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Rapid Prototyping to Roll-to-Roll Manufacturing of Microfluidic Devices

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RAPID PROTOTYPING TO ROLL-TO-ROLL MANUFACTURING OF MICROFLUIDIC DEVICES

By

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Microfluidics constitutes a widely applicable field of enabling technologies with great potential to revolutionize healthcare and biotechnology. The ability to miniaturize and parallelize processes with microfluidics is seen as a solution for many problems with diagnostics technologies and accessibility. Unfortunately, fabricating microfluidics often require extremely expensive, time consuming, and specialized high-precision methods, making both prototyping and commercial-scale mass manufacturing difficult to accomplish. In this work, we evaluate the feasibility of using a unique roll-to-roll (R2R) micropatterning manufacturing process coupled with Additive Manufacturing (3D printing) to rapidly prototype and produce microfluidic devices at high-volume on film or paper backings for applications in biotechnology. The first part of this process involved using Innovation Engineering approaches to navigate the customer discovery process to define the market areas in microfluidics that were of most value. Next, we identified key feasibility metrics for assessing products made with this process by looking at both manufacturability and functionality. Feature dimensions of products fabricated in the R2R process were evaluated at each step of production to determine manufacturability. Functionality was then assessed using microfluidic mixing patterns to compare the mixing efficiency of our film product to those manufactured with a current industry standard method. Ultimately, we found that fabrication of microfluidic patterns was feasible in the R2R production method, and that the devices created had

functionality comparable to traditional microfluidic devices. This work will serve as a platform for further investigations into the high-volume manufacturing and prototyping of microfluidic patterns for applications in diagnostics and other areas of biotechnology.

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INTRODUCTION

1.1. Introduction to Microfluidics in Medicine

Microfluidic devices are liquid handling systems that manipulate and use small fluid volumes at sub-millimeter scale lengths.[1] The dominating physics and fluid phenomena of liquids on this small scale are significantly different from those on the macro scale. Among the most important differences is the lack of turbulence associated with laminar flow streams, where convection is no longer the dominant mechanism by which fluids mix, as well as the presence of capillary forces and the increased dominance of surface and interfacial tension.[2] Microfluidics can be used to carry out functions for various applications that are not possible on the macro scale by exploiting these scaling properties.[3–5] On the microfluidic scale it is possible to miniaturize and automate many processes with lowered reagent consumption and material handling. These characteristics give microfluidics the potential for use in applications in a wide range of fields, spanning outside of their origin in research labs and into industry. This technology was predicted early on to have a major revolutionary impact in science by using these properties, and has contributed to major advancements in related fields such as chemical engineering and biotechnology.[1,6]

Some of the most lucrative markets for the development of microfluidic technology are those that require high-volume but low-cost manufacturing.[1] The focus of most research effort in microfluidics is in the field of healthcare and diagnostics, where single use platforms of this nature are practical for applications which involve contact with and processing of biological samples. Within this field, point-of-care (POC) diagnostics are those which use rapid and precise miniaturized liquid manipulations, low cost, and portability of microfluidics to support decentralized testing of patients and personalized medicine.[7–9] Microfluidic technologies play a key role in enabling POC diagnostics applications.[2,10,11] They have been shown to be useful for analytical purposes by effectively controlling flow of sample fluids

from reaction and detection zones to result readouts, supporting the main functions necessary for these healthcare and diagnostic applications.[12–16]

1.1.2. Microfluidics Market

The microfluidics market is steadily growing and represents a lucrative opportunity for product and technology development. The market value has grown steadily from $1.59 billion USD in 2013[17] to $3.6 billion USD in 2017[18] and is projected to reach over $10 billion USD in 2022[19], representing a growing opportunity for innovative developments and applications. The global market for POC diagnostics is similarly poised for growth, projecting significant increases from $16.5 billion USD in 2016[20] to $34.6 billion in 2021[21]. The demand for commercialized microfluidic products in this market is driven by the need for sterility and disposability of devices that come directly into contact with biological fluids, where the probability of fouling and clogging of channels is high.[22,23] Both fields together represent an opportunistic landscape ripe for innovative new microfluidic technologies, as supported by the rising number of microfluidic-related scientific publications from 1 in 1994 to 1499 in 2018 (Figure 1).

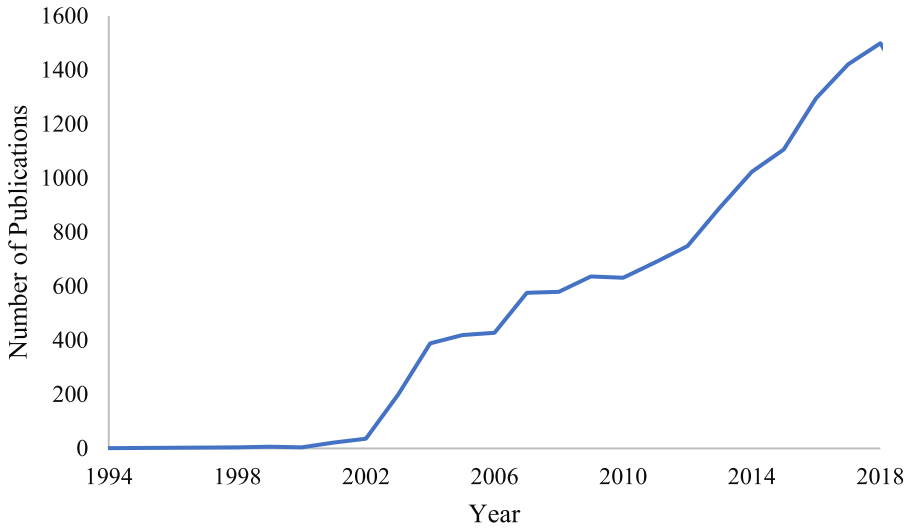

Figure 1.1. Number of Microfluidics-Related Journal Articles Published Between 1994 to 2018. Annual publication figure reproduced from PubMed.

1.1.3. Microfluidics Development Challenges

The field of microfluidics has mainly been confined within academic research laboratories despite its originally-speculated potential for widespread revolutionary use.[1,6,13] Many of the microfluidic technologies developed for POC applications serve only as a proof-of-concept, and translation into marketed products is limited. Microfluidics have not yet reached full maturity in commercial applications because they are limited by both technological and production bottlenecks.[24] Technological problems include the inherent low throughput of microfluidic systems and therefore long sample analysis time, which may be overcome in some cases by parallelization of devices.[25,26] Clogging of devices is also a common issue which typically requires iterative changes to designs[27,28], but prototyping in this way is not easily done due to the expensive and time consuming processes involved in fabrication.[29]

Despite being low-cost in terms of materials for production of miniaturized systems, conventional manufacturing methods are expensive and laborious. Traditional microfluidic devices are fabricated out of glass or silicon using planar fabrication techniques used by the microelectronics industry, such as lithography and etching.[30] Both methods enable the creation of sub-micron scale structures for applications with critical feature sizes and robust material properties.[31] These early techniques were suitable for applications in research labs, where the higher cost and limited materials were feasible for the smaller production volumes required.[32] Although devices manufactured with these methods are extremely precise, they are also expensive and rigid, and therefore limited in potential applications.[33] Lithography requires manufacture of a costly master, specialized training, and use of a cleanroom. These methods are specifically ill-suited for exploratory work and prototyping, because the designs are not easily customizable and cannot be adapted to the many applications that require a low cost and flexible substrate for allowing or improving function. Planar fabrication methods also impose geometrical limitations in the final design, where feature shapes and heights are limited by each step

size.[30,31] Applications within the field of microfluidics vary widely and often require intricate and free-form shapes. Commercial production of designs require that the technology can produce a dynamic range of structural dimensions, as applications within the field of microfluidics vary widely and often require intricate free-form shapes.[30] The fabrication and usage limitations inherent to these conventional lithographic techniques would require management of significant hurdles for any commercial use, driving the demand for more feasible, standardized, and mass producible platforms.

It is speculated that this drive has been limited over the past three decades by an ineffective search for a new "killer application".[34,35] Microfluidics is considered a platform enabling technology instead of a product in itself, so development of the technology must be translated to a viable application case to realize commercial success.[36] Numerous academic publications feature proof-of-concept designs with novel technical functions, but diffusion into consumer markets is limited by a lack of market-need validation, appropriate customer development, and high financial entry barriers. Instead of focusing on the search for a revolutionary new application, many stakeholders agree that developers should shift this focus from innovative new product demonstrations to marketable mass-producible products with well-defined market routes.[17]

Lower-cost manufacturing methods are necessary to achieve clinical impact and diagnostic utility in the POC diagnostics applications within the highest value market routes. To perform the necessary diagnostic tasks[37] it must also be possible to customize and integrate designs, which are difficult to do with traditional low-throughput fabrication methods where turnaround time is very slow. Soft lithography with polydimethylsiloxane (PDMS) has remained a common method for fabricating microfluidics devices, and is considered an industry standard by many despite the need for a cleanroom for production. [33,38]

An increased use of thermoplastic polymers and their manufacturing technologies such as injection molding, hot embossing, and casting initiated movements from expensive cleanroom

fabrication methods to lower-cost and higher-throughput methods more suitable for the commercial scale.[39,40] One newer manufacturing method that aims to achieve this more effectively is additive manufacturing, or 3D printing, which has previously been explored and characterized as a method of fabricating microfluidics.[41–45] 3D printing can bypass many limitations of methods like soft lithography and embossing by lowering machinery and material costs to make the fabrication process easier and more adaptive. Compared to soft lithography, in which every change of design requires the fabrication of a new master mold, design change in additive manufacturing can be directly transferred from the CAD file to the device, enabling the significant advantage of rapid prototyping over other more complex methods. However, 3D printing is not translated to a commercial scale for microfluidics because of limitations on available resolution of printers, throughput, and compatibility of resins.[46]

One approach to bridging the existing gap for low-cost and high-volume production is with roll-to-roll (R2R) production methods, such as nanoimprint lithography and roller embossing. R2R methods allow large-scale and high-throughput manufacturing solutions,[47,48] and have been investigated as methods for the creation of functional microfluidic devices.[49–51] Although these are promising approaches for large-scale manufacturing, the embossing cylinders require an expensive and complicated lithographical or chemical etching process and are not suitable for prototyping production.[48,52] Feature sizes and resolution are also limited by the thin film substrates used.[48,53] An ideal solution to the overarching problem would allow more rapid and accessible mass-manufacturing of microfluidics with enhanced design flexibility and resolution.

1.2. Sappi

Sappi North America, Inc. is a global pulp and paper company that supplies printing, packaging, and specialty papers for a wide range of applications. One of these specialty products is a line of casting and release papers, which are used to create textures on the surface of synthetic leathers, laminates, and films. Release papers are made using a unique, high-throughput, roll-to-roll (R2R) electron-beam (E-

beam) coating process that can replicate patterns on paper or film backings with superior fidelity, reproducibility, and stability.[54] With this technology surfaces can be patterned with feature dimensions ranging from macroscale to nanoscale. For producing coated fabrics, the release papers or films are coated with polyurethane (PU) or polyvinyl chloride (PVC), a fabric backing is applied, the aesthetics of the paper (gloss level and texture) are replicated onto the coated fabric, and the paper is peeled away. These coated fabrics then act as textiles for use in products such as handbags, shoes, flooring, and furniture.[55]

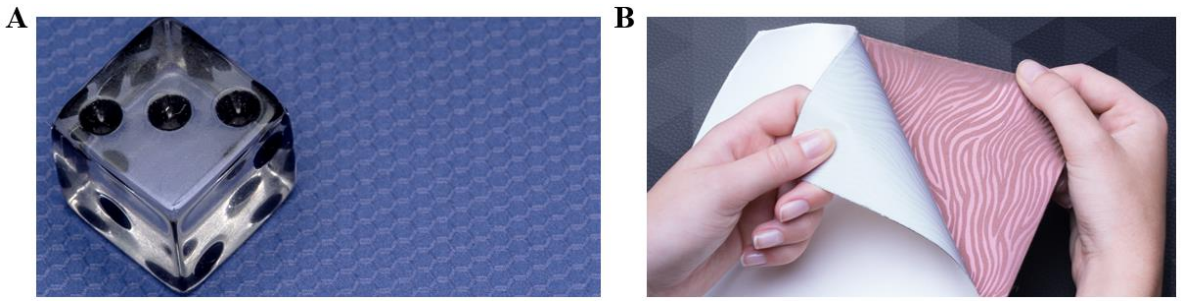

Figure 1.2. Sappi Release Paper Product Textures and Coated Textile Replication. (A) Apex, a hexagonal texture used in release paper products. (B) Demonstration of release paper product, where the paper (left) is stripped away from coated textile, resulting in pattern replication on fabric backing. (Images from Sappi.com[55])

This project involves collaboration with Sappi for exploring new uses of this E-beam coating process. This specialized fabrication process[56] allows enhanced design flexibility compared to other roll-to-roll R2R methods, as well as a novel method of prototype production using 3D printed master components. The final patterned products manufactured with this process are thin, flexible, and optically transparent when produced with a film backing (see Figure 1.3 for an overview of material properties). Although the exact composition of the matrix is proprietary, similar thermoplastic polymers such as perfluoroalkoxy polymer (PFA), polydimethylsiloxane epoxy acrylate (PSEA), and Polyurethane

(PU) have also been used and have been shown to have an acceptable resistance to corrosive solvents such as piranha[57], acetone[58], and chloroform[59], respectively.

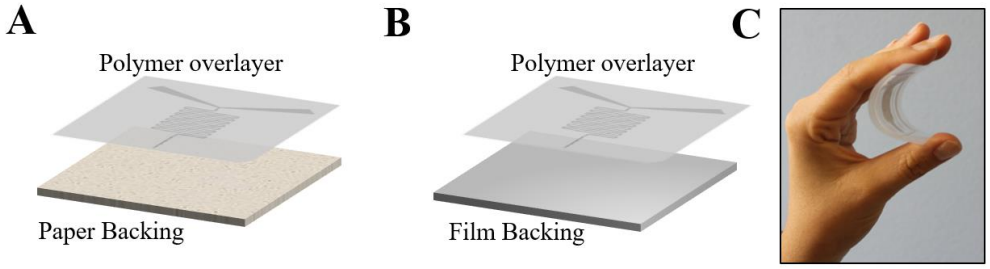

Figure 1.3. Features of Microfluidic Patterned Products Manufactured at Sappi. Exploded view depiction of microfluidic patterned polymer overlayer with (A) paper backing and (B) film backing. (C) Demonstration of flexibility and transparency of film-backed products.

