Cell Sorting & Cell Counting Using Passive Microfluidic Devices

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Thesis Supervisor

Dr. Jawad Aslam

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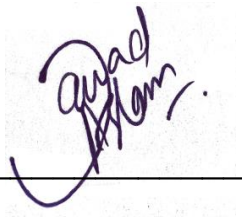

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2019-NUST-MS-Mech-319885

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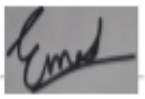

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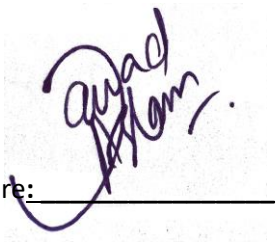
Signature: 

Copyright Statement

Acknowledgements

First and foremost, starting with the name of **Allah Almighty**, the most beneficent, the most merciful, all praise and thanks to Allah for His endless blessings in letting me through all the difficulties. Without His never-ending help, my efforts would have meant nothing.

I would like to extend sincere thanks to my supervisor **Dr. Jawad Aslam** for all stages of my research and thesis work. I would like to thank the rest of my examination committee & a special thanks to **Dr. Emad Ud Din** for guiding me throughout my project, boosting up my morale and giving valuable insights as the GEC member.

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Muhammad Mansoor Ud Din

Abstract

This research work focuses on the development of high-performance capillary pumps for low-cost point-of-care diagnostic devices using printed circuit board (PCB) technology. The study explores the design and fabrication of capillary pumps using PCBs and polydimethylsiloxane (PDMS) to create microfluidic devices. Two different designs of PCB-based micropumps with hexagonal-shaped micropillars are proposed, offering different vertical distances between rows to achieve varying flow rates and fluid volumes. The fabrication process involves designing the PCB microchannel, cutting the PCB fiber sheet, creating silicon molds, pouring and curing PDMS, bonding the PDMS replicas to a substrate, and testing the micropump's performance for both the designs. Experimental setups are established to measure the flow rate and pressure drop of various glycerin ratio solutions in the microfluidic system. The results indicate that as the glycerin content increases, the flow rate decreases due to increased fluid viscosity. Design 1 consistently exhibits higher flow rates than Design 2 due to the smaller gap distance between micropillars. The findings demonstrate the effectiveness of PCB-based capillary pumps in controlling fluid flow and offer valuable insights for the development of low-cost point-of-care diagnostic devices. The design of micropumps for studying blood flow at low flow rates offers significant advantages in investigating blood-related conditions. The precise control overflow rates, realistic simulations, integration with microfluidic systems, drug delivery studies, and reduced sample requirements all contribute to a deeper understanding of blood disorders and the development of personalized treatment approaches.

Key Words: *Microfluidics, Capillary action, Micropump, Self -Perpetuating*

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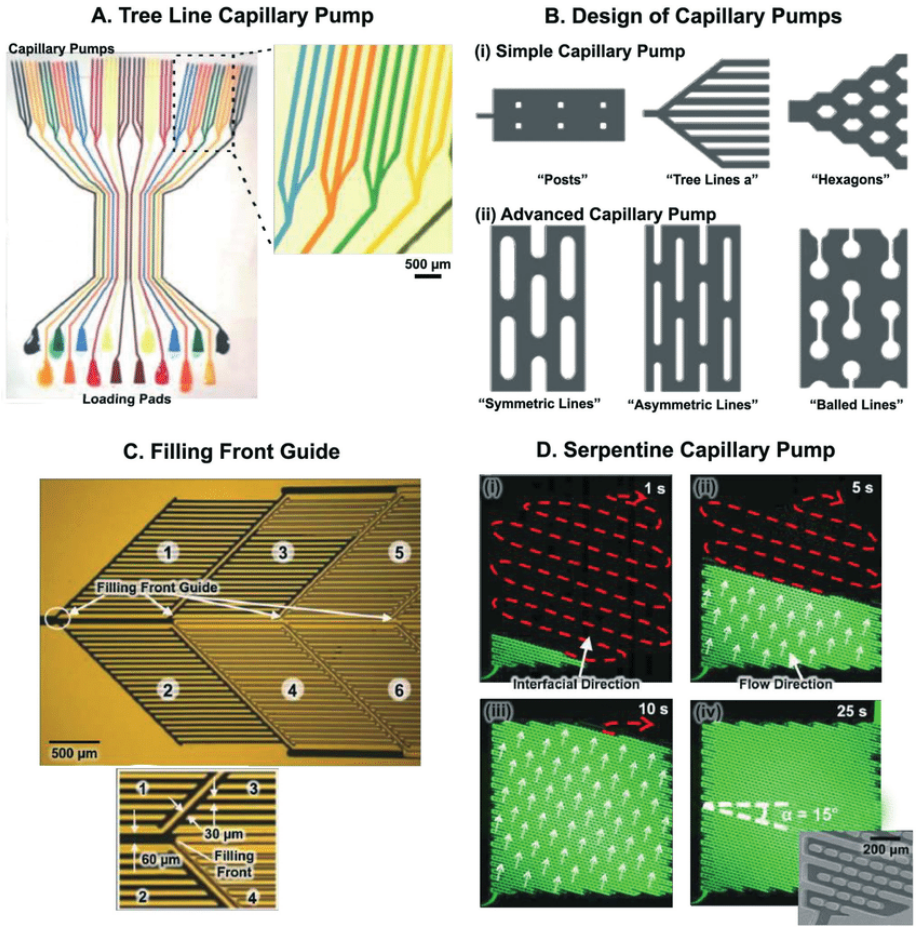
Chapter 1 - Introduction

Self-perpetuating pumps are those which work on capillary action to transfer fluid toward its destination, and it does not require any external source [1]. The liquid keeps flowing because of the capillary action, the propulsive force that helps cause the flow. The design of a capillary pump is significant in this scenario. Out of all available technologies, the suitable and appropriate method for designing and fabricating capillary pumps assimilates PCB (Printed Circuit Board) technology. It allows a more efficient and reliable capillary pump that can be used in affordable point-of-care diagnostic devices.

1.1 Capillary Micropump

A self-priming capillary micropump works by utilizing the phenomenon of capillary action to pump fluids through small channels. Capillary action is the ability of a liquid to flow in narrow spaces without the assistance of, or in opposition to, external forces like gravity. The micropump



typically consists of a channel with a small diameter, which is filled with a liquid. Applying external pressure to one end of the channel results in the liquid being compelled to

move through the channel, thanks to capillary action. The flow of the liquid will persist until the pressure is relieved, causing the capillary action to cease and the liquid to stop flowing. The micropump's ability to initiate operation without the presence of liquid is attained through the utilization of a liquid that can easily adhere to the channel walls, enabling the liquid to be drawn into the channel and commence flowing.

1.1.1 National Needs

Capillary self-priming micropumps offer numerous potential applications that address important national requirements, including:

- **Medical diagnostics:** Capillary micropumps can be integrated into portable diagnostic devices, such as point-of-care diagnostic systems, to enable efficient and accurate testing in remote or resource-limited settings.
- **Environmental monitoring:** Capillary micropumps can be used to pump and analyze small samples of water or other environmental fluids, making it possible to detect and

Figure1: Different Designs of Capillary Micropumps

monitor contaminants or pollutants in remote or hard-to-reach locations.

- **Food and water safety:** Capillary micropumps can be used in food and water safety testing, to detect bacteria, viruses, or other pathogens.

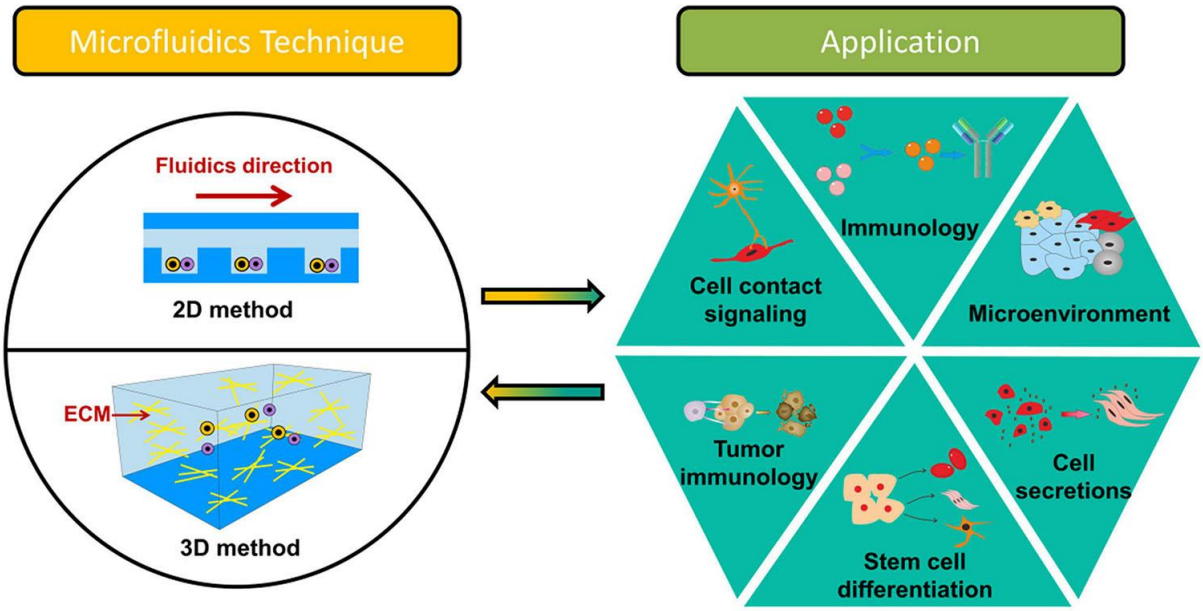


Figure 1: Frontiers of Capillary Pump Usage in Ecology

1.1.2 Advantages of Capillary Micropumps

Capillary self-priming micropumps exhibit various benefits in comparison to alternative micropump types, including:

- **High flow rate:** The small channel diameter of capillary micropumps enables them to achieve high flow rates, facilitating the rapid pumping of substantial liquid volumes within a brief timeframe.
- **Self-priming:** Capillary micropumps are capable of self-priming, meaning that they can start pumping liquid without the need for manual filling or priming, making them more convenient and user-friendly.
- **Low power consumption:** Capillary micropumps typically use minimal power, making them suitable for portable or battery-powered applications.

