cutting, alignment and assembly processes, several layers of films with different properties and thickness were stacked and microfluidic devices were fabricated. The entire fabrication process takes less than 1 h and is scalable to fabricate several tens of devices within this time.



Figure 2.2: Process flow for fabrication of multi-layer and multi-material microfluidic devices using xurography and cold lamination technique (a) patterning layers by a cutting plotter (b) assembly of the layers by a cold laminator.

# 2.3 Results and discussion

## 2.3.1 Fabrication of multimaterial microchannels

Using the described layer by layer manufacturing technique, layers with different materials and thicknesses were assembled efficiently. Polymers films that are commercially available range from 25  $\mu$ m to 1.5 mm in thickness and can be easily patterned with cutter plotter and bonded to other materials by sandwiching a transfer adhesive tape between them. One sided or double-sided adhesive tapes that are available in thicknesses in the range of 100–200  $\mu$ m can be used with cold lamination to bond the plastic layers with each other. The variety of adhesive tapes that are available provide a suitable combination that is appropriate for the different film materials that need to be bonded. For instance, silicone based adhesives are suitable choices for bonding silicone elastomers to other polymers and acrylic based adhesives are suitable for high surface energy materials. Also, silicone-based adhesives are more chemical resistant and they are less auto fluorescent while acrylic adhesives have variety range of hydrophobic/hydrophilic surfaces. Most of the devices are passive microfluidics and they do not require external connectors. However, for the burst pressure testing and pneumatic valves, the connectors attached to the devices by transfer adhesive tapes.

#### 2.3.1.1 Burst pressure testing

Leakage in microfluidic devices due to bonding issues has been the bane of many microfluidic fabrication methods that have been developed. Since the devices made by our technique have several layers bonded to each other by adhesive materials, characterization of strength of adhesive bonding was key to establishing this as a viable fabrication method. To demonstrate the strength of adhesive bonding in the method, several devices with different adhesives were fabricated. Each device consists of three layers. The top layer was an adhesive tape into which appropriate patterns for the inlet and the outlet reservoirs have been cut out. The middle layer was a PET film (125  $\mu$ m thickness) into which a microchannel (20 mm Length, 0.5 mm Width) has been cut out. The bottom layer was the same adhesive film as the top layer without any patterns and functioned as the bottom substrate (figure 2.3(a)). The layers were aligned and laminated according to the procedure described above. The alignment accuracy was 100  $\mu$ m. Various adhesive tapes such as 7951MP-3M<sup>TM</sup> (acrylic based-hydrophobic), 9795R-3M<sup>TM</sup> (silicone based-hydrophobic) and 93049-AR (acrylic based-hydrophilic) were used to identify the adhesive best suited for this purpose.

In order to find the failure point of the devices made by adhesive tapes, the burst pressure test was conducted as follows: After assembly of the layers, Tygon tubes were connected to the inlet and outlet of each microfluidic device via connectors (17625, QOSINA, US). Then, the outlet was connected to a pressure transducer (Omega PX273, 300DI) and the inlet to a syringe pump (Harvard Apparatus, Holliston, MA). Water was infused to the tube with the flow rate of 1 ml min<sup>-1</sup>.

The pressure at the inlet of the microfluidic devices made of different adhesive tape recorded. The failure depends on the strength and properties of adhesives used for bonding the layers. For each adhesive tape, the experiment was repeated five times. The hydrophobic acrylic adhesive tape (7951,  $3M^{TM}$ ) produced a burst pressure of  $395\pm6.54$ kPa showing a very strong bonding. The hydrophobic silicone adhesive tape (9795R,  $3M^{TM}$ ) had a burst pressure of  $323\pm21.89$  kPa while the acrylic hydrophilic tape (93049-AR) indicating a relatively weaker bonding with burst pressure of  $98\pm8.07$  kPa (figure 2.3(b)). These results reveal that microfluidic devices made by lamination technique have sufficient bond strength and can form leak proof seal suitable for many common microfluidic applications. As a comparison, PDMS to PDMS bonded by O<sub>2</sub> plasma has burst pressure of 300 kPa [20].

#### 2.3.1.2 Controlled filling of microchannels

Use of capillary forces to transport samples has been used in many biochemical assays, most notably in the glucose biosensor. This passive method of sample transport eliminates the need for external instrumentation such as pumps and syringes and enables easy and inutitve operation of a point of care device. However, capillary filling is highly dependent on the surface properties of the materials used and it is often difficult to modulate it. Nevertheless, new capabilities such as control of residence time to perform an in situ reaction can be realised if an effective technique to modulate the capillary filling were achieved.



Figure 2.3: (a) Schematic view of the layers and patterns used to fabrication a microfluidic channel. This channel was used in burst pressure testing, (b) burst pressures obtained using various adhesives for bonding (n = 5). Hydrophobic adhesive tapes generally have higher bond strength compared to hydrophilic adhesives.

The speed of filling can be approximated by a modified Hagen–Poiseuille flow equation
[21]:

$$\nu = \gamma \frac{h^2}{S\mu} \frac{\triangle P}{L} \tag{2.1}$$

Where v is velocity of the filling, L is the length of the channel by time, h is the height of the channel,  $\mu$  is the liquid viscosity and  $\Delta P$  is the pressure difference inside the channel. Also, S is a constant depending on the geometry of the channel (S = 12 for slit, S = 32 for circular, S = 28.45 for square) [22]. Finally,  $\Delta P$  or capillary pressure inside the rectangular microchannel can be modeled by [23]:

$$\Delta P = -\gamma \left(\frac{\cos(\alpha_b) + \cos(\alpha_t)}{h} + \frac{\cos(\alpha_l) + \cos(\alpha_r)}{w}\right)$$
(2.2)

Where  $\gamma$  is the surface tension of the liquid, h and w are height and width of the channel and  $a_{(b,t,l,r)}$  represents the contact angles of the liquid–solid–air on the bottom, top, left, and right wall, respectively. The equation indicates that the capillary pressure can be easily controlled by changing the contact angle of the microchannel walls. In multi-layer

multi material structure fabricated by the lamination technique, one could control the surface contact angle of each of the walls constituting the microchannel by incorporating the appropriate material in that respective layer.

In order to demonstrate the unique functionality that is possible with a channel with multi material surfaces, we fabricated two different microfluidic devices with combination of hydrophobic and hydrophilic surfaces. One channel was fabricated with a hydrophilic top and bottom layer and the other with the top hydrophilic and the bottom hydrophobic. The channel had dimensions of 1 mm (W), 89  $\mu$ m (H), 10 cm (L) and was cut through a double sided adhesive tape (90178, AR) which formed the channel layer in both the devices. The top surface was a hydrophilic film (9984, 3M<sup>TM</sup>) for one device and a PVC film (Graphix) for the other device. Finally, the bottom surface a hydrophilic film (9984, 3M<sup>TM</sup>).

After fabrication of the device, 100  $\mu$ l of water containing methylene blue for visualization was placed at the inlet and the position of the filling front of liquid was measured by a camera (CoolpixNikon, Tokyo, Japan)(figure 2.4(a)).

The results (figure 2.4(b)) shows that these channels support capillary filling of water as expected. The speed of filling was about 24 mm s<sup>-1</sup> at the first second and gradually reduces as it proceeds in the case when the top surface was hydrophobic and the bottom was hydrophilic. When it reached to 10 cm position, it has an speed of 3 mm s<sup>-1</sup>. On the other hand, by changing the top wall to hydrophilic the speed of filling increased. At the first second it had a speed of about 33 mm s<sup>-1</sup> and it became about 7 mm s<sup>-1</sup> when it reached to 10 cm position. More importantly, the speed of filling and the filling distance follows calculated values closely. Finally, channels with hydrophobic top and bottom surface did not fill at all. Thus multimaterial combinations with different surface properties can be combined with xurographic patterning to provide different filling speeds in different regions of the microfluidic devices.



Figure 2.4: (a) Position of meniscus of capillary flow versus time in two microfluidic devices with the same geometry but made of different materials, (a) meniscus' positions at different times, (b) comparison of position of meniscus in two devices versus time (n = 5).

## 2.3.2 Fabrication of valves using multimaterial combinations

Integrated values are critical in microfluidic devices for various operations including, aliquoting, mixing and sequencing of reagents. Passive values that use change in surface property from hydrophilic to hydrophobic has been used as a way to stop and position the fluid in capillary flow devices [24]. Similarly, use of an elastic membrane that can be pneumatically actuated so that the underlying fluidic channel can be closed has been used widely in externally pumped microfluidic devices [25]. Both of these values require the integration of multiple materials with different properties into the geometry and we demonstrate the use of xurogrpahy and lamination technique for these purposes.

#### 2.3.2.1 Super hydrophobic valve barrier

Passive values are used in capillary flow devices to stop the fluid filling at a particluar location. The value provides sufficient resistance to balance the capillary pressure. The value can be opened by applying a small external pressure to overcome the resistance. It is often a onetime use system and once the value area is inundated fully with fluid, its value function is lost. An abrupt opening in channel geometry has been used to pin the fluid air interface and function as a passive valve [24]. Alternatively, a hydrophobic surface barrier has also been used to stop capillary filling [26].

In order to integrate a passive microfluidic valve the following fabrication process was developed. First, a 1 mm diameter hole was patterned on a non-adhesive liner (AR) using the cutting plotter. Then, this liner was used as a mask, placed on the hydrophilic adhesive, aligned and a super hydrophobic spray was used to coat the surface of the tape in the hole. This patterned hydrophilic layer was used as a bottom layer of the device. A second layer with a thickness of 100  $\mu$ m containing a microchannel pattern with dimensions of 400  $\mu$ m (W), and 20 mm (L) was cut from 9795R-3M<sup>TM</sup> polyolefin adhesive tape. Finally, the top layer with patterns for inlet and outlet (circles with radius of 2.25 mm) was made of 9795R-3M<sup>TM</sup> adhesive tape (figure 2.5(a)). The device was designed in a way that the top wall of the channel was hydrophobic and the bottom wall was hydrophilic that allows the liquid to wick in. However, in the valve region both the top and bottom surfaces were hydrophobic which stops the flow. The layers were assembled and laminated with each other and the final fabricated valve region is shown in figure 2.5(b).

To test the functioning of the valve, a droplet of DI water mixed with methylene blue dye was placed at the inlet of the channel. The liquid wicked into the channel rapidly but stopped at the barrier as shown in figure 2.5(c). The hydrophobic barrier was found to be stable for more than 5 min. Application of a small pressure (of 1.5 kPa) at the inlet was sufficient to overcome the resistance at the valve and cause the liquid to quickly flow past it and fill the rest of the channel up to the next barrier (figure 5(d)). The capillary pressure inside the microfludic channel dictates the fluid flow in it. At the inlet and inside the channels both the top and the bottom surface is hydrophilic. The capillary pressure calculated from equation 2.2 was 490 Pa and was sufficient to pull the liquid into the channel from the inlet. However, when it arrives at the valving region, it encounters a bottom surface that is hydrophobic. The capillary pressure changes at this region to -910 Pa which provides a resistance to flow. The edge where the bottom surface changes from hydrophilic to hydrophobic functions like an energy well as the system energy is minimum when the liquid has filled upto that location. Therefore, the liquid column is stable and this configuration serves as a passive valve. When a positive pressure was applied at the inlet, it overcomes the energy well and pushes the liquid past the passive valve. Once the liquid reaches the other side where both the top and bottom are hydrophilic, the capillary pressure becomes positive again and the liquid quickly continues to fill the channel beyond the valving region till it reaches another barrier.