1.2.1. Goal of Project

The goal of this project is to identify the most commercially viable opportunity for new application of Sappi's R2R micropatterning process. Applications within the field of biotechnology were explored and through customer discovery efforts, the field of microfluidics was identified as a key opportunity. Typical microfluidic applications can be generalized into 2 categories: continuous-flow microfluidics, where the two major opposing tasks are mixing and separation, or droplet microfluidics, where individual droplets of liquids are handled as opposed to continuous streams.[60] For microfluidics to be successfully employed into miniaturized analysis systems, the ability to rapidly mix two or more reagent streams is often a required function.[61–65] For this reason, mixing was selected as a functional test to assess microfluidic device function; specifically, passive mixing, as it is preferred in most applications due to ease of fabrication and design simplicity.[66] Within the scope of work, we optimized a method that allowed us to couple the benefits of 3D printing with the output of R2R manufacturing for rapid iterative design of microfluidics that can be directly translated to mass manufacturing. The use of additive manufacturing allows the customization of designs for a variety of target applications and end use settings. An overview of this process is illustrated in Figure 1.3.

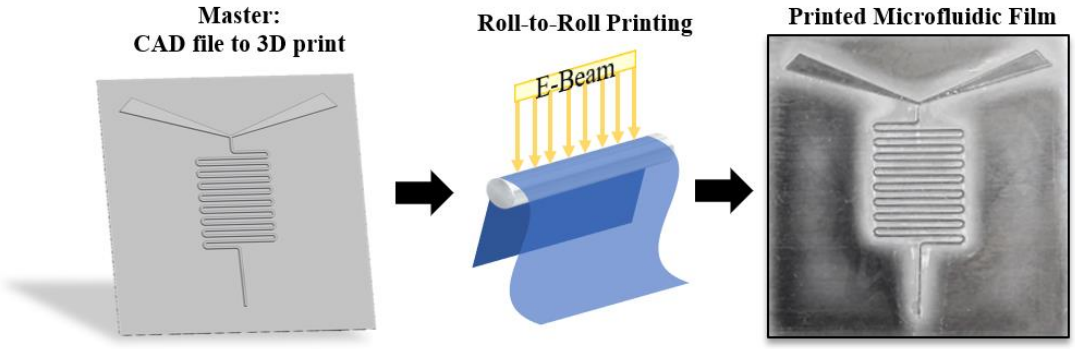

Figure 1.4. Overview of Microfluidic Manufacturing Concept. Patterns are designed in SolidWorks, 3D printed, incorporated into the R2R printing process, and replications of the 3D printed master are created.

CHAPTER 2

CUSTOMER DISCOVERY AND INNOVATION ENGINEERING

2.1. Introduction

Innovation Engineering (IE) is a framework of thinking created by innovators at the University of Maine in collaboration with Eureka! Ranch to systematize the innovation process which is divided into components of creation, communication and commercialization. In this project, IE principles were explored and applied in an accelerator-style program called MIRTA (Maine Innovation and Research Technology Accelerator). MIRTA teaches university-based teams that have the potential to commercialize a product or service about the process of business model development, customer discovery, market analysis, intellectual property, and commercialization, with the goal to advance research innovation towards marketable new products and services.

This chapter defines the key principles applied from IE during participation in the MIRTA program, and describes how they were applied to understand the Sappi technology core strengths, identify potential customer problems, ideate solutions, develop prototype systems to test feasibility to meet the demands of the necessary solutions, and rapid prototype solution experiments to reach proof-of-concept of Sappi's platform technology and ability to serve key market opportunities.

2.2. Innovation Engineering

The inception of Innovation Engineering was to provide structure to the process of thinking, learning and doing, when it comes to new products, services or general innovations. This concept was built into systematizing what were termed the three core steps to innovation; creation, communication and commercialization. The Innovation Engineering platform provided tools and methodologies for ideation, concept generation and testing, and cycles of prototype iteration, discussed in more depth in following sections. IE further evolved at the University of Maine into development of an entire

curriculum for undergraduate and graduate students, as well as tools and implementation strategies to nurture innovation from startups to larger corporations.

2.3. Maine Innovation, Research and Technology Accelerator

The Maine Innovation, Research and Technology Accelerator (MIRTA) is a program that teaches university-based teams that have the potential to commercialize a product or service about business model development, market analysis, and intellectual property, all with the goal to advance research innovation to marketable new products and services. In this project, MIRTA served as a means of executing Innovation Engineering principles and tying market feedback into the engineering processes of research and development (R&D) to focus efforts, enhance resource use and maximize the chance for success or market adoption. The program helped to define parameters for what was needed to predict and communicate success and function. MIRTA also helped to refine skills for listening to the actual problems of customers and develop a systematic way to turn the problems into pragmatic solutions using Sappi's technology. Overall, the program framework assisted with the process of innovation and development of the market analysis and customer discovery process.

2.4. Systems Thinking

One of the keystones of Innovation Engineering is the adoption of systems-level thinking, which is broadly defined as the process of innovating as an intentional and structured system.[67] Systems thinking was introduced by Russell Ackoff in 1997, and involves the idea that a "a system's essential properties and function derive from the interaction of its parts, not from the action off its parts taken separately"[68] . The components of a healthy system work cohesively together to accomplish a goal, rather than as a series of consecutive tasks loosely directed to accomplish what typically results in being a derivative of the intended goal. Application of a systems-level thinking mindset is appropriate for each stage of the innovation process; create, communicate and commercialize. Examples of such systems include mining for problems, generating new ideas for solutions by using approaches to gather and

process stimulus, translating ideas to pragmatic solutions that effectively and efficiently solve the problem, and rapidly prototyping these solutions to minimize time and resources, maximize the frequency of solution prototypes, and ultimately maximize chances of meaningfully solving the problem. An overview of this logical progression is depicted in Figure 2.1.

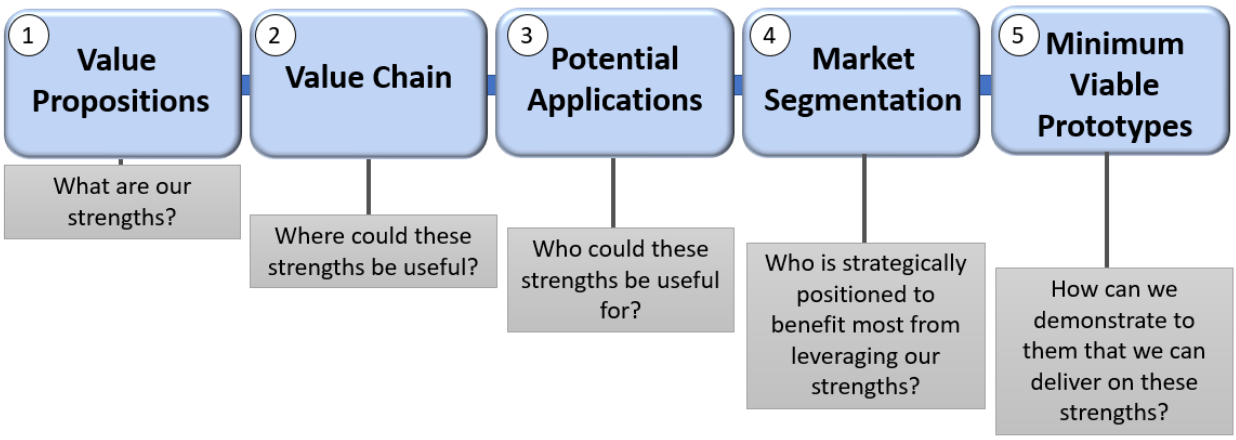

Figure 2.1. **Innovation Engineering Process to Systematically Identify Technology Applications.** An overview of the process used to identify the most lucrative potential applications of Sappi's platform technology.

In this flow of logic, the first step is to identify the core strengths with the value proposition, and then find where these strengths could be useful by developing a value chain. Potential applications are identified next by specifying who the strengths could be useful for within the value chain. The "who" in this situation represents different types of customers which make up the market. The market can be broken down into segments, where customers within a segment all experience the same problem and can benefit from a product that solves that problem. The final step of this process is to identify which specific segment in the market stands to benefit the most from the strengths identified in the value proposition, and then to develop prototypes to demonstrate the ability to deliver on these strengths.

2.5. Articulating the Value Chain

One of the most important systems to understand when strategizing new product or company development is the value chain. The value chain is the process of how a product or service is created,

distributed and used, that provides a visualization for the key touch points from players in your value chain and jobs to be done by those key players.[67] For example, a player in the beginning of the value chain is the raw ingredient supplier, and their job is simply to be a trustworthy partner in the supply of the ingredients/parts needed to build the product. A high-level chart of Sappi's value chain is provided in Figure 2.2.

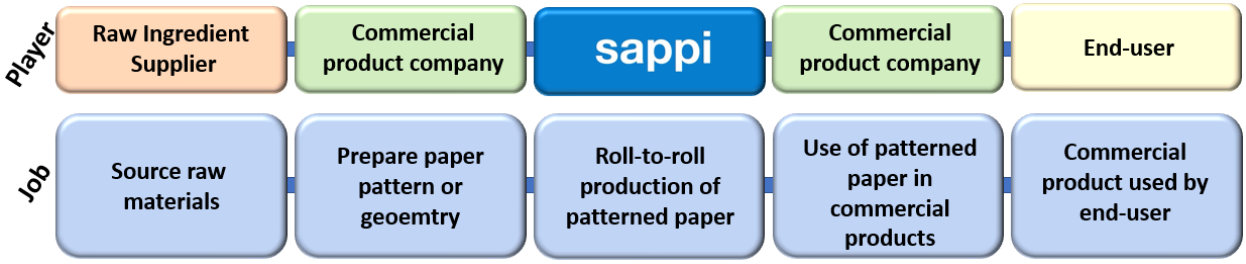

Figure 2.2. **Value Chain of Sappi's R2R Manufacturing Industry.**

Sappi approached the project described in this thesis with a very clear intention of serving solely as the large-scale manufacturer of role-to-role pattern. Therefore, the customer is not necessarily the end-user, but the company that commercialized a product from the manufactured patterned paper. This also meant, in many cases, that the party responsible for selecting what pattern to print could either be Sappi or the customer, depending on the uniqueness and specificity of the customer's needs.

2.6. Value Propositions

Regardless of the customer, it is necessary to identify the key value propositions that the role Sappi plays in the value chain provided to their customer. Value propositions are the core essence of benefits provided to customers through a product (e.g. faster, better or cheaper)**.** In the case of Sappi, due to the highly scalable nature of their existing R2R manufacturing process, their value propositions are providing large volumes of high-precision patterned papers or films with tunable surface chemistry. Commonly, the greater the number of value propositions provided by the technology, the more problems the technology is able to solve, resulting in greater commercial potential.

2.7. Mind Mapping

Identification of value propositions offered by the technology allows for visualization of the wide range of potential markets and their individual respective problems that the technology can service. With a value proposition as broadly applicable as a high-volume, high-quality and highly consistent manufacturing process, the applications become expansive – introducing the potential for oversight or lack of proper organization to lead to missed opportunities, or the inability to generate a strategy for beachhead market launch and penetration into parallel markets. An appropriate Innovation Engineering concept for such technology application ideation is the mind map, which structures free-association of thoughts generated in response to four stimuli relating to the prompt, where the prompt is an open ended statement in the style of "I need ideas for _____". A method of mind mapping employed in this work is a derivative of the Mind Mapping process developed by Tony Buzan, which uses a diagram to visually display or map information radially using branches.[69]

In the mind map generated for this project, the prompt was "We need ideas for Sappi platform applications", and the categories of diagnostics, mechanical devices, optical and treatment as stimuli. This resulted in the generation of a range of possible technology applications, the outcome of which is shown in Figure 2.3.

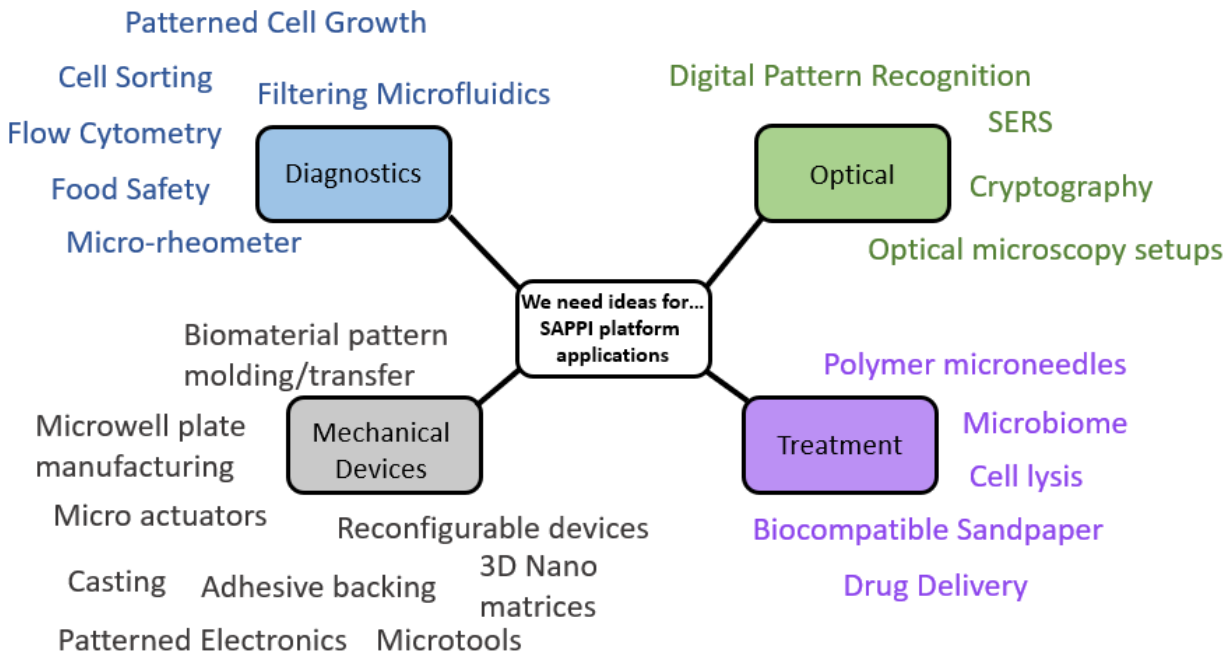

Figure 2.3. Mind Map of Sappi Platform Applications. Ideas generated for Sappi platform applications, spanning out from initial stimuli of Diagnostics, Mechanical devices, Optical, and treatment.

