THESIS

DESIGN, FABRICATION AND TESTING OF AN ELECTRICALLY CONTROLLED MICROFLUIDIC CAPILLARY MICROVALVE BASED ON HYDROPHOBICITY

Submitted by

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ABSTRACT

DESIGN, FABRICATION AND TESTING OF AN ELECTRICALLY CONTROLLED MICROFLUIDIC CAPILLARY MICROVALVE BASED ON HYDROPHOBICITY

Microfluidics is a promising disciple that combines "micro" amount of fluid handling in "micro" sized channels and has found applications in diverse fields such as biotechnology and environmental monitoring. Combination of microfluidics with digital electronics technology has spurred creation of Lab-on-a-Chip (LOC) devices that are field-deployable and bought to market in the last few decades. In these devices, positioning/transportation of liquids has remained a critical issue. A sample of fluid needs to be acquired from a specimen reservoir and moved to a different reservoir location for analysis. Inexpensive, reliable and straightforward methods to do this transportation makes such instruments low-cost and robust for use in the field for a variety of purposes. Current ways to do fluid movement require high electric field and hence requiring the use of high voltages (thousands of volts), making the device bulkier. Another approach to use a pneumatic pump for droplet movement is also detrimental in making LoC devices portable due to sizes of associated electronics and electrical parts.

This thesis presents the design of a microfluidic valve using capillary action, hydrophobicity, and low voltages (several volts). The use of low voltages brings the "micro" realm to the digital electronics part of LOC. It could lead to better portability, low-power operation of LOC devices, and consequently more adoption in field applications. The design process is based on practical considerations found during experimentation. This method was tested, and results are presented for various biochemical mediums, including KCl, PBS, GMOPS, Cell culture and FBS.

ACKNOWLEDGEMENTS

I thank Dr. Thomas Chen for his constant inspiration and putting me back in the maker's frame of mind. Special thanks to my friend and senior colleague Ming-Hao Cheng for his time-to-time guidance and kind support. I acknowledge numerous discussions with William Tedjo - those helped me consolidate my ideas. Thanks to Daniel Ball and Caleb Begly for fun-filled and educating conversations during the hard work that was being put in. It wouldn't have been same without you. Thanks to Lang Yang and Yusra Obeidat for their words of advice and caution during the experiments. In doing the lab work at the Physics department, August DeMann provided all needed support, and I am indebted to him for that.

DEDICATION

To my wife Chaitali, her unwavering support made this possible

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Chapter 1

Microfluidic Devices

Microfluidic devices are a particular class of devices which process fluids in tiny quantity, typically a few micro-litres to nano-litres using channels whose dimensions are correspondingly small in the order of microns [1]. Fluids (and possibly powders) are manipulated and analyzed in these micro-channels using various means such as electro-chemistry and spectroscopy. Applications of microfluidic devices are in healthcare delivery and monitoring, home healthcare, outpatient diagnosis, homeland security, counter-terrorism, first responders, veterinary medicine, environmental and food safety monitoring [2].

Creation of microfluidic devices uses knowledge derived from physics, chemistry, microbiology, material science and software development. It relies heavily on the technology of microfabrication. Industry reports estimate global microfluidics market to reach $8.64 billion by 2023 [3].

Due to small dimensions in microfluidic technology, these devices use a very small quantity of sample (a critical need in some applications such as biology). They can carry out separations and detection with higher efficiency in lesser time [4]. Furthermore, they are low cost due to mass-production and have small footprints due to miniaturization.

Origins of microfluidics can be traced to miniaturized gas chromatography systems pioneered by Terry et al. [5], Manz et al.'s proposal of a miniaturized total chemical analysis system [6], and a prototype of blood gas analyzer created by Shoji et al. [7]

Microfluidic devices use generic components of micro-channels, microvalves and micro-mixers as elements to manipulate fluids. These are used to introduce, move and mix liquids [2]. Electronics based analysis/detection system is typically used at the backend. Together with associated electronic components and software, a Lab on a chip (LOC) gets formed. LOC devices are complete devices serving a single unique function that traditionally would be accomplished by a multi-step lab process involving multiple lab instruments. To that end, Lab-on-chip devices are promising

- They are portable, high-throughput and low-cost. Some prominent examples of commercially successful LOC products are Triage cardiac panel [8] and Abbott Laboratories' i-Stat [9].

1.1 Design of Microfluidic devices

A modern typical microfludic system still looks very similar to one proposed by Terry et al. [5] with added components for doing software-based processing of generated data. Figure 1.1 shows those components -

- Sample injection inlet or reservoir
- Microfluidic operation
- Detector
- Digital Data processing unit
- Cloud-based platform for data analysis

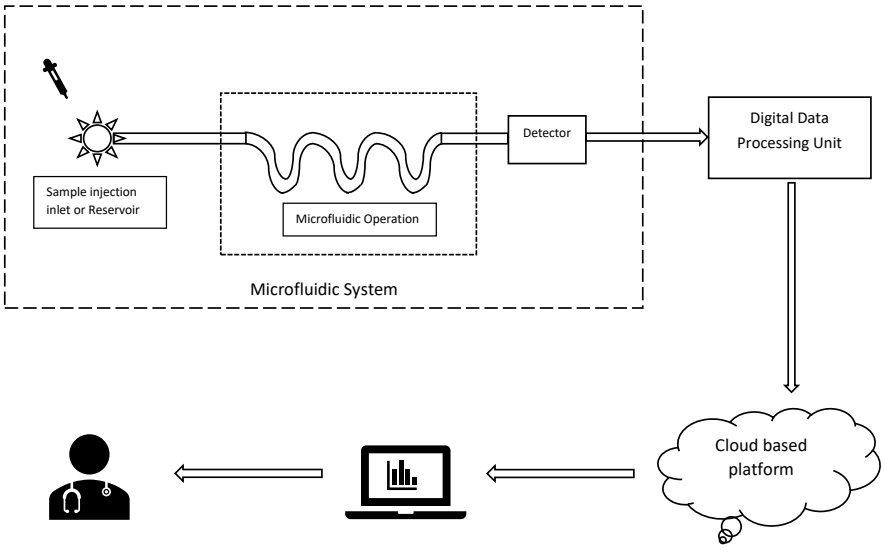

Figure 1.1: Structure and Components of a Typical Microfluidic system

Sample/working fluid that needs to be investigated is inserted at the "Sample injection inlet or reservoir". It is stored there for subsequent use by the device. During the measurement/analysis cycle, a droplet from the reservoir is moved to the area of "Microfluidic operation" to be manipulated such as separation of an enzyme might be done in this step. Afterwards, it is taken to a detector/sensor area where conversion from chemical to electrical property is done by optical or electro-chemical means. The output of the detector is then fed to "Digital Data processing unit" where raw data from detector is converted to a machine-readable format and sent to a Cloud platform for storage. A PC/Mobile based analysis and graphing software connected to the cloud then enable further interpretation of the data.

In these steps, the movement of sample from one stage to the next is performed by a physical gating mechanism using microvalves and micro-pumps.They use external forces such as pressure or high voltage to drive liquids around which are not portable. This has become one of the significant issues that inhibit adoption of microfludics in portable instruments. Effective transport of an analyte to sensors is a crucial aspect performance-wise as well. It affects the limit of detection and analysis time [10]. Transport independent methods to improve performance have been tried, but they depend on more advanced nanotechnology [11].

In this thesis, a microvalve based on the principle of capillary action and hydrophobicity is designed, fabricated and tested. The creation process and parameters of such microvalves were found by experimentation. Results from liquid movement experiments using KCl, Gmop, PBS, FBS and Cell culture are presented.

Another issue that needs to be addressed in the LOC field is a easy use of data from electrochemical experiments done in microfluidics. Currently, data from sensors is collected using discrete measurement instruments and then analyzed manually. To make an instrument portable, data needs to be collected automatically and then presented to the user in easy to perceive graphical format. A programmable framework based on Python is proposed in this thesis to collect sensor data and provide graphical elements to interact with the data collected.