- **Compact size:** Capillary micropumps are small and lightweight, making them easy to integrate into microfluidic devices or other compact systems.

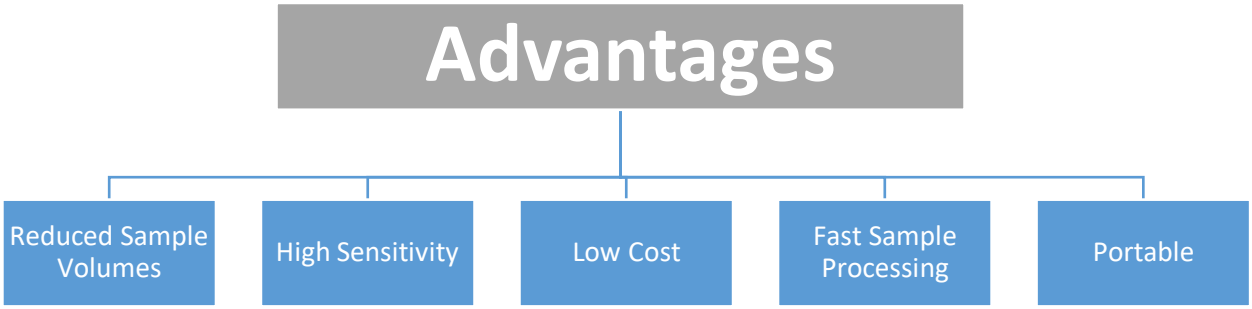


Figure 2: Advantages of Capillary Motor Pump

1.1.3 Area of Application

Capillary self-priming micropumps find utility in a diverse array of applications, encompassing:

- **Medical diagnostics:** Capillary micropumps can be integrated into portable diagnostic devices, such as lab-on-a-chip systems, point-of-care diagnostic systems, and biosensors, to enable efficient and accurate testing in remote or resource-limited settings.
- **Environmental monitoring:** Capillary micropumps can be used to pump and analyze small samples of water or other environmental fluids, making it possible to detect and monitor contaminants or pollutants in remote or hard-to-reach locations.
- **Food and water safety:** Capillary micropumps can be used in food and water safety testing, to detect bacteria, viruses, or other pathogens.
- **Biotechnology:** Capillary micropumps can be used in biotechnology applications, such as cell culture or gene therapy, to precisely control the flow of fluids and maintain optimal conditions for cell growth.
- **Energy:** Capillary micropumps can be seamlessly incorporated into energy production and storage systems, such as micro fuel cells and micro heat exchangers.
- **Automotive:** Capillary micropumps can be integrated into vehicles to pump and control the flow of fuel, coolant, and other fluids, leading to the development of more efficient and reliable vehicles.

- **Industrial:** Capillary micropumps can be integrated into industrial systems to improve the efficiency and precision of fluid handling tasks, and thus leading to the optimization of production processes.
- **Pharmaceutical and chemical industry:** Capillary micropumps can be used to handle small volumes of fluid in chemical and pharmaceutical applications, such as drug delivery, and sample preparation.
- **Analytical Chemistry:** Capillary micropumps are used in the analysis of small samples in analytical chemistry, such as capillary electrophoresis, and capillary chromatography.
- **Microfluidics:** Capillary micropumps are used in microfluidic systems to precisely control the flow of fluids and create complex microfluidic systems with other microscale components.

1.2 Method of Fabrication

The fabrication of microfluidic chips encompasses various methods that can be categorized into two primary approaches: top-down and bottom-up methods.

1.2.1 Top-Down Approaches

In top-down approaches, microfluidic channels and structures are created through direct machining or etching processes on a substrate material, such as glass or silicon. These approaches include photolithography, which uses light-sensitive resists and etching to pattern the substrate; laser ablation, which uses a laser beamto vaporize material from the substrate; and milling, which uses a rotary tool to cut the channels into the substrate.

1.2.2 Bottom-Up Approaches

Bottom-up approaches involve the assembly of microfluidic devices from smaller units or building blocks. These approaches include the use of microfluidic "inks," which are viscous fluids containing particles or other materials that can be printed or drawn into desired patterns; self-assembly.

It relies on the natural forces of attraction or repulsion between particles or molecules to spontaneously form structures; and microinjection molding, which uses a mold to shape molten polymer into the desired microfluidic structure.

There are also hybrid approaches that combine elements of both top-down and bottom-up fabrication methods. As an illustration, microscale 3D printing methods can be employed to construct microfluidic structures by layering materials, effectively merging the accuracy of photolithography with the versatility of various "inks" or materials.

In general, the selection of a fabrication technique for microfluidic chips is contingent upon the particular demands and limitations of the application. Factors such as the materials employed, the size and intricacy of the structures, and the desired production volume all play a role in determining the most suitable fabrication method.

1.2.3 Rapid Prototyping

Rapid prototyping refers to the swift generation of a physical model for a design or concept using additive manufacturing or other related technologies. This enables designers and engineers to promptly assess and refine their ideas, bypassing the expenses and time associated with traditional manufacturing processes.

Several varieties of rapid prototyping technologies exist, including:

- **3D printing:** This method entails the construction of a physical model by depositing successive layers of materials, such as plastic or metal, in a predetermined pattern.
- **CNC machining:** This technique utilizes computer-controlled cutting tools to selectively remove material from a solid block, thereby shaping it according to the desired specifications.
- **Vacuum casting:** This involves creating a mold of the prototype using a silicone rubber mold, and then casting the prototype using a liquid resin.

Rapid prototyping allows designers and engineers to quickly create physical models of their designs and test them in real-world conditions, which can save time and money in the development process.

1.2.4 PCB Manufacturing

PCB (Printed Circuit Board) manufacturing for microchannels involves the fabrication of a PCB with intricate and miniaturized channels designed for fluid flow. These microchannels are typically used in applications such as microfluidics, where precise control and manipulation of fluids at the microscale are required.

1.3 Aims and Objectives

- **High flow rate:** The micropump should be able to pump large volumes of liquid at a high flow rate.
- **Self-priming:** The micropump should be able to start pumping liquid without the need for manual filling or priming.
- **Low power consumption:** The micropump should be able to pump liquid using minimal power, making it suitable for portable or battery-powered applications.
- **Compact size:** The micropump should be small enough to be integrated into microfluidic devices or other compact systems.
- **Low cost:** The micropump would be relatively inexpensive to manufacture and maintain, making it accessible to many users.
- **Durability:** The micropump should withstand repeated use and exposure to different liquids without experiencing significant wear or damage.
- **Precision control:** The micropump should be able to control the flow rate and direction of the liquid with high precision, making it suitable for applications that require accurate fluid handling.
- **Scalability:** The micropump should be scalable and adaptable to a different volume of liquid, channels, and pressure.
- **Compatibility:** The micropump should work with a wide range of liquids and be compatible with other microfluidic devices or systems.

1.4 Methodology of Research

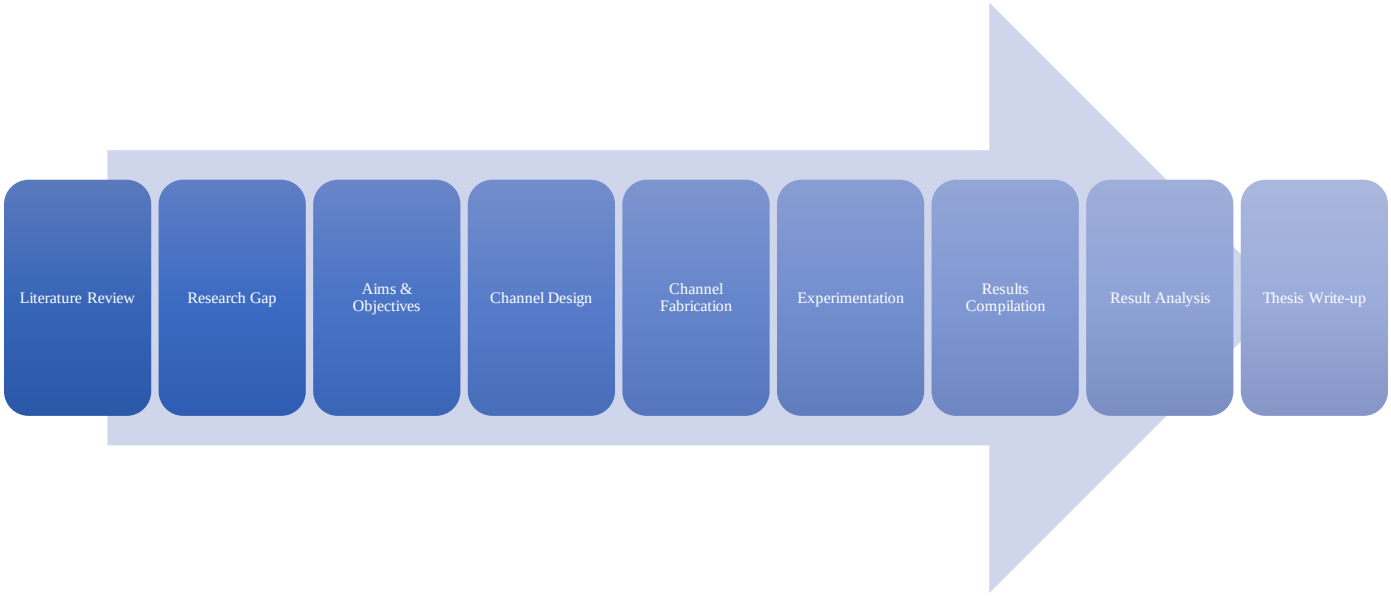


Figure 3: Research Methodology

Chapter 2 – Literature Review

Microfluidics is a branch of technology and science that examines the fluid behavior in micro-channels. Microfluidics uses miniaturized micro devices called micro channels for fluids flow or to process or manipulate small volumes of fluids. Microfluidics has a long history, beginning in the 1950s with the development of inkjet printers. The printers' mechanism is based on microfluidics, which includes the use of very small tubes to transport the ink for printing.