2.8. Mining

Although an array of applications was generated and visualized the mind map exercise, it is of critical importance that meaningful ideas are arrived at through more than one medium – a diverse spectrum of stimuli is the key ingredient that leads to an abundance of good ideas. To find more stimuli, one must go 'Mining', or searching for information through various channels. Innovation Engineering helps systematize this mining process, categorizing the types of mining (shown below) to help 'spark ideas and fresh thinking'[67]:

- Patent: 'Referencing existing patents and inventions'
- Wisdom: 'Referencing academic research'
- Insight: 'Reference the voice of the customer'
- Future: 'Referencing trends and predictions'

- Market: ‘Referencing information about direct/indirect competitors, and internal/supply chain assets’

In this work, the core methods of mining that yielded the most significant returns were patent mining, future mining and market mining.

2.8.1. Patent Mining

Through patent mining, we referenced existing patents and inventions to use as stimulus, which involved searching for patents that could be identified using key term relevant to the Sappi platform (e.g. precision manufacturing, high-volume manufacturing, roll-to-roll manufacturing, paper-based platform, paper-based biotechnology) in the USPTO patent search database. Thousands of patents meeting this basic criteria have been applied for and granted, therefore we referenced such patents from an array of applications, as well as formed a collection of patents close to our niche. With these, we compiled a table illustrating the patent number, what entity it was issued to, an abstract-style description of the patent, and claims made relevant to our work. As patenting a design or a process is typically a first-line means to establish a competitive differentiator (as a right to block competitors from entry into the space), an abundance of patents can be found in virtually every application of technology relevant to ours, which provided a salient visualization for the breadth of applications of the Sappi platform technology.

2.8.2. Future Mining

The process of future mining guided the search for trends and predictions in the industry to not understand what is possible and common now, but what is anticipated to occur, become a large driver, or even disrupt an entire industry in the future. As Sappi was interested in a broad understanding of biotechnology applications of their platform, the search for future trends was broadly spanned to

capture trends in biotechnology and medicine, resulting in primary mining sources such of seminars, market projections, talks and blogs delivered by industry thought leaders, and literature to be insightful mechanisms of stimuli. From these, it was clear that point-of-care diagnostics and personalized medicine were two emerging fields where a high precision, low-cost and potentially disposable medical device could have significant use-cases.

2.8.3. Market Mining

The component of market mining involving looking to market research reports as an indicator of future trends also falls in the category of market mining, which broadly looks to direct and indirect competitors, and internal and supply chain assets as stimuli. There are several channels by which market mining can be an effective practice: searching online for market research reports to understand industry category break down and sizing, looking to competitors to understand what they're doing and how they're differentiating themselves in a competitive landscape, and talking to stakeholders in the industry to first-hand understand what the un-met pains or potential gains are.

Market mining revealed one of the largest emerging medical device markets within healthcare is point-of-care (POC) diagnostics devices, which can be thought of as a 'total addressable market', or TAM. Identification of this TAM shed light on an array of benchtop to bedside applications for Sappi's technology, which warranted further investigation into the applications within POC diagnostics where the Sappi technology may best fit, also known as the serviceable addressable markets (SAMs). A comprehensive list of applications identified during these mining efforts is shown in Appendix A.

2.9. Customer Discovery

Knowing that the goal was to find the SAMs within the TAM, or the applications in the POC market, an effective means to identify such information is to directly ask stakeholders in the industry

about how they would perceive a high volume micropatterning technology, what feasible applications they could imagine and see a need for in their industry, and what size of an economic opportunity might each use-case represent.

Customer discovery is the process of generating and testing hypotheses about what the customer's problems are, testing the quality of a solution to address that problem, and iteratively honing in on the fundamental components of the problem, while simultaneously iterating the solution to best meet the dynamically evolving perception of what the true problem(s) are.[67] The ultimate goal is to gain clarity of the problem (value propositions desired) and quality of solutions to address the problem (value propositions delivered) to eventually arrive at product/market fit, where the nature of and quality of value propositions delivered to the customer are so meaningfully unique that they feel compelled to renounce the way they currently solve their problem and adopt the new solution. The practice of customer discovery was spread mainstream by Steve Blank, a highly successful serial entrepreneur that established processes and methods for doing so within his own companies, and subsequently brought the process to the public through the form of curriculum development, literature and workshops. Customer discovery has become a powerful process for learning, adapting and arriving at product/market fit for small to large organizations. For this project, customer discovery was used at different stages for ideation, iteration, and honing in on product/market fit.

The first iteration of customer discovery was oriented towards the goal of finding SAMs within the POC TAM, so interview efforts were directed towards the right audience to yield the type of answers and insight sought after. To do so Matt Talbot, a team member, attended BioMedDevice (Boston, MA, 18th-19th April 2018), which gave way to numerous pivotal conversations with companies in the biotechnology materials and plastics industry. During these interviews, open-ended questions (further detail in Appendix B) were used to probe for applications of microfabrication and high-volume manufacturing to industry stakeholders such as raw ingredient suppliers, manufacturers, distributors,

operating companies that use manufactured goods in their products, and end-users of those products. The goal was to understand the value chain of major companies in the industry and with this information, render an intuitive visualize applications and where the Sappi technology could most organically achieve product/market fit, and whether there was an opportunity for substantial financial upside in doing so. During this process, we asked open-ended questions in a high-level introductory portion of the conversation to understand who the person is, what they think/feel about, and the challenges they face. Following these questions were more inquisitive questions that aimed to get down to the fundamental truths about the real problems and perceptions of the current solutions. The flow of questions was typically as follows:

- 'Tell me about how you current do/solve ____'
- 'Why is it important that you do/solve ____?'
- 'What happens if you don't do/solve ____?'
- 'What do you wish you were able to do/had in the way you do/solve ____, that you aren't able to do currently?'
- 'Tell me more about ____' (specific application or topic)
- 'What is it that you love/hate about ____'
- 'What would happen if you weren't able to ____'
- 'How does it feel when you're finally able to ____'

This event provided an abundance of learnings about the different applications and a more educated perspective on how to view each individual opportunity. Three opportunities were ultimately identified.

2.10. Market Identification and Segmentation

After synthesizing information from each form of mining and applying a more well-rounded perspective on the state of the industry from the conference, several factors to vet new opportunities

were employed: market size, current breadth of use-cases, and up-and-coming use-cases. With these, opportunities were filtered until three key applications were reached. These were:

1: Microfluidic mixing, which involves mixing of two or more small fluid volumes on the microscopic scale, is one of the most commonly published-on concepts in point of care diagnostics literature[11,65,70–72], as it is a key function for diagnostic applications. From market research, the mixing market is maturing but ripe for innovation, and likely represents the largest current ability to commercially deploy the Sappi technology on a broad scale.

2: Droplet generation, an technology which involves the formation and manipulation of discrete micro-scale droplets, constitutes a field that seeks to create microfluidic droplets for biological screening platforms[73], cell based assays[74], pharmaceutical applications[75], and many others. In medicine, microdroplet generation enables high-throughput testing, including an individual's cells for reactivity to a range of drugs for personalized medicine. Microdroplets are also relevant in the cosmetics industry, with late stage French startup Capsum collaborating with CHANEL to produce a new range of microdroplet rich products made in microfluidics to provide a unique texture, preservation method, and aesthetic. Conversations with potential strategic partners at the conference revealed that companies in the droplet generation space are actively seeking a manufacturing partner that can lower their margin and produce high-precision devices for them in their commercial droplet generation applications. Microfluidic droplet generation was also identified from conversations with the CEO of Dolomite, a leader in microfluidics that is heavily interested in the droplet generation space.

3: Cell sorting, which is a new up-and-coming diagnostic measure that can be used for early detection of a range of diseases. Initial scoping of cell sorting began during the MIRTA program as a result of a phone call with Stephen Pelsue of BBI Solutions in Maine, as he expressed their

customers in biopharma were increasingly interested in flow cytometry and cell sorting. Cell sorting was also one of the most common presented-on topics at the BioMed Device conference and the Microfluidics Consortium. This indicates that sorting is a growing sector in the market and one that companies will inevitably seek high-precision and high-volume manufacturing partners in the drive to create better products at lower costs.

Again, these applications can be thought as 'serviceable obtainable markets' or SOMs, which are specific markets where a clear understanding of value propositions drives a quantifiable size of the market. A SOM is a market opportunity that can realistically be obtained in a discrete amount of time. SOMs all fall within a series of SAMs, or 'serviceable addressable markets', which in this case is generally microfluidics. Finally, the series of SAMs fit in the overarching 'total addressable market', which engulfs all applications in each market, therefore in this case is point of care. This hierarchy is illustrated below in Figure 2.4.

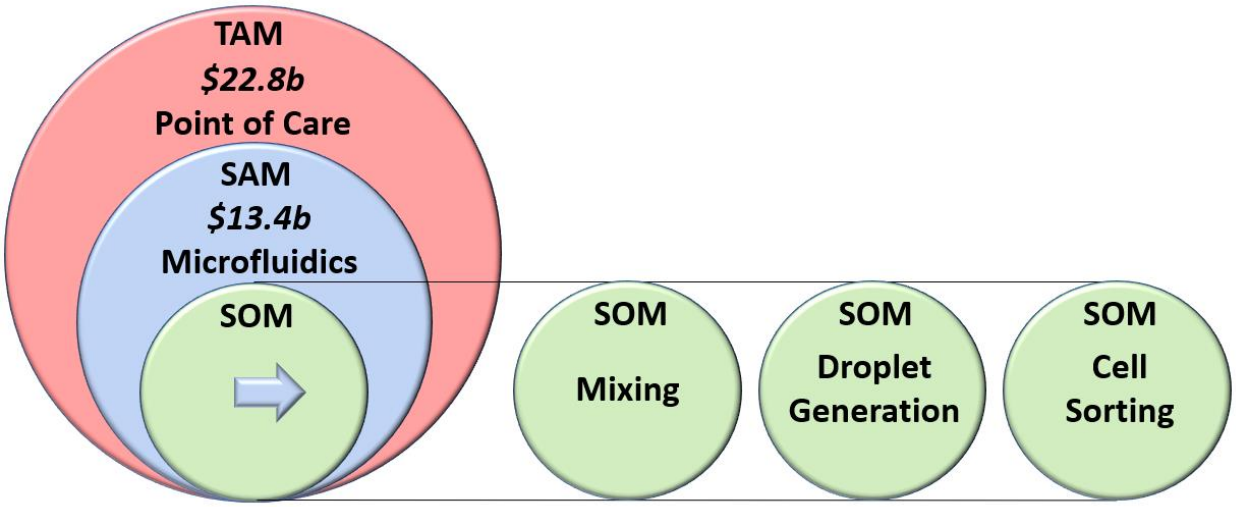

Figure 2.4. TAM, SAM, and SOM of Key Sappi Applications. The total addressable market (TAM)[76], serviceable addressable market (SAM)[77], and serviceable obtainable market (SOM) broken down into 3 key identified applications: microfluidic mixing, droplet generation, and cell sorting.

2.11. Concept Prototypes

An important takeaway from in-person customer discovery efforts was unearthing the common use of concept prototypes to communicate value (before deploying the time and resources to develop physical prototypes) and garner actionable feedback to drive future cycles of prototype development. With the three key applications identified (microfluidic mixing, droplet generation, and cell sorting), the next step was to produce such concept prototypes that demonstrated that the Sappi technology had the ability to be applied. Initially, the goal was to make early prototypes to begin preliminary testing, which involved prototyping by creating a model to minimally demonstrate the concept. For these 'lean demonstrations', CAD models were generated for each pattern or geometry, resulting in finalized designs for all three applications. The generation of these designs is covered in section 3.2.1.

2.12. SAM Customer Discovery

After the designing microfluidic mixer, droplet generator and cell sorter concept prototypes, the next step was to add a summarized description of key value propositions provided to the concept prototype and present them to industry stakeholders to gauge potential interest. For this, attendance to biotechnology-focused conferences relevant to our industry (PEGS Protein Engineering Summit, Boston, MA, 8th-12th April 2018. 2. NPE Plastics show, Orlando, FL, 7th-11th May 2018. 3. Microfluidics Consortium, Boston, MA, 25th-26th June 2018) provided critically valuable learning opportunities. In this phase of customer discovery, a recurring focus was homing in on many of the specifics about our technology use-cases, design constraints, desired/undesired features and some preliminary gauges of adoption readiness for numerous types of customers.

The first conference was the PEGS Protein Engineering Summit, where the most notable interaction was meeting a sales representative from Perkenelmer. One example of a specific need required of devices was less than a 10% tolerance in thickness of films. The next event was the NPE Plastics

show, which reinforced previously stated findings, as well as found that there is a lack of mass-manufacturing options for fabrication of microfluidic devices outside of plastic injection molding and embossing.

The final event was the Microfluidics Consortium, where there were many key companies and stakeholders in the field of microfluidics in attendance. It was evident through interactions with stakeholders within these companies that those who have microfluidic manufacturing capabilities are more actively pursuing life science market opportunities. Representatives from key industry players (Micronit, Dolomite, Fluigent, etc) were also in attendance, resulting in the finding that Micronit was looking at new, roll-to-roll manufacturing processes. Furthermore, the three key applications that were the focus of concept prototype development (microfluidic mixing, droplet generation, and cell sorting) were among the most commonly discussed applications by these players. One last key takeaway from this event was the lack of standardization, which all in attendance unanimously agreed on. This is a problem that our innovation with large scale manufacturing of microfluidics could potentially solve.

2.13. Lean Learning

Through attending the three conferences on microfluidics between the Spring and Summer of 2018 and having the ability to speak with potential customers/competitors/partners, an abundance of use-cases were uncovered, but it took and would continue to take a significant amount of time and resources to validate each application. Overall, interviews initially revealed superficial gaps and pain points experienced by potential customers, and with careful listening, following threads, and objective analysis of what was heard, several underlying core needs from each type of stakeholders could be revealed. This shotgun approach of asking stakeholders open ended questions and presenting concept prototypes was an effective way to validate what the fundamental problems are, however, validating

our ability to deliver on core value propositions (in this case, Sappi's core technology capabilities) would require a different methodology.