This thesis is organized into six chapters. This chapter introduced the field of microfluidic devices from engineering and scientific point of view. Chapter 2 2 reviews origins, evolution and current research on various mechanisms and technologies used to create different types of microvalves. It also discusses the pros and cons of each microvalve type. Wherever applicable suitability for adoption in portable devices is also discussed. Chapter 3 3 discusses the design, fabrication and testing of capillary hydrophobicity effect based microvalve created by me based on existing research using glass and SU-8 as primary elements. Chapter 4 4 presents the results and observations made during the creation of the proposed valve design. Chapter 5 5 provides a discussion on improvements that can lead to better success in creating a valve for microfluidic devices; it also makes concluding remarks about the research done for the proposed microvalve. Appendix A A discusses additional information on micropumps. Appendix B B covers the design of a Python-based software package for capturing data from electro-analytical experiments performed in a microfluidic device.

Chapter 2

Review of Fluid Control Systems in Microfluidics

The positioning of liquids is vital in micro-analytical instrumentation. A sample of fluid needs to be acquired from a specimen reservoir and routed to a different location for analysis. Inexpensive, straightforward and reliable methods to do this movement would make such instruments low-cost, portable and robust for use in chemical analysis.

Current technology to do this is to use a pneumatic pump [12] or a large amount of electric field (electrohydrodynamics) [13] [14]. High voltage is needed to generate an electric field sufficient to move multiple types of liquid. Pneumatic pumps contain moving parts which are prone to wear and tear, leading to leaks and contamination. Also, such moving parts contribute to dead volume - a small quantity of fluid that remains in valve due to the crevices created by the valve's microstructures. But more importantly, these techniques to move fluids are not portable, and this thesis focuses on the portability aspects of microvalves that would make LOC more adaptable in field.

Fluid movement can be done in two ways: active, using micro-pumps to direct flow in the desired channel and passive, using microvalves that shut on-off to route flow in a pre-defined path. In this thesis, the main focus is on microvalves and hence a review of microvalves is covered in detail henceforth.

2.1 Microfluidic valves

Microfluidic valves move fluids by routing them in an existing network of micro-channels. Various physical phenomenon has been found useful in creating microvalves.

Electrokinetic microvalves [13] [14] [15] uses electro-osmotic flow (EOF) of the fluid induced by the electric field created by a high voltage between a source and destination reservoir. EOF is generated in a network of channels, as shown in Figure 2.1 to route fluid across reservoirs.

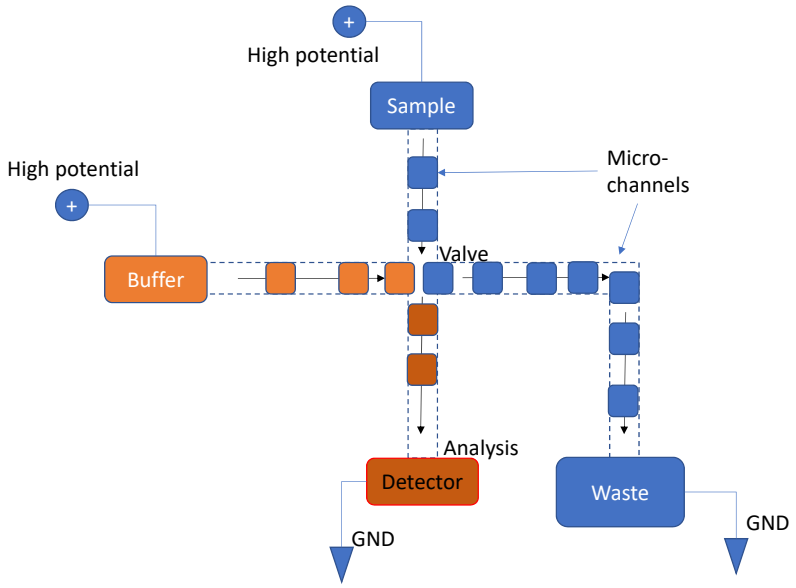

Figure 2.1: Principle of Electrokinetic Valve

Due to rectilinear channels of length between 1 and 5 cm, these design needs the use of high voltage. This doesn't make the technique useful in portable applications. In [16], an attempt was made to remove the limitation of high voltage by using a circular microchannel with equi-spaced electrodes along its circumference. Since the gap between electrodes was now much lesser, a small amount of voltage was sufficient to create a large amount of electric field needed to move the fluids. But it was observed that the fluids accumulated at the electrodes.

Complementary Metal-Oxide Semiconductor (CMOS) process was used to create a strong electric field using small voltage in [17] but no information could be found about using this high electric field to move fluids. These type of devices suffer adsorption of analytes on walls of micro-channels. This issue was addressed by surface modifications and coatings on the micro-channel walls [18] [19].

Use of electroosmotic flow (EOF) has evolved on its own into the creation of microcapillary electrophoresis LOC devices with commercial implementations [20] available for application in

point of care as well as more resourceful lab settings in clinical, environmental and industrial applications. Also, its use as a pumping mechanism is more widespread than valving [12].

Pneumatic valves [21] consists of two micro-channels, one above the other in separate layers with an elastomer membrane in between at the junction points. One of the layers acts as a control channel while other is a flow channel - the white and blue colored channels respectively, in Figure 2.2. To stop the flow channel, air or fluid is forced in the control channel. A compression due to the fluid pressure at the cross-bar of both channels prevents fluid in the flow channel. These valves can be easily fabricated in a small footprint of a 100-micron by 100-micron area enabling a high level of integration [22] akin to silicon large scale integration. Though attractive due to these factors, they need external devices to generate and hold pressure to activate valves. This requirement would not make it a portable instrument. Also, these valves tend to be leaky, prone to closing permanently during the fabrication process [12] and hence unreliable.

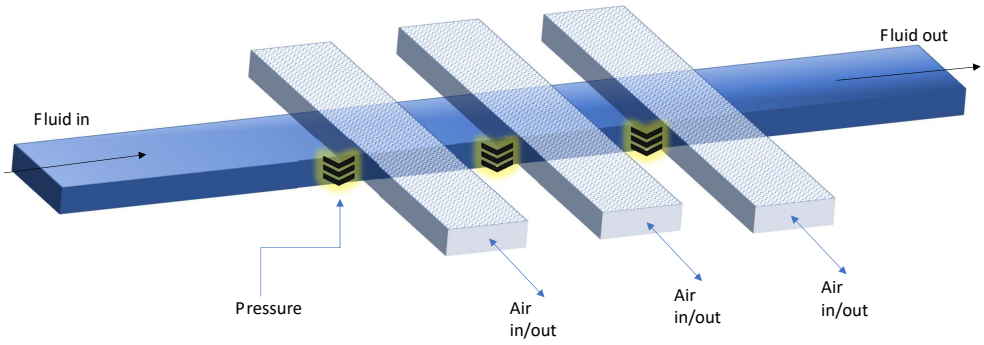

Figure 2.2: Principle of Pneumatic Valve

With a 3D pneumatic bistable design [23], the need to hold pressure can be removed. The use of magnetic actuation of elastomer membrane [24] and polymer membranes that expand and exert mechanical force on stimulus [25] could remove the need of vacuum/pressure completely. Pincer [26], spherical dome [27], helical [28], 4-walled [29], and parallelogram-shaped [30] cross-section structures were proposed to overcome the problem of leaky valves. One dimensional structure was proposed to solve the issue of permanent bonding between valve walls during the fabrication process [31]. Modular designs which can make the valve design more portable were proposed in [32] and [33].