In the 1970s, a silicon wafer was used to create a tiny gas chromatograph. By the end of the 1980s, the first silicon micro-machined micropumps and microvalves had been demonstrated. Researchers spend a lot of effort inventing new microfluidic devices for fluid conveyance, mixing, metering, or valving, and split in tiny volumes of fluids throughout time. Fluigent was the first business to propose a disruptive new approach of handling fluids in microfluidics in 2006 microfluidics pressure pumps. The adoption of a pressure-based pump provides for extremely quick response and pulse-free flow. Fluigent initially only had the ability to control the pressure of liquids in microfluidic chips, but with the addition of a flow sensor and a novel feedback control loop, it was able to control both pressure and flow rate. The exact control of fluids in a microfluidic device enables previously unimaginable complex applications.

The main principle behind microfluidics is to combine tasks that would normally need an entire laboratory into a small micro-sized system. Multiplexing is currently being used to replace traditional scale-up in microfluidic systems, thanks to the device's small size, which substantially reduces the time it takes to go from formulation to production. This leads to the adoption of microfluidic technologies in process industries, such as food, environmental, and pharmaceuticals, fine chemistry, not only for analytical purposes but also for large-scale manufacturing. Microfluidic devices have been widely used as analytical instruments in molecular biology and biochemistry applications in recent years.

Microfluidic systems also provide great data quality and enhanced parameter control, making it possible to automate processes while maintaining performance. They are capable of processing and analyzing materials with minimal sample handling. The connection between the microfluidic chip and the fluid handling system has been refined such that the integrated automation allows the user to construct multi-step reactions with a low level of skill and many

functions. Nowadays, microfluidic based microchannel devices growing fast day by day. Microfluidics are hitting the market, developed by both tiny start-ups and biomedical corporations and large pharmaceutical.

Numerous designs for self-perpetuating pumps start with Autonomous capillary systems (CSs), a type of self-perpetuating pump that also works on the principle of capillary action [2]. The vast application of these pumps is bioanalytical because of their amenity, rapidness, and effectiveness. The capillary pump is designed to regulate the flow characteristics of CSs, and the microchannel is devised to offer small flow resistance. Adjusting the microchannel dimensions and pumped liquid properties helps achieve a specific flow rate [2]. However, the design does not consider the impact of temperature and other external factors on the workings of capillary pumps.

In some situations, high flow rates for capillary pumps are preferred. High flow rates are achievable by creating micropillars and integrating them into microfluidic devices, which provides diverse applications in micro-fluidic based analytical systems [3]. Two designs for acquiring high flow rates with low-pressure one is a serpentine pump. It has a series of serpentine channels that increase in width to create flow by setting up a pressure gradient along the length of the channel. Second is a leading-edge pump in which the liquid flows over the sharp leading edges, creating a pressure gradient [4].

Pulmonary alveolar capillaries are small blood vessels that interchange oxygen and carbon dioxide between the blood and the air in the lungs. Red blood cells depict a range of behaviors and are prone to adhere to the walls of microfluidic channels causing blockages in blood flow. A mathematical model can predict the behavior of Red Blood Cells (RBCs) in a biomimetic microfluidic device of pulmonary alveolar capillaries which aids in formulating better blood flow models in the lungs [5]. A portable device that tracks fluid flow and temperature changes are beneficial in the biomedical field. This device can supervise fluid flow in microfluidic chips and then sends the data to a person's smartphone, where it can be kept an eye on, and in case of blockages, adequate measures can be taken [6].

The fluid flow in microchannels can be directed by utilizing capillary forces in a capillary-based microfluidic system. The wet and tension forces assist in the flow. The phenomenon proves instrumental in creating capillary pumps, valves, and mixers. Nevertheless, these forces have some restraints, such as weak driving fluid flow and less regulation over the flow direction and rate [7].

A low-cost, high-performance design on a printed circuit board (PCB) is another novel approach for designing and fabricating a capillary pump. The design creates a series of pressure-driven pumping chambers that move the liquid without external power [7]. The microfluidic device is developed for executing complicated biological and chemical processes for its rapidness measurements and efficiency of using microscopic devices [8] [9]. The midget devices are made of polymers and paper, which are cost-friendly, easily disposable, and multifunctional. The challenge is to design point-of-care (PoC) tests that execute numerous functions monolithically while fulfilling requirements. The assimilation of microfluidics, sensing, and signal processing in a single platform is critical for a successful PoC device [10] [11] [12]. As a result, an alternative microfluidic system based on PCB manufacturing technology, the LoPCB (Lab-on-PCB), merges microfluidic components with electronics, heaters, electrodes, and biosensors into a monolithic device [13] [14] [15]. The O2 plasma treatment is used, and the wetting qualities of the core material fame retardant grade 4, FR-4 can be adjusted, resulting in channels with varied capillary flow characteristics. The essential component of this technique is a capillary pump that uses the super hydrophilic characteristics of O2 plasma treated FR-4 [16] [17] [18]. The micro pump is based on micropillar arrays and enables precise and adjustable fluid flow control across a wide range of flow rates. The LoPCB technology's overall design meets the majority of the criteria for autonomous monolithic PoC platforms [19] [20].

The technique is created through a series of steps, including the development of the capillary pump's circular chamber design. Several chambers on the PCB are connected to the microfluidic system. During the fabrication process, capillary pumps are constructed on the PCB using a mix of photolithography and electroplating processes. Initially, the PCB is coated with photoresist and subjected to UV light through a mask. The exposed areas are then covered over, producing a network of canals and reservoirs. To reinforce the channels and establish a stronger structure, the PCB is electroplated with copper. The capillary pumps' efficacy and performance are evaluated. This requires measuring the flow rate, pressure, and ability of the pumps to pump fluids of varied viscosities.

Self-perpetuating pumps are those which work on capillary action to transfer fluid toward its destination, and it does not require any external source [1]. The liquid keeps flowing because of the capillary action, the propulsive force that helps cause the flow. The design of a capillary

pump is significant in this scenario. Out of all available technologies, the suitable and appropriate method for designing and fabricating capillary pumps assimilates PCB (Printed Circuit Board) technology. It allows a more efficient and reliable capillary pump that can be used in affordable point-of-care diagnostic devices.

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The paper presents a method for developing high-performance capillary pumps that can be employed in low-cost point-of-care diagnostic devices. It embodies a printed circuit board (PCB) technology to develop capillary pumps that are more efficient and reliable than current options. The procedure is developed by going through several processes, including the design of the capillary pump, which uses a circular chamber. The PCB has an array of these chambers linked to a microfluidic system. The fabrication process is then built, which entails creating the capillary pumps on the PCB using a mix of photolithography and electroplating processes. The PCB is covered with photoresist before being subjected to ultraviolet light through a mask. The exposed sections are then eliminated, leaving a pattern of channels and reservoirs in their place. The PCB is electroplated with copper to enhance the thickness of the channels and produce a more sturdy

structure. To confirm the functioning and performance of capillary pumps, they are tested. The pumps' flow rate and pressure, as well as their capacity to pump fluids of varying viscosities, are measured throughout the testing.

For battle against COVID-19, Microfluidics played an important role for the vaccine development technologies and different detection method. Microfluidics sorting methods can be split into two categories: active and passive. Microfluidic structure filtration, inertial, bionic, and hydraulic sorting, DLD (deterministic lateral migration), inertial sorting, bionic sorting, and other ways are examples of passive sorting processes. They usually have a large flux and don't require an additional force field. Magnetic sorting, Di-electrophoresis sorting, acoustic and light sorting are examples of active sorting procedures that offer the advantage of high sorting accuracy.

Micron-sized items must be sorted in a continuous flow for several applications, including mineral processing, chemical synthesis, and biological studies. Separation and sorting procedures are divided into three types called passive, active, and combination techniques. Passive sorting approaches rely on interactions between particles, flow field and microchannel structure. Active sorting approach use an external flow field to sort microparticles.

Microfluidic systems can incorporate several cell sorting methods based on physical factors. It is offering an ideal interface for access different and manipulating single type of cells in a variety of ways. This allowing for fully independent assessment of physical type parameters [17].

Active technologies, which are based on microelectromechanical systems, increase fluid control by using external forces mechanically. This can be founded on mechanisms such as dielectrophoretic, magnetophoretic, acoustophoresis, or optical tweezers [18].

For cell separation, Bhagat et al. [19] offered a variety of separation and sorting approaches. Gosset et al. described label-free technique for cell sorting and separation procedures [20]. Most of the methods for sorting and separation based on active and passive techniques are given in these publications, although there is little discussion of the devices that implement the operating principles. Furthermore, the influence of separation technique and sorting processes on cell viability is not considered.