To determine our ability to deliver on core value propositions, it became necessary to design test experiments to demonstrate and de-risk the Sappi platform's core functionalities. In such experiments, positive outcomes would provide validation for not one application of the platform, but all of them, thereby working through innovation and de-risking cycles in a leaner fashion. This is a common practice in numerous fields- from agile development in software to lean startup methodology in early-stage startup companies- all of which require clarity for what the core competencies truly are in the prospective SAMs.

When considering the SAMs of microfluidic mixing, droplet generation and cell sorting, features in each category possess distinct characteristics relative to one another, that serve distinct roles; however, all of these unique features (e.g. channel size and wall curvature for droplet generation, artifact or peg placement to direct cells in cell sorters) are based on the ability of the device to manipulate fluid flow, with the overall outcome different, but the core process is the same. Additionally, in each of these commercial use-cases, a strong differentiator lies in the unit economics – the ability for each device to be high-precision mass manufactured, resulting in a low-cost microfluidic product that performs the desired fluid flow manipulation.

2.14. Pivot to Minimum Viable Product Design

Having a succinct understanding for what is required of the platform in the SAMs of microfluidic mixing, droplet generation, and cell sorting, two core competencies emerged that would be necessary to test: the ability for the devices to manipulate fluid flow and the ability to manufacture these devices at a high-volume with high-precision. With these two high-level testable metrics in mind, it became necessary to select experiments that allow for adequate analysis of these two competencies, in (ideally)

the most time and cost-effective manner, to maximize the cycles of learning and testing. This testing process termed the generation of a minimum viable product (MVP), or the most basic version of a product or component necessary to demonstrate feasibility of, and test fidelity of, the desired feature. Considering these variables, we selected microfluidic mixing as the ideal test platform to gauge the Sappi platform's ability to manipulate fluids towards a simple end-goal (mixing) and manufacture these fine fluid channel patterns at a high-resolution in large-batch volumes.

Microfluidic mixers are a valuable extension of patterned paper microfluidics, and in conversations with potential diagnostics strategic partners/customers, we found that they were interested in reproducing what mixing patterns they currently used on a most cost-effective, bendable and disposable platform to reduce plastics and improve immunoassay testing with a pre-mixing step. In microfluidic devices, diffusion is the dominant transport mechanism for mixing.[65] Under typical conditions, flows in these channels are laminar, and molecular diffusion across the channels is slow because the two streams move parallel to the direction of flow. Turbulent mixers achieve mixing based on chaotic advection, which stretches and folds the solutions to increase the interfacial area between the two fluids.[70] The goal of the microfluidic mixer MVP prototype development was to create microchannel patterns for mixing streams of steady pressure-driven flows, with low Reynolds numbers. The designs were intended to decrease the length necessary for diffusion, using purely the geometry of the channels to induce chaotic advection. The development of these microfluidic mixing prototypes is described in section 3.2.2.

CHAPTER 3

MATERIALS AND METHODS

3.1. Overview

Described in this chapter are the materials and methods for developing prototypes, performing the MVP testing, and relevant metrics for each feature. The initial step of the experimental processes in this work is the digital design of microfluidic mixing patterns and printing of patterns using additive manufacturing. These were then incorporated into Sappi's R2R manufacturing line and used to generate prototype film replications of open-face microfluidic patterns. The 3D prints were also used to create PDMS soft-lithography molds to serve as an industry standard product for comparison. These patterns were encapsulated in a housing device that allows effective sealing of channels and ports for fluid introduction and disposal, which was designed to allow swapping of the internal pattern for cycles of rapid experimentation. This setup was used to quantitatively assess the mixing of fluids in the channels by using a method for measuring mixing efficiency as a metric to compare function of our products to those manufactured by current industry standards.

3.2. Computer Aided Design Development

All microfluidic prototype patterns were designed using SolidWorks CAD modelling software (SolidWorks 2018–2019). The following sections outline the design process for both concept prototypes and MVP prototypes.

3.2.1. Concept Prototypes CADs

This section outlines the creation of the initial concept prototypes for the microfluidic mixers, droplet generators, and cell sorter applications as described in section 2.11. These drafts of patterns were created to illustrate the basic functionality of each application and served as an initial step towards identifying and validating key feasibility metrics.

A. Initial Microfluidic Mixer Prototype

A search of relevant literature was conducted to find microfluidic mixing patterns with dimensions feasible within Sappi's R2R process. One common method of inducing mixing involves a staggered herringbone mixer (SHM), which uses periodically-placed grooves in the bottom of microfluidic channels to induce transverse flows.[78] The first microfluidic mixing prototype was designed with features similar to a SHM used by Williams et. al..[79] This CAD file was imported into COMSOL Multiphysics software in order to assess mixing performance with dimensions that were adapted for use in the R2R process (Figure 3.1.) as an initial study before investigation of other mixing patterns.

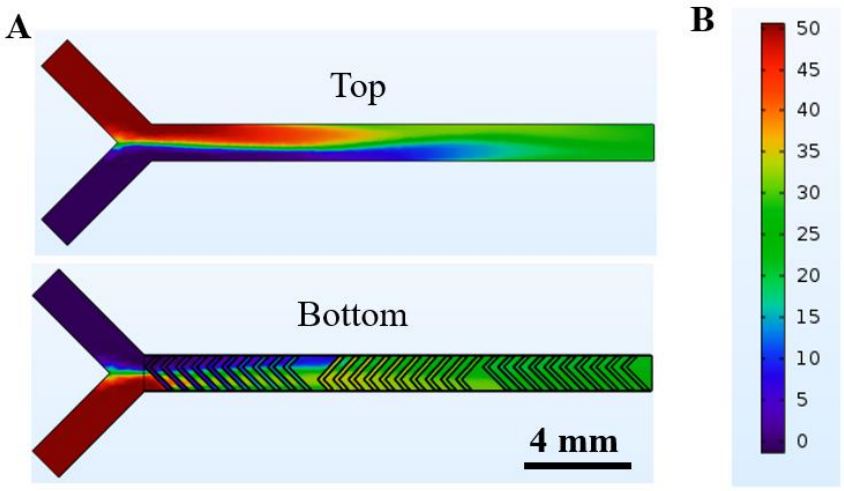

Figure 3.1. Initial Microfluidic Staggered Herringbone Mixer Concept Prototype. A common microfluidic mixing pattern was drafted in Solidworks and imported into COMSOL for initial investigation into mixing efficiency. (A) Top and bottom views of SHB pattern. (B) Relative concentration scale of diluted species flows.

B. Initial Microfluidic Droplet Generator Prototype

A droplet generator pattern used by Tan et. al. was identified due to the simple geometries and mechanism for droplet formation.[80] A droplet generator of this kind was drafted in Solidworks with modified geometries to allow production in Sappi's R2R process (Figure 3.2).

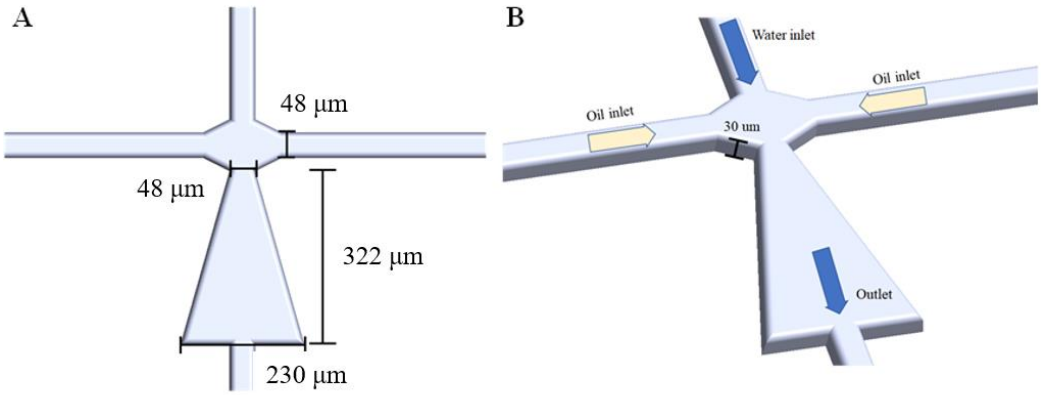

Figure 3.2. Initial Microfluidic Droplet Generator Concept Prototype. Adapted from Tan et. al.[80] (A) Critical feature sizes of droplet pattern. (B) Diagram of droplet generation design concept.

C. Initial Microfluidic Cell Sorter Prototype

Microfluidic cell sorting methods were explored in literature and a passive sorting mechanism called deterministic lateral displacement (DLD) was identified due to the simplicity of design and function. DLD achieves sorting by using the physical interactions between fluids/particles and pillars (which act as physical barriers) to sort by size as opposed to an active sorting mechanism.[81] An initial iteration of this design was drafted in Solidworks based off of a pattern found in literature that was shown to sort blood cells and platelets by size[82] (Figure 3.3). The concept prototype provided in Figure 3.3 allowed for clear visualization of the components and size scale dimensions of a DLD sorter.

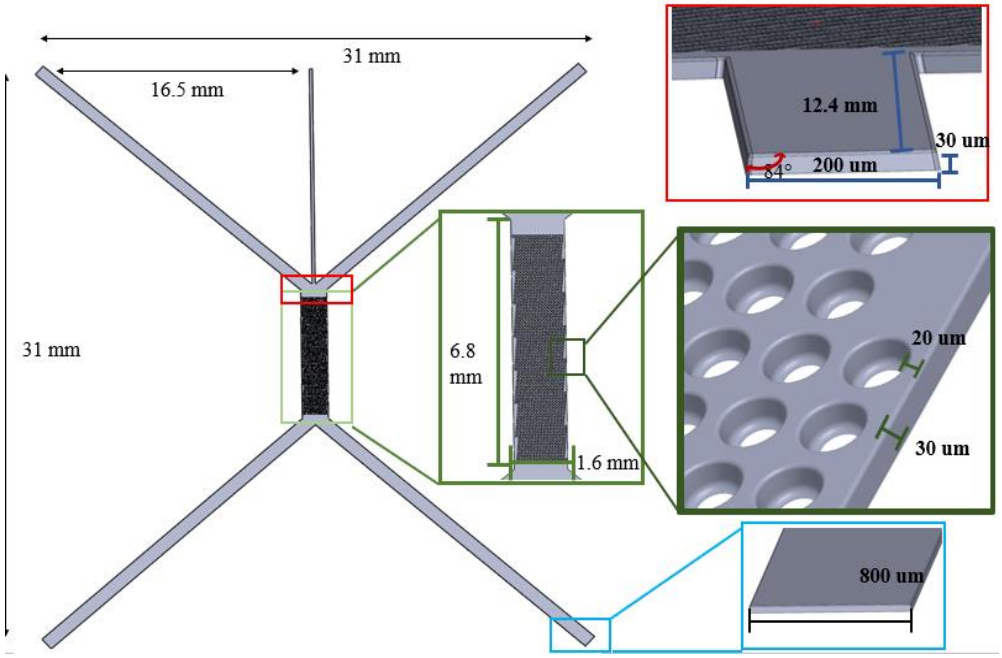

Figure 3.3. Initial Microfluidic Droplet Generator Concept Prototype. Critical feature sizes of a microfluidic cell sorter design prototype, using deterministic lateral displacement (DLD) to separate blood cells based on size. Adapted from Li et. al.[82]

3.2.2. Microfluidic Mixer CADs

Four passive mixing patterns with various shapes were selected to demonstrate a dynamic range of geometric features. The Serpentine pattern in Figure 3.4. (A) was inspired by similar serpentine patterns used for mixing studies found in literature.[41,83] The Diamond mixer pattern in Figure 3.4. (B) was inspired by early experiments conducted to create fluid mixers using transparency sheets and double stick take, where the most successful design featured a “diamond” pattern. The Semicircle pattern in Figure 3.4. (C) was designed as a 2-dimensional rendition of a 3D “twisted microfluidic mixer” used for mixing studies by Sivashankar et. al.[84] Lastly, the Spiral mixer was inspired by a mixing pattern used by Duryodhan et. al. to investigate mixing characteristics in spiral microchannels.[65] The designs functioned as the masters used for molding of the final product, so features were created in the opposite phase. All channel designs had a constant height of 400 µm, and width of 400 µm.

In this work, the serpentine pattern shown in Figure 3.4. (A) was used for the mixing quantification studies.

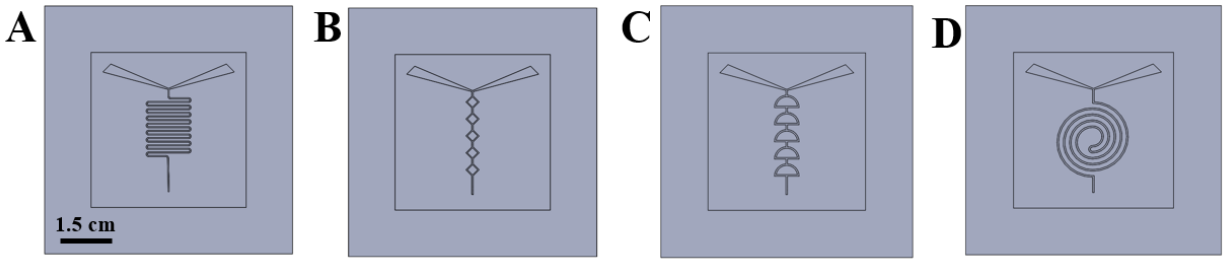

Figure 3.4. CAD Files of Microfluidic Mixing Patterns. Microfluidic patterns designed to demonstrate dynamic range of geometrical features. (A) Serpentine mixer, (B) Diamond mixer, (C) Semicircle mixer, and (C) Spiral mixer.

3.3. 3D Printing Master Molds

Following CAD design, patterns were printed with an Objet30 Desktop 3D Printer[85] housed in the Advanced Manufacturing Center at the University of Maine, using DurusWhite, a polypropylene-like material. Within this 3D printing process several iterations of feature dimensions and conditions were varied to allow optimization of print quality, including minimizing the thickness of the print, aspect ratio resolution, and feature heights. For use in the R2R process it was vital that the thickness of all prints was minimized, but the resolution of the printer limited the minimum thickness to approximately 650 μm in order to retain structural integrity. Figure 3.5. shows the printed mixing patterns used as master molds in the fabrication of both film and PDMS replications.