Figure 2.5: Hydrophobic valve barrier, (a) schematic view, (b) before filling, (c) filling stopped at the barrier (d) after applying pressure at the inlet in order to push the liquid to pass the barrier and reach the next barrier. Scale bar 500  $\mu$ m.

#### 2.3.2.2 Hydrophobic valve bridge

A completely xurographic based approach using multiple layers with different materials can also be used to create passive valve structure. The schematic view of such a device is shown in figure 2.6(a). In this design, a base layer consists of two channels that form the inlet and the oulet for the valve. These channels have a hydrophilic bottom surface and a hydrophobic top surface and are disconnected from each other by a small gap. The second or the valve layer consists of a short bridging channel that has both its top and bottom surfaces as hydrophobic. The bridging channel is aligned and positioned such that it connects the inlet and the outlet channels.

In order to realise this passive valve structure, a four layer microfluidic device was fabricated. The bottom layer of the device was made of the hydrophilic PET film (9984,  $3M^{TM}$ ) and was not patterned. The second layer containing two separated channels with dimensions of 1 mm (W), 125  $\mu$ m (H), and 14 mm (L) was cut through another PET film and formed the sidewalls of the inlet and outlet channels. The third layer was made of hydrophobic adhesive (9795R,  $3M^{TM}$ ) and the bridging channel design with dimension of 400  $\mu$ m (W), 100  $\mu$ m (D) and 1 to 5 mm (L) was cut into it. This layer forms the top surface of the inlet and the outlet channels as well as the bottom surface of the bridging channel. The fourth layer was an unpatterned film made of the same material as the third layer and formed the top surface of the bridging channel.

After assembly of the devices consisting of a passive valve, a droplet of deionized water mixed with methylene blue was place on the inlet of the device. Initially, the speed of the front filling of the liquid was  $24 \text{ mm s}^{-1}$ , but when it reaches the hydrophobic region, it completely stopped. After about 5 min, the liquid a small inlet pressure was applied by squeezing the inlet interconnect made of elastic Tygon tube (outer diameter 1 cm). This pressure was sufficient to overcome the resistance offered by the hydrophobic bridging channel and the liquid flowed across the bridge, quickly filling the outlet channel (figure 2.6(b)). Also, in order to determine the impact of using multimaterial for functioning of the device, another

device in the same geometry but made of only hydrophilic materials were fabricated and the valve was not able to stop the flow (supplementary figure S2).

The valving effect in this device is due to the changes in surface energies as the liquid attempts to flow from the inlet channel into the valving region. As equation 2.2 shows, the pressure inside the capillary depends on channel dimensions and contact angles of the water with walls. The liquid in the inlet channel encounters a hydrophilic  $(45^{\circ})$  bottom surface while its top surface is hydrophobic. The capillary pressure generated in this configuration was 298 Pa which is sufficient to allow wicking till it reaches the valve region. In the bridging channel the top and the sidewalls are highly hydrophobic while the bottom surface is mildly hydrophobic  $(95^{\circ})$ . Thus the capillary pressure changes to -312 Pa which effectively stops any flow past this region. This energy well thus formed is stable enough to hold capillary flow for a long duration of time till it is actuated by a pressure pulse.



Figure 2.6: Hydrophobic valve bridge, (a) schematic view, (b) time wise images for different valve sizes, step 1- before filling, step 2- liquid stopped at the entrance of the valve, step 3-liquid passed the bridge by applying pressure at the inlet. Scale bar 2 mm.

#### 2.3.2.3 Pneumatic valve

Passive values are generally one time use components and an active mechanism is needed to dynamically control the flow across a value structure. Active values switch between an open and closed state by using an external actuator. One class of active values, known as diaphragm values, have a flexible membrane, adjacent to the flow channel, which can be deflected by an actuator thereby constricting or stopping flow in the channel. The external actuator can be electrical [27], magnetic [28], pneumatic [29], thermal [30] or optical [31]. These valves have been made using shape memory alloy wires of Ni/Ti [32], phase changing materials, PEG [27] and permanent magnets [33].

A widely used active valve format in microfluidics is based on deflection of PDMS membrane that is adjacent to a microchannel by pneumatic pressure [34]. A thin membrane of PDMS is sandwiched between two intersecting channels and when pressure is applied through channel, the membrane deflects into the other channel and constricts flow. Although effective, PDMS membrane based active pneumatic valves have been demonstrated only in all-PDMS devices where the rest of the microfluidic structures are also made of PDMS. This is due to the strong oxygen plasma initiated bonding that is achievable between PDMS layers.

Here we demonstrate the integration of elastomeric PDMS membrane inside rigid polymeric microfluidic devices for active valving using the xurographic approach. The device design consists of a thin PDMS membrane that is sandwitched between two plastic layers composed of two channels. The channel on top carries the liquid whose flow is to be controlled. The channel at the bottom is the actuation channel through which pneumatic pressure is applied to deflect the PDMS membrane at the region where these two channels intersect.

The schematic design of the active valve structure is shown in figure ??(a). The fabrication process of the device is as follows: The bottom layer was made from silicone adhesive tape (9795R-3M<sup>TM</sup>) and served as the bottom surface of the fluid channel with no patterns on it. The second layer was made of 9795R-3M<sup>TM</sup> adhesive tape and served as side walls of a microchannel with dimensions of 600  $\mu$ m (W), 10 mm (L) and 100  $\mu$ m (H) that was used for pneumatic activation of the valve. The third layer was made of a thin membrane of PDMS which was fabricated as follows. 1 ml of PDMS was poured on top of a silicon wafer placed on a spin coater (6800, SCS Inc., Indianapolis, IN). The spinning

rate was set to 2500 rpm for 1 min to obtain 25  $\mu$ m thickness. The wafer was placed on a hotplate set to 70 °C for 40 min. After curing, the membrane was peeled off and bonded to the second layer. Next, the fourth layer, made of 9795R-3M<sup>TM</sup> adhesive tape, was cut in shape of a microchannel with dimension of 600  $\mu$ m (W), 10 mm (L) and 100  $\mu$ m (H) to serve as the liquid flow channel and bonded to the membrane by cold lamination. Finaly, the last layer was made of 9795R-3M<sup>TM</sup> adhesive tape and was patterned in shape of circles with 2.25 mm radius which served as the inlet for air and the inlet and outlet for liquid (figure 2.7(a)).

After assembly, the inlet and outlet of the device were bonded to two male luer locks (Qosina)using a 7951-3M<sup>TM</sup> transfer adhesive tape (supplementary figure S3). Tygon tube was connected to the luer locks and water with methylene blue was infused to the microchannel by a syringe pump (Harvarad Apparatus, Hollistion, MA) at flowrate of 5 ml  $h^{-1}$ . Also, a compressed air line was connected to the air channel. When the compressed air line was at ambient pressure and the liquid easily flowed through the liquid flow channel (figure 2.7(b)). When the valve was pneumatically actuated and the air channel was connected to a 103 kPa pressure source through a switch, the thin PDMS membrane sandwiched between the xurographically cut plastic layers deflected into the flow channel and closed it (figure 2.7(c)). As a result, by switching the compressed air line to on or off, the silicone membrane was pneumatically actuated and the fluid flow in the lower channel regulated. By increasing the back pressure, the compressed air pressure was increased to completely block the liquid pathway. For 6.5, 7.8, 9.1 and 10.4 kPa back pressures, 138, 172, 207 and 241 kPa pressure of compressed air was needed. At a pneumatic pressure of 280 kPa pressure the valve failed due to delamination of the PDMS layer from the adhesive. Therefore, device fabricated with the lamination method enables us to integrate PDMS membrane with other materials and due to high bonding strength, the failure was low. Also, since PDMS has low surface energy, most adhesive types, especially acrylic based ones do not bond with it. However, silicone based adhesive types are ideal for
bonding with low surface energy materials, especially PDMS. Therefore, a silicone based adhesive was chosen to bond with PDMS surface. Consequently, the pneumatic failure of the valves was significantly reduced.



Figure 2.7: Active pneumatic valve using PDMS membrane, (a) schematic view, (b) valve not activated, (c) valve activated. Scale bar 600  $\mu$ m.

#### 2.3.3 Gel integration

Hydrogels have been widely used in microfluidics for biochemical assays [35, 36], bacterial chemotaxis [37] and cell migration [38]studies. In many of these devices, hydrogels are required at certain regions of the device and have to form an interface with the sample solution. Hydrogels have been patterned and integrated in microfluidic devicesusing soft lithography [39], flow confinement [40] and UV patterning [41] methods. In soft lithography, structures and patterns on a mold were replicated on casted hydrogels which were then integrated into plastic channels. Weak sealing between the hydrogel and the

plastic channels can cause small gaps along the interface that make this method not suitable for many applications. In the flow confinement method, microchannel network with hydrophobic [42] or hydrophilic surfaces [37] were used to confine the flow to certain regions of the device and solidify. In hydrophobic surface control, the gel was pushed into microchannel by small and precise back pressure while in hydrophilic surface control, capillary pressure inside the channels pull the gel solution into microchannel. UV-cure method is easy to integrate into microfluidic devices, since it uses a laser to pattern and polymerize hydrogels inside microchannels [43]. However, this method is expensive and require sophisticated instrumentation and it has not been widely used.

An example of a microfluidic device requiring integration of gels is one that has been recently developed for quantification of cfDNA in whole blood sample for early diagnosis of septic conditions [44, 45]. Here the gel is used as a mobility trap to concentrate and collect cf-DNA from the sample using electrophoretic methods. Although this prototype demonstrated rapid quantification of cf-DNA, integration of hydrogel into the device and confining it to only one of the intersecting channels was found to be difficult leading to long and complicated process of loading which resulted in low yield of functional devices.

For this purpose, a device capable of autonomous wicking of gel and samples was designed as shown in figure 2.8(a). It consists of a gel channel intersecting with a sample channel. By appling an electric field through channels, the DNA from sample channel can be attracted into the gel channels and made to accumulate at the intersection area. The amount of accumulated DNA is quantified for diagnostic purposes.

The fabrication process for the devices is as follows: The bottom layer was made of hydrophilic adhesive tape (93049, AR) that was not patterened and served as the bottom surface of the gel channel. The second layer was made of PVC film and was cut in the shape of the gel channel with dimension of 700  $\mu$ m (w), 175  $\mu$ m (H), 6 mm (L). This layer was served as the side walls of the gel channel. The third layer was made of hydrophobic adhesive tape (9795R, 3M<sup>TM</sup>) and was cut in the shape of sample channel with dimensions of 200  $\mu$ m (W), 80  $\mu$ m (H) and 6 mm (L). The fourth layer was made of hydrophilic adhesive tape (93049, AR) and was cut in the shape of a small circle, 0.35 mm (radius), above the intersection of the two channels. The last top layer was made of hydrophobic adhesive tape (9795R, 3M<sup>TM</sup>) and was patterned in the shape of circles, 2.25 mm, functioning as inlets and outlets (figure 2.8(a)).



Figure 2.8: Multilayer intersectional channel valve, (a) schematic view, (b) confining liquid in only one of the intersectional channels.