TWIST valves [34] [35] [36] were proposed to overcome the need for external pressure supply. As shown in Figure 2.3, they use a simple principle of pinching the PDMS flow channel itself by using a moving rod/screw above it to block or unblock the flow of fluid. They can be made modular [37] and can do automatic operation using a Braille type display [38] which was an improvement compared to need of pressure or vacuum source.

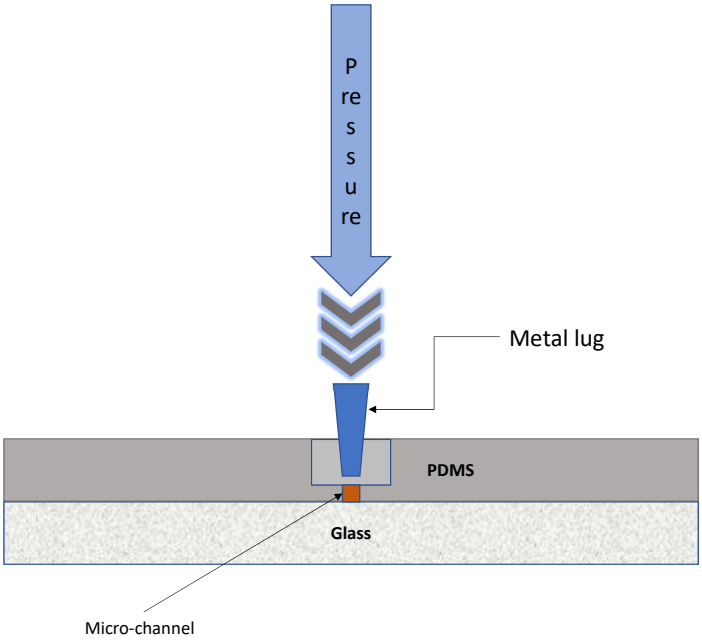

Figure 2.3: Principle of Pinch Valve

Thermopneumatic valves [39] [40] [41] use a heating element, such as the Peltier device [42] to heat actuation fluid [43], PDMS, Shape Memory polymer [44] or Silicon membrane that presses on the flow channel. As seen in Figure 2.4, this closes the gap between inlet and outlet ports, stopping the flow. In one novel type, surface acoustic waves were used to heat paraffin oil droplet that heated a Shape Memory Alloy (SMA) wire. Expansion of SMA wire compressed a PDMS microchannel, thereby closing it [45].

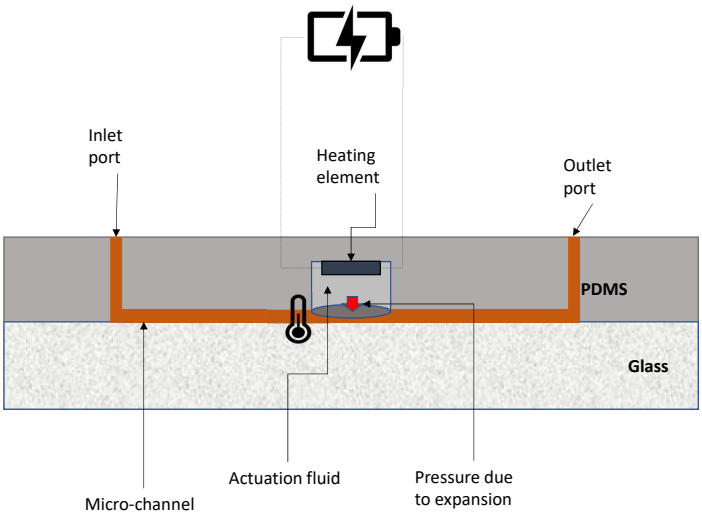

Figure 2.4: Principle of ThermoPneumatic Valve

Due to the use of heating which is often not efficient in converting thermal to mechanical energy, this type of valves consume more power. They also have a high response time since materials take time to expand. To make these valves more power-efficient, a bistable design can be used which employs magnet to hold ON/OFF condition [46]. The use of electro-static latching [47], and insulating heater [48] was able to reduce power consumption to some extent in the design.

To improve the thermal responsiveness, to dope PDMS with expandable micro-spheres [49] and to use liquid-crystalline elastomers [50] has been proposed. Corrugated diaphragm and raised heaters have been suggested in [51] to improve thermal responsiveness in microvalves made with Silicon.

Leakage issue in this type is due to a gap that is created when deformed valve membrane presses against a cross-section profile which is rectangular. A round-shape geometry of valve solves this problem [52].

The technology to develop these valves is sophisticated. Each valve needs to be created individually - This reduces the repeatability and increases the cost. These types of valves are normally open so may not be useful to start and stop the flow of liquid. The heat generated by the heating element can coagulate some analytes under test such as proteins though this problem can be prevented by using a two-chamber configuration [53] in which heating element is in a separate chamber connected to actuation chamber via a connecting path. But the two-chamber valve is slow due to indirect heating of actuating fluid. Heat can evaporate analytes in PDMS valve due to its porous nature; Polyurethane can be used as an elastomer to mitigate this problem [54]

Optopneumatic valves are similar [55] in working principle as thermopneumatic. Instead of using a heating element, they use laser light as a source of heat. A glass micro-capillary is coated with carbon-powder mixed PDMS. When laser light is incident on this photo-thermal material capillary, light energy is converted to heat. The air inside capillary expands due to heating and fills connected micro-channel. This causes the flow to stop.

Thermomechanical valves [56] use a bimetallic diaphragm of metals, as shown in Figure 2.5 to cover the inlet to the outlet connection. The two metals have different coefficients of thermal expansion. On passing current, the heat generated changes the shape of the diaphragm, causing opening and closing of ports. Bimetal alloys used are Aluminium/Silicon, Shape memory alloy (Nickel-Titanium) [57], or Nickel-Silicon.

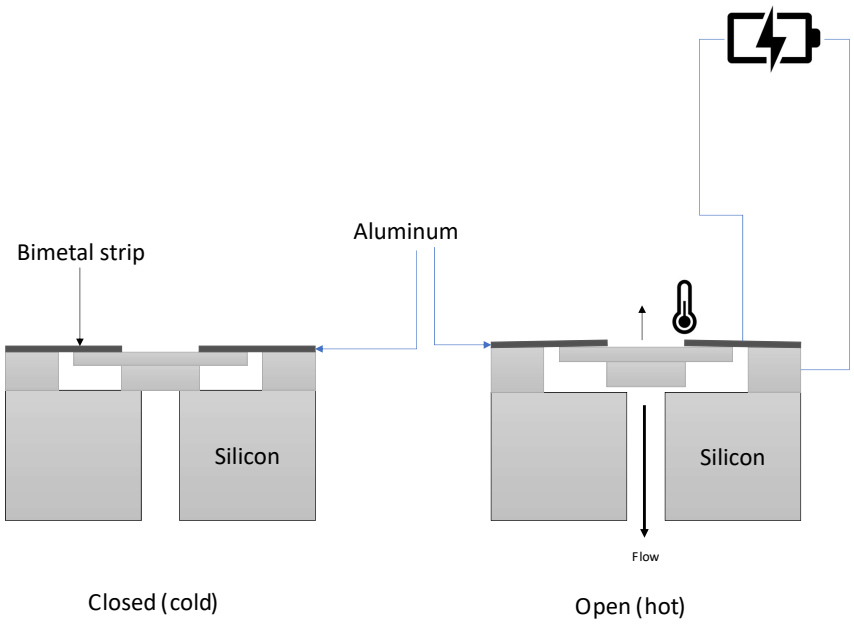

Figure 2.5: Principle of Thermomechanical Valve

These valves suffer from the drawback that diaphragm is sensitive to ambient temperature, limiting the useful operating temperature range. Also, due to inefficient heating, the power consumption is quite high in hundreds of milli-Watts which is not suitable for portable applications. The heat generated by the valve may cause degradation of the biochemical analyte under consideration.