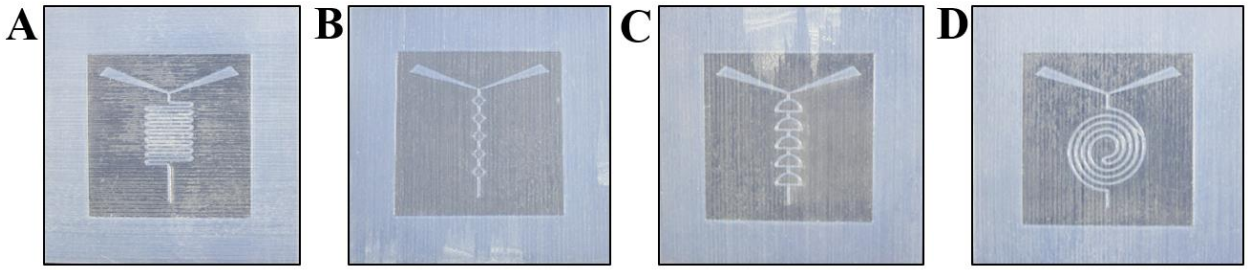

Figure 3.5. 3D Printed Microfluidic Mixing Patterns. (A) Serpentine mixer, (B) Diamond mixer, (C) Semicircle mixer, and (C) Spiral mixer.

3.4. Silicone Moulding

Prototype molds were fabricated out of PDMS using soft lithography techniques to allow comparison of function between industry standard patterns and R2R-printed film patterns. The 3D printed masters were adhered directly to the bottom of a petri dish using epoxy (Elantas Easypoxy® K-230). The prepolymer of PDMS was mixed with the curing agent (Sylgard 184 Silicone Elastomer Curing Agent and Base) in the ratio of 1:10, then mixed at 2000 rpm for 1 minute with a desktop planetary mixer (Thinky). The polymer mix was poured into the petri dish and placed in a vacuum for 60 minutes to degas. The dish was then placed in an oven at 70 °C for 60 minutes. The dish was removed and the PDMS mold was separated from the master 3D print.

3.5. Sappi Printing

The 3D printed patterns were used as masters in the patented electron beam R2R process at the Sappi North America, Inc. Technology Center (Westbrook, Maine). This trade secret process involves direct attachment of printed components to the cylindrical shim to rapidly prototype product manufacturing. A metallic coating on the surface of the 3D prints was necessary to allow effective replication of pattern features and release of the cured acrylate material. To accomplish this all 3D prints were sputter coated with a 35 nm layer of gold-palladium before incorporation onto the shim. The modified shim was then run in the process to produce high volume replicas of patterns in an acrylate material over a transparent film web with a width of 28.0 inches (Figure 3.6.).

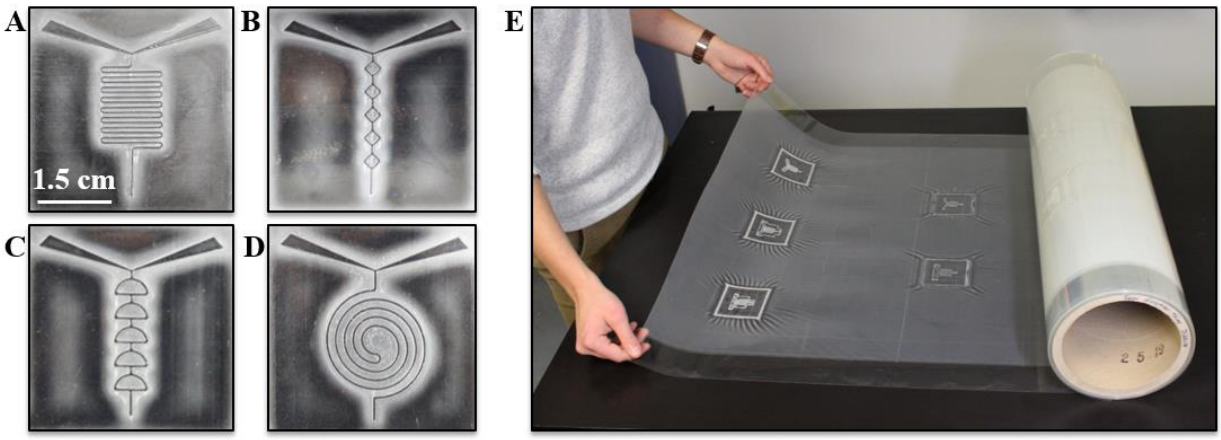

Figure 3.6. Final Film Microfluidic Mixing Patterns. (A) Serpentine mixer, (B) Diamond mixer, (C) Semicircle mixer, and (C) Spiral mixer. (E) Full roll of Microfluidic mixing patterns before separating individual films.

3.6. Device Assembly

The device housing was designed to allow rapid assembly and disassembly of a closed microfluidic channel system for both film and PDMS patterns. The device is composed of laser-cut acrylic sheets with permanently fastened barbed adapters for tubing at the inlets and outlet. All microfluidic pattern substrates were cleaned with isopropanol and air dried prior to assembly to remove residuals from manufacturing and handling. Adhesive sheets (Fellowes 3-mil Self-adhesive sheets) were pierced with a 5.0 mm mm biopsy punch (World Precision Instruments) at the location of the inlets and outlets and placed over the microfluidic pattern substrate. Adhesive tabs (Scotch 12.7mmx12.7mm Mini Tabs) were also pierced with the 5.0 mm biopsy punch and placed with holes aligning those on the adhesive sheet. This unit is aligned with the inlets of the acrylic sheet, and all layers are held in place and provided additional even pressure distribution by 4 sets of magnets (McMaster-Carr Twist-release paired magnets) arranged around the 4 corners of the device. An illustration of this assembly is shown in Figure 3.7. Tubing is attached between the inlet adaptors and two syringe pumps (New Era Pump Systems, Inc.), as well as to the outlet adaptor and a beaker to exhaust fluid. For each experiment, the pattern with attached laminate sheet and adhesive tabs are swapped out in the acrylic housing. For imaging the

entire unit is placed in a 30”x30” light tent (Westcott Digitent), which reduced the reflection of light and evenly illuminate the microfluidic setup for imaging.

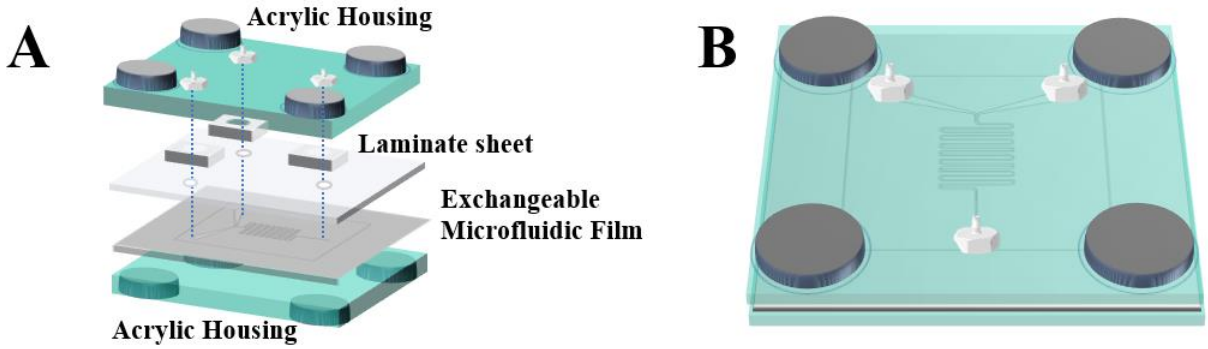

Figure 3.7. Diagrams of Microfluidic Housing Device. (A) Exploded view of assembly. (B) Top view of sealed device with encased microfluidic film.

3.7. Mixing Analysis Experiments

The mixing tests were conducted by flowing two solutions into the microfluidic channels with the aid of syringe pumps. A 3ml syringe containing deionized water and a second 3ml syringe containing a 1% mixture of black ink (Higgins) and water were mounted on syringe pumps (New Era Pump Systems, Inc.) to accurately control flow rates. The pumps were programmed to dispense fluids at 0.15 ml/min, a rate selected as an average representation of ranges of flow rates observed in relevant mixing studies.[50,86–88] The system was run for 60 seconds to ensure equilibrium was reached before images for each trial were taken. Digital images of the flow were obtained using a digital camera (Canon EOS Rebel T5) with a 0.25m Macro Lens mounted on a post and stand.

3.7.1. Mixing Index Formula

Mixing indices are calculated using the intensity values of pixels across a section of a gray-scale image where a mixing event has occurred.[89] All indices involve some metric of the standard deviation of pixel intensities to quantify a profile that is more homogeneous and thoroughly mixed with a low standard deviation, to a profile that is less thoroughly mixed with a higher standard deviation. The

absolute mixing index (AMI) is a method of comparing the standard deviation of pixel intensities to the mean intensity value for a more direct measure of the extent of mixing.[89] The AMI is calculated using Formula (1).

$$AMI = \frac{\sigma}{<I>} = \frac{\sqrt{\frac{1}{N}\sum_{i=1}^{N}(I_i - <I>)^2}}{<I>} \quad (1)$$

Where I_i is local pixel intensity, <I> is average of the pixel intensities in the cross section, N represents the total number of pixels, and σ represents the standard deviation of the pixel intensities.

3.7.2. Normalization of Pixel Data

Although the AMI is a direct measure of the extent of mixing, this method of quantification is not sufficient for the comparison of mixing events across different studies. The mixing index values vary greatly depending on the lighting conditions or variations in the color of inks used even for mixing events that are hydrodynamically identical. This problem can be solved by artificially scaling or normalizing each pixel to the same span of intensities as 0 to 255 on a gray-scale image.[89] AMI calculations done on normalized pixel data result in values that represent the mixing index with modified intensities. This method was used to normalize data from mixing experiments in this experimental process.

3.7.3. Image Analysis and Calculations

The experimental images were analyzed using ImageJ software. Images were converted to 8-bit, and pixel intensity measurements were made at the cross sections of all locations of interest on the serpentine channels using the line tool. Intensity values for the pixels along this line were extracted, and each set of pixel values were normalized as described in section 3.7.2. These values were then exported into Microsoft Excel, where Formula (1) was applied to each set to calculate the absolute mixing

intensity for each location of interest along the length of the channel. The absolute mixing indices with modified intensities were plotted to compare the mixing efficiency for both PDMS and film micromixer experiments.

CHAPTER 4

RESULTS

4.1. Early Microfluidic Prototypes

The patterned surfaces manufactured by Sappi mimic microfluidic channel function when the top surface is sealed with an adhesive laminate sheet, where introduction of fluids through sealed inlets allows visualization of fluid flows in channels. With an early microfluidic prototype, shown in Figure 4.1, a simple system to create microfluidic channels was designed with a pattern designed for aesthetics and demonstrates basic microfluidic function.

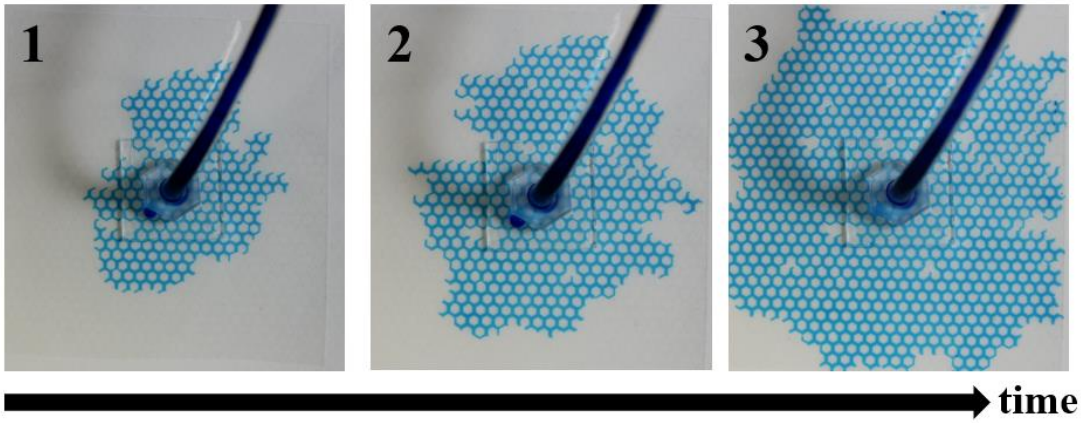

Figure 4.1. Early Microfluidic Function Prototype. A laminate sheet with a 5 mm hole was placed over a paper-based pattern product from Sappi, designed purely for aesthetic applications, sealing the gaps between raised features as closed channels. An adhesive tab was used to attach an inlet connector and tubing over the hole to allow introduction of colored fluids into the channels to visualize fluid flow over time.

The result showed that products manufactured by Sappi could effectively function as microfluidic channels with an adapted sealing mechanism as simple as a laminate sheet. This confirmed that the acrylate material composing the top of the patterns was suitable for microfluidic function, and that feature dimensions were within a range that could be used for microfluidic flows, warranting further exploration into microfluidic applications.

4.2. Manufacturability

The first metric for comparing feasibility of the microfluidic film products and industry standard PDMS products was successful replication of patterns from 3D printed masters and high-volume R2R production of products. This was assessed by analyzing profilometry data of the 3D printed patterns and final film patterns and assessing the discrepancies and how they change over time.

4.2.1 Replication Fidelity

The process of fabricating film microfluidic mixers involves two components of design or feature transfer; the first being the transfer between CAD file to 3D print, and the second being the transfer between 3D print to the final film product. These components are summarized in Figure 4.2. It is important to assess the pattern replication at both components to identify where any sources of discrepancies may arise. These components were investigated for different phases of the Serpentine mixer pattern.