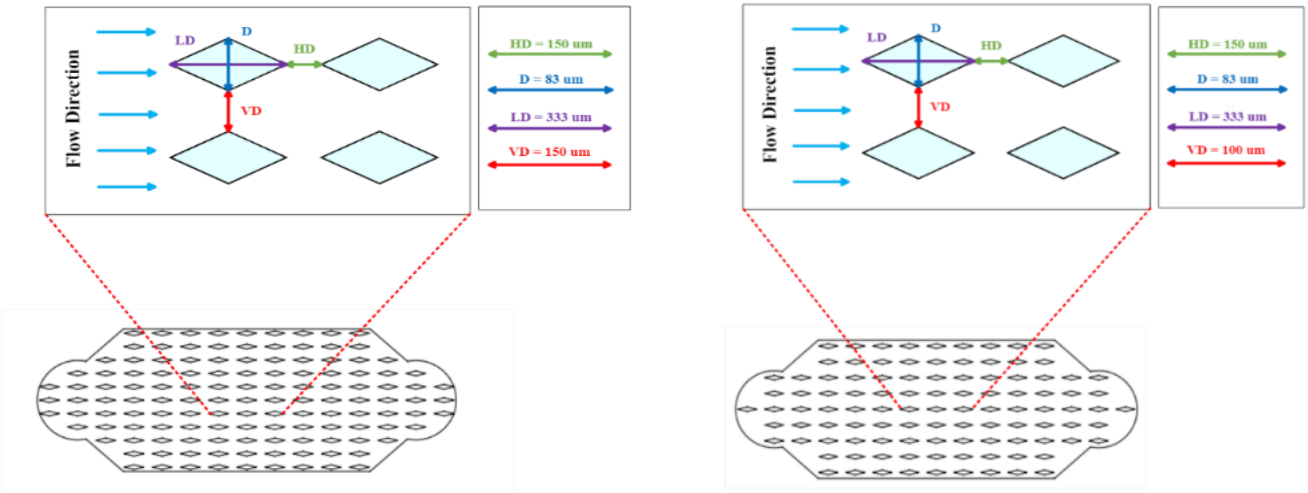
Doddabasavana et al. [21] discussed the several ways for separating blood cells into its constituents. Pamme et al. [22] described different microfluidics continuous separation and sorting approaches. However, some techniques on passive separation methods such as inertial flow and dean flow fractionation, as well as the micro-hydrocyclone, are not covered. Some passive type microfluidic separation techniques and sorting techniques were described in additional review work by Lenshof and Laurell [23], but few other techniques, such as crossflow filtration and the Zweifach–Fung effect, were not.

[24]E.L. Tóth et al worked on a system for particle sorting for pollution monitoring application. In this paper, the hydrodynamic behavior of the system was modeled by using COMSOL(FEM). The passive microfluidic sorting and separation system used with environment pollutant particles of different physical and geometrical parameters. By using inertial separation methods, size dependent particle sorting achieved by utilizing the lateral and dean separation, pinched flow. The 10 and 16 micrometer particle trajectories were visualized. The particle was mixed uniformly at the inlet, and the particle sorted at the outlet according to their sizes.

Chapter 3 – Manufacturing Methodology

Micropump Design:

Micropump is one of the most essential entity in any microfluidic system because it allows for an exact control and manipulation of fluids on a microscopic scale. Among various options, PCB-based micropillar designs with a hexagonal shape are widely favored for micropumps due to



easy fabrication process and capability to generate high flow rates. Two unique designs of PCB-based hexagonal micropillars have been created, with both designs maintaining a constant space between columns. However, the vertical distance between rows differs, with one design set at 100um and the other at 150um. The first design features a vertical distance between rows of 100um, which facilitates high flow rates owing to the smaller gap between rows, allowing for a larger number of pillars to be densely packed within a given area.

Table 1: Dimensions of Design 1 and 2

	LD (um)	VD (um)	HD (um)	D (um)
Design 1	333	100	100	83
Design 2	333	150	100	83

The greater concentration of pillars leads to an expanded fluid interaction surface area, which in turn improves mixing and reaction rates. The second design features a vertical gap of 150um between rows, offering increased versatility by accommodating larger fluid volumes for transportation via the micropump. The wider spacing between rows also facilitates convenient sample loading and unloading, making it an ideal option for applications that involve frequent fluid changes.

3.1. Fabrication of Micropump

The technology uses the Printed Circuit Board (PCB), a practical and affordable alternative, to build a capillary pump. In order to create the micropump, a PCB microchannel and Polydimethylsiloxane (PDMS), a silicon-based polymer substance that creates the capillary pump system, are used. To create the different geometries required to create microfluidic channels, PDMS can be molded. To make a completely working device, it can also be seamlessly combined with glass, plastic, or other materials. Multiple steps are involved in the fabrication of a micropump from a PCB microchannel and PDMS, although the procedure is quite simple and yields precise results.

3.1.1. PCB Microchannel

Designing the PCB microchannel is the first step, which is completed with the use of CAD (Computer-Aided Design) software. The PCB's copper layer has the design for the microchannel etched onto it. It is an important step that must include the necessary breadth and depth to permit fluid movement. The following stage includes using a laser or mechanical cutter to cut the PCB fiber sheet along the planned microchannel layout. The PCB will develop microchannels as a result. The creation of a PCB (Printed Circuit Board) with detailed, miniature channels intended for fluid flow is referred to as PCB (Printed Circuit Board) production for microchannels. These microchannels are frequently employed in microfluidic applications, where precision control and microscale fluid manipulation are necessary.

Here is a broad outline of the PCB manufacturing process for microchannels:

- **Design:** Making the PCB layout, which includes the microchannels, is the first step. The design is created using specialized software, such as computer-aided design (CAD) tools, while accounting for the appropriate microchannel diameters, forms, and connectivity.

- **Substrate selection:** Based on the particular needs of the application, the substrate material for the PCB is chosen. Common materials include FR-4 (Flame Retardant 4), an epoxy laminate reinforced with fiberglass, or specialized materials with superior thermal or electrical qualities like polyimide or ceramic substrates.

- **Substrate preparation:** The chosen substrate is prepared by cleaning and ensuring its surface is free from contaminants or debris. This step is crucial to ensure good adhesion and quality of the subsequent layers.

- **Copper deposition:** A thin layer of copper is deposited onto the substrate surface through various techniques such as electroless deposition, electroplating, or sputtering. This copper layer serves as the conductive pathway for electrical connections and will also form the walls of the microchannels.

- **Photoresist application:** A layer of photosensitive material, called photoresist, is applied over the copper layer. The substrate is then exposed to ultraviolet (UV) light through a photomask that defines the microchannel pattern. The photoresist undergoes a chemical change upon exposure, either becoming soluble (positive resist) or insoluble (negative resist).

- **Photolithography:** The UV-exposed photoresist is developed, selectively removing either the exposed or unexposed areas, depending on the type of photoresist used. This step transfers the microchannel pattern onto the photoresist layer.

- **Etching:** An etching process is performed to remove the exposed copper or the copper in the unexposed areas, depending on the type of resist used. This creates the channels in the copper layer, following the microchannel pattern defined by the photoresist.

- **Resist removal:** The remaining photoresist is stripped away, leaving behind the copper microchannels embedded in the substrate. This exposes the copper surfaces for further processing and ensures the microchannels are open for fluid flow.

- **Surface finish:** The exposed copper surfaces are treated with surface finish techniques, such as immersion tin, immersion gold, or HASL (Hot Air Solder Leveling), to protect them from oxidation and improve solderability.

- **Additional layers (optional):** Depending on the complexity of the design and the requirements of the application, additional layers, such as solder mask, silkscreen, or protective coatings, may be applied to the PCB.

- **Assembly and testing:** After the PCB manufacturing process, the microchannels are integrated with other components, if necessary, and undergo testing to ensure functionality and quality.

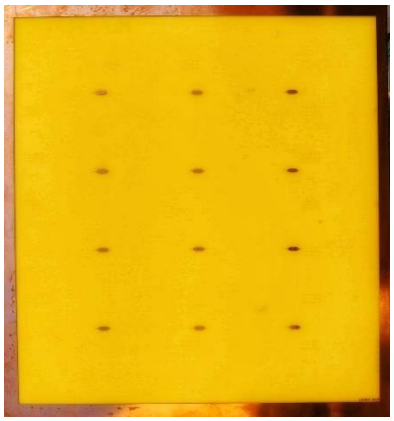


Figure 5: PCB Sheet

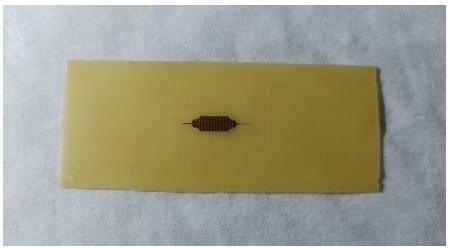


Figure 6: PCB Microchannel

3.1.2. Mold Fabrication

After that, using photolithography or other microfabrication methods, flat silicon molds are created as the next step. It is essential to note that the molds have a flat, smooth, and level surface. In order to ensure that the PDMS will take the shape of the micropump, the micropumps are then adhered to silicon molds.

Figure 7: Flow Chart of Mold Preparation

3.1.3. PDMS Preparation Procedure

In order to thoroughly mix the two components, it is also important to combine the PDMS base and curing agent in a 10:1 ratio and rapidly swirl the mixture. The PDMS mixture is then carefully poured over the silicon molds, making sure to completely cover the micropumps and the surrounding area. It's crucial to check that the PDMS has a uniform thickness and covers the mold's whole surface.