Piezoelectric valves [58] [59] typically consist of two separate structures - the upper one is an inverted mesa structure on a stacked piezoelectric actuator, and lower one is the actual micro-channel with inlet and outlet port topped by a flexible polymer in seating as seen in Figure 2.6. On the application of a voltage, the mesa structure moves out of plane due to the piezoelectric effect and impinges the polymer membrane to close the valve or moves away from it to open the valve. These valves can be fabricated in glass, and large scale integration is possible [60].

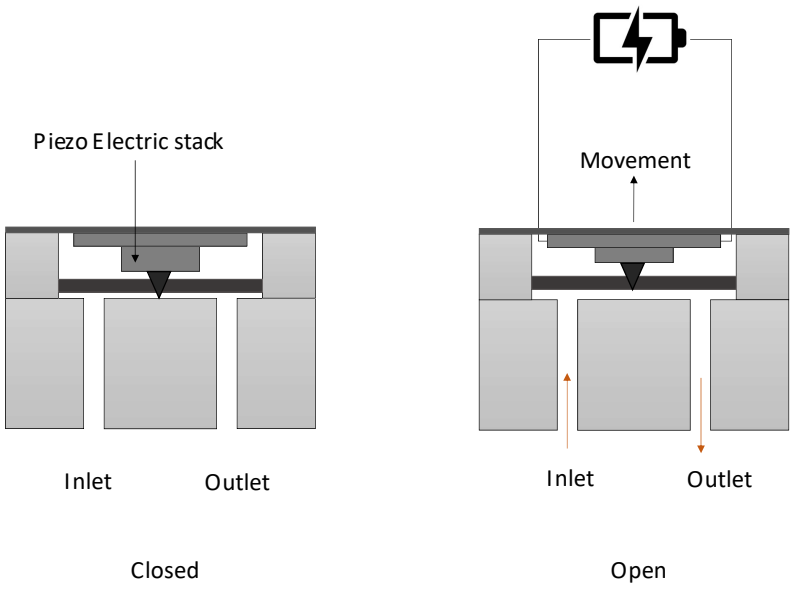

Figure 2.6: Principle of Piezoelectric Valve

Voltages applied is in tens of volts which may not be suitable for portable applications. A lower voltage operation is possible using a bulk piezoelectric uni-morph actuator [61]. The displacement of the valve to achieve an open position is very small - this leads to dependence on temperature due to thermal expansion of stack. These valves are challenging to fabricate. Ease of assembly was proposed by using an unconstrained poppet attached to the piezoelectric actuator [62]. These valves suffer from the problem of leakage. This can be solved by using narrow concentric seat-

ing rings that provide additional pressure points increasing the seating pressure and consequently reducing leakage [63]. Still, due to high voltage usage in portable applications is limited.

Electrostatic valve [64] is made of a closure plate resting on a base plate - brown colored plate on green colored one in Figure 2.7. The closure plate is attached only on one side of the base plate, leaving a gap that allows flowing from inlet to outlet port (normally open valve). On creating a high potential between the base plate and the closure plate, an electrostatic force attracts the closure plate over the base plate, closing the gap to shut-off the valve. These plates are made using surface and bulk micromachining technique of depositing silicon nitride on silicon.

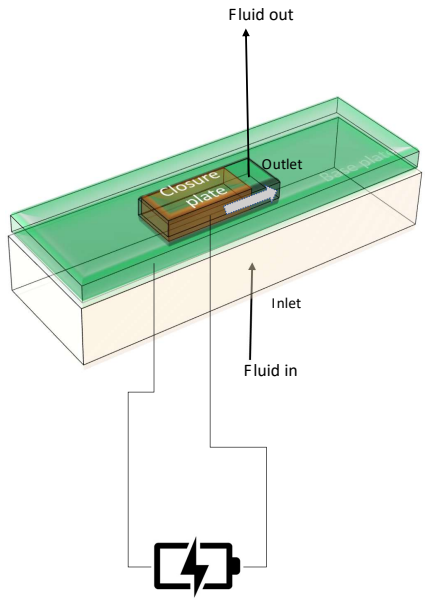

Figure 2.7: Principle of Electrostatic Valve

Voltages applied are still in tens of volts, making it not suitable for portable applications. Actuation voltage can be reduced by using curved-cantilever-beam-type actuator [65]

In this type of valves, voltages applied to affect actuation may cause electrolysis of the working fluid [66]. Careful design that doesn't involve application of voltage potential across fluid can

result in mitigating electrolysis and making it independent of fluid used [67]. The voltage required to operate this type of valves can be reduced by using the electrostatic zipping phenomenon [68] in which distance between electrodes is lesser at one end effecting a high electrostatic force at that end. This causes a zipper-type effect to close the valve from the closest to the farthest end.

The valve opening obtained is very small in this type of valve, leading to an inadequate flow. S-shaped actuator membrane [69] [70] can be used, which results in a better flow. These valves are typically made using metals, silicon, glass or thermoplastics which make their fabrication difficult. Elastomers are a preferred method due to extensive use of soft-lithography methods and is proposed in [71].

The **Freeze-Thaw/Ice Valves** [72] freezes and thaws a small portion of working fluid in micro-channel to start and stop the flow. For example, in the valve shown in Figure 2.8, the Y-shaped arms are the portions on which cryogen is sprayed to stop the flow.

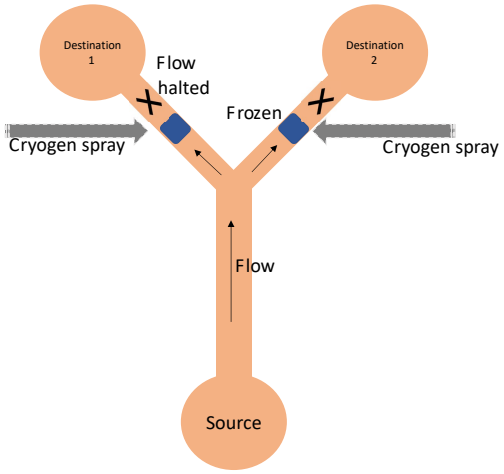

Figure 2.8: Principle of Freeze-Thaw Valve

Though this method doesn't involve any moving parts, it needs a suitable cryogen to freeze analyte inside micro-channel. Using cryogens is not ideal for portable devices. Also, the low

temperature must be maintained for some time. This is not easy unless a continuous flow of cryogen is available. This again proves to be difficult for a portable LOC device. The use of thermoelectric (TE) modules can remove the requirement of using cryogens.

Since freezing and thawing back takes time, these valves have slow response times. Also, they are normally open, so they are usable only in scenarios where flow needs to be stopped. Repeated freezing and thawing may adversely affect some analytes under consideration.

A two-level TE module can reduce the time to freeze/thaw, thereby improving response time [73]. It can be reduced using ice-nucleating proteins (INPs) buffers that provide ice nucleation sites, accelerating ice formation at much warmer temperatures [74]. By using a high thermal conductivity aluminium cylinder and eliminating thermal inertia by using a pre-cooled movable thermo-electric unit it was possible to reduce the response time of this type of valves to less than a second [75].

Instead of freezing/thawing the fluids under consideration, temperature-dependent viscosity changes of phospholipids have been used to create micro-channels with different flow resistances. This can steer fluids in sections of channels [76]. Similarly, dimethyl sulfoxide (DMSO) slugs can be solidified at the end of the capillary microchannel to seal [77] instead of freezing working fluid.

Freezing/thawing of channels structures created on an ice platform can be used as a microfluidic system. In this system, a scanning IR laser beam is used to selectively melt the regions required and create flow [78]. Use of low temperatures and bulky freezing equipment make this unsuitable for LOC device adoption.