Next, a droplet of 1% agarose gel was dropped on the accumulation channel inlet. As a result of the hydrophilic nature of the bottom surface of the gel channel, the agarose solution wicked rapidly into the channel. At the intersection region, the circular cutout in the valving reagion was crucial in ensuring the reliable confinement of the gel to the bottom channel and prevent its wicking in the to top channel. It formed the required tight interface with the sample channel and had a 90% yeild producing consistent and functional device. Next, a droplet of the sample was dropped on the sample channel inlet. Due to hydrophilicity of the top channel, the sample fills the channel automatically creating a bubble free interface with the gel layer.

In order to investigate the applicability of this device,  $\lambda$ -DNA was diluted with Picrogreen DNA intercalating dye (Thermo Fisher Scientific, Waltham, MA) that resulted in the final concentration of 5 µg ml<sup>-1</sup> of DNA. The sample (<10 µl) was loaded into the device by placing a drop of solution at the sample channel inlet. Due to the hydrophilic top surface of the sample channel, it quickly wicks in and forms a bubble free interface with the hydrogel at the intersection region. Next, anode and a cathode electrodes were placed at the accumulation channel inlet and the sample channel outlet, respectively. A 9 V DC potential was then applied for 5 min to accumulate the DNA from the sample on to the gel. Therfore, DNA from the sample was extracted and concentrated into the gel at the intersection by electrophoresis. The concentration of Picogreen labeled DNA into the gel was measured by its fluorescence intensity (figure 2.9). The results reveal that  $\lambda$ -DNA was clearly trapped into the gel after electrophoretic accumulation. It is gel was prevented from wicking up into the sample channel due to the hydrophobic top surface of the circular passive valve region and was confined to the bottom channel (figure 2.8(b)) where it continued to flow to the gel channel outlet. The interesting to note that the leak proof sealing was obtained between the gel and the channels as the agarose fills the channels quickly before solidifying in position.



Figure 2.9: DNA accumulation by electrophoresis in agarose gel, (a) before applying 9 V, (b) after 3 min, (c) after 5 min.

A control experiment was also performed by fabricating the same geometry using only hydrophilic material to identify if the multimaterial combination is needed. The results (shown in supplementary figure S4) revealed that the wicking gel material was able to breakthrough the intersection region and also filled the top channel. This demonstration shows the need for the use of multimaterial combinations in certain applications.

In order to demonstrate the scalability of this approach to integrate gels into microfluidic devices, another device with multiple intersection regions was designed. It has one long channel for flowing the gel into appropriate locations that intersects with sample channels at multiple points. The configuration of layers was the same as before. In this device the bottom channel was a serpentine path with total length of 30 mm and six parallel microchannels on top of the bottom channel (figure 2.10(a)). The same process was conducted to fill the device with a serpentine channel and six parallel channel on top (figure 2.10(b)). Since the gel channel was long and it required longer time to be filled, the device was placed on a hot plate (VWR, Radnor, PA) set on 85 °C to avoid gelation of the agarose during the filling. As it can be seen, during filling of the gel channel, the gel was confined to the channel without wicking the top channels which demonstrates the robustness of this approach. Also, the top channels filled with the sample without allowing the sample to go through the gel channel. The device has 12 analysis spots and can be used with four different samples. This demonstration shows that multimaterial combinations can be used to integrate other functional materials such as gels easily and precisely into microfluidic devices.



Figure 2.10: Multilayer intersectional parallel channels, (a) bottom channel filled with hydrogel (blue), (b) loading sample in top channel (red).

# 2.4 Conclusion

In this study, a fast and inexpensive technique for fabrication of microfluidic components is introduced. By combination of xurography and cold lamination, multimaterial multilayer

structures were integrated into microfluidic devices. The speed of capillary wicking was controlled by changing the surface energy of the walls inside microchannel. In one case, water filled a slit channel with top and bottom hydrophilic by speed of 33 mm s<sup>-1</sup> at the beginning and  $7 \text{ mm s}^{-1}$  after 7 s. While for the other case in which the top wall was changed to hydrophobic, the speed of filling was 24 mm s<sup>-1</sup> at the beginning and 3 mm s<sup>-1</sup> after 16 s. Also, a passive valve was integrated into microfluidics by creating a superhydrophobic barrier on the way of a hydrophilic channel. Furthermore, another passive valve was created by changing the geometry of the channels along with change in surface wettability of the walls. The sudden change in surface energy resulted in the formation of an energy well that stopped fluid flow at a precise spatial position in the channel. This bridge valve had multilayer structure and different lengths of it were successfully tested. Additionally, a pneumatic active valve was fabricated by integration of elastic membrane with thermoplastic microfluidic channels. A thin membrane of PDMS was sandwiched between two intersectional channels and when compressed air applied through one of the channel, the membrane blocked the liquid channel due to deflection. By applying 240 kPa compressed air, the active valve blocked the liquid channel with back pressure of 10 kPa. Finally, integration of gels and its confinement into certain regions of the microfluidic device was also demonstrated using a multimaterial stack. The device was capable of autonomous wicking of hydrogels and biomedical samples and demonstrated that robust gel regions with tight sealing between the gels and channels can be fabricated in a scalable manner for DNA quantification applications. The fabrication methods described here and the application examples shown demonstrate that this platform technology of combining xurography with cold lamination is broadly applicable and can be used for manufacture of a wide range of microfluidic devices with applications in diagnostics, cell culture and as microreaction engineering.

# Acknowledgements

The authors wish to acknowledge funding from NSERC and CIHR through the Collaborative Health Research Program (CHRP 493620-16). AM wishes to acknowledge support from Ontario Graduate Scholarship Program. PRS wishes to acknowledge support from the Canada Research Chair Program and the Discovery Accelarator Supplement award.

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# Chapter 3

# Rapid and inexpensive method for fabrication and integration of electrodes in microfluidic devices

#### Complete citation:

Mohammadzadeh, Aliakbar, Alison E. Fox-Robichaud, and P. Ravi Selvaganapathy." Rapid and Inexpensive Method for Fabrication and Integration of Electrodes in Microfluidic Devices." Journal of Microelectromechanical Systems, 2019, Digital Object Identifier: 10.1109/JMEMS.2019.2914110.

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#### Contribution:

*Mohammadzadeh A*: Designed and perfomed all experiments, interpretation and analysis of data and wrote drafts of the manuscript including all figures and text.

Selvaganapathy P.R.: Supervised A. Mohammadzadeh and provided guidance with the research focus, idea development, analysis of the results, manuscript revision, and was responsible for the final manuscript submitted to the journal.

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# Abstract

Electrodes are essential components in a number of microfluidic devices for sensing and actuation. Current methods for electrode fabrication in microfluidic devices are mostly derived from the electronic industry and rely on expensive photolithography and sputtering processes. Here, we demonstrate that a combination of xurography and cold lamination can be used to fabricate and integrate electrodes in microfluidic devices. This method is fast, inexpensive, direct and does not require any intermediate layer for pattern transfer. This method utilizes thin metal foils that are commercially available at low cost and with a large variety of materials in fabrication of electrode structures. We demonstrate that using xurography, electrode sizes down to 66  $\mu$ m and pitch sizes as small as 25  $\mu$ m can be obtained using these foils. After patterning, the electrodes were bonded to plastic films using pressure sensitive adhesives and integrated into microfluidic devices which were also fabricated using xurography approach combined with cold lamination. We demonstrate various applications of these electrodes as electrochemical sensors, as heaters for temperature control and as electrokinetic mixers. This simple method is low cost and produces electrode structures that are ideally suited for application in microfluidic and lab-on-a-chip devices.

**Index Terms**: Microfabrication, xurography, lamination, electrochemical sensors, labon-a-chip

## 3.1 Introduction

Electrodes are essential part of lab-on-a-chip devices and have been used in a broad range of applications such as electrochemical detection and electrokinetic transportation [1]. A number of fabrication methods to integrate electrodes into microfluidic devices have been investigated over the past 30 years [2]. However, most of these methods are suited for electronic fabrication that require high resolution, densely packed metal interconnects and are unsuited and expensive for lab-on-a-chip devices that typically do not need high resolution or density [1].

Photolithographic patterning combined with sputtering or evaporation are the most commonly used method for fabrication of electrodes in most microfluidic devices [3, 4, 5]. These thin film methods originate from the electronic industry and may be more suitable for electronic fabrication where sub micrometer precision is required rather than for microfluidic applications. Although precise and scalable, these microfabrication processes require vacuum conditions, clean room facilities and multiple process steps, making them expensive and unsuited for the needs of microfluidic devices that have low density of electrodes and don't in many cases require sub-micrometer resolution. For example, electrodes in size of 40  $\mu$ m was fabricated by sputtering technique for electrochemical detection chip [6]. In another work, 250  $\mu$ m size platinum electrodes were used in a real time polymerase chain reaction (RT-PCR) device [7].

Recognizing these limitations, alternate approaches to fabricate and integrate electrodes into microfluidic devices have been developed. A simple approach is to create grooves or channels in microfluidic chips into which wire electrodes can be inserted prior to bonding. An example of this approach is where carbon fiber electrodes were inserted into Polydimethylsiloxane (PDMS) device made by soft lithography [8]. Similarly, platinum wires have been inserted into grooves created in Poly (methyl methacrylate) (PMMA) device made by hot embossing [9]. McCreedy et al. showed that Ni-Cr wires can be easily inserted into a PDMS solution in a serpentine shape before curing [10]. Pt, Au or Cu wires are also inserted into a glass chip grooved by chemical etching using HF [11]. Recently, Liu et al showed insertion of microwires into PDMS microfluidic devices by xurography [12]. In this method, the choice of material is limited to wires and electrodes cannot be fabricated in planar forms. Also, wires are only integrated into PDMS and cannot be integrated with other materials likes thermoplastics. Alternatively, conductive (carbon) paste is used to fill electrode channel made of PDMS [13] or laser-ablated PET [14]. These methods require post processing of each and every device and are not cost effective in a scalable manufacturing process.

Screen printing and inkjet printing are inexpensive methods for fabrication of electrodes in microfluidics. In these approaches, conductive inks such as Ag, Carbon, Au and Pt [15] are printed at low temperature and transferred on the chip surface after which they can be sintered. Although this technique is easily operated and inexpensive, nanoparticle inks can clog of nozzles of inkjet printers [16]. Also, it is difficult to produce high quality electrodes using sintered nanoparticle materials [17].

Another simple method for integration of electrode is based on photoresist patterning and chemical etching [18]. In this method, a three-layered foil of  $50\mu$ m polyimide coated with 5  $\mu$ m copper in both sides is used. The foil is coated with photoresist, patterned and then etched using a liquid etchant. Then, plasma etching is used to create liquid channel into the polyimide layer. Although scalable, this method still uses photolithographic approach which requires a number of steps.

An ideal approach for fabrication of electrodes in microfluidics should be low cost, easy to fabricate in a non-clean room environment, capable of incorporating a variety of high quality materials and have sufficient resolution of few 10s of micrometers. Xurography is a robust method that can fulfill these requirements and create features in the size range that is needed. Xurography is a low cost fabrication approach that has been used previously to demonstrate fabrication of microfluidic structures [19]. In this method, a razor blade connected to a cutting plotter is used to create patterns on polymer films. It has also recently been combined with cold lamination to integrate a variety of polymeric materials to fabricate and integrate essential parts of microfluidic devices like as pumps and valves [20]. So far, this method has not been adapted to fabricate and integrate electrodes in microfluidics. Here, we combine xurography with cold lamination to create microelectrodes embedded into microchips. Also, we demonstrate its functionality by electro sensing, electromixing and electro heating.