In the following step, the PDMS is cured by putting the molds in an oven or incubator. The PDMS is normally solidified and shaped to fit the molds during the curing process, which usually lasts several hours at a temperature of about 80°C. After the PDMS has fully hardened, the replicas are carefully removed from the molds while being careful to trim away any additional PDMS that may have built up around the borders of the micropumps. Next, a substrate made of glass, or

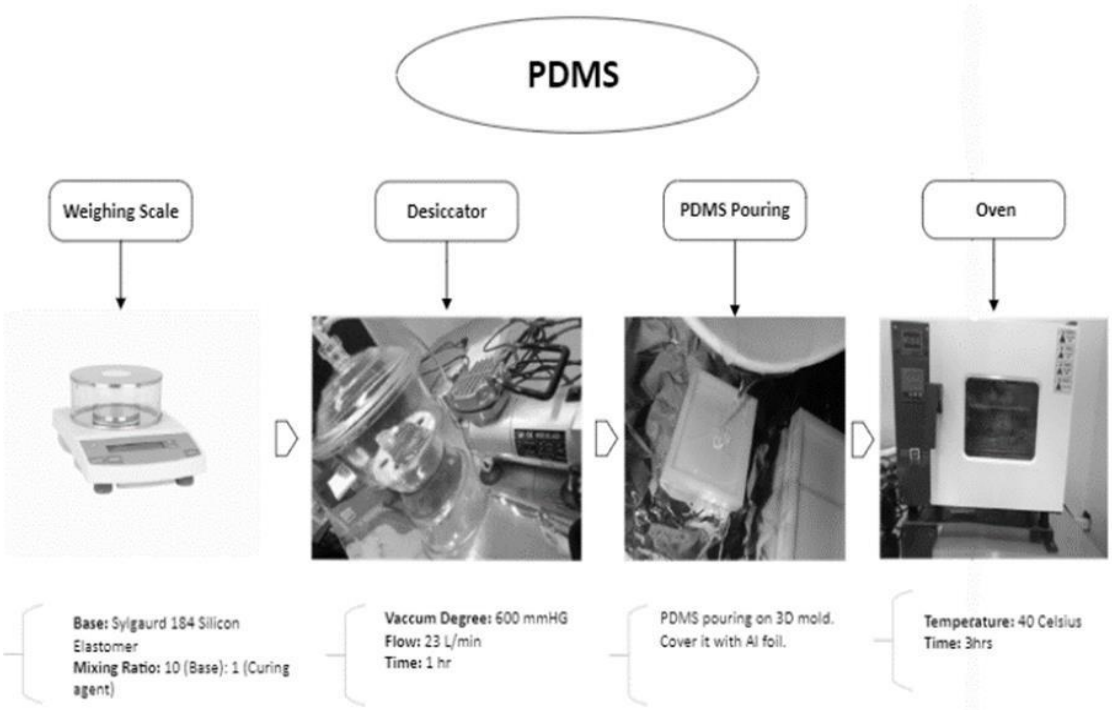


Figure 8: PDMS Preparation

another polymer is placed on top of the PDMS copies, and a plasma cleaner is used to permanently glue the two surfaces together. This bonding procedure creates a solid bond between the substrate

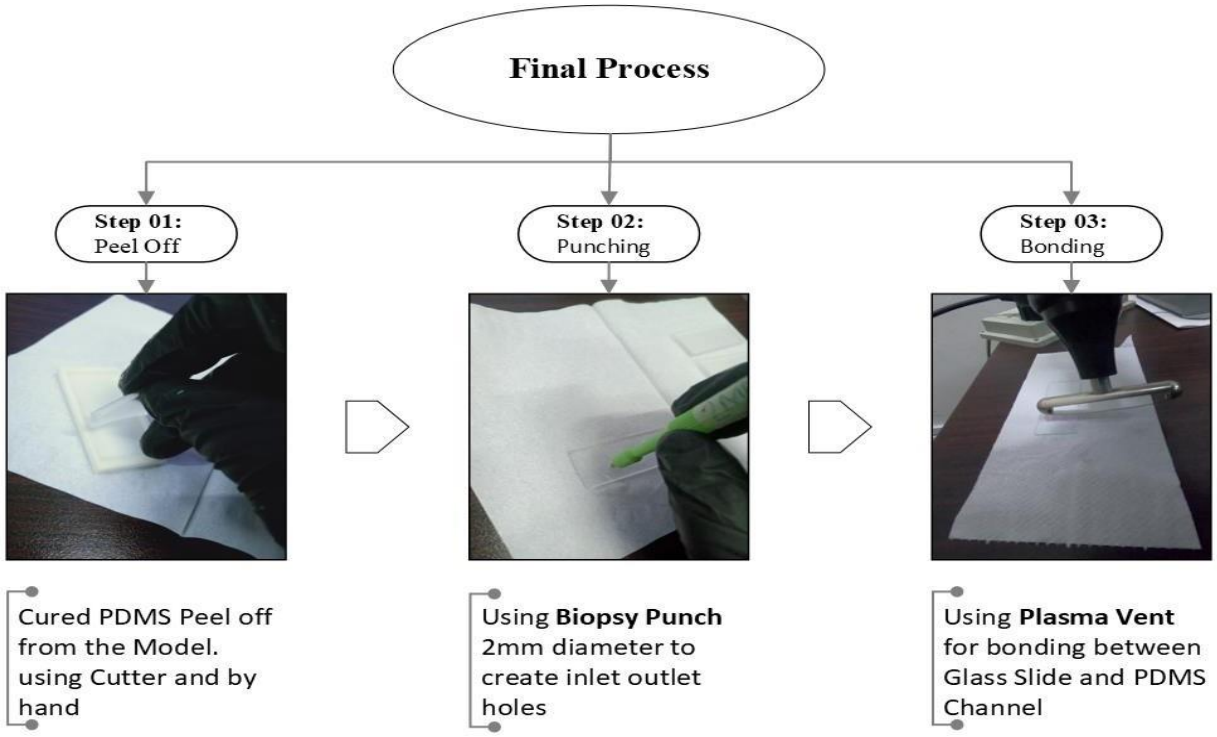


Figure 9: Final Steps of Microchannel Fabrication

and the PDMS, guaranteeing the stability and dependability of the micropump. The PDMS replicas are punched or laser-cut with holes to allow for fluid input and output. The intake and outlet ports are furthermore connected by tubing. Lastly, fluids are pushed to test the micropump's performance. through it, while measuring the flow rate and assessing the pressure.

This particular step holds great significance as it serves to optimize the design of the micropump and validate its performance.

In general, this process can be customized to accommodate diverse applications, rendering it a versatile and invaluable technique for researchers and engineers operating within the realms of microfluidics and nanotechnology. The design and fabrication of micropumps using PCBs and PDMS necessitate meticulous and methodical procedures to develop functional microfluidic devices with varying degrees of intricacy. Consequently, the meticulous execution of each step guarantees the precise and dependable performance of the micropumps.

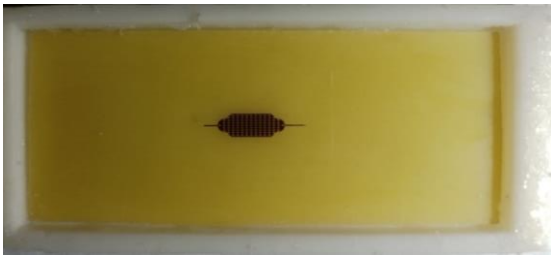


Figure 11: PCB Capillary Micropump in Silicon Mold

Figure 10: Final Design 1 and Design 2

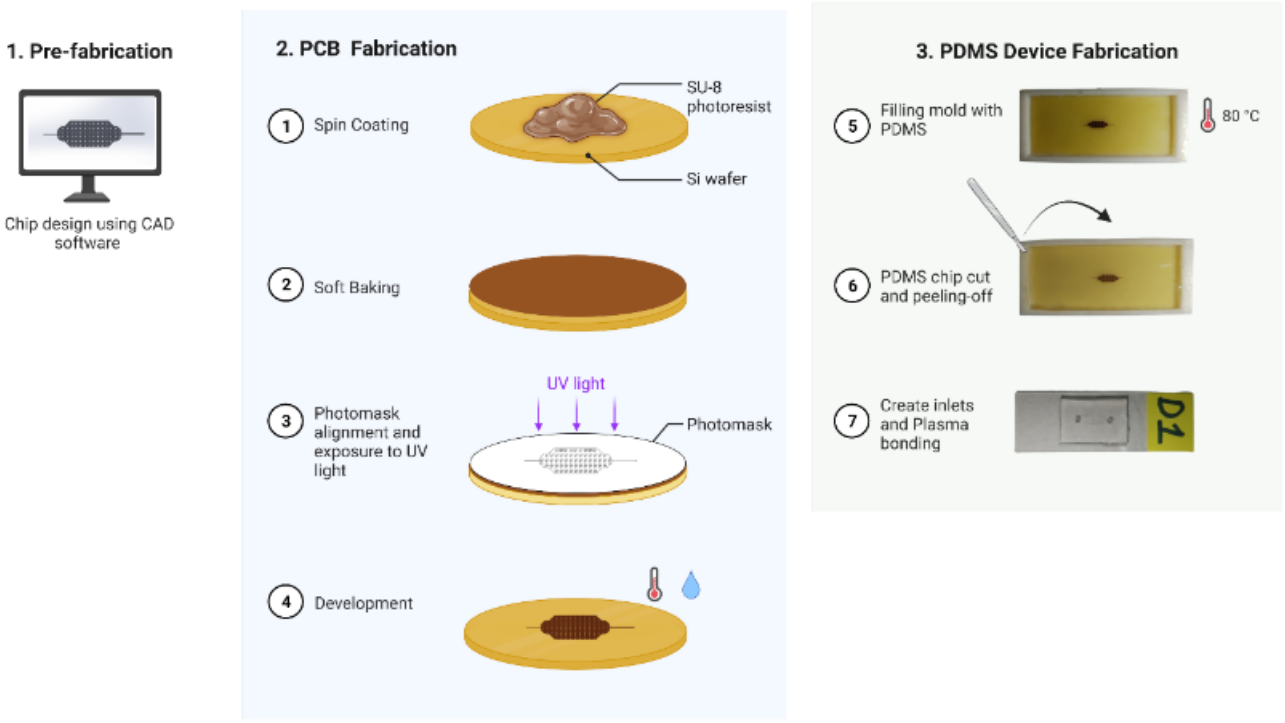


Figure 12: Flow Chart of Fabrication Process

Chapter 4 – Experimentation

Experimental Setup:

Sample Preparation:

For the series of experimentation, 7 samples of glycerin in water were prepared with various concentrations: 5%, 7%, 12%, 24%, 40%, 60% and 79%. For adding color to each sample for visibility, a drop of ink was added in each of the sample solution. After preparing the samples, they were filtered using a syringe filter to remove any possible impurities or particles that may have been introduced in the solution during the experiment.

Figure 13: 7 Glycerin-in-Water Solutions

Flow Rate: The series of experimentation was conducted in a fully sterile environment, specifically a clean room, to minimize any peripheral contamination that could affect the results in any way. The working fluid, solution, was dropped over a capillary micropump inlet to ensure a controlled and exact delivery spot. A 1 ml syringe filled with the working fluid solution of different glycerin ratios, one to two drops, were dispensed onto the capillary micropump for a completely controlled delivery through the microchannel. The working fluid was cautiously observed under a vertical microscope equipped with a camera (BioCam Microscopy BIC-E3S-

1.5C, 1.5MP) to ensure the proper flow of the fluid throughout the microchip. The microscope was connected to a laptop to collect the data for analysis and post-processing.