Optothermorheological valves [79] are similar in working to the freeze-thaw valves, but they use optothermorheological liquids which undergo reversible sol-gel transition on heating due to incident laser light. The micro-channel in which flow needs to be stopped is filled with optothermorheological fluid. Low-power laser light is used to illuminate it. The optothermorheological liquid present in micro-channel gelates and stops the flow. This stoppage can be used to redirect the flow in another direction. Though promising the chemical interaction between the working fluid and optothermorheological fluid needs to be further studied.

Magnetic/Electromagnetic Valving uses micro-fabricated nickel-iron (NiFe) cantilever membranes to act as a valve attached to a silicon substrate. The magnetic valve is moved using an external electromagnetic field of micro-coils, as seen in Figure 2.9.

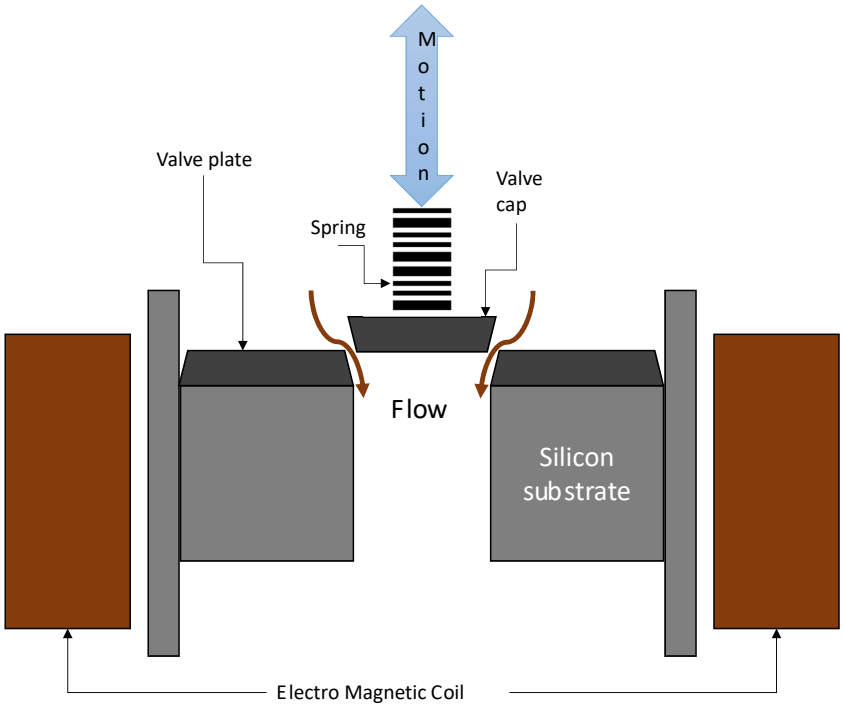

Figure 2.9: Principle of Electro Magnetic Valve

Though this is promising, it involves the use of the advanced process of 3D microforming with an aspect ratio of 10:1 and near-vertical walls which is challenging to achieve in practice [80]. A simpler version [81] uses a NiFe valve cap attached to a magnetic spring, placed on an orifice on a valve plate. The valve cap is moved up/down using an external magnetic field to plug/unplug the orifice. These valves need a continuous current to keep the valve open or close. To overcome this need, bistable electromagnetic valves were created [82] [83]. In all of these valves, the creation

of an integrated coil for the electromagnet is a technologically sophisticated process [84]. An electromagnetic actuator made of a permanent magnet at top, PDMS diaphragm in middle and easy to fabricate planar copper micro coil at the bottom seems to make the process of creation simpler [85]. Another more straightforward method to build the valve structure is proposed by using a micro-pattern of magnetorheological (MR) fluid topped on PDMS membrane [24]. The fluid flow channel is sandwiched between this membrane and a magnet. When the magnet is activated, MR fluid at the top gets attracted to it exerting pinch pressure and thus closing the valve. A simple fabrication method based on photolithography that uses SU-8/Fe composite as the actuator is proposed in [86]. This yields a flow-control (not ON/OFF) type valve. Another design that is simple to fabricate and also makes large scale integration of valves possible involves creating magnetic PDMS coated tips of metal rod that move and close a PDMS channel underneath on magnetic field activation [87]. A similar use of magnetic PDMS is proposed without using photo-lithography, but rather using a cutting plotter [88]. Another way that avoids photo-lithography uses laser-cut Polyvinyl chloride (PVC) adhesive stencils to create a stacked design of the valve [89]. It uses magnetic PDMS as a valve membrane. An in-plane U-shaped valving system made of PDMS mixed with iron powder provides another simple method to fabricate this type of valve [90]. Such magnetic composite polymers might make adoption of electro-magnetic actuation widespread in microvalves [91]. This type of valve can be combined with TWIST type of valve, which makes it easy to fabricate [92] [93].

Ferrofluidic valves [94] [95] use colloidal suspensions of mono-domain ferromagnetic nano-size particles in a carrier medium (water, diesters, hydrocarbons or fluorocarbons) that act like plug depicted in blue color in Figure 2.10, inside a capillary tube. They are held in place under magnetic field. They can be used to provide a flexible routing scheme [96]. Ferrofluid plug as valve helps in preventing evaporation of fluids that need heating such as in Polymerase chain reaction (PCR) [97]. Instead of using Ferrofluid as a valving liquid, a non-magnetic stopper floating in Ferrofluid that is pre-magnetized by permanent magnets can be used as microvalve and provides the same force at the size [98]. One significant advantage of these valves is ferro-fluid can conform to any non-

uniform shapes of micro-channel. Due to this, they can form a good seal even in imperfectly manufactured microchannels [99]. Alternative to injecting ferro-fluids which complicates steps in a microfluidic assay, recent research [100] suggests the use of magnetorheological fluids consisting of micrometer-scale particles suspended in a carrier or working fluid. External magnets can be brought in close proximity to aggregate these particles. This causes a viscosity increase to the point that flow is stopped.

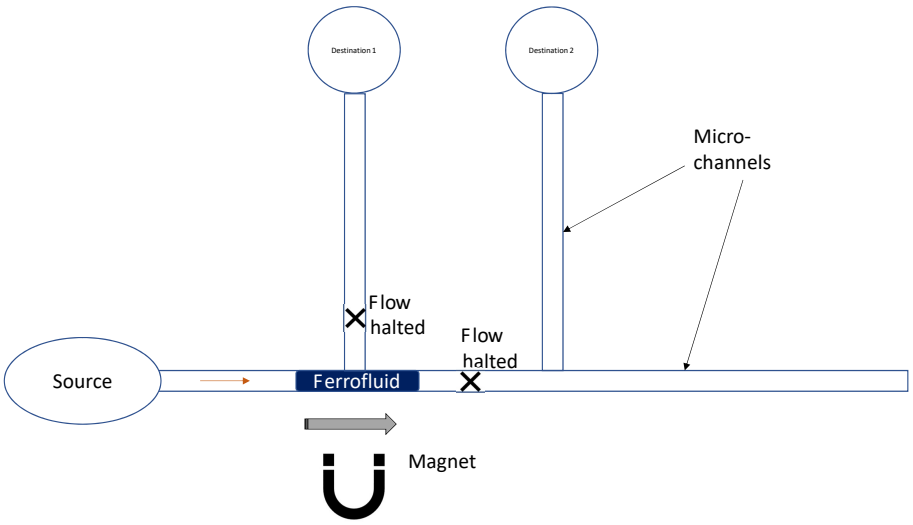

Figure 2.10: Principle of Ferrofluidic Valve

Though found useful, other physicochemical interactions of ferrofluids and biochemicals need to be understood before applying them since ferrofluid need to be in direct contact with working fluid. To overcome this issue, indirect actuation is proposed [101]. It consists of working fluid channel sandwiched between an electromagnet and a ferro-fluid filled microchannel. On activation of electro-magnet, ferro-fluid channel gets attracted to electro-magnet, compressing the working channel to stop fluid flow.