## 3.2 Experimental details

#### 3.2.1 Materials

The metal foil used was a copper-polyimide composite foil (9 $\mu$ m-Cu and 12 $\mu$ m-PI thickness, Pyralux®, AC091200EV, DuPont, US). The transfer adhesive tape was acrylic adhesive (7952MP, 50  $\mu$ m thickness, 3M<sup>TM</sup>, US). The one-sided adhesive tapes used was polyolefin film with silicone adhesive (9795R-3M<sup>TM</sup>, 100  $\mu$ m). The dicing tape used was UV curable acrylic adhesive on PVC film (95 $\mu$ m, 1020 UV adhesive, Ultron Systems, US). The PVC film (Clear-Lay, 125  $\mu$ m) was from Grafix (US).

Potassium hexacyanoferrate (II) trihydrate ( $K_4Fe(CN)_6.3H_2O$ ), sodium sulfite ( $Na_2SO_3$ ), sodium thiosulfate ( $Na_2S_2O_3$ ), potassium metabisulfite ( $K_2S_2O_5$ ) and gold chloride hydrate (HAu(III)Cl<sub>4</sub>) were purchased from Sigma Aldrich (US). Nickel (II) sulfate ( $NiSO_4$ ), potassium nitrate ( $KNO_3$ ), potassium Chloride (KCl) and boric acid ( $H_3BO_3$ ) were purchased from Calden (Canada). Silver nitrate ( $AgNO_3$ ) was purchased from Alfa Aesar (US).

#### 3.2.2 Fabrication

The fabrication process to construct microelectrodes is shown in Fig.3.1. First, two layers of dicing tape (composed of a base film and an adhesive layer) were laminated on back and on top of a copper composite foil by a cold laminating machine (ASC365 LTD, Canada) (Fig.3.1a). Then, a cutter plotter, (FC-8600, Graphtec America, US) was used to create patterns on the foil. Blade CB15U was used and its length (depth of cut) was set to about 115  $\mu$ m, in order to cut only the foil and the top dicing tape (Fig.3.1b). The top dicing tape helps the foil to not catch on the blade and tear before cutting. After cutting, the foil with the dicing tapes was exposed from top to the UV light in 246 mWcm<sup>-2</sup> for 30 seconds (Fig.3.1c). The exposure changed the UV adhesive to be non-sticky, which enabled the easy peeling of the top dicing tape (Fig.3.1d). After that, the foil with the back dicing tape was exposed to the UV light as before (Fig.3.1e). The exposure enabled easy peeling of the unwanted regions of the foil (Fig.3.1f). For the final step, a layer of transfer adhesive tape  $(50\mu \text{m}, 7952\text{MP}, 3\text{M}^{\text{TM}}, \text{US})$  with appropriately positioned holes and patterns was aligned on top of the patterned foil and then laminated on it (Fig.3.1g). The holes were previously cut out from the transfer adhesive layer using xurographic process. They were patterned in such a way that they will expose specific regions of the underlying metal foil while protecting or serving as an insulation for the rest of the electrode surface. Also, using a transfer adhesive tape enabled us to bond the electrode layer to other microfluidic components such as microchannels and integrate the electrodes into microfluidic devices easily.



Figure 3.1: Process flow for fabrication of microelectrodes, a) lamination of dicing tapes on both side of a metal foil, b) creating pattern on the foil and the top dicing tape by a cutter plotter, c) exposure of UV light from top, d) peeling off the top dicing tape, e) exposure of UV light from bottom, f) peeling off unwanted regions of the foil, g) lamination of transfer adhesive tape on top of the foil.

# 3.3 Results and discussion

#### 3.3.1 Xurographic patterning of metal foils

In order to determine the parameter space suitable for use of xurographic method to pattern metal foils, we conducted cutting experiments to fabricate electrodes of width from 50  $\mu$ m to 400  $\mu$ m. Five electrodes of each width separated by a pitch of 400  $\mu$ m were created to investigate the reliability of the process (Fig.3.2a). The cutting force and speed were set to

2.55 N and 1 cm/s, respectively. They were the minimum speed of the machine and least cutting force that can completely cut the foil and the top dicing tape. In another experiment, 400  $\mu$ m wide electrodes separated by various pitch sizes from 50  $\mu$ m to 400  $\mu$ m were also fabricated. For each pitch, five electrodes were fabricated (Fig.3.2b). After fabrication, measurement of the width and pitch sizes was carried out by a camera (Infinity3, Lumenera, US) mounted on a microscope (SZ61, Olympus, Japan).



Figure 3.2: Characterization of fabrication of electrodes, a) designed feature sizes of 100, 200, 300 and 400  $\mu$ m from left to right, b) designed pitch sizes of 50, 100, 200 and 300  $\mu$ m. (scale bar= 400  $\mu$ m)

The results (Table.3.1) revealed that electrodes as small as 66  $\mu$ m can be fabricated using this method. Electrodes with designed width of 200  $\mu$ m or larger were consistently reproduced (with variation of 6  $\mu$ m or less) while that 100  $\mu$ m designed size electrodes were fabricated with larger variation in their width (about 12  $\mu$ m). It was also noted that there was a significant but consistent difference between designed width on the CAD file and the actual fabricated width. For designed width larger than 200  $\mu$ m, the fabricated width was consistently 15-25  $\mu$ m less than the designed width. While for designed width of 100  $\mu$ m, the difference was found to increase (about 34  $\mu$ m). In all the cases, the difference between the CAD file and the actual fabricated electrode was decreased with increase in the electrode

Designed dimension(µm)		Measured dimension (µm)				
		Straight electrodes (width)	Straight electrodes (pitch)	Triangular patterns	Rectangular patterns	Circular patterns
	50		25.28±5.43			
	100	66.31±11.87	93.29±4.02	$239.55 \pm 20.12$	224.39±15.13	259.90±9.03
	200	175.37±5.77	210.23±2.69	316.87±25.55	307.69±25.22	349.19±9.38
	300	280.24±4.94	321.70±4.56	432.13±9.08	435.08±10.77	400.23±10.77
	400	385.67±5.80	427.78±5.24	$531.36 \pm 19.72$	481.32±31.29	524.35±7.93

Table 3.1: Average measured dimensions for different electrode patterns based on designed dimensions.

size. Also, the electrodes with designed size of 50  $\mu$ m were not produced. This is due to the fact that in smaller width cuts, the shear force is less than the lateral force that moves the blade toward the first cut.

Also, it was observed that pitch size between electrodes as small as 25  $\mu$ m can be fabricated. Electrodes in all designed pitch sizes were consistently reproduced with small variation in their width (about 5  $\mu$ m or less). For pitches with designed size of 50  $\mu$ m, the blade could not pass the second cut due to the lateral force. Therefore, 25  $\mu$ m fabricated pitch size was the footprint of cut. Also, it was noted that there was a significant but consistent difference between designed pitch size on the CAD file and the actual fabricated electrodes. For designed pitch size larger than 200  $\mu$ m, the pitch was consistently 10-27  $\mu$ m more than the designed size. While for designed size of 100  $\mu$ m, the actual size was found to be 9  $\mu$ m less.

In another experiment, different shapes with sizes (side length or diameter) of 100 to 400  $\mu$ m were fabricated on the metal foil. The results, as shown in Fig.3.3, demonstrated that the circular patterns were consistently reproduced in all sizes while in the case of triangular and rectangular shapes, designed feature sizes of 100  $\mu$ m did not represent the shape. Also, the circular shapes were noted to have more smooth edges compare to the other shapes. Finally, the difference in size between designed and actual shapes were found to be larger compared to the straight electrodes (Table 1). These characterizations show that the resolution range for the xurography process was as small as 66  $\mu$ m in feature size for straight electrodes, 25

 $\mu$ m for pitch size between electrodes, individual circular shapes with diameter of 260  $\mu$ m and individual triangular and rectangular shapes with side length of 317 and 308  $\mu$ m.



Figure 3.3: Multiple patterns of different shapes forming an array. (a-c) patterns with different designed sizes \_side or diameter\_ of 400, 300, 200 and 100  $\mu$ m from left to right in (a) triangular, (b) rectangular and (c) circular shapes (scale bar = 200  $\mu$ m)

#### 3.3.2 Integration of the metal patterns with insulation: heater

In order to demonstrate fabrication of complex features using this method for practical applications, several designs were fabricated. This included a heater which has a wide range of application in microfluidics. They can be used to amplify DNA in polymerase chain reactions (PCR)[21], control flow as valves and pumps [22] or stabilize the conditions in microreactors [23]. Since the heating elements are typically isolated from the sample or reagents that are to be heated, they have been protected by an insulation layer. The conventional lithographic based fabrication process would require several steps for deposition and patterning of both electrode and insulator elements in order to fabricate the heaters. However, by the xurography-lamination technique, insulated heaters with complex patterns can be easily fabricated in a cost-effective manner using low-cost tools and in a non-clean

room environment.

The heater element was designed to be serpentine in shape to cover a wide area. The lines were designed to be of 9  $\mu$ m, 500  $\mu$ m and 12 cm in thickness, width and length, respectively (Fig.3.4a). It also consisted of two large 3 mm diameter contact pads at is ends. It was xurographically cut from the copper foil on top of a layer of dicing tape (Ultron Systems, US). Electrical potential was applied on the contact pads from a power source. A thermal imaging camera (FLIRONE®, US) was used to measure the temperature and its uniformity at steady state (Fig.3.4b). By applying 0.7 V, mean temperature of 51.4° degrees with distribution of  $\pm 1.4^{\circ}$  across the area of heater was obtained. While by applying 1.1 V, mean temperature of 89.7° degrees with distribution of  $\pm 7.3^{\circ}$  across the area of heater was obtained. Because of high conductivity of copper, high temperature was achieved with relatively low voltage. Also, at higher temperatures, there was not any noticeable change in electrodes because of high thermal stability of the composite foil.



Figure 3.4: Heater fabrication and operation. a) microscope image of an electro heater, b) infrared image of an electro heater exposed to 1V DC voltage

This heater was then integrated with a microfluidic channel to demonstrate the ease with which such integration could be performed. The various layers that constitute this integrated structure is shown in Fig.3.5a. A base layer of dicing tape was used without any patterning. Next, metal foil layer (9 $\mu$ m Cu- 12 $\mu$ m PI thickness) was cut in the shape of the

heating element. Following it, a 40  $\mu$ m thick layer of PDMS that was made separately by spin coating was used as an insulating layer as well as the bottom surface of the microfluidic channel. This layer was adhered to the adhesive dicing tape in the regions where the heating element was not present and formed a conformal coating on the heater. Next, the fourth layer, made of 9795R-3M<sup>TM</sup> adhesive tape, was cut in shape of a microchannel with dimension of 500  $\mu$ m (W), 19 mm (L) and 100  $\mu$ m (H) to serve as the liquid flow channel and laminated to the PDMS layer. The inlet and outlet of the channel was positioned 2.3 mm away from the heater element. Finally, the last layer was made of 9795R-3M<sup>TM</sup> adhesive tape and patterned with circular openings of 1 mm radius which served as the inlet and outlet for liquid channel. The final fabricated structure is shown in Fig.3.5b where heating strips with width of 400  $\mu$ m and 800  $\mu$ m pitch can be seen integrated underneath the microchannel. After fabrication of the device, DI water injected through the channel with flow rate of 100 ml/hour by a syringe pump (Harvard Apparatus, US). A thermocouple was placed at the outlet to monitor the temperature of the water flow instantly. Potential from 1 to 2.5 V was applied to the heating element. Temperature in the range of  $25^{\circ}$  C to  $75^{\circ}$  C degrees was achieved after 5 minutes (Fig.3.5c). As expected, increase in the applied voltage produced a higher steady state temperature and higher rate of increase of temperature.