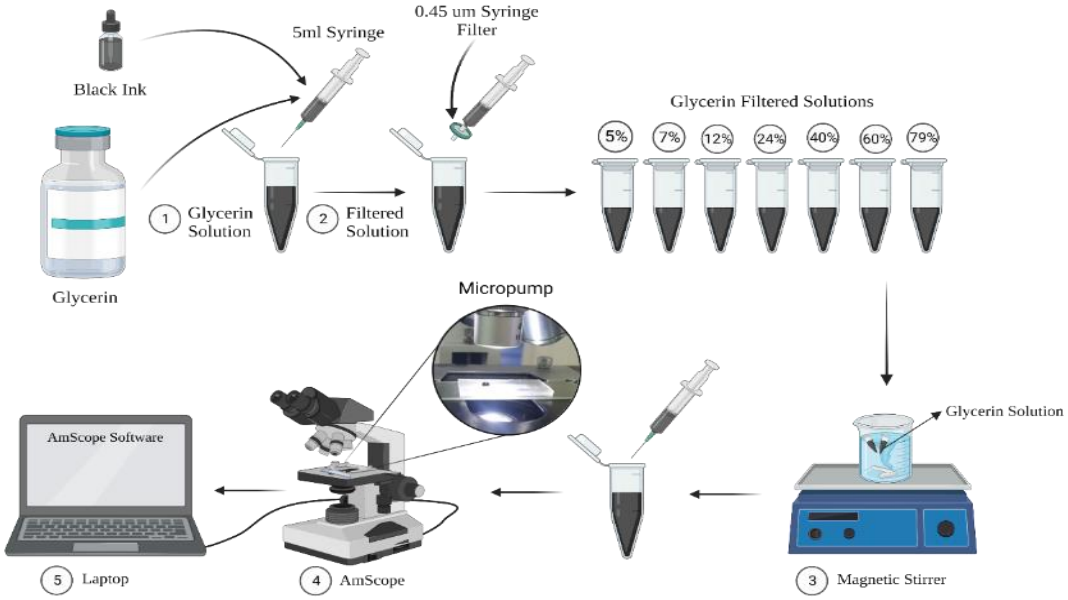


Figure 14: Schematic of Experiments based on Flow Rate

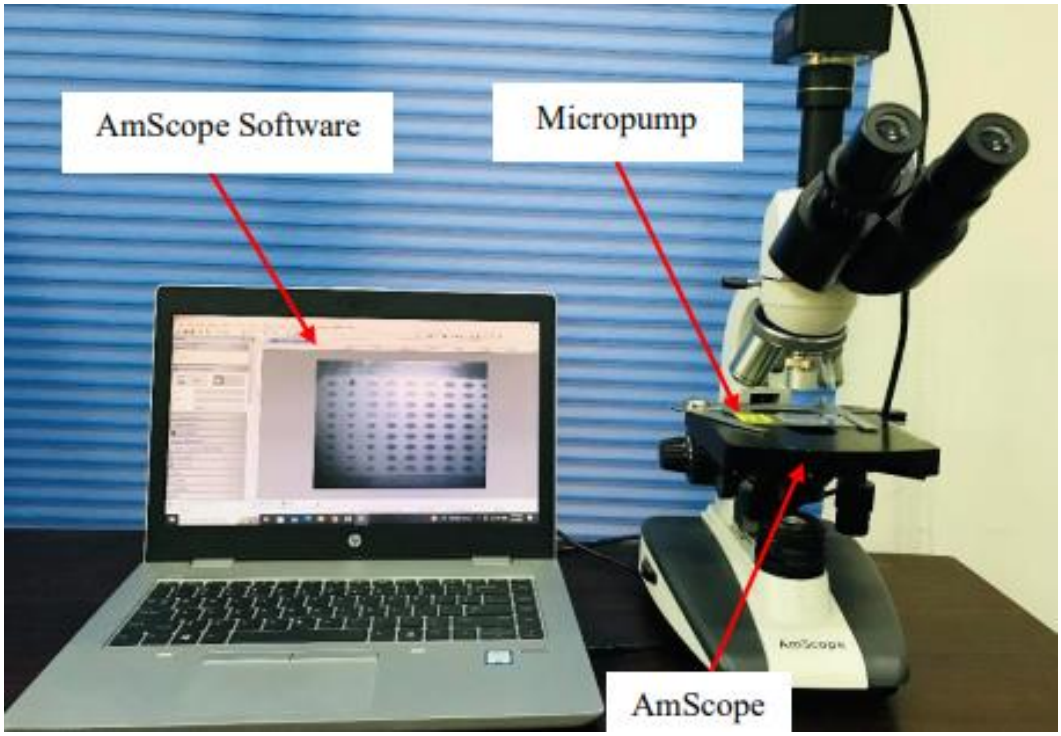


Figure 15: Experimental Setup based on Flow Rate

Pressure Drop: The series of experiments were performed in a clean room. The working fluid solution was injected in the microfluidic chip using a syringe pump (Darwin Microfluidic Pump). A 1 ml syringe filled with the working fluid solution was passed through the microchannel by varying the flow rates from the syringe pump. Flow from the chip was observed through a vertical microscope furnished with a camera (BioCam Microscopy BIC-E3S-1.5C, 1.5MP) and connected to a laptop to collect the data for analysis and postprocessing of the under-observation microchip. The tubes (Scalp Vein Infusion Set) were connected for inlet fluid flow between the syringe pump and the microchip.

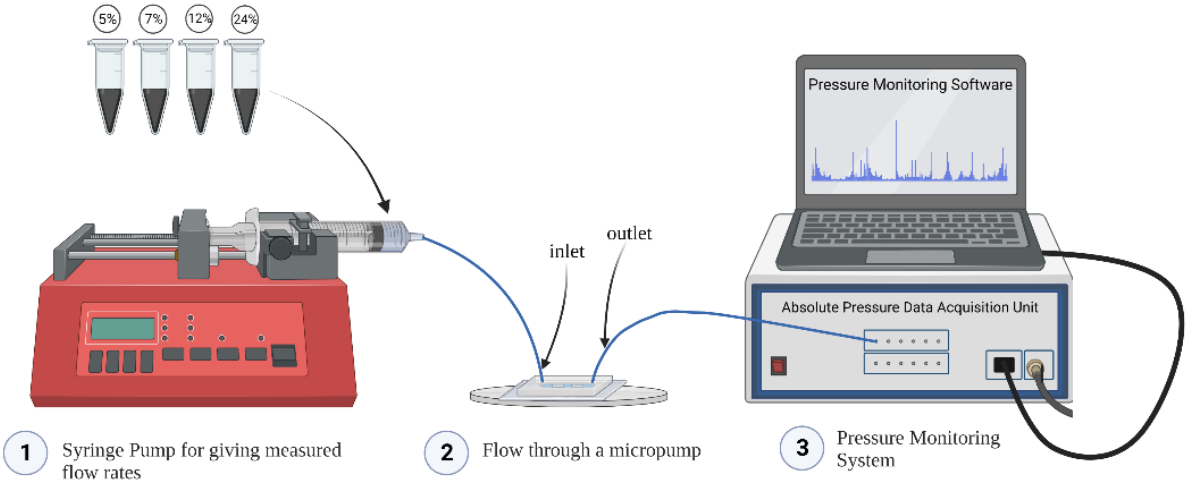


Figure 16: Schematic of Experiments based on Pressure Drop

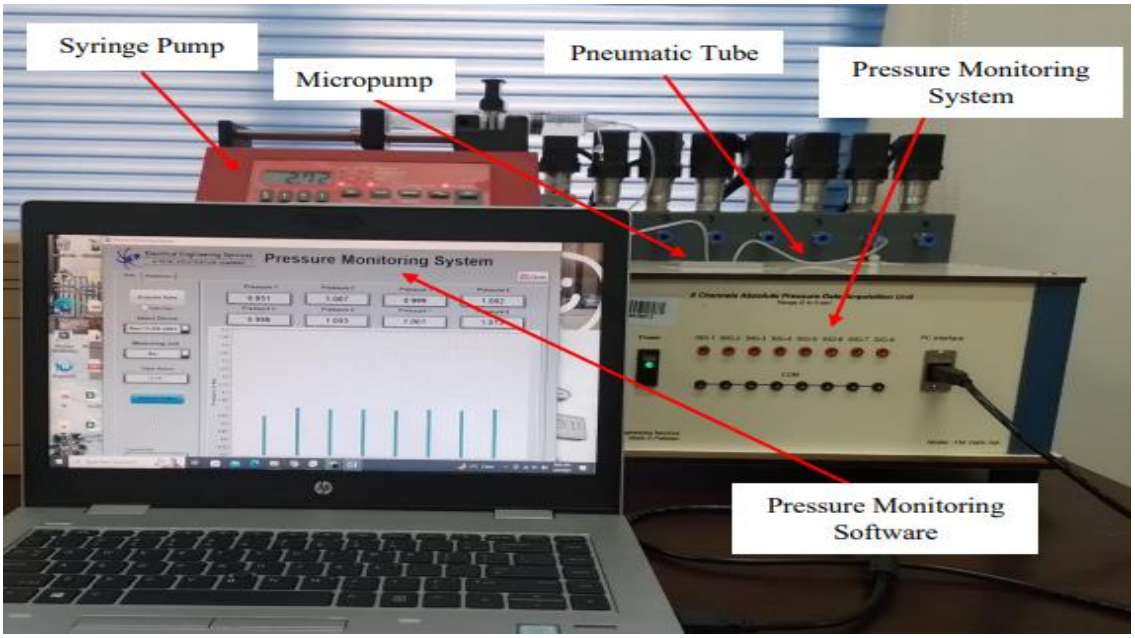


Figure 17: Experimental Setup based on Pressure Drop

Chapter 5 – Results & Discussion

The study examined the effect of the content of glycerin on the flow rate in two microchannel designs. Design 1 had a 100 μm gap distance while the Design 2 had a 150 μm gap distance. On the two designs, the flow rate was measured for various glycerin ratios, including 5%, 7%, 12%, and 24% solutions using a generated microfluidic system. The results depicted that both of the designs observed great decrease in the flow rate as the glycerin content increased. However, because of the narrower gap distance and a higher pressure drop, the Design 1 consistently depicted a greater flow rate in comparison to Design 2 for all the glycerin ratios.