Hydrogel valves [102] promise to be simple in construction with little or no power consumption. They are based on expansion and contraction of phase changing chemical compounds, the hydrogels, on stimuli. As depicted in Figure 2.11, a small amount of hydrogel is wedged between a fixed and a movable membrane. On applying a stimulus, hydrogel expands, pushing the flexible membrane over a channel between input and output ports, thereby closing the valve. The ways to provide stimulus include pH [103], heat [104] [105], electric potential [106], glucose level [107], DC electric field [108], AC electric field [109], light [110] [111], pH change due to light [112], water [113], and alcohol concentration [114]. Since they can be activated by chemical properties of working fluid, they afford autonomous activation [115] by making use of these chemical properties for activation.

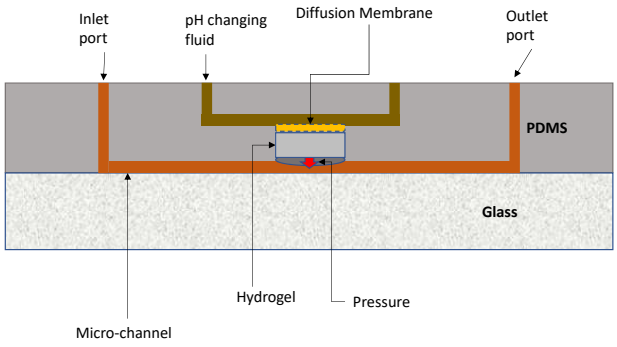

Figure 2.11: Principle of hydrogel Valve

Remote control is possible by application of alternating magnetic field (AMF) to a valve made of nanocomposite hydrogel: a mixture of magnetic nanoparticles dispersed in N-isopropylacrylamide (NIPAAm) hydrogel [116] which is temperature-sensitive. Similarly, remote swelling of temperature-sensitive Poly-N-isopropylacrylamide (PNIPAAm) hydrogels was possible by mixing Graphene

oxide (GO) nanoparticles in it [117]. GO nano-particles help in absorption and conversion of light energy to heat.

Various designs of valves have been proposed [118] [119] [120] [121]. Though attractive due to low power consumption, these valves had a long response time [122], which makes them not useful in applications that pose a requirement of a quick measurement result. Ultrafast response hydrogels were created by using x-ray lithography and a novel "synchrotron-radiation-induced polymerization" process [123]. Redox-active polymers such as polyferrocenylsilanes with electrical potential as a stimulus are found to be faster than the stimulus of temperature, pH, or ionic strength [124]. Fabrication of this type of valve is easy and can scale to micron-size using photo-lithography [125] [126]. One benefit of scaling the size down is the faster response time of valves [115] [127].

Because of large swelling characteristics, hydrogels can be applied to create re-configurable structures in microfludics. For example, an active wall made of the hydrogel can reconfigure a channel network for the protection of system components or redirect flow in a new direction. Similarly a delivery piston made of the hydrogel can reposition an object such as a filter [128].

The hydrogel can be applied in non-uniform shapes by embedding a mesh layout heater [129]. Activation using low voltages and currents may be possible using electrically actuated hydraulic solids [130].

Hydrogels based on cellulose [131] are bio-degradable and hence promise to address the environmental concerns arising due to disposable nature of microfludic devices.

Bubble valves use mechanical force of a gas bubble. In one implementation, shown in Figure 2.12, the process of electrolysis created a bubble that moved a micro-gate on an opening [132] over inlet and outlet port. This caused the flow to start or stop.

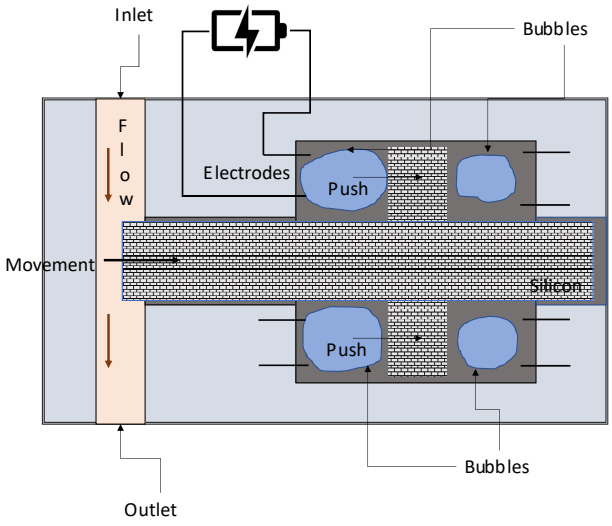

Figure 2.12: Principle of Electrolysis Bubble Valve

[132]

In another type of implementation [133], a gas-filled actuation chamber is adjacently connected to a microchannel containing working fluid. Actuation chamber has a micro-heater which heats the gas in it. Expanding gas moves in the micro-channel to block fluid movement. On removing the heat the gas volume decreases reopening the valve. Microchannel has a narrow neck downstream to the actuation chamber - this helps in creating a capillary force that holds the bubble at the actuation window. A similar type of valve but with heater placed in the main channel [134] moves a bubble from attached micro-cavity into the main channel due to thermal gradient (Marangoni effect [135]).

In one implementation [136] a cantilever is created using SU-8 between openings that connect two micro-channels. A bubble is grown by water electrolysis. It pushes a cantilever on the opening to close it. The cantilever is in the same media as working fluid. One implementation that avoids the creation of gas using electrolysis injects a gas bubble into a working channel via a side vent.

The gas bubble is held at the junction by use of micro-pillars [137]. Another implementation connects directly to the flow channel [138].

The capillary force has been used in valves in different forms. **Capillary-force valve** uses a gas bubble to force open a valve created by capillary pressure [139]. In Figure 2.13, a pressure barrier exists between a wide and a narrow opening between an inlet and an outlet. The bubble created by electrolysis in the broader part creates a capillary pressure that overcomes the pressure barrier between the inlet and the outlet to cause flow.

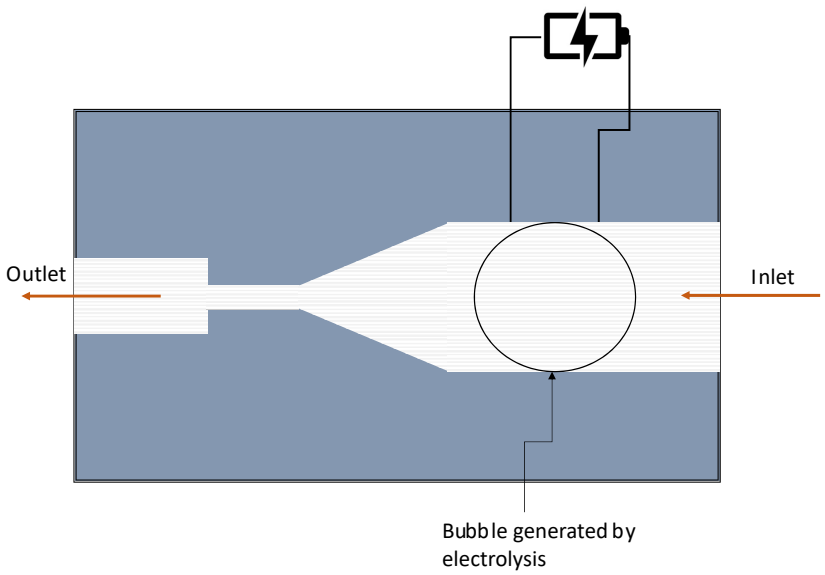

Figure 2.13: Principle of Capillary Force Valve

Apart from these, fluid motion has been achieved by making the use of just the **Capillary action** so that fluids move or block autonomously [140] [141]. Capillary valves typically consist of a narrow micro-channel connecting two wider micro-channels. The valve action is due to the change of hydrophobicity across the valve, which in turn depends on the surface energy or the geometry of the valve channel.