Figure 3.5: Heater integrated with a microfluidic channel, a) schematic of a multilayer microfluidic device with heater, b) microscope image of the integrated heating elements, c) controlling the temperature at the outlet of a microchannel by applying different voltage to the heater

The xurography-lamination technique is capable of combining multiple materials

including, thermoplastics, elastomers and metal foils through adhesive bonding between the layers to form complex microfabricated structures that are expensive and time consuming to achieve using conventional lithographic methods.

# 3.3.3 Integration of the metal patterns with fluid contact: electrochemical sensor

Electrochemical sensing is one of the most widely used methods for chemical [24, 25] and biochemical analysis [26, 27, 28] in microfluidic lab on a chip devices. Electrochemical methods are ideal for miniaturization as they only require metal electrodes, have high sensitivity, and low-power consumption. Nevertheless, they require high quality metal electrodes made of specific materials such as gold and are often sputter deposited or evaporated. This process is time consuming and expensive.

In order to demonstrate that high quality electrodes can be fabricated and integrated using the xurographic method, a microfluidic device consisting of an electrochemical sensor was designed. The first layer was made of dicing tape without any patterns and served as a carrier for the working and counter electrodes on top of it. The second layer was cut from the copper foil that consisted of working and counter electrodes with dimension of 1 mm (W) and 20 mm (L). The pitch size between two electrodes was 11 mm. Then, the electrode layer with its carrier was immersed in a nickel electroplating bath containing 2M nickel sulfate and 0.5M boric acid. Current density of 30 mA cm<sup>-2</sup> was applied for 1 minute. After that, it was immersed in a gold electroplating bath and current density of 3 mA cm<sup>-2</sup> was applied for 3 minutes. The gold electroplating bath was prepared with solution of 0.42M sodium sulfite and 0.42M sodium thiosulfate mixed with 0.05M gold chloride [29].

After that, the third layer was made of 7952MP-3M<sup>TM</sup> transfer adhesive tape with two rectangular holes with dimension of 2 mm (W), 2 mm (L) and 50  $\mu$ m (H) cut into it at appropriate locations. These openings are aligned to the electrodes underneath so that the sample flowing in the microchannel can be in contact with the electrodes. It was laminated

to the second layer and served as the bottom wall of the microchannel. Next, the fourth layer, made of PVC film, was cut in shape of a microchannel with dimension of 2 mm (W), 20 (mm) and 125  $\mu$ m (H). The fifth layer was made of 7952-3M<sup>TM</sup> transfer adhesive tape and served as the top wall of the microchannel. This layer had one hole with dimension of 2 mm (W), 2 mm (L) and 50  $\mu$ m (H) to enable the flow to be in touch with the reference electrode. The sixth layer was cut from the copper foil and consisted of a reference electrode  $(9\mu \text{m Cu-} 12\mu \text{m PI thickness})$  with dimension of 1 mm (W) and 20 mm (L). Before assembly, this layer with its carrier (dicing tape) was immersed in the same nickel electroplating as described previously and plated to provide a nickel base layer coating with plating conditions similar to those described before. After that, it was immersed in a silver electroplating bath and current density of 60 mA  $\rm cm^{-2}$  was applied for 1 minute. The silver electroplating was prepared with solution of 30 gL<sup>-1</sup> silver (as chloride), 500 gL<sup>-1</sup> sodium thiosulphate and  $30 \text{ gL}^{-1}$  potassium metabisulfite [30]. Finally, the last layer was made of dicing tape in which two circular holes with 1 mm radius was patterned to serve as inlet and outlet for liquid channel (Fig.3.6a). After assembly, the device was filled with 1 M potassium chloride solution and 2 V DC anodization was applied for 20 seconds to deposit silver chloride on the silver electrode. Thus, a microfluidic device with integrated electrochemical sensor was designed and fabricated.

In order to test this sensor, the device was filled by a solution containing 5mM Ferrocyanide in 1 M potassium nitrate. Cyclic voltammetry was performed using a potentiostat (Palm Sense 2, EmStat, US). Various scan rates were applied, and the data was recorded (Fig.3.6b). As it can be seen, the cathodic and anodic peaks associated with ferrocyanide/ferricyanide redox couple was clear in each scan rate. Also, the magnitude of peaks was found to be proportional to the scan rate, as expected.

The layer by layer lamination technique enabled the integration of electrodes into microfluidic devices in an easy and rapid way. The whole process from the cutting layers to assembly was carried out in about 30 minutes whereas conventional techniques require



Figure 3.6: Electro chemical sensing, a) schematic view of the structure of the device, b) cyclic voltammetry of 5 mM ferrocyanide in 1 M potassium nitrate.

several time-consuming processing steps to integrate multimaterials into microfluidic devices. Also, xurography method enabled us to fabricate electrodes made of various materials precisely. The copper foils used in this technique made this process cost-effective.

# 3.3.4 Multi level integration of the metal patterns: electrokinetic mixer

Although homogeneous mixing of reagents is critical for many microfluidic operations, it is difficult to perform in straight microfluidic channels due to the low Reynolds number of the flow [31]. Therefore, several different mixers have been introduced to enhance the mixing performance. In passive mixers, the molecular diffusion is enhanced by increasing the contact area or contact time between the species in the flow [32, 33]. In active mixers, the diffusion process is enhanced by external forces such as acoustic waves [34], thermal actuation [35], magnetic [36] or electrokinetic forces [37]. Lately, simple mixers using Induced charge electro-osmosis (ICEO) [38] have been used where electrodes need to be integrated within the microchannels. Many of the ICEO mixers have electrode structures fabricated on only the bottom surface due to fabrication complexity and difficulties. However, mixing could be enhanced if electrodes could be integrated on two surfaces, both the bottom and top of the microfluidic channels. Here we demonstrate the capability of the xurography-lamination approach to easily integrate electrodes into both the top and bottom of the microfluidic channel to create effective microfluidic mixer.

The microfluidic device that included an electrokinetic mixer was designed as follows: The first layer was made of dicing tape without any patterns and served as a carrier for the electrodes on top of it. The second layer was cut from the copper foil that consisted of two field electrodes (9 $\mu$ m Cu- 12 $\mu$ m PI thickness) with 5 mm length. The pitch size between each electrode was 750  $\mu$ m and the electrodes were arrayed in a way that they generated the electric field perpendicular to the flow direction (Fig. 3.7a). After that, the third layer served as the side wall of the microchannel were made of two 7952-3M<sup>TM</sup> transfer adhesive tapes laminated on both sides of a PVC film. The composite layer was cut in shape of a Y-shaped microchannel with two inlet branches with dimension of 500  $\mu$ m (W), 7.5 (mm) and 125  $\mu$ m (H) merging into a main channel with dimension of 1000  $\mu$ m (W), 20 mm (L) and 225  $\mu$ m (H). The fourth layer was cut from the copper foil and consisted of eight conductor electrodes  $(9\mu \text{m Cu-} 12\mu \text{m PI thickness})$  with dimension of 250  $\mu \text{m}$  (W) and 1 mm (L) (Fig.3.7b). The conductor electrodes were designed to be in the middle of the field electrodes. Finally, the last layer was made of dicing tape in which three circles with 1 mm radius was patterned to serve as the two inlets and one outlet for liquid channel (Fig. 7a). Thus, Y-shape mixer microfluidic with electrodes on top and bottom of the channel was designed and fabricated.

In order to demonstrate mixing in the microfluidic channel, AC voltage was applied to the field electrodes. The frequency was set to 100 kHz and the amplitude was between 0 V to 180 V. Therefore, electric field from 0 to 2400 V cm<sup>-1</sup> was generated inside the microchannel. The conductor electrodes between field electrodes polarized the electric field. DI water colored with food dye was infused to the channel with flow rate of 500  $\mu$ l hr<sup>-1</sup> by a syringe pump (Harvard Apparatus, US). The mixing in flow was captured at different voltages by a microscopy camera (Infinity3 Lumenera, Canada) (Fig.3.7c).

The mixing efficiency was calculated from the color distribution [39]. First, the microscope images were converted to grey scales. Then, the image pixel intensity was



Figure 3.7: Electro-osmosis mixing by integrated electrodes in microfluidics, a) schematic view of the structure of the device, b) microscope image of the integrated conductor electrodes, c) mixing under different applied AC voltage (scale bar =  $500 \ \mu m$ ).

measured across the channel width at 1 mm after the mixer. The red flow had intensity of about 255 while the blue flow had intensity of about 0. The values were divided by 255 to obtain normalized intensity (Fig.3.8). Also, the standard deviation (stdev) of the normalized intensity was calculated as measure of mixing efficiency in which stdev of 0.5 represents two fluids are not mixed at all while stdev of 0 represents two fluids are fully mixed. The results indicated that before applying voltage, the stdev of the flow after the mixer was about 0.31, while for 140 V, 160 V and 180 V, it was decreased to 0.16, 0.10 and 0.05, respectively. Therefore, at 180 V, the mixing was enhanced by more than 6 times.

In this electrokinetic mixer, the field electrodes and conductors were arrayed in small pitch size, thus requiring less voltage to generate strong electric fields. Also, construction of electrodes enhanced the mixing effects due to generation of electric fields and electroosmotic flows perpendicular to the flow direction. The microfluidic device was fabricated in an easy



Figure 3.8: Mixing efficiency of the electrokinetic mixer under different applied AC voltage and rapid way while conventional fabrication techniques required several and complicated processes [40].

# 3.4 Conclusion

In conclusion, a fast, robust, low cost and novel technique for fabrication and integration of electrodes in microfluidic devices was demonstrated. This method is a direct as it does not require any intermediate layer for pattern transfer and uses xurography to pattern commercially available thin copper foils. Feature sizes as small as 66  $\mu$ m are shown to be achievable and higher resolutions can be feasible with higher precision xurographic equipment. Also, this method uses cold lamination of pressure sensitive adhesives that enables us to integrate electrodes easily into microfluidic devices made of different types of materials. Using localized electroplating a variety of metals such as gold, silver and platinum could be incorporated which are important for electrochemical sensing in Lab-on-Chip devices. Incorporation of metal patterns in multiple layers was demonstrated and is relatively easy as compared with other lithographic methods. This fabrication

method is expected to be of widespread interest and use in many microfluidic applications including those requiring electrical field (such as DNA sequencing by electrophoresis), heating elements (such as DNA amplification), electrical sensors (such as water contamination monitoring) and actuators (such as pumps and valves).

# Acknowledgements

This paragraph of the first footnote will contain the date on which you submitted your paper for review. (Corresponding author: P.R. Selvaganapathy) The authors wish to acknowledge funding from NSERC and CIHR through the Collaborative Health Research Program (CHRP 493620-16). AM wishes to acknowledge support from Ontario Graduate Scholarship Program. PRS wishes to acknowledge support from the Canada Research Chair Program and the Discovery Accelerator Supplement award.