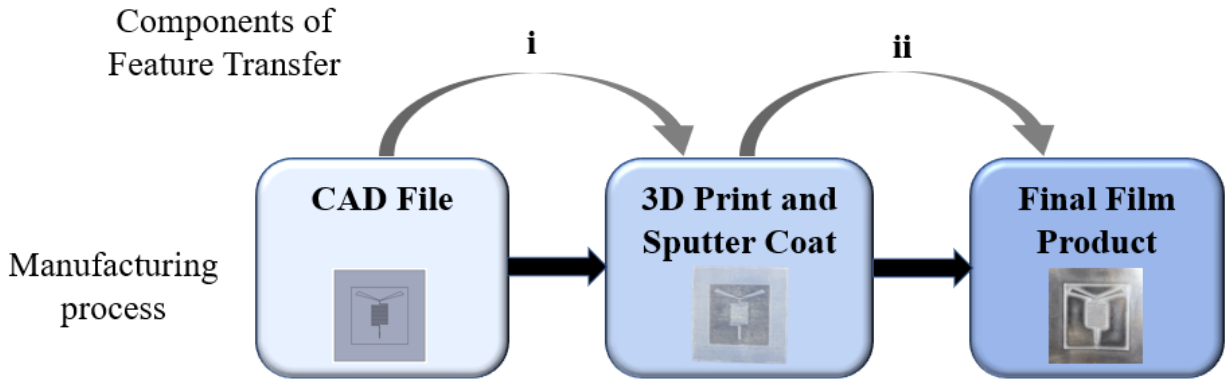

Figure 4.2. Overview of Manufacturing Process and Components of Feature Transfer. (i) Represents the transfer of feature dimensions from CAD file to 3D printed pattern, and (ii) represents the transfer of features from 3D print to the final film product.

Measurements were taken of serpentine channel dimensions at each stage of the manufacturing process. The results are shown in table 4.1., where the dimensions of the raised channels in the CAD file and 3D print are compared to the dimensions of the recessed channels in the final film pattern.

Table 4.1. Feature Dimensions of CAD File, 3D Printed, and Final Film Mixers.

Production Phase	Channel Width (µm)	Channel Height (µm)
CAD File	400	400
3D Print	502.32	390.45
Film	589.32	248.89
Overall difference between CAD file to film:	- 189.32	+ 151.11

The results in Table 4.1 show significant discrepancies between all three production phases. The features of the CAD file and 3D print are in opposite phase of the final film patterns, so the larger measured width of the film channel showed that the resulting film replication is 189.32 µm wider than the CAD file. The film channel was also 151.11 µm shallower than the CAD file. This means that the manufacturing process resulted in a final replication that was incomplete or flawed due to possible errors between the two components of design feature transfer: from CAD file to 3D print or from 3D print to final film product.

4.2.2. High Volume R2R Production

Assessment of the quality of the prints over several sequential printing cycles consisted of a topographical analysis of 3D printed film samples taken from the beginning, middle, and end of roll production. Each consecutive sample created during production is referred to as a pass, where the first sample represents pass number 1, the middle sample represents pass number 68, and the last sample represents pass number 117 at the end of the roll. Measurements were taken at the two locations shown in Figure 4.3, on each mixer sample shown in Figure 4.4.

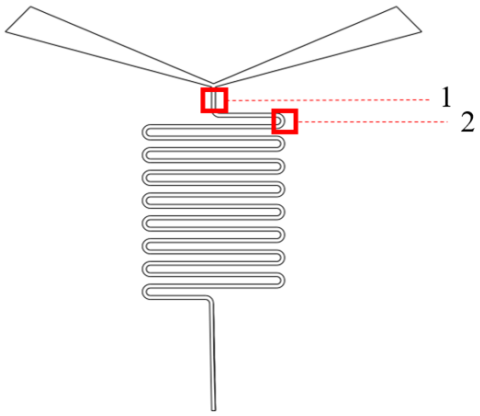

Figure 4.3. Measurement Locations for Feature Replication Analysis in R2R Process. Locations 1 and 2 mark where profilometry measurements were taken for each of the 3 samples taken from the roll of printed mixers to compare dimensions from the first pass, a middle pass, and end pass.

The two locations in Figure 4.3. were chosen to isolate feature sizes of the microfluidic channel in areas of both straight channel geometry (location 1) and curved channel geometry (location 2). Measurements of feature dimensions in location 1 are presented in Figure 4.4, and measurements for location 2 are presented in Figure 4.5.

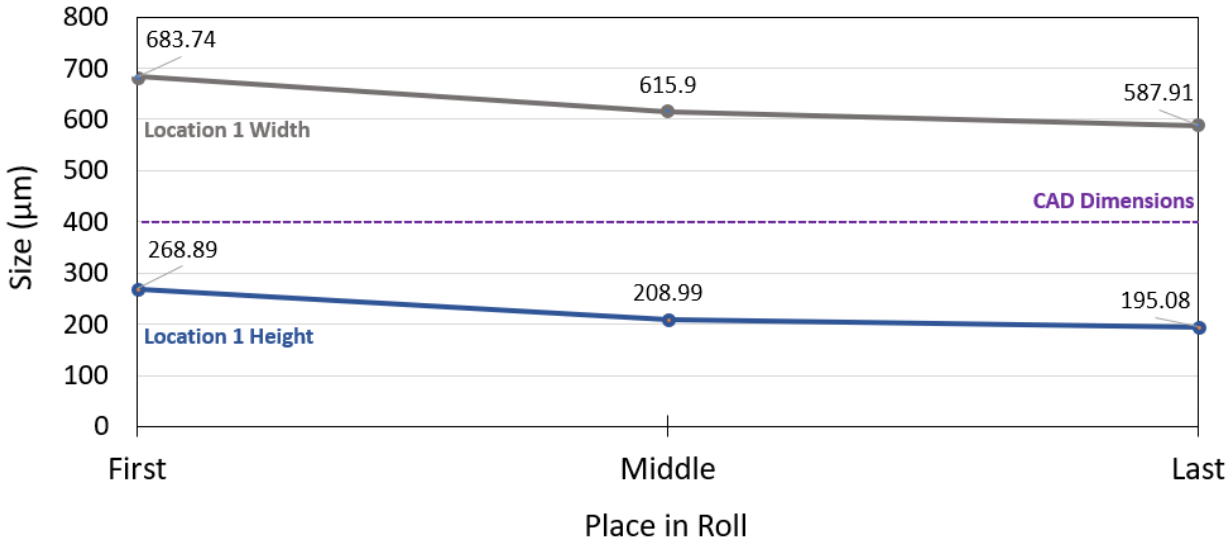

Figure 4.4. Measurements of Serpentine Channel Width and Height in Location 1. The serpentine channel width and height are shown for samples taken from the first, middle and last pass at location 1. These values are compared to the height and width dimensions of 400 µm from the CAD file, shown in the dashed line.

These results show that compared to the CAD file dimensions, the channel width in location 1 is larger for all passes and the height is smaller for all passes. Both the height and width of the channels in location 1 decrease from beginning to the end of the roll.

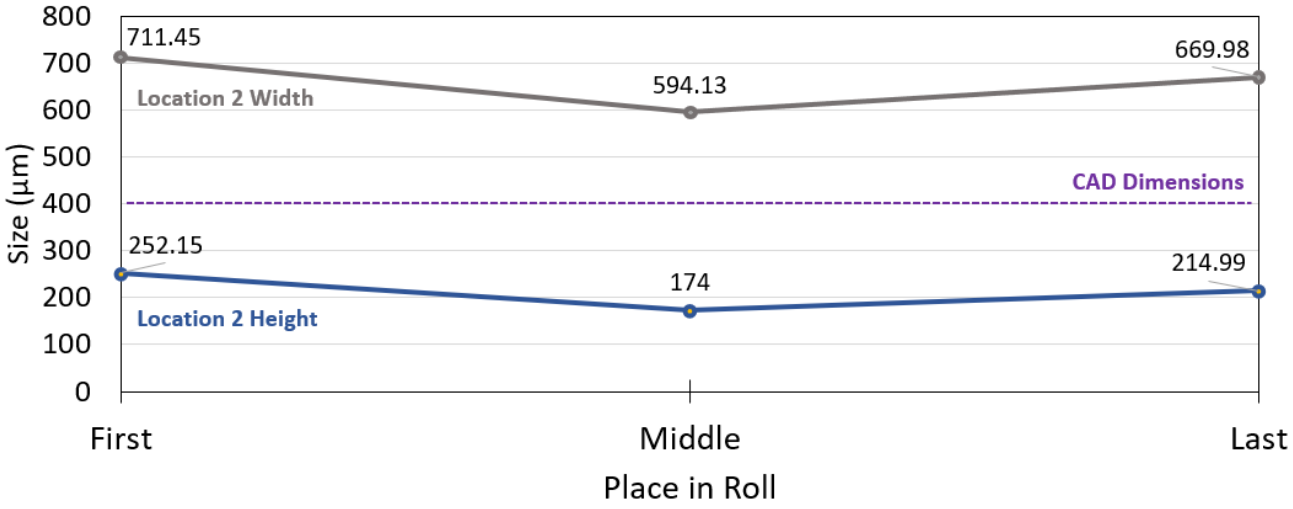

Figure 4.5. Measurements of Serpentine Channel Width and Height in Location 2. The serpentine channel width and height are shown for samples taken from the first, middle and last pass at location 2. These values are compared to the height and width dimensions of 400 µm from the CAD file, shown in the dashed line.

These results show that like the measurements for location 1, the width is larger than the CAD file and the height is smaller for all passes. Unlike the pattern observed in location 1, these feature dimensions decrease from the beginning to the middle pass and increase by the last pass. Results from both Figure 4.4. and Figure 4.5. show that the dimensions change significantly between the 3 chronological sample measurements, indicating a degradation in pattern fidelity from the first pass to the last. To further investigate this, images from the profilometry scans were analyzed in Figure 4.6. to visualize the qualitative print changes in samples from the beginning to end of the roll in both locations.

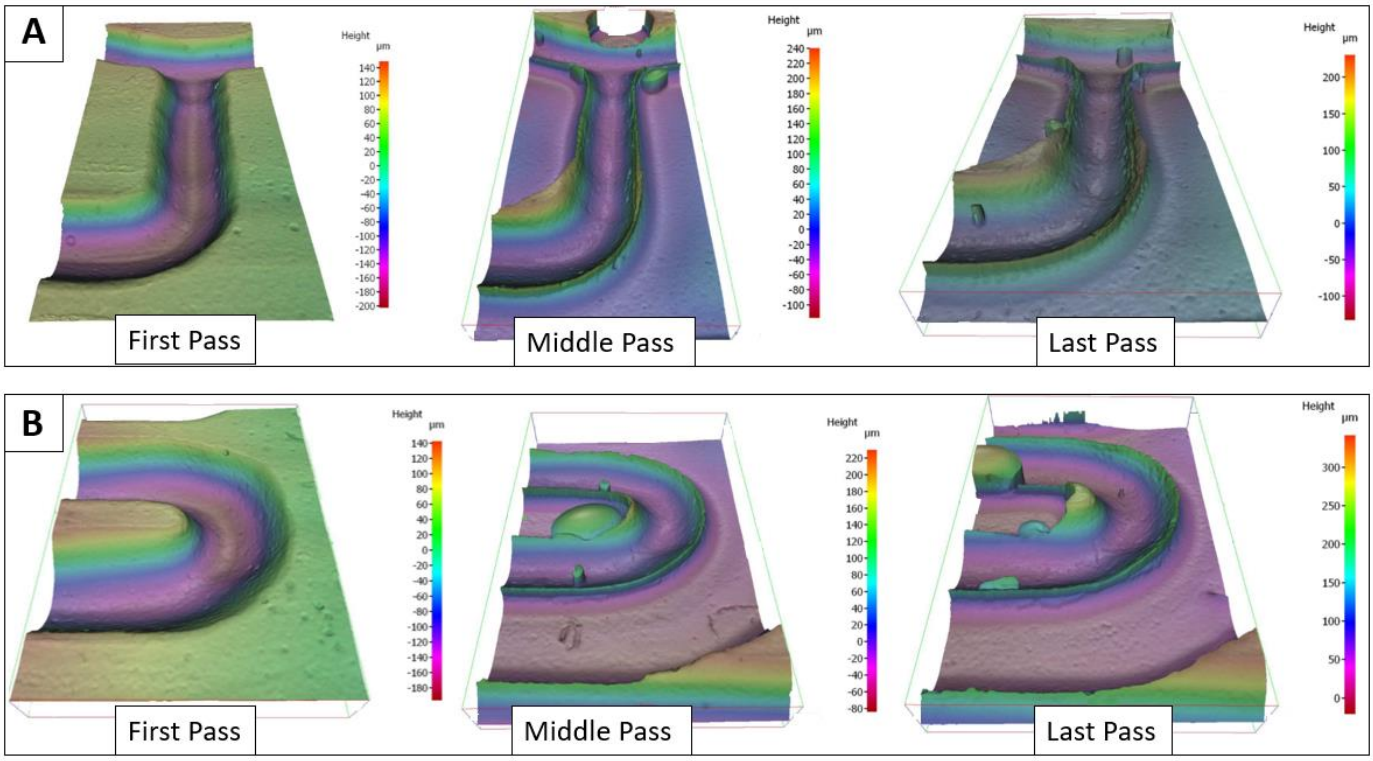

Figure 4.6. Profilometry Scans of Serpentine Channel at Locations 1 and 2. (A) Profilometry scans for the serpentine pattern in location 1, showing degradation in print quality from the first to the middle pass. (B) Profilometry scans for the serpentine pattern in location 2, showing significant decrease in print quality from first to last pass, and the presence of bubbles interfering with channel replication in the middle and last pass.

These results clearly show a degradation in print quality from first to last pass in both locations, with a more significant change in quality in the channels of location 2. These scans show the presence of bubbles in the curved section, which likely acted as a pocket to trap air during the printing process. These bubbles were the cause for the increase of both channel height and width between the middle and last pass. This further validates the degradation in print quality throughout production. Film patterns are also compared side-by-side for each phase of production in Figure 4.7. to assess the quality of print samples qualitatively.