Capillary action based valve offers various advantages - they are easy to fabricate using simple manufacturing techniques such as conventional plastic molding, laser [142], and 3D printing [143]. They don't need active elements for flow control. With a careful system-level design of micro-structures' geometry it can be used to create delay valve that gives a timed flow of working fluid, flow resistances valve that gives measured flow and "AND" logical function valve that starts/stops the flow of working fluid using another fluid [144]. Combination of various capillary elements can lead to complex "capillarics" [145] - circuits similar to electronic circuits. Capillary force can be combined with gravitational force [146] to create more accessible designs for a low-resource setting.

To get better control over fluid movement in capillaries, striped/ridge pattern of material perpendicular to the direction of flow - "Phaseguides" [147] [148] can be used. These patterns guide the flow in a channel. They are useful in efficiently filling and emptying microfluidic structures. Further to this, liquid flow can be confined using continuous undercut edges an application of Gibbs inequality [149].

Hydrophobic zones in the capillary channel can be affected by electric field or centrifugal force [150]. One innovative technique that uses electric field, makes use of release of electrical discharge by a handheld corona device in a capillary microchannel [151]. This ionizes air in it changing surface energy that leads to a reduction in contact angle for fluid. Due to this reduction in contact angle liquid flows.

Capillary soft valves are created by the space below an elastic PDMS membrane placed between two micro-channels. On pressing the PDMS membrane, capillary pressure barrier between the two channels is reduced, leading to the flow of working liquid [152].

Orientation and concentration [153] can also be used to move fluids across micro-channels.

Check valves mimic biological valves, as seen in Figure 2.14, they are flaps which opens on applying the right pressure [154] [155]. Traditional silicon micro-machining techniques [154], PDMS [156], SU-8 [157] has been used in the fabrication of these devices. Manufacturing on PCB has been found feasible [158].

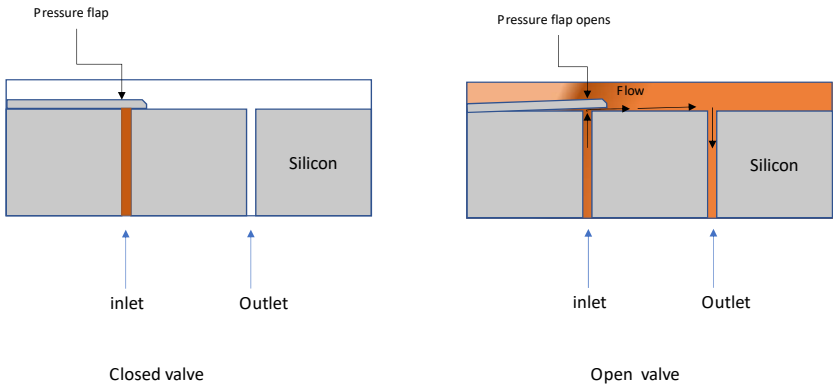

Figure 2.14: Principle of Check Valve

An embedded elastic arch in a micro-channel can be used as a valve by the mechanism of "snap-through" [159]. Recently a novel design that uses a comb-shaped free-moving plug as valve was created [160]. It employed a comb-shaped microstructure that moved and engaged in downstream microchannel's opening on applying pressure. This closed the flow. On release of the pressure, the comb tooth disengaged and allowed fluid to flow.

These valves need no power to operate, use bio-compatible material, have a straightforward and fast fabrication process. They are expensive to develop because of the need to tailor for each application. Also, they operate on pressure, generating that in portable devices is difficult.

Apart from these valves discussed, which are mechanical in nature, a new entirely different type of valves based on cell biology have been investigated. Protein aggregates, forisomes from Fabaceae family, exhibit swelling on exposure to Calcium ions and pH change. This protein was integrated into a micro-channel. On change in calcium concentration or pH change using electric current, they were able to block micro-particle flow [161]. A similar result was observed using a

stalk of Vorticella convarallia. A stalk of it was implanted on the microchannel wall. On addition of Calcium ions, the stalk extended to block the channel and constrict the flow [162].

Burst/One-shot valves are formed by a narrow constriction between two connecting microchannels. A functional element such as solder [163], alloy [164] or wax [165] is present at the compression. It is opened in a "burst" using external means such as pressure, temperature, opto-thermal energy [166] [167].

Piezo-thermal valve [168], is a novel type of valve which extends the use of one-shot valves for multiple purposes. It has a top actuator made of a piezo-electric plate that moves out-of-plane on the application of voltage. At the bottom is an orifice plate that contains an inlet with solder ring around it. A resistive heater is connected to this solder. The valve seals on simultaneous action of the piezo plate moving towards the bottom plate and solder getting melted by application of current in the base plate. This can be invoked multiple times with no leakage.

Mechanical valve use principles from macrovalves to stop fluid flow. In one design microvalve was created like a "water tap" by inserting a cylindrical rod across the micro-channel flow. Rod has a hole of the same dimension as microchannel. On aligning the hole with micro-channel, the flow of fluid could be affected [169]. In another implementation, a pentagonal-shaped elastomer rotor had orifices that aligned with stator orifices allowing flow [170].

The **Molecular valve** was created using a nanoporous membrane. A 3D structure in PDMS consisting of two microchannels perpendicular to each other in two different layers was built. A nanoporous polycarbonate nuclear track-etched (PCTE) membrane was placed between them. The flow between these crossed channels was found dependent on pore size and polarity of nanochannel surface charge [171].

Hydrophobic valve uses a hydrophobic region in a hydrophilic channel to stop the fluid. As seen in Figure 2.15, a hydrophobic patch exists between a hydrophilic inlet and outlet which doesn't allow fluid to pass through. Fluids can move across the patch by applying a sufficient amount of pressure. Various means exist to create such a hydrophobic region. For example, it can be formed by depositing Octafluorocyclobutane(C4F8) [172]. In [173], anisotropic oxygen

plasma etching was utilized to texture the bottom of microchannel before depositing Octafluorocyclobutane(C4F8). To tune burst pressure (opening pressure) either geometrical dimensions or the etching time can be varied.

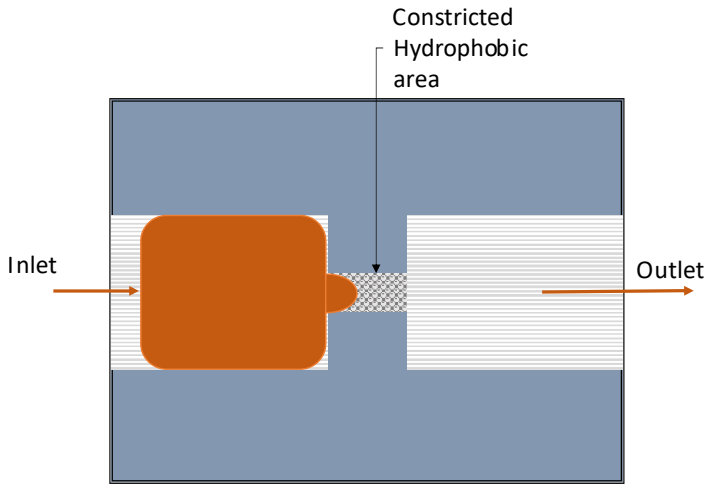

Figure 2.15: Principle of Hydrophobic Valve

Electrowetting - increase in wettability of surface on the application of electric potential, is used in hydrophobic valves for actuation. In one implementation [174] screen printed carbonaceous electrode at the bottom of micro-channel formed the hydrophobic stop valve in micro-channel with screen printed silver walls at two ends. The fluid stopped at the valve, and on the application of low potential, wettability of valve region changed to start the flow again.

Similarly, reversible hydrophobicity of silver deposited at the bottom of micro-channel was used to create a stop valve [175]. On applying voltage, the surface roughness of the solid electrolyte changed to induce stoppage and flow rate changes. Instead of metal, Perfluorodecanethiol [176], 1-

hexanethiol [177] was used as a hydrophobic monolayer, which turned hydrophilic due to reductive desorption allowing fluids to flow.