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# Chapter 4

# Parallel Electroplating of Multiple Materials Using Patterned Gels with Applications in Electrochemical Sensing

#### Complete citation:

Mohammadzadeh, Aliakbar, Alison E. Fox-Robichaud, and P. Ravi Selvaganapathy. "Parallel Electroplating of Multiple Materials Using Patterned Gels with Applications in Electrochemical Sensing." Submitted to Journal of Frontiers in Chemistry.

#### Contribution:

*Mohammadzadeh A*: Designed and perfomed all experiments, interpretation and analysis of data and wrote drafts of the manuscript including all figures and text.

Selvaganapathy P.R.: Supervised A. Mohammadzadeh and provided guidance with the research focus, idea development, analysis of the results, and manuscript revision.

*Fox-Robichaud, Alison E.*: Provided advice with analysis of the results and manuscript revision.

# Abstract

Electrodeposition is a widely used method to fabricate electrodes in microscale electroanalytical devices. In this method, low cost materials such as copper are coated with higher cost but functional materials such as gold or silver. Conventional methods of electroplating, which use a sequential process of coating one material at a time, consumes a significant amount of time for deposition of multiple materials. In addition, they also use a large volume of electrolytes which may be reasonable if large areas are coated but are wasteful and unnecessary when fabricated small area microelectrodes. Here, we introduce a new method where gels are used to immobilize plating reagents close to the surface on which it is to be plated. We show that such gels could be patterned either using spot printing or using microfluidic flow and confined to some regions using xurographically patterned films attached to the surface. This method allows gel patterns containing different metal salts to be placed in different locations. Such patterned surfaces can then be dipped into a common working electrolyte and produce a complex multimaterial pattern of deposition in parallel.

**Keywords**: parallel electroplating, electrodeposition, gel printing, electrochemical sensors, microfluidics

## 4.1 Introduction

Significant amount of research has been performed towards the development of micro total analysis systems for over the past three decades [1] for applications in point of care medical diagnostics [2, 3], drug delivery [4] and environmental monitoring [5, 6]. These microfluidic devices typically have microchannel networks integrated with electrodes for sensing, heating or actuation purposes [7]. Often, expensive materials such as gold and silver are used to make functional components such as electrochemical sensing microelectrodes. However, current methods for fabrication and integration of electrodes in microfluidic devices are mostly derived from the electronic industry and rely on sequential, time consuming and expensive processes.

Sputtering or vapor deposition of noble metals are the most commonly used method for fabrication of electrodes in microanalytical systems [8, 9, 10, 11]. These methods combined with photolithography are used to pattern desired microelectrode features. Due to their origins in the electronic industry where only one type of conductor is used to connect electronic components, these processes are suited to deposit and pattern only one material at a time. Deposition of multiple materials requires repetition of the deposition and photolithography steps multiple times in sequence, which along with the high vacuum conditions and clean room facilities that are required make the process expensive.

Electrochemical deposition has gained increasing attention in fabrication of microelectrodes because of its relatively inexpensive equipment [12, 13] Electrodes made through electroplating have favorable electrical and mechanical properties that have been used in electronics and microfluidics. However, similar to vapor deposition techniques, conventional methods of electroplating require sequential processes of depositing one material at a time. In addition, conventional methods are suitable for coating of large area electrodes because of using a large volume of electrolyte while it is not cost effective for small area electrodes. In order to overcome the limitation, inkjet and screen printing techniques have been introduced [14].

Screen and inkjet printing are non-vacuum, low cost and direct patterning techniques for deposition of thin conductive films [15]. In these approaches, multiple conductive inks containing nanoparticles such as silver (Ag), Carbon, gold (Au) and platinum (Pt) [16, 17] can be printed at low temperature and transferred on the chip surface after which they can be sintered. Variety of microfluidic devices have been developed using these techniques such as heaters [18] and dielectrophoresis chips [19]. Despite the ease of operation and cost-effectiveness of this technique, there are significant issues associated with the mechanical properties of printed electrodes that they are easily cracked by thermal
expansion or mechanical bonding [20]. Also, clogging of inkjet printer nozzles due to use of nanoparticles is a frequent problem [21]. Additionally, these printed electrodes have less conductivity than bulk materials [15].

An ideal fabrication method for microelectrodes in microanalytical system should be able to integrate multiple functional materials in a low cost, rapid, and parallel process with minimal or no need for expensive high vacuum or clean room environments. Here, we introduce a novel technique in which gold and silver are electroplated in parallel in a single process by placing only droplets of plating solutions mixed with agarose gel over nickel coated electrodes. The whole process is performed in a non-clean room environment in which electrode base substrates and masks are patterned as described in our recent work by xurography and cold lamination [22, 23]. Using gel droplets enable us to electrodeposit different metals at the same time without cross deposition. Also, using small amount of solution as droplets minimizes the use of electrolyte that is crucial for rapid prototyping of micro analytical systems. We show the ability of this method by creating arrays in form of dots and lines. In addition, we demonstrate its functionality by electrochemical sensing in a three electrode system integrated in a microfluidic device. Finally, using gel droplets for electroplating has potential to be utilized by other additive manufacturing techniques such as inkjet printers for fully automation of the technique.

# 4.2 Materials and methods

## 4.2.1 Materials

Potassium hexacyanoferrate (II) trihydrate ( $K_4Fe(CN)_6.3H_2O$ ), sodium sulfite ( $Na_2SO_3$ ), sodium thiosulfate ( $Na_2S_2O_3$ ), potassium metabisulfite ( $K_2S_2O_5$ ) and gold chloride hydrate (HAu(III)Cl<sub>4</sub>) were purchased from Sigma Aldrich (US). Nickel (II) sulfate (NiSO<sub>4</sub>), potassium nitrate (KNO<sub>3</sub>), potassium chloride (KCl) and boric acid (H<sub>3</sub>BO<sub>3</sub>) were purchased from Calden (Canada). Silver nitrate (AgNO<sub>3</sub>) was purchased from Alfa Aesar (US). Agarose was from BioShop Canada Inc (Canada).

Metal foil was copper-polyimide composite foil (9 $\mu$ m-Cu and 12 $\mu$ m-PI thickness, Pyralux®, AC091200EV, DuPont, US). Transfer adhesive tape was acrylic adhesive (7952MP, 50  $\mu$ m thickness, 3M<sup>TM</sup>, US) and one-sided adhesive tape used was polyolefin film with silicone adhesive (9795R-3M<sup>TM</sup>, 100  $\mu$ m). Hydrophilic low contact angle was polyester (9984-3M<sup>TM</sup>, 99  $\mu$ m). Double-sided adhesive tape used was acrylic adhesive on polyester film (90176, 89  $\mu$ m) and was from Adhesive Research aka AR (US). Dicing tape was UV curable acrylic adhesive on PVC film (95 $\mu$ m, 1020 UV adhesive, Ultron Systems, US). PVC film (476  $\mu$ m) was from McMaster-Carr (US).

## 4.2.2 Substrate fabrication

The fabrication process to construct array of base electrodes for electroplating was described in our previous work [23]. Briefly, two layers of dicing tape were laminated on back and on top of a copper composite foil by a cold laminating machine (ASC365 LTD, Canada). Then, a cutter plotter, (FC-8600, Graphtec America, US) was used to create patterns on the foil and the dicing tape on top. The top dicing tape was critical to ensure that the foil does not catch on the blade and tear during cutting process. After cutting, the foil with the top dicing tape was exposed from top to the UV light in 246 mWcm<sup>-2</sup> for 30 seconds. The exposure changed the UV adhesive to be non-sticky, which enabled it to be separated from the cut foil easily and cleanly. Finally, the foil with the back dicing tape was exposed to the same dose of UV light as before. The exposure enabled easy separation of the unwanted regions of the foil (figure 4.1a) thereby creating the pattern of the base Copper electrode.

Then, the base electrode layer with its carrier was immersed in a nickel electroplating bath containing 2M nickel sulfate and 0.5M boric acid (figure 4.1b). Current density of 2 A dm<sup>-2</sup> was used to plate nickel for five minutes (figure 4.1c). After that, a layer of onesided adhesive tape (100 $\mu$ m, 9795R, 3M<sup>TM</sup>, US) patterned with xurography and working as electroplating mask was aligned on top of the foil and then laminated on it (figure 4.1d).

# 4.2.3 Preparation of gold and silver electroplating bath mixed with agarose gel

The gold electroplating bath was prepared with solution of 0.84M sodium sulfite and 0.84M sodium thiosulfate mixed with 0.1M gold chloride [24]. The silver electroplating was prepared with solution of 30 gL<sup>-1</sup> silver (as chloride), 500 gL<sup>-1</sup> sodium thiosulphate and 30 gL<sup>-1</sup> potassium metabisulfite [25] and then was diluted fivefold. Agarose was prepared by concentration of 2 gL<sup>-1</sup>. It was placed on oil bath with temperature of 90° Celsius. Then, gold and silver plating were mixed separately with agarose solution in ratio of 1:1 in two different containers and kept at temperature of 90 Celsius°.

## 4.2.4 Electroplating procedure

Small amount of mixture of plating bath and agarose gel was deposited on the mask laminated on top of the electrodes (figure 4.1e) in the form of droplet. Due to the viscosity of the gel, this mixture was confined to the region defined the electroplating mask layer that was previously cut. Then the electrodes are placed in a beaker containing working electrolyte of 1 M potassium nitrate. The anode was connected to a platinum wire electrode. The cathode was connected to the base electrode layer. A 675 mV DC voltage was applied by a source meter (Keithley Instrument-Model 2636, US) for five minutes (figure 4.1f). After that, the electrode substrate was taken out of the working electrolyte bath and washed away. The plated electrode was integrated into a microfluidic system (figure 4.1g) by cutting the contact pad and separating the electrodes. Also, the mask layer could be peeled away for other applications (figure 4.1h).



Figure 4.1: Process flow for electrodepositon of metals by gels, a) creating patterns on a copper foil laminated on a dicing tape, b) placing the substrate on nickel electroplating bath and applying voltage, c) nickel coated substrate, d) laminatin of a xurography patterned mask to the substrate, e) placing droplets of gold and silver solution over the substrate, f) placing the substrate in a 1 M potassium nitrate bath and applying voltage, g) the substrate with electrodeposited layers of silver and god, h) peeling off the mask and separation of electrodes by cutting the contact pad.

# 4.3 Results and discussion

## 4.3.1 Electroplating using printed gels

In order to demonstrate the ability of the technique to electroplate a single noble metal, a copper substrate with dimension of 20 mm (L) and 50 mm (W) was prepared by xurography technique. The substrate was coated with nickel and laminated with a mask consisting circular holes with radius of 1.5 mm. Then,  $10 \ \mu$ l droplets of gels containing gold electrolytes were dispensed onto these locations by a micropipette. The deposited droplets automatically self aligned themselves to the patterned circular holes due to surface tension. Figure 4.2a shows an example of sequences of substrate preparation including initial copper foil, nickel coating, mask laminating and dispensing of gels (blue color dye was added to the gels for better visualization). After that, the substrate was connected to an external DC voltage

source, dipped into a beaker containing a common working electrolyte and electroplating was performed as described above.Figure 4.2b shows microscope image of electrodeposited layers of gold on nickel. The same experiment was repeated with silver plating solution to produce silver electroplated layer as shown in Figure 4.2c.