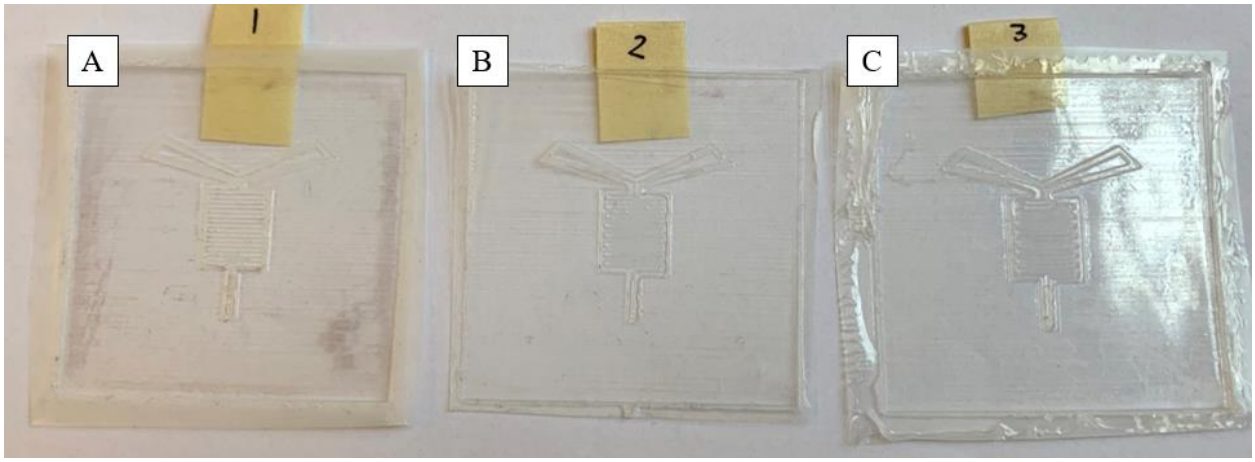

Figure 4.7. Film Product Samples Taken from Different Points of Production in R2R Process. Samples were taken from the beginning (A, pass number 1), middle (B, pass number 68), and end (C, pass number 117) of the R2R patterning process and demonstrate changes in print quality as seen in the presence of pigmentation in (A) and the lack of pigmentation in (B).

Although the printing process is able to replicate microfluidic features, these results further demonstrate degradation of pattern fidelity throughout the production process. The gold coating used to allow release of the cured resin is clearly being stripped away from the 3D printed samples during production. Sample (A) shows a darkened pigmentation around the edges of the otherwise clear patterned surface. This pigmentation is less visible on sample (B) and is not seen on sample (C) from the end of the roll. It is also observed in these results that the border of the prototype patterns changed significantly between sample (A) and sample (C). This loss of gold coating results in a decreased ability of the acrylic matrix to release from the 3D print after curing, and therefore a loss in replication fidelity.

4.3. Functionality

The second metric for comparing feasibility of the microfluidic film products and industry standard PDMS products was assessing the functionality of the microfluidic patterns. This was done by conducting mixing experiments in which microfluidic patterns were used to enhance mixing a solution of black ink and water as described in section 3.7. In early stage of mixing experiments there were significant issues with leaking, both around the inlets and out of the channel boundaries, likely due to unequal pressure distribution from a previous housing setup that used screws in the 4 corners of an acrylic sheet to

provide the pressure to seal channels. After months of experimental cycles, the housing setup shown in Figure 3.7 was derived to counteract the issues with leaking and fluid containment. This was done to use the microfluidic patterns that had been previously printed, and the modified setup included adhesive tabs that often overlap the channel boundaries.

4.3.1. Microfluidic Mixing Function

Using the experimental setup described in section 3.7, the film or PDMS micromixer patterns were enclosed in an acrylic housing for fluid manipulation within the channels. With the final assembly protocol using the setup in Figure 3.7, microfluidic flow was successful for both PDMS and film patterns. A qualitative side by side comparison of both PDMS and Film setups is shown in Figure 4.8. The results qualitatively showed that both channels were successful in achieving microfluidic function and served as an initial demonstration that the film products would function comparably to the PDMS molds.

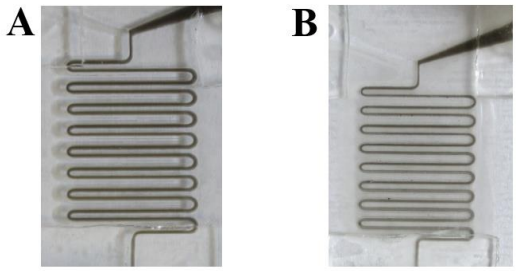

Figure 4.8. Qualitative Microfluidic Mixing Results. Microfluidic patterns demonstrating mixing of water and black ink. (A) PDMS serpentine micromixer, (B) Film serpentine micromixer.

4.3.2. Mixing Index Results

Figure 4.9 (A) shows locations 1 through 6 where the cross sections of the channels were analysed to calculate the mixing efficiency. These locations were used because the channels were not blocked by any components of the acrylic housing and adhesive tabs, so mixing could be assessed without any interference. In Figure 4.9 (B), the absolute mixing index (AMI) with modified intensities was calculated and averaged over 5 trials for both film and PDMS micromixer patterns and plotted as a function of location along the path length. The results showed mixing index ranges that remained above

0.40 for both the film and PDMS patterns, indicating that the fluids did not reach complete mixing within the channel length of the serpentine mixers. Theoretically, the value of AMI varies from 1 (for non-mixing) to 0 (for complete mixing).[90] However, due to background noise in the experimental images the range of values is smaller, between 0.57 to 0.41. For both categories of patterns, the mixing index values decreased along the length of the channel, indicating an increase in mixing without reaching a fully mixed state.

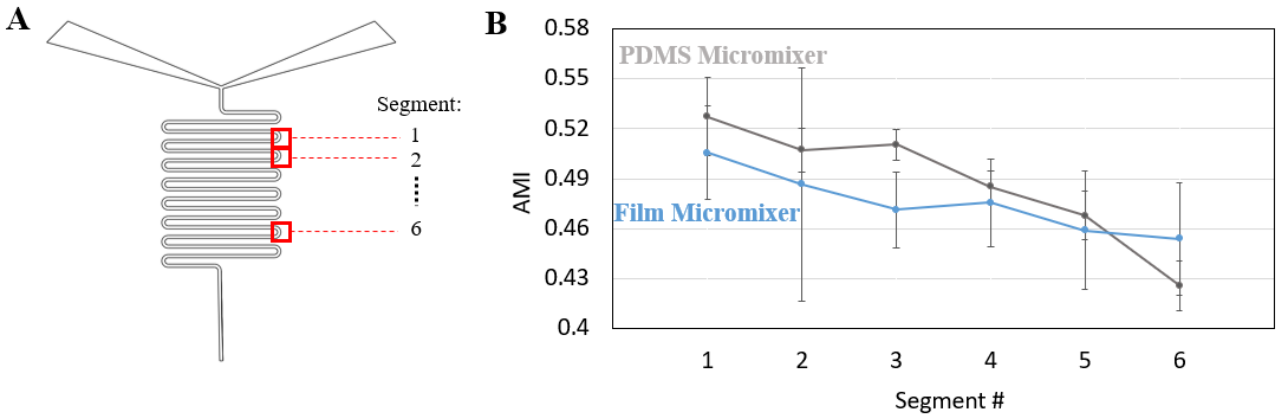

Figure 4.9. Mixing Efficiency Quantification of Film and PDMS Micromixers. (A) Geometry of serpentine mixer; boxes indicate locations for mixing examination. (B) Plot of absolute mixing index (AMI) vs segment location along length of microchannel to quantify function of mixing patterns.

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1. Discussion Overview

The results displayed in Chapter 4 outline the data collected for analyzing the feasibility of the film microfluidic patterns created in the R2R manufacturing process as compared to those made with the industry standard methods of soft lithography using PDMS. This comparison was segmented into two functions with the first segment being that which explored the manufacturability of film patterns, including the ability to replicate the patterns from the 3D printed master, as well as the ability to manufacture the patterns in a high volume in the R2R process. The second segment was assessing the function of the microfluidic patterns using the mixing as a quantifiable metric.

5.2. Metric 1: Manufacturability

Section 4.2.1 presented data on the feature replication of patterns produced in the R2R process. By comparing differences between the features measured at each phase of the manufacturing process it can be concluded that there is a source of error during one of the two components of feature transfer (from CAD file to 3D print, or 3D print to final film product.)

A major source of this observed error is likely resulting specifically from the prototyping process rather than the R2R production process itself. This is supported by the fact that Sappi's release paper manufacturing process is known for its ability to precisely replicate features down to the 100 nm scale.[56] This process requires an extremely high tolerance, as the patterned products are designed for aesthetic purposes and the human eye is extremely effective at detecting visual defects. This means that surfaces manufactured in the same high-volume R2R production process show successful replication of features on the sub-micron scale, demonstrating that the process has the capability to precisely replicate extremely fine feature sizes. The other source of error is from the transfer of features from CAD file to 3D print, where the 3D printer used to fabricate the CAD patterns contributed to these discrepancies. It

was demonstrated in Appendix C that the 3D printer has varying resolutions for different feature sizes, with a higher average percent error found for the width of features in the x- and y-directions than for the height of features in the z-direction. This discrepancy is also presented in section 4.2.1., where there is significant error between the design feature transfer from CAD file to 3D print. Similarly, it has been found in literature that 3D printing has limited applications in microfluidics due to problems with the variations in resolution.[38,42–44] Despite this flaw, 3D printing represents a suitable option for prototyping in microfluidics due to the low cost and accessibility compared to other fabrication methods.[91,92]

Use of a higher-resolution 3D printer would allow for greater control over final product dimensions by limiting the discrepancies in the feature transfer from CAD file to 3D print. The errors resulting from the 3D printing process could also be minimized without changing printers by using the average percent error values for feature height and width in Appendix C as a scaling factor in the design of patterns. Offsetting the dimensions in the CAD file to account for these percent errors would likely reduce the discrepancies that occur during the 3D printing process.

Section 4.1.2 presented data on the high-volume R2R production of microfluidic patterns. Figure 4.4 and Figure 4.5 showed changes in channel width and height of samples from the beginning, middle and end of production in a location with straight features (location 1) and curved features (location 2). For the channels in location 1, both width and height of channels decreased from the beginning to end of the roll, indicating a general loss of print fidelity. Channels in location 2 showed a decrease in measurements from the beginning to middle of production, but there was an unexpected increase in both height and width between the middle to end of production. Qualitative assessment of profilometry scans in Figure 4.6 revealed that air bubbles were being trapped in the curved areas of the pattern during production. The increased presence of these bubbles in the later passes was the cause for the unexpected trend in channel dimensions for location 2.

One likely source for the general degradation of print replication observed in section 4.1.2 is a flaw in the patterning method used for this prototyping protocol. The 3D printed masters were sputter-coated with a 35nm layer of gold-palladium before incorporation into the R2R manufacturing process to allow effective release of the resins used for pattern replication. It was observed in Figure 4.7 that the film patterns produced in the beginning of the roll had a pigmentation on the surface that was not present on the samples from further on in the roll. The pigmentation indicates that some of the gold coating was picked up and retained in the resin. With the gradual removal of this protective coating it is likely that replication fidelity would decline significantly during production due to a decreased ability for the acrylic matrix to release from the 3D printed master pattern after curing.

This issue could be overcome by using a different material for the protective sputter coating that allows release of the cured resins in production. Some examples of potential coatings are polytetrafluoriethylene (PTFE) or fluorinated ethylene propylene (FEP), which are non-stick fluoropolymer coatings that are commonly used as release agents in various moulding processes.[93] Another potential solution could be tiling multiples of the sputter coated master prints on one roll to get a greater number of replications in fewer passes before the coating is removed. On a 28” roll it would be possible to tile approximately 40 of the coated serpentine mixers. Even if the coating is stripped away after 2 passes, running a roll with 40 mixers would generate 80 film patterns before degradation occurs. Prototyping production in this way is still incredibly valuable as it would allow testing of patterns for phenomena like the bubble formation observed in Figure 4.6 before investing the significant resources necessary for creating a full-scale patterned roll.

Another potential source for the trend observed in replication fidelity is degradation of the 3D printed master pattern over time by mechanical deformation or melting, but this can’t be confirmed as the masters were not retained after production for inspection. A solution to this problem could be using a metal-extruding 3D printer to fabricate the master patterns. Metal masters would be more durable

than the flexible polymer masters and would likely limit the degradation in print quality resulting from the loss of gold-palladium coating or damage to the master itself. It is also possible that the acrylic matrix used in production has built up on the surface of the 3D printed masters and filled in the structures, and these modified surfaces are replicated rather than the intended features. These hypotheses could be tested by measuring the profilometry of the master pattern both before and after use in roll production in future work. This would most effectively allow the quantification of any effects of degradation on the master mold to pinpoint the source for replication fidelity changes during production.

5.3. Metric 2: Functionality

In section 4.1., an early-stage prototype was presented to demonstrate microfluidic function using a pattern designed solely for aesthetic purposes. By using a simple adhesive sheet and adhesive tabs for connectors to introduce fluids, it was shown that channels manufactured in the R2R process were able to contain and manipulate fluids like those in microfluidic devices. Section 4.3.1 demonstrated the qualitative microfluidic mixing function of both film and PDMS patterns.

The function of film patterns was further demonstrated in section 4.3.3, where the quantified mixing efficiency of both products was calculated to effectively compare function of both the film and PDMS patterns. In microfluidic channels with straight planar geometries, mixing occurs purely by diffusion.[70] In curved channels like those used in the mixing experiment, transverse secondary Dean flows arise due to the interaction between centrifugal and inertial forces.[94] The curved geometries used in the Serpentine mixer enhance these secondary flows, causing the fluid to travel from the outer to the inner regions where the radius of curvature is smallest. Since the direction of rotation of the secondary flows is not sustained over the length of the mixer it is expected that their strength would not be significant enough to perturb the laminar profile, and over a shorter mixing length the primary mixing mechanism would still be diffusion.[65] For this reason, it was expected that fluids would not reach

complete mixing within the channel length of the serpentine mixers. This was confirmed by the mixing index results in Figure 4.9 (B), which showed ranges that remained above 0.41 for both the film and PDMS patterns.

As the mixing index values presented in Figure 4.9 also show significant areas of overlap, it is reasonable to conclude that mixing performance in the film-based channels is comparable to that in the PDMS channels. Differences in the mixing efficiencies are most likely due to the different material properties of the acrylic matrix (composing the top of film patterns) and PDMS. PDMS is hydrophobic in its native form[95], and it was determined by measuring an average contact angle of 30 µl water droplets on the film patterns that the acrylic matrix is slightly hydrophilic (47.0716°). Hydrophobic and hydrophilic materials have different surface energies and therefore interact with fluids differently, which change the fluid dynamics in microfluidic channels and can result in varying microfluidic performances.[96,97] The different material properties for the film and PDMS were likely a major contributor to the differences in mixing efficiency. Discrepancies in values may also be due to errors in the more variable PDMS moulding process, as well as potential debris in microchannels due to a lack of cleanroom conditions. There were likely discrepancies also resulting from the slightly varying optical transparencies of the pattern. The films have an increase in opacity in the regions surrounding the mixing channel, and the PDMS channels were evenly transparent. This may have resulted in variations in the adjusted focus length of the camera between mixing trials, and ultimately variations in pixel resolution.