Autonomous actuation without applying potential was made possible through an electrochemical reaction. The system is composed of two channels. In working fluid channel, the base of the stop valve is composed of hydrophobic self-assembled monolayer (SAM) on a platinum electrode. Parallel control channel has Zn/Pt electrode. Aqueous fluid travelling in working fluid microchannel halts at SAM-Pt electrode due to hydrophobicity. Oxidization of the Zn layer of the Zn/Pt electrode happens when an electrolyte is passed in control microchannel. This results in SAM layer getting removed by reductive desorption due to the negative mixed potential created. This reduces the hydrophobicity allowing the flow of working fluid [178].

A pH-sensitive hydrophobic valve was proposed in [179]. It needed a fixed potential to be applied at a valve which activated when a fluid with a particular pH was injected in the channel.

Methods described till now used chemicals and have multiple fabrication steps which make it difficult to manufacture. A fast way to create a hydrophobic valve was proposed using a laser printer [180]. The unit was composed of three transparency layers. The middle tier had printer toner coated uniformly on both sides. Top and bottom had a patch of toner printed on the inner side to form a hydrophobic region. Hydrophobicity in the valve region was found to be directly proportional to the density of the printed ink, i.e. toner density which was controllable using a laser printer's grey-scale setting. Fluid stopped at the valve and started on applying a burst pressure.

Modulation of wettability can be used in the passive movement of fluids in a micro-channel. This is done by creating an alternate pattern of hydrophilic and hydrophobic surface, In [181] hydrophilic TiO2 nanoparticles and hydrophobic octadecyltrihydrosilane(OTHS) were used. Similarly, [182] used an alternate pattern of SiOH and PFS perfluorooctyl silane (PFS).

A delay valve was created by using a checkered hydrophobic pattern [183]. Hydrophobic material for the pattern was created by mixing PDMS with chloroform. Checkered pattern was imprinted by using a master stamp made of PDMS that had the pattern formed on it.

In this thesis, a hydrophobic valve that gets actuated on potential such as the type mentioned in [174] and [175] is created. It is studied for its applicability in a portable lab-on-chip device.

Chapter 3

Hydrophobicity effect based microvalve

3.1 Current research

At micro volumes, fluids behave differently from conventional fluid dynamics. It is found that mixing of two micro volumes of fluids is not convective as in bulk fluids; instead, they don't mix at all and flow is laminar when bought together in a channel. The movement is predicted by Reynolds number (Re), the ratio of inertial to viscous forces on fluids [1] [184]. Due to low Re, flow is laminar.

Electrowetting is a change in wettability on the application of electric potential. Electrowetting is of two types - Direct electrowetting and electrowetting on dielectric (EWOD). The fluid is in contact with the electrode in direct electrowetting. In EWOD, a dielectric layer separates electrode and fluid.

Hydrophobicity effect based microvalve use principle of capillary action and direct electrowetting for actuation. Capillary action causes movement till the valve area. Bottom of valve area is typically made of metal [175] [185] or SAM [176]. In the valve region, movement through it is controlled by electrowetting of this bottom electrode area.

In this thesis, the hydrophobic valve has been realized using direct electrowetting of metal - Gold. Fluid moves in a microchannel due to the hydrophilic nature of glass-bottom till it stops at the hydrophobic valve area made of the gold electrode. The flow starts again after application of a potential between fluid and metal electrode. Valve width needs to be adjusted to stop the fluid [185]. The flow velocity is linked to flow microchannel geometry as well as wettability. It is defined by the Washburn equation [185] as :

$$v = \frac{\gamma_{LV}}{8\eta x}\left(\frac{hw}{h+w}\right)^2\left[\frac{2cos\theta_{PDMS}}{w} + \frac{cos\theta_{PDMS} + cos\theta_{Glass}}{h}\right]$$

where "v = average flow velocity, h = height of the flow channel, w = width of the flow channel, η = viscosity of the solution, x = distance between the inlet of the flow channel to the meniscus of the moving liquid column, γ_{LV} = interfacial tension between the solution and the capillary wall, θ_{PDMS} = contact angles on PDMS, θ_{Glass} = contact angles on glass", as mentioned in [185]

Based on this relationship, the geometry of the valve was designed. Nine models of valves with widths - 80μmeter, 100μmeter, and 120μmeter with three heights - 40μmeter, 60μmeter, and 80μmeter were created. Width of flow microchannel was kept constant at 300μmeter for all.

3.2 Construction of hydrophobicity effect based microvalve

As seen in Figure 3.1, the valve was made of two components: PDMS slab with microvalve and glass substrate with gold electrodes. Figure 3.2 of valve cross-section depicts the alignment needed during bonding. The valve electrode aligns with the microvalve, the reservoir electrode, and the reservoir.

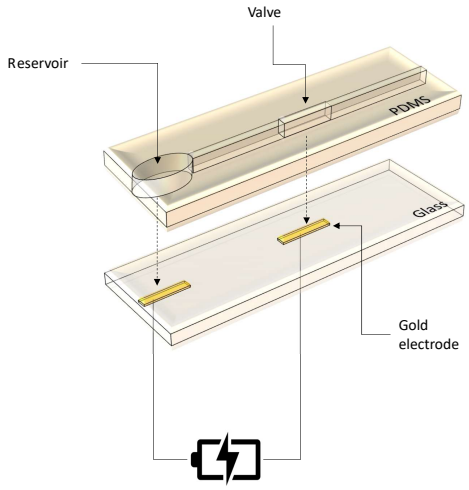

Figure 3.1: Construction of Hydrophobic Valve

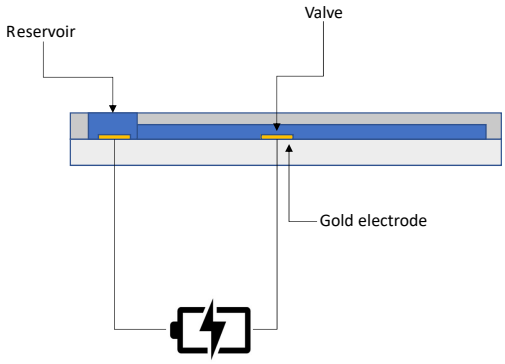

Figure 3.2: Cross-section of Hydrophobic Valve

The glass surface at the bottom of microchannel connecting microvalve is hydrophilic. The gold electrode surface in microvalve is hydrophilic immediately after cleaning, but on exposure to air, a hydrophobic monolayer of carbonaceous contamination is formed on the gold electrode surface [186]. This layer is used as a valve in this work. The contact angle of the gold electrode surface was reduced by doing plasma treatment. Bare PDMS surface, with no plasma treatment on it, has a contact angle of 110 °C [185]. No change in contact angle was done for the PDMS surface. If PDMS surface is treated, then valve action is not seen, and fluid flows from one end to another with a minimal plasma treatment.

3.3 Procedure to create hydrophobicity based microvalve

To create microvalve, PDMS was poured on a master mold of the microvalve. On solidification of PDMS, microvalve got formed in it. The master mold was created using SU-8 2050, a perma-

nent epoxy negative photoresist [187]. SU-8 has been used to construct Microelectromechanical Systems (MEMS) for years and has been found very well suited in producing near vertical, and tall structures [188].

Gold electrodes on glass slides were made using a vapour deposition process on the glass. Then joined to PDMS valve by doing oxygen plasma treatment on glass with electrodes. PDMS surface was not treated with plasma to keep it hydrophobic. Hydrophobicity of gold only was changed by doing oxygen plasma treatment.

Broad steps to create a hydrophobicity based valve are shown in Figure 3.3 below. Each of these steps is further detailed in later sections.