The microscope images of electroplated layers demonstrate the layers of gold and silver were precisely and uniformly defined. Additionally, since the transportation of species in gel environment was extensively limited, the diffusion of ions near the cathode surface was a key element in the electrodeposition process. Therefore, setting current density for both gold and silver electroplating as small as 30 mA dm<sup>-2</sup> for duration of about 4-8 minutes formed uniformly bright surfaces while current density lower or higher than this value produced non-uniform deposition or black surfaces. Accordingly, applying potential between cathode and anode in range of 600-700 mV was found most favorable to generate the appropriate current density for gold and silver electrodeposition.

In order to demonstrate formation of continuous deposits by the electroplating method using printed gels, images from layers of Cu, Ni, Au and Ag were obtained by scanning electron microscopy (SEM. SEM images were obtained using TESCAN VP system and the accelerating voltage was set at 30 kV. Figure 4.2d shows low and high magnified (as inset) images of layers of Cu, Ni, Au and Ag from left to right. The low magnification SEM images shows uniform and well-defined coverage of the electrode by Ag and Au deposited layers. The speckle features that are visible are due to the roughness of the starting Cu substrate. SEM images presented in the high magnification images demonstrate that around one to five microns clusters of Cu are presented initially on the substrate. After deposition of layers of Ni, Au or Ag, the surface roughness did not change indicating a uniform and conformal plating of the functional material over the underlying nickel base layer.



Figure 4.2: Electroplating of gold and silver, a) Sequence in preparation of the substrate by nickel coating, mask placing and gel dispensing (scale bar= 7mm), b,c) microscope image of deposited layer of (b)Au and (c) Ag (scale bar =  $600\mu$ m), d) SEM images with inset of higher magnification for layers of Cu, Ni, Au and Ag from left to right, (Scale bar =  $100\mu$ m\_inset = $10 \mu$ m).

## 4.3.2 Parallel electroplating of silver and gold

In order to demonstrate the ability of the technique to electroplate silver and gold in parallel, a copper substrate with dimension of 14 mm (L) and 35 mm (W) was prepared by xurography technique. The substrate was coated with nickel and laminated with a mask consisting two circular holes with radius of 1 mm and separated by 7 mm (center to center). Then, a 10  $\mu$ l droplet of gel containing gold electrolytes was dispensed by a micropipette on one of the holes. Similarly, another droplet containing silver electrolytes was dispensed on the other hole. Subsequently, the substrate was immersed in the common working electrolyte and electrodeposition was performed as describe above. Therefore, Ag and Au were simultaneously electrodeposited on nickel coated electrodes.

In order to investigate the elemental composition of electrodeposited layers, the surface of electrodeposited layers was analyzed comprehensively by X-ray photoelectron spectroscopy (XPS) using PHI Qanutera II system. Figure 4.3 shows XPS spectra of the samples. The results demonstrate that for each circle, XPS peaks associated for only silver or gold were observed. This means that Ag and Au were electrodeposited perfectly on the confined region without cross deposition. Since gel was used as an environment for electroplating, it limited convective transportation of metal ions and therefore avoided cross deposition. Additionally, 7 mm distance (center to center) between two holes with radius of 1mm was found to be the smallest pitch size without any cross deposition. However, using automatic dispenser to precisely place droplets and designing smaller size holes to place smaller droplets will reduce that distance.



Figure 4.3: XPS sepctra of simulatenously electropdesposited layers of gold and silver

## 4.3.3 Pattern electroplating-array of dots

In order to demonstrate the scalability of the technique to electroplate metals in parallel, a mask consists of circular patterns with radius of 500  $\mu$ m, placed 5 mm apart (center to center) forming an array of 14 × 4 was fabricated by xurography. The mask was laminated on a nickel coated copper foil with dimension of 70 mm (L) and 45 mm (W). 2 $\mu$ l droplets of gel containing gold and silver electrolyte were dispensed on alternate circular holes (patterns) on the substrate by a micropipette and electroplating was performed as describe above. After electroplating, the mask was peeled off. Figure 4.4a shows parallel electrodeposited layers of gold and silver on nickel coated substrate. Also, magnified image of the array is shown in figure 4.4b. In addition, microscopic images of individual circles show layers of Ag and Au were deposited only in confined regions defined by the prepared mask (figure 4.4c,d).



Figure 4.4: Parallel electrodeposition of gold and silver in shape of circles on a nickel coated substrate, a) an array of  $4 \times 14$  alteranate dots (scale bar = 5mm), b) microscope image of patterns (scale bar = 1mm), c,d) microscope image of deposited layer of (c) gold and (d) silver (scale bar = 0.5 mm)

This result demonstrates that gel printing can be used as a comprehensive method to fabricate electrode that is fundamentally different from conventional electroplating approaches. Conventional methods of electroplating require a set of process including coating and removal of mask that is time-consuming and expensive when multiple materials are to be electroplated. Also, the substrate needs to be immersed in a large volume of electrolytes which is suitable for large production level, but expensive for fabrication of small area electrodes in prototyping fabrication. On the other hand, electroplating with gels eliminates the need for mask coating/removal, since gel has the ability to immobilize the electrolyte solution and can be used as a direct patterning technique. This ability becomes more important when multiple materials need to be electroplated. The method of gel deposition used here is manual. However, it can be easily automated by incorporating inkjet or drop printers in order to deposit smaller volumes of gel loaded with electroplating solutions with much closer spacing. Although xurographic patterned layer was used as a mask on the substrate, this step can be also eliminated by inkjet printing thin layer of insulating material as covering layer alongside the printed electrolytes.

## 4.3.4 Pattern electroplating-lines

In order to demonstrate ability of the gel printing method to simultaneously electrodeposit Ag and Au in variety of structures, masks patterned by xurography in shapes of microfluidic channel with width of 1 mm were used. For this purpose, masks with higher thickness were required to carry on more amount of plating solution uniformly across the open microfluidic channels. Therefore, masks made of PVC (476  $\mu$ m thickness) laminated on double-sided adhesive tape (89  $\mu$ m) were used. In order to perform the experiment, a copper foil with dimension of 30 mm (L) and 45 mm (W) was cut and coated with nickel as described above. Then, the substrate was laminated to the prepared mask and placed on a hot plate (VWR, Radnor, PA) set on 70 °C to avoid gelation of the solutions during the filling. Between 20-30  $\mu$ l of gel plating solution of gold and silver were placed at the beginning of each channel and using capillary forces, the plating solution wicked into the open microchannels automatically (Figure 4.5a). Then the substrate was placed in a common working electrolyte bath and electroplating was performed as described above. After electroplating, the mask was peeled off from the substrate.

Figure 4.5b shows electrodeposited layers of Ag and Au on nickel coated substrates. As it can be seen, edges of electrodeposited layers were well-defined compared to the nickel coated layer (Figure 4.5c). Therefore, using microfluidic flow, gel solutions were patterned, and parallel electroplating of silver and gold was performed. Additionally, use of capillary wicking eliminated manual dispensing of gels over entire patterns that facilitated printing process. However, for longer distance patterns, capillary flow slows down toward end of the pattern. For that purpose, modification to channel design such as using slightly conical shape channels or placing a temporary sealing layer on top of the open channel will enhance the capillary pumping [26, 27].



Figure 4.5: Parallel electrodesposition of gold and silver in shape of English alphabet letters on a nickel coated substrate, a) schematic view of process for printing gels by using microfluidic flow (from left to right), b) microscope image of deposited layer of gold in shape of "M", and deposited layer of silver in shape of "A" and "C", c) microscope image of deposited layer of gold and silver showing well-defined edges. (scale bar= 1mm)

## 4.3.5 Electrochemical sensing

Electrochemical sensors have gained increasing attention for chemical [5]) and biochemical analysis [28] in microfluidics. Electrochemical methods have significant characteristics such as high sensitivity and low-power consumption that made them an ideal choice for miniaturization. However, the conventional techniques for fabrication and integration of electrodes are time consuming and require expensive facilities.

In order to demonstrate that high quality electrodes can be fabricated by the parallel electroplating technique and integrated using the xurography-lamination method, a microfluidic device consisting of an electrochemical sensor was designed. In this device, the first layer was made of dicing tape without any patterns and served as a carrier for electrodes on top of it. The second layer was cut from the copper foil, consisted of working, counter and reference electrodes with dimension of 2.5 mm (W) and 20 mm (L). The pitch spacing between each electrode was 20 mm. After cutting, the electrode layer was coated with nickel as described above. The third layer was made of 9795MP-3M<sup>TM</sup> one-sided adhesive tape with three circular holes with radius of 1 mm cut into it at appropriate locations. These openings are aligned to the electrodes underneath so that the sample flowing in the microchannel can be in contact with the electrodes. This layer was laminated to the second layer and served as the bottom wall of the microchannel. After that, electroplating using printed gels was performed in a way that gold and silver were electroplated on two side electrodes and on a middle electrode, respectively. Next, the fourth layer, made of double sided adhesive tape (90176, AR), was cut in shape of a microchannel with dimension of 2 mm (W), 20 (mm) and 89  $\mu$ m (H). Finally, the last layer was made of hydrophilic film (9984, 3M<sup>TM</sup>) in which two circular holes with 1 mm radius was patterned to serve as inlet and outlet for liquid channel (figure 4.6a). This layer automatically wicks the microchannel by capillary forces that eliminates need of any equipment for sample injection. After assembly, a droplet of 1 M potassium chloride solution was placed at the inlet that filled the microchannel. Then, 2 V DC anodization was applied for 20 seconds to deposit silver chloride on the silver electrode. Thus, a microfluidic device with integrated electrochemical sensor and reference electrode was designed and fabricated (figure 4.6c).

In order to test this sensor, a droplet of solution containing 100 mM Ferrocyanide was placed at the inlet of the device that filled the microchannel by capillary wicking. Cyclic voltammetry (CV) was performed using a potentiostat (Palm Sense 2, EmStat, US). Various scan rates were applied, and the data was recorded (figure 4.6b). The result showed the cathodic and anodic peaks associated with ferrocyanide/ferricyanide redox couple in each scan rate. Also, the magnitude of peaks was found to be proportional to the scan rate, as expected.



Figure 4.6: An electro chemical sensor, a) schematic view of the structure of the device, b) cyclic voltammetry of 100 mM ferrocyanide, c) microscope image of integrated electrodes inside a micofluidic device (scale bar = 2mm)

The parallel electroplating technique combined with the layer by layer lamination technique enabled the integration of high quality electrodes into microfluidic devices in an easy and rapid way. The whole process including cutting the layers, electrodeposition and assembly was carried out in less than 30 minutes whereas conventional techniques require several time-consuming processing steps to integrate multimaterial into microfluidic devices. Also, gel printing method enabled us to electrodeposit silver and gold simultaneously in a single process on a single layer. Automatic filling of the device by using a hydrophilic film made this sensor suitable for end-users. Also, the small amount of electroplating solution among the copper and plastic films used in this technique made the entire process cost-effective and suitable for commercialization.

# 4.4 Conclusion

In conclusion, a novel technique for parallel electroplating of gold and silver was introduced. This technique can be used for fabrication of high quality electrodes in electroanalytical systems. In this method, silver and gold electrolytes were mixed with agarose gel and printed in form of gel droplets on nickel coated substrates. Agarose working as immobilizing environment reduced the amount of plating electrolytes and enabled parallel electroplating of gold and silver without cross deposition. We showed the reliability of this method by parallel electrodeposition of gold and silver in form of arrays of dots and lines. We also demonstrated the functionality of the method by fabrication of a three electrode system integrated in a microfluidic device performing electrochemical sensing. This fabrication method is widely applicable and can be used for a vast range of micro analytical systems with bioanalytical and environmental applications such as disease diagnosis and water monitoring.