Relationship between the glycerin ratio and associated decrease in flow rates can be depicted by the fluid's increased viscosity. Glycerin has a viscosity higher than water. Right as the glycerin ratio in the solution increases, the total viscosity of the fluid also increases. By then, because of the greater barrier to the flow caused as a result of increased viscosity, the flow rate is compromised. Drop in pressure was also observed for both the designs to actually quantify the effect of glycerin concentration on the flow rate. The data depicted a similar trend: right as the concentration of glycerin grew, so did the decrease in pressure, which was as a result of the increased viscosity of fluid. The data collected for each glycerin ratio and the design is compared in the table below.

Table 2: Data for Various Glycerin Ratios

Glycerin in Water	**Flow rate D1**	**Pressure Drop D1**	**Flow Rate D2**	**Pressure Drop D2**
%	ul/min	bar	ul/min	bar
5	0.04527	0.011	0.02964	0.006
7	0.04069	0.009	0.02731	0.006
12	0.03525	0.007	0.02377	0.005
24	0.01981	0.004	0.0174	0.003

Flow rate was affected by the interspacing distance between the diamonds as well as the vertical space between them. Far as the designs are concerned, the vertical distance between two diamonds of Design 1 was narrower than the vertical distance between two diamonds of Design 2, resulting in a higher flow rate for Design 1. A comparison graph showing the flow rate data for both of the designs, Design 1 and Design 2, is depicted below to graphically highlight the effect of diamond-shaped hollow cut design on the flow rate. The graph regularly trends that the Design 1 has a better flow rate than the Design 2, highlighting the significance of using a diamond-shaped hollow-cut design while developing a capillary micropump.

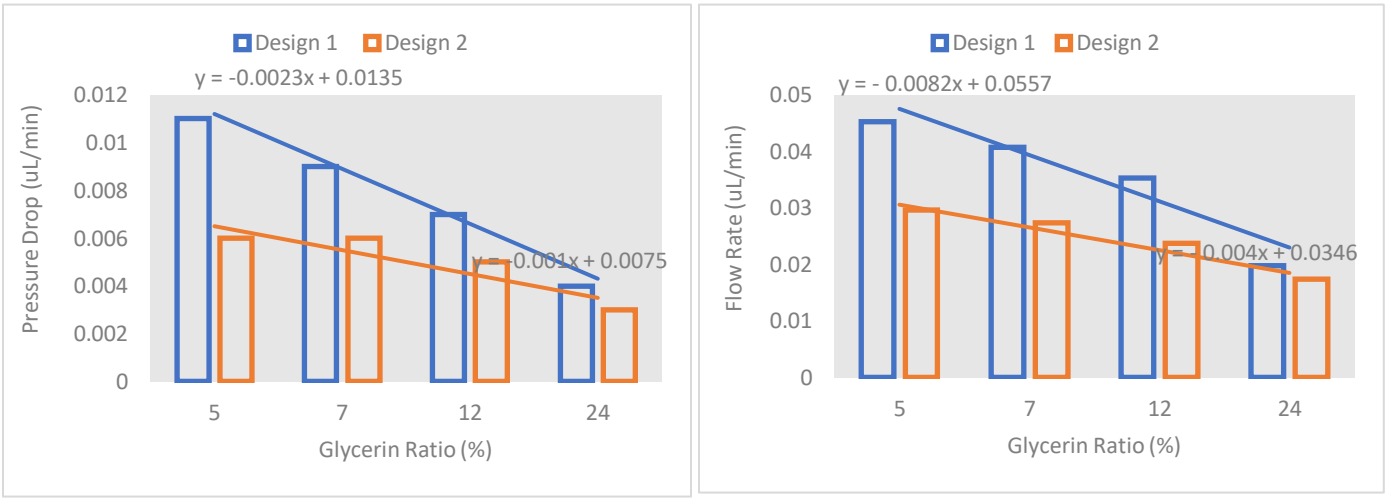


Figure 18: Comparison of the pressure-drops & flow-rates of Design 1 and Design 2

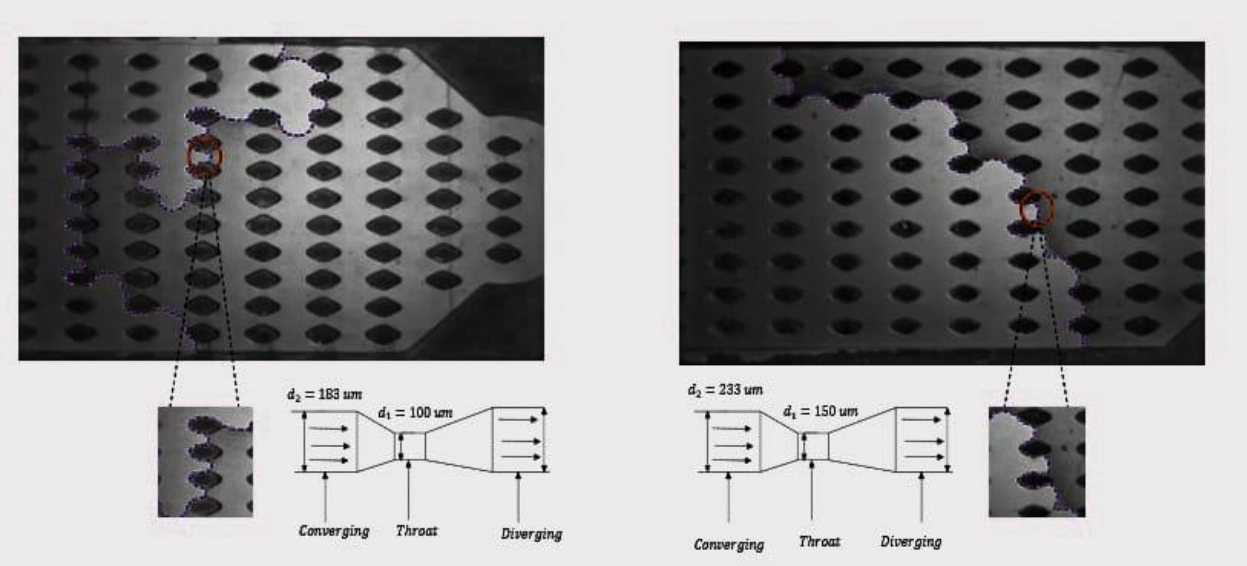
In the pressure drop versus glycerin ratio graph, Design 1 has a slope of -0.00034, suggesting that for every 1% increase in glycerin content, the pressure drop drops by 0.00034 bar. Design 2, however, has a slope of -0.00017, suggesting a pressure reduction of 0.00017 bar for every 1% increase in the glycerin content. Consequently, as a result of its increased sensitivity, Design 1 proves be more sensitive to variations in the glycerin content. Similarly, Design 1 exhibits a slope of -0.0013 in the flow rate vs. glycerin content graph, suggesting a drop of 0.0013 ul/min in flow rate for every 1% rise in glycerin concentration. Design 2 has a slope of -0.00062, suggesting a drop in the flow rate of 0.00062 ul/min for every 1% increase in glycerin content. This emphasizes that Design 1 is more sensitive to glycerin content fluctuations, when cross compared with Design 2.

The sharper slopes in Design 1 indicates that it is more prone to changes in glycerin content than Design 2. This might be as a result of Design 1's smaller gap distances between the diamonds, which results in a larger total pressure drop and flow rate. The negative slopes in both figures can be explained by glycerin's greater viscosity than water. Glycerin provides higher flow resistance, resulting in a drop-in flow rate as the glycerin content of the micropump increases.

Concludingly, the negative slopes and differences in steepness between the designs show that the amount of glycerin has a very high impact on the performance of micropump, and different designs may respond differently to changes in glycerin concentration.

The difference of flow rates can be associated to the Venturi effect, which occurs when a reduction in flow area results in an enhancement of flow velocity, resulting in a larger flow rate. The smaller vertical space between the diamonds in Design 1 generates a tighter flow area, triggering a faster flow velocity, henceforth a higher flow rate. Because of the conservation of mass principle, the fluid's velocity increases as it passes through this constriction. According to Bernoulli's theorem, this increase in velocity corresponds to a drop in the pressure of fluid. This loss of pressure adds to the pressure decrease measured over the micropump.

Figure 19: Venturi Effects in Design



The existence of Venturi effect in Design 1 of the micropumps result in a larger pressure drop due to a smaller gap distance between micropillars. This causes increased fluid velocity, and as a result, a higher flowrate. Design 2, on the other hand, has a reduced Venturi effect, resulting in a smaller pressure drop and slower fluid velocity, resulting in lower flowrate. However, it is critical to access that the Venturi effect is not the only element impacting variations in pressure drop and flow rates within the micropump. The viscosity of glycerin, as previously noted, also plays a crucial role in causing these variances.