It was demonstrated that prototyping the high-volume production of microfluidic patterns on film was feasible in this unique R2R manufacturing process. Ultimately by achieving success by both manufacturability and functionality metrics, it was reasonable to infer that that these conclusions translate to the other applications of interest identified in the customer discovery segment of the project, including microfluidic droplet generation and cell sorting. Towards the next phases of product

development, the droplet pattern has been printed in the same high-throughput R2R process as the microfluidic patterns. It was reasonable to assume that a microfluidic cell sorting pattern could also be manufactured successfully in this manner.

5.4. Future Work

Having proven feasibility to manufacture film microfluidic patterns in this R2R process, additional steps may be taken to further quantify and compare the functionality and manufacturability for microfluidic applications. An important modification for future printing of microfluidic patterns should include an adjustment to the inlet and outlet locations for all patterns. In the adapted housing device proposed in Figure 3.7, it was necessary to include the adhesive tabs to seal the junction between the film pattern and the inlets on the acrylic sheet. The location and size of these tabs interfered with the intensity measurements in the channels located directly below them, and this limited the number of channel cross sections that could be used for calculation of the mixing index. Preventing this overlap with channels in the future will allow for a more thorough analysis of the mixing performance.

Another important step towards effective comparison between film and PDMS pattern function will require a deeper characterization of both materials. Several factors likely contributed to the discrepancies in mixing performance between both pattern types including differences in surface energies which were primarily shown with the differences in hydrophobic properties. The PDMS that was used in this study was chosen due to its availability in the lab, but future work should involve a selection of PDMS with surface properties more similar to those of the films in order to isolate the surface energy as a control for both mixing studies. This would most effectively allow comparison between two different patterns for microfluidic applications. Another important consideration specifically for developing microfluidic patterns for applications involving biological fluids should involve analysis of the surface properties of the film and the interactions with the fluids of interest. Biological fluids can have vastly different properties and the acrylic material used in printing may not be suitable

for all applications. The tendencies of the fluid and constituents to adsorb to the film surface should be assessed to prevent issues with clogging, fouling, and undesired changes in fluid mechanics. Investigation of the ability to tune the surface chemistry of films during production at Sappi may help narrow down applications to those that are feasible.

For future prototype scale production, it was hypothesized in section 5.2 that applying the average percent errors for height and width as a scaling factor in the CAD file may result in a more accurate 3D print and final film pattern. These percent error values should be applied to separately scale the width and the height of a microfluidic pattern, and a profilometry assessment would reveal if this strategy is effective. Based on these results it may be necessary to adjust the scaling factor to achieve the most accurate dimension sizes and minimize errors in production overall.

Improvements to the high-volume production process that were proposed in section 5.2 should also be explored to potentially achieve enhanced manufacturability of film prototypes. Analysis of the 3D printed masters following production would provide greater insight into the specific sources contributing to the errors reported in print fidelity. A method to investigate errors without making major changes to the process would involve printing and coating the masters, as described in sections 3.3 and 3.5, and tiling a greater number of masters onto a single roll for higher volume replication production in fewer passes before the gold coating is stripped away. This would enable cost-effective analysis of feature printability, including the effects of pattern orientation and presence of errors in printing like air bubbles. Future analysis of manufacturability should also involve using more durable materials to 3D print masters, such as a metal-extruding printer.

A general direction for future work on this project should consist of a similar process of characterizing function of the microfluidic droplet generation and cell sorting patterns discussed in Chapter 2. A modified channel-sealing and housing mechanism will likely be necessary for both applications, where the smaller feature sizes will require modified inlet ports and potentially more

permanent sealing to account for the higher pressures of flow in more miniaturized channels. There are likely other applications (or TAMs, SAMs, and SOMs as described section 2.10) where the Sappi platform technology may be able to provide value. An example of one potential application is microcontact printing, where the ability to precisely replicate sub-micron features could be particularly useful. Application of the Innovation Engineering principles described in Chapter two would help process stimulus for idea generation and vet potential markets to find future commercialization opportunities outside of those identified in biotechnology for this project.

5.5. Conclusion

In this work, we evaluated the feasibility of using a unique R2R micropatterning process coupled with 3D printing to rapidly prototype and produce microfluidic devices at high-volume on paper or film backings for applications in biotechnology. First, Innovation Engineering approaches were used to systematize the process of discovering and evaluating applications of the manufacturing process. Microfluidic diagnostics were identified as the primary application, where the ability to prototype and manufacture high volumes of flexible patterns is extremely valuable in developing cost-effective solutions in healthcare. To identify the most lucrative applications within this field we performed customer discovery interviews with industry stakeholders, which lead to the identification of three key applications. These were microfluidic mixing, microdroplet generation and cell sorting, all of which share a core set of technological capabilities for device functionality: the ability to be mass manufactured and to effectively manipulate fluids. We then designed low fidelity concept prototypes and minimum viable products to validate if microfluidic devices produced in our process could meet these capabilities. This was done using microfluidic mixing as the demonstrator, as mixing of solutions is a core component of many diagnostic devices.

Microfluidic mixing patterns were designed in Solidworks and 3D printed for use as masters in the R2R process at the Sappi Technology Center. Prints were coated with a 35 nm layer of gold-

palladium before incorporation into the printing process in order to allow release of the cured acrylate material and effective replication of pattern features. The coated masters were integrated with the cylindrical shim and run in the R2R process to produce high volume replications of patterns on rolls of film.

Metrics were developed to assess the feasibility of the film mixing patterns for manufacturability and fluid handling functionality. Manufacturability was assessed by analyzing the feature dimensions at different stages in production to verify that patterns could be effectively replicated in the R2R process. The manufacturability results indicated that despite some degradation in print quality, likely due to loss of the gold-palladium coating, pattern replication was successful in the process. The quality of prints could potentially be improved by using a different printing material or surface coating with enhanced durability. Functionality was proven using microfluidic mixing experiments, where the mixing efficiency of the film device was shown to function comparatively to a device created with PDMS using industry-standard fabrication methods. Meeting these key metrics validated that the technology could also be applied to patterns used for cell sorting and droplet generation as well as other applications within diagnostics.

The ability to produce microfluidics in a high-volume but low-cost process is potentially highly valuable for realizing success in commercial applications, and this manufacturing method could be the key to developing major advances in diagnostic technologies and revolutionizing healthcare. Microfluidics is a flourishing field where the ability to miniaturize and parallelize processes is a powerful tool for enabling advancements spanning well beyond diagnostics and biotechnology. This work lays the foundation to demonstrate the broad applicability of this high throughput micropatterning technology, setting the stage for others to rapidly and cost effectively validate and develop novel micropatterned products.

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APPENDIX A: MASTER LIST OF IDEAS GENERATED DURING THE MINING PROCESS

Section 2.8 discussed the concepts applied during the idea generation process of customer discovery. A comprehensive list of potential applications of Sappi's R2R patterning process was assembled by searching through mind mapping, relevant patents, academic research, conversations with customers, and market information. This master idea list is provided below:

1. Sappi Neoterix as a colorimetric smartphone-compatible contamination sensor
2. Template for realistic medical simulation mannikin "skin" patterning
3. Oil and Gas Testing: Asphaltene measurements in crude oil
4. Patterned Cell Growth - 3D Culturing in Channels
5. Filtering Microfluidics
6. Food Safety - Sticker with responsive hydrogel encapsulating a food dye within channel
7. Cryptography/Digital Pattern recognition
8. Adhesive Baking Biomimetic Recognition
9. Microbiome
10. Cell Lysis
11. Reconfigurable Simple Microfluidics
12. Drug Delivery
13. Micro-rheometer
14. Microwell Plate Manufacturing
15. Biomaterial Pattern Modeling and Transfer
16. Microtools- casting micro scale tools
17. Miscellaneous Casting
18. Controlled Root/Produce Growth: paper channels direct growth for control of produce
19. Controlled Root/Produce Growth
20. "Blister" Membrane - Reagent/drug release by breaking seal of film covering pattern
21. Sample pretreatment for analytical microfluidics
22. Micro cooling- takes advantage of surface area to volume ratio
23. Molecular diagnostics
24. Cell sorting – viable option for future work
25. Protein Patterning
26. Microreactor
27. Micro-Dessicator
28. Protein Quantification, Bradford Assay
29. HPLC, MS, GC
30. Inkjet deposition
31. Flexible Electronics
32. Pressure Sensitive Conduction (Actuator Driven)
33. Matrix of Nanoparticles or Nanowires Incorporated into Paper
34. Surface Enhanced Raman Substrate
35. Optics with Silver (Dichroics, Mirrors)
36. Polymer Microneedles

APPENDIX B: OPEN ENDED QUESTIONS USED IN CUSTOMER DISCOVERY

Chapter 2 reported efforts conducted during the customer discovery and Innovation Engineering phase of the project development. A critical component of these efforts involved conversations or interviews with companies in various subsets of biotechnology and materials science industries, including industry stakeholders such as raw ingredient suppliers, manufacturers, distributors, and end users. Below are sample questions that were used to guide discussion in different stages of the conversation:

Introductory Questions

Tell me about your role in X organization?

How long have you been with X organization?

What gets you most excited about your job and company?

What are your primary 'jobs to be done' in X organization? What is their role in the industry?

Inquisitive Questions toward intended learning outcomes

What are the primary 'jobs to be done' of your products/services?

What are your products/company are you not able to do currently, that you wish you could?

How much time do you spend on that problem/opportunity?

How are you currently solving the problem?

What do you like about the current solution? What do you dislike?

Probing Questions for deep learning on value propositions and systems

Why is it important that you solve the problem? If you had a solution, what would this mean to you?

How would it change the current way you/your company does things?

What about the problem really keeps you up at night?

What would happen if you weren't able to solve the problem, or what are the biggest risks that accompany your current solution?

If you could wave a magic wand and have any imaginable solution, what might this look like?

If your ideal solution could do only one thing, what might that be?

APPENDIX C: ASSESSMENT OF 3D PRINTER RESOLUTION

Chapter 3.3 described the materials and methods for 3D printing the mixing designs used as masters in the R2R printing process. Technical specifications for the printer used (Objet30 Desktop 3D Printer) reported a resolution of printers down to 28 µm[85], but this resolution can vary depending on a number of other printing parameters and conditions. It is critical to assess the printer resolution for fabricating features with sizes relevant to the microfluidic mixing patterns. To do so, a test chip was designed with tabs of varying height and width dimensions ranging from 200 µm to 1200 µm in Solidworks (Figure C.1.). The tab was printed using the Objet30 Desktop 3D printer. Printer resolution was assessed by measuring the height and width of each tab with an Alicona InfiniteFocus optical 3D surface measurement system and comparing these to the expected feature dimensions from the CAD file. Below is an overview of this process.

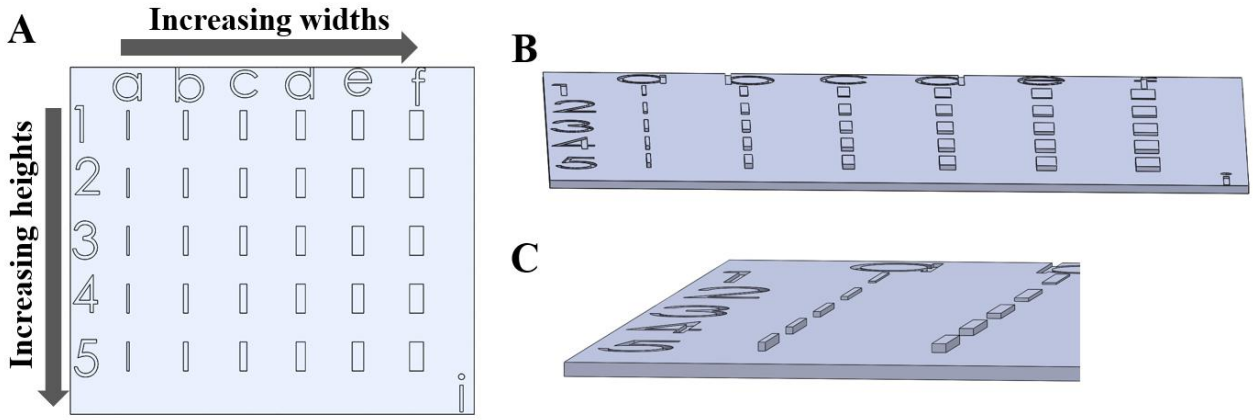

Figure C.1. Test Chip Designed for Assessment of Printer Resolution. The test chip designed with varying tab dimensions for comparison to printer dimensions. (A) Overview of chip, showing the design scheme for tabs with increasing widths along rows and increasing heights along columns. (B) Side view of chip. (C) Close up of isotropic tabs, showing increasing aspect ratios.

The tab shown in Figure C.1. was printed with the Objet30 Desktop 3D printer in Durus White. These prints were measured with the Alicona InfiniteFocus optical 3D surface measurement system, and tab height and width dimensions were analyzed separately to determine z- and x- or y- resolution independently in the tables below.

Table C.1. Tab Height Comparisons Across Rows 1-5.

Row #:	**1**	**2**	**3**	**4**	**5**
CAD Dimension Height (μm):	50	100	150	200	250
Average Measured Height (μm):	52.6497	110.4855	169.1701	197.4114	246.682
Percent Error:	5.2994%	10.4855%	12.7800%	1.2943%	1.3272%
				Average Height % Error:	**6.2373%**

In general, the heights presented a larger percent error when the ranges were between 100-150 microns. The average percent error for the heights of all printed features is 6.2375%.

Table C.2. Tab Width Comparisons Across Columns a-f.

Column:	**a**	**b**	**c**	**d**	**e**	**f**
CAD Dimension Width (μm):	200	400	600	800	1000	1200
Average Measured Width (μm):	309.9697	380.2963	531.3169	687.0535	846.8313	1055.456
Percent Error:	54.98487%	4.9259%	11.4471%	14.1183%	15.3169%	12.0454%
					Average Width % Error:	**18.8064%**

The average percent error for the widths of all features is 18.8064%, with the highest percent error found for features with widths of 200 microns. These numbers indicate that the printer has higher resolution in the z-direction compared to the resolution in the x- and y-directions.

BIOGRAPY OF THE AUTHOR

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