# Funding

This research was supported by NSERC and CIHR through the Collaborative Health Research Program (CHRP 493620-16) and the Ontario Research Foundation.

# Acknowledgements

The authors wish to acknowledge funding from NSERC and CIHR through the Collaborative Health Research Program (CHRP 493620-16). AM wishes to acknowledge support from Ontario Graduate Scholarship Program. PRS wishes to acknowledge support from the Canada Research Chair Program and the Discovery Accelerator Supplement award.

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# Chapter 5 Conclusion and future work

# 5.1 Conclusion

Microfluidics has recently gained popularity as a tool for biochemical analysis since it can automate all the process steps in a continuous flow stream by using small volume of samples. Significant progress has also been made in the development of fabrication techniques in order to broaden the application of microfluidics. Clearly, each of these techniques has its own advantages; however, limitations still exist with respect to using clean room facilities thus high cost and/or using only specific materials. Therefore, an easy, inexpensive and robust fabrication technique that can integrate different materials into a single device is highly demanded. Also, essential microfluidics components such as electrodes need to be fabricated in an easy and inexpensive way with minimum process steps.

A rapid and inexpensive technique for fabrication of microfluidic components was developed. In this technique, xurography and cold lamination were combined to construct multimaterial multilayer microfluidic devices. Using xurography, feature sizes as small as 100  $\mu$ m can be created that is enough for microfluidic and LoC devices. Also, polymer films are commercially available in range of  $25\mu$ m - 1.5mm in thickness and can be easily patterned by xurography and bonded to other materials by sandwiching a transfer adhesive tape between them. The wide variety of adhesive tapes provide a suitable combination that is appropriate for the different film materials that need to be bonded. For instance, silicone based adhesives are suitable choices for bonding silicone elastomers to other polymers and acrylic based adhesives are suitable for high surface energy materials. In addition, metal foils such as copper, stainless steel, aluminum and metalized PET are commercially available in ultra-thin format and can be patterned by xurography and integrated into microfluidic devices.

Multimaterial combination provides unique functionality that may not be possible otherwise. For example, using hydrophobic and hydrophilic materials enable us to control fluid flow in passive microfluidics. Passive microfluidics is attractive for applications such as bedside diagnostics, since they are portable and do not require off-chip equipments such Also, multimaterial combinations can be used to integrate other functional as pumps. materials such as gels easily and precisely into microfluidic devices. Integration of hydrogel in certain regions of a microfluidic device is useful for wide range of applications such as biochemical assay and cell migration studies. In one study, confinement of agarose gel in a certain region of a device with potential application in prognosis of sepsis proceeds with 90% success rate. However, this method has some drawbacks. Use of adhesive layers introduce unwanted material to the microchannel walls. Also, for analysis of samples containing organic solvents, compatible materials are needed to be selected for microfluidic construction including plastic films and adhesives. Additionally, further development such as automatic and more controllable alignment of layers will enhance the accuracy and success rate of the technique.

Integration of electrode components is necessary to perfrom biochemical analysis in most of microfluidics applications. Therefore, fabrication and integration of microelectrodes in microfluidic devices by xurography-lamination technique was introduced. Thin commercially available copper foils as electrode layers can be patterned by xurography and integrated in microfluidics using adhesive films. Also, electrode feature sizes as small as 66  $\mu$ m can be created. In fabrication of electrode layers, patterns with feature size smaller than 300  $\mu$ m are sometimes peeled off undesirably that leads to 80% success rate within this size range. Integration of electrode components is crucial for microfluidics and can be used for variety of applications such as electrochemical detection, mixing and heating. However, this method has some limitation. For example, 3D structures or side wall electrodes that are critical to provide uniform electric field for dielectrophoresis application cannot be achieved. Also, for electrochemical detection, multiple metals such as gold and silver are needed to be deposited on the electrode substrate that led to use additional process steps.

In order to reduce the process steps for fabrication of electrochemical sensors, a novel method for parallel electroplating of noble metals such as gold and silver was introduced. Silver or gold electrolytes can be mixed with agarose and printed as droplets of gel on a conductive substrate. Agarose as an immobilizing environment enables immersion of the substrate in a common working electrolyte without cross mixing of gold and silver electrolyte. Using this method, a large volume of metal electrolyte can be conserved, since only small droplets of noble metals electrolyte are needed. However, the success rate of electodeposition is 75%, which lies below the standard electroplating techniques rate. This is mainly due to the extensively limited transportation of ions in gel environment. Further development of the technique is required to fulfill the limitation. For example, incorporation of the method in inkjet printers for automatic dispensing and gel preparation is necessary. Also, thin layer of insulating material as covering layer can be printed simulatanously with electrolytes to eliminate need of a patterned mask. Finally, deposition of other functional metals such as platinum and palladium are required to be investigated.

# 5.2 Research Contribution

My research contributions are:

(i) Integration of multiple materials into a single chip by xurography: We developed a robust fabrication technique that combines xurography and cold lamination technique to construct microfluidic devices made of different materials. Different polymers such as thermoplastics, elastomers and thermosets and metals such as copper foils can be integrated into a single microfluidic device by a rapid and inexpensive method. Using this technique, the cost of microfluidics fabrication was significantly reduced.

- (ii) Controlling rate of capillary wicking and designing passive valves in devices fabricated by xurography: Using polymers with different properties, we were able to control fluid flows in passive microfluidics. Rate of capillary wicking was controlled by changing surface energy of walls in microchannels. Also, different passive valves were designed to stop fluid flows.
- (iii) Fabrication and integration of electrodes: We developed xurography-lamination technique to fabricate and integrate electrodes in microfluidic devices. Commercially available thin foils were patterned by xurography and integrated into microfluidic chips by pressure sensitive adhesives. The cost of fabrication was significantly reduced compared to conventional techniques such as PVD.
- (iv) Parallel electroplating of multiple materials: We developed a technique to electroplate multiple materials simultaneously. In this method, we used gels to immobilize and pattern electroplating electrolytes on substrate surface. Using this approach, significant volume of electrolyte was conserved since it only used droplets of gels. Also, significant amount of time was saved as multiple metals were electroplated in a single step.

# 5.3 Recommendations for future work

Some works associated with fabrication of multimaterial microfluidic devices are recommended as follows:

(i) Fabrication and integration of actuators: Development of micro total analysis systems requires progression in actively controlling the fluid flow. Active valves and pumps have been developed in recent years to control the flow in channels more efficiently. PDMS valves couples by pneumatic actuator have been most widely used in microfluidics. However, pneumatic actuators use off-chip equipments and thus incorporation of other systems is difficult.

One alternative way for simple on-chip actuation is using Shape Memory Alloys (SMA). SMA has the ability to return to its original memorized shape after deformation. This feature is resulted from phase transition between austenite (high-temperature) and martensite (low-temperature) phase. By heating a shape memory alloy (either in form of wire or foil), it shrinks, while by cooling down, it becomes back to its original length. However, there are some challenged that need to be addressed. Thin foil of SMA are relatively thick and cannot be patterned by xurography. Other methods, such as chemical etching, milling and laser cutting should be used for patterning. Use of SMA in form of wires required development of wire integration techniques. Although rapid heating can be achieved by joule heating, rapid cooling mechanism is needed to be addressed. Also, programming and forming of SMA requires high temperature furnace that led to additional steps in fabrication process.

- (ii) Integration of metal leaves as electrodes in microfluidics by xurogaphy : A metal leaf, is an ultra-thin foil that mostly used for decoration. Metal leaves are commercially available in variety of materials such as gold, silver, copper and platinum. Lamination of these foils with pressure sensitive adhesives and patterning with xurography can be used to integrate electrodes in microfluidic devices. One of the main advantage of using metals leaves is that it reduces process steps such as electroplating. These leaves can be used in microfluidic with application of electrochemical sensing. One of the challenges should be aware of is mechanical properties of these electrodes. For example, they are susceptible to crack upon bending or damage upon contact. Also, laminated adhesive should be not dissolvable by liquid samples.
- (iii) Parallel electroplating of multiple materials: In chapter four, parallel electroplating of

silver and gold by using gels were studied. For further development of this technique, electroplating of other functional metals such as palladium and platinum can be investigated. Palladium and platinum are functional materials that have been extensively used in electrochemical sensors. One of the challenges should be aware of is that these metals have different deposition potential. The deposition potential can be adopted by adjusting concentration or changing pH. Also, additive manufacturing techniques such as inkjet printers can be used for fully automation of the technique. By using inkjet printers, electroplating gel along with an insulting material can be printed simultaneously to eliminate need of mask.

# Appendix

#### A) Creating 2D patterns on plastic films

- 1. Cut large films and tape rolls in smaller sizes by a mat cutter (Logan Graphics Product ,US)
- 2. Place and laminate films on a cutting mat (Silhouette Portrait mat,  $8'' \times 12''$ )
- 3. Place the cutting mat into a cutting plotter (Graphtec FC8600, US)
- 4. Draw 2D model of the design in a 2D CAD design software (AutoCAD, US).
- 5. Open the CAD file with Corel Draw Software (US) and send it to the cutting plotter controller software (Cutting Master 3, Graphtec, US)
- Choose appropriate blade based on the thickness of the film (CB09UB for films up to 0.25 mm, CB15U for films up to 0.5 mm and CB15U-K30 for films up to 1.5 mm)
- 7. Adjust the blade length slightly longer than thickness of the film
- 8. Run a test cut by the plotter to find appropriate force, speed and offset setting.
- 9. Send the 2D design to the plotter.

## B) Creating 2D patterns on metal foils

- 1. Laminate two layers of dicing tape on back and on top of a foil by a cold laminator
- 2. Place the substrate on a cutting mat

- 3. Use blade CB15U and set its length slightly longer than overall thickness of the foil and the top dicing tape
- 4. Create patterns on the substrate by a cutting plotter
- 5. After cutting, place the substrate under UV light to change dicing tape on top of the foil to be non-sticky
- 6. Peel off the top dicing tape
- 7. Place the substrate again under UV light to change dicing tape on bottom of the foil to be non-sticky
- 8. Peel off the unwanted regions of the foil

## C) Making alignment stage

- 1. Place a 6 mm acrylic sheet as the material to be cut in a laser cutter (Epilog, US)
- Draw 2D model of stage design in a 2D CAD design software with same dimension (width and length) as individual layers and having small holes functioning as alignment marks (diameter size 1/8")
- 3. Open the CAD file with Corel Draw Software, change the line thickness as 25  $\mu m$  and save the file as PDF
- 4. Send the PDF to the laser cutter to cut thoroughly the acrylic sheet

### D) Assembly of multilayer devices

- 1. After cutting and patterning two individual films (at least one of them has adhesive layer on it), place each layer on one alignment stage
- Secure layers by insertion of alignment pins (Dowel pins, diameter size 1/8", McMaster-Carr, US)
- 3. Place a non-sticky liner between layers to avoid adhesion of adhesive surfaces to the adjacent films during the assembly and alignment process

- 4. Remove the dowel pins and the alignment stages, and place stacked layers under the cold laminator
- 5. Move the stacked layers into the laminator and meanwhile remove the non-sticky liner to allow the entire area of adhesive to be activated.
- 6. Repeat the process to add additional layer to the stacked layers.