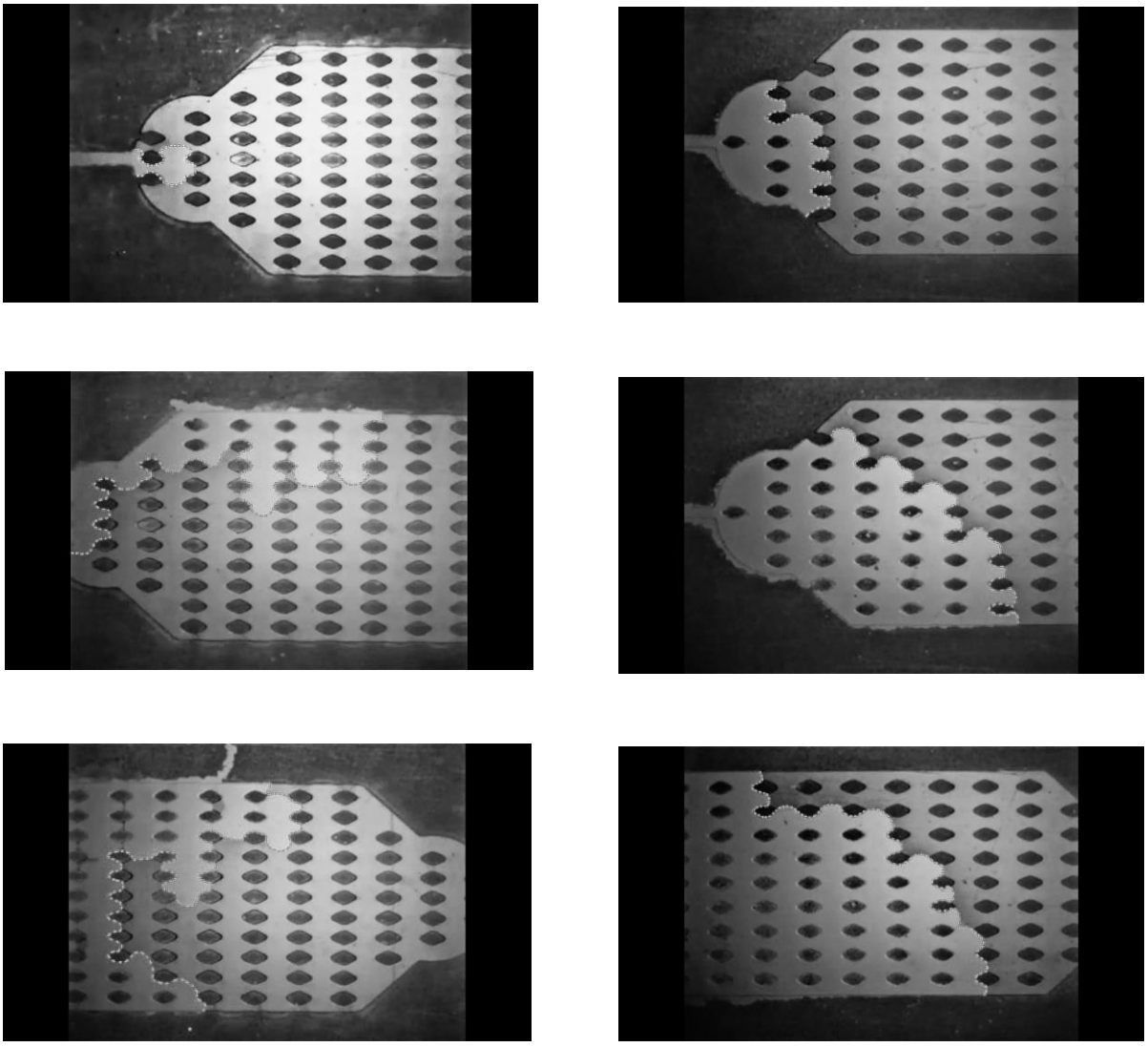


Figure 22: Diamond Shape Cuts in Design

The diamond-shaped hollow cuts used in the series of experiment were made up of PDMS, a plastic polymer with a very low surface energy and a high surface tension. The surface tension of the fluid influences the flow rate within the micropump by creating a negative pressure or suction at the vena contracta, which refers to the flow path's narrowest portion. This negative pressure can increase the flow rate and improve the micropump's capability of self-priming.

In addition to it, the wall shear stress was recongized as another factor impacting the flow rate. As the fluid traverses the surface of the PDMS diamond-shaped hollow-cuts, friction arises between the fluid and the PDMS surface, generating a shear stress referred to as wall shear stress. The heightened surface tension of the PDMS can yield a hydrophobic surface, thereby intensifying the wall shear stress and resulting in a reduction in the flow rate.

Chapter 6 – Conclusion & Recommendations

Conclusion:

The study presents a methodology for the design and fabrication of cost-efficient capillary pumps which are viable for point-of-care diagnostic devices utilizing the printed circuit board (PCB) technology. These pumps leverage the self-perpetuating phenomenon of the capillary forces, eradicating the need for external power sources and therefore making them viable for portable and cost-efficient diagnostic devices. The incorporation of PCB technology increases the efficiency and effectiveness of such capillary pumps. This research basically emphasizes on the design and fabrication of micropumps using the PCBs & PDMS (Polydimethylsiloxane). As the part and parcel of experimentation, two discrete designs of PCB-based micropillars with hexagonal shapes were developed, looking for characteristics such as high flow rates and adaptability towards the varying volumes of fluid. The process of fabrication involved creating the microchannels on PCB, shaping PDMS replicas using silicon molds, treating the PDMS to achieve desired characteristics, and bonding it to an adherent substrate. The feasibility and performance of the micropumps were assessed through the rate of flow and the pressure testing, confirming their reliable operation. The experimental findings revealed a reduction in flow rate with an increasing glycerin amount due to the corresponding increase in the viscosity of fluid. Remarkably, the Design 1 consistently developed higher flow rates when compared to the Design 2, owed to its smaller gap distance, which was as a result of a greater pressure drop. In addition to it, drop in the pressure value increased as the amount of glycerin in the solution increased further, affirming a significant effect of the viscosity of fluid on the performance of these micropumps.

Recommendations:

There are plentiful mandatory recommendations and improvements for taking the capillary micropump technology ahead. With the priority given to optimize the performance factors such as flow rates, power consumption, and control accuracy, a lot in the field is yet unveiled. This can be achieved by investigating sophisticated processes of microfabrication, incorporating new designs, and using novel composites with superior characteristics and specifications.

Moreover, the capillary micropumps should be coherently synchronized with the modern sensing technologies such as biosensors and the nail-sized lab-on-a-chip microsystems. This assemblage would allow for the real-time monitoring of fluid and analysis in bringing up novel opportunities for applications in the sectors such as medical diagnostics, monitoring systems and chemical analysis.

Another noteworthy field of study is increasing the compatibility of the capillary micropumps for a wider range of microfluids. This involves dealing with the abnormalities that come with exploring and handling complex biological samples, viscous fluids, and multiphase systems. The capillary micropumps can find even larger applications in sectors such as biotechnology, pharmaceuticals, and industrial FMCG processes of food and beverage industry, if techniques to address these problems are rightly developed. It is critical for the actual installations of capillary micropumps to provide a long-termed durability and long-termed dependability. Thus, the future efforts should focus on enhancing the robustness and lifecycle of these devices. This includes investigating and testing the suitable materials, refining device sealing and bonding techniques, and conducting thorough long-termed reliability tests.

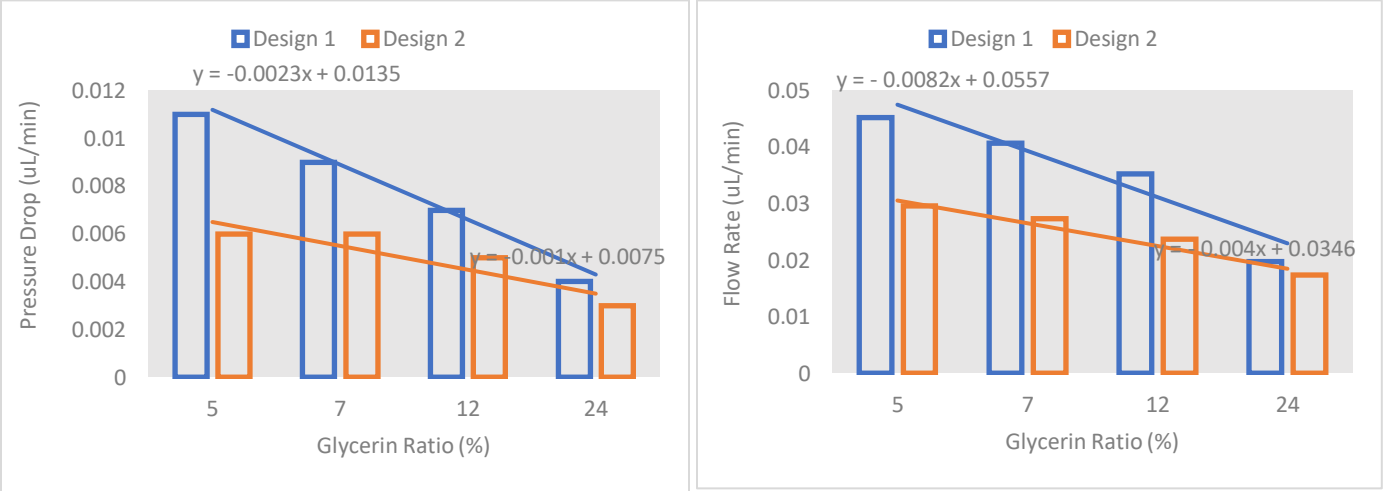
Developing modern-day scalable manufacturing methods will enable even cost-effective production and mass customization of capillary micropumps, making them more accessible to an even wider range of users and industries.

Lastly, acknowledging the significance of application-specific design considerations is elemental. Different fields and uses have discrete requirements, and tailoring the design parameters, the geometries of channels, and the materials accordingly will improvise the performance and functionality of capillary micropumps in every application domain.

Focusing these future recommendations, the capillary micropumps will continue to evolve, offering enhanced capabilities, reliability, and versatility. This, in turn, will develop ways for their widespread adoption and revolutionize the handling of fluid and analysis in multiple fields, driving advancements in medicine, environmental monitoring, industry and far beyond.

Appendix A

The graph regularly trends that the Design 1 has a better flow rate than the Design 2, highlighting the significance of using a diamond-shaped hollow-cut design while developing a capillary micropump.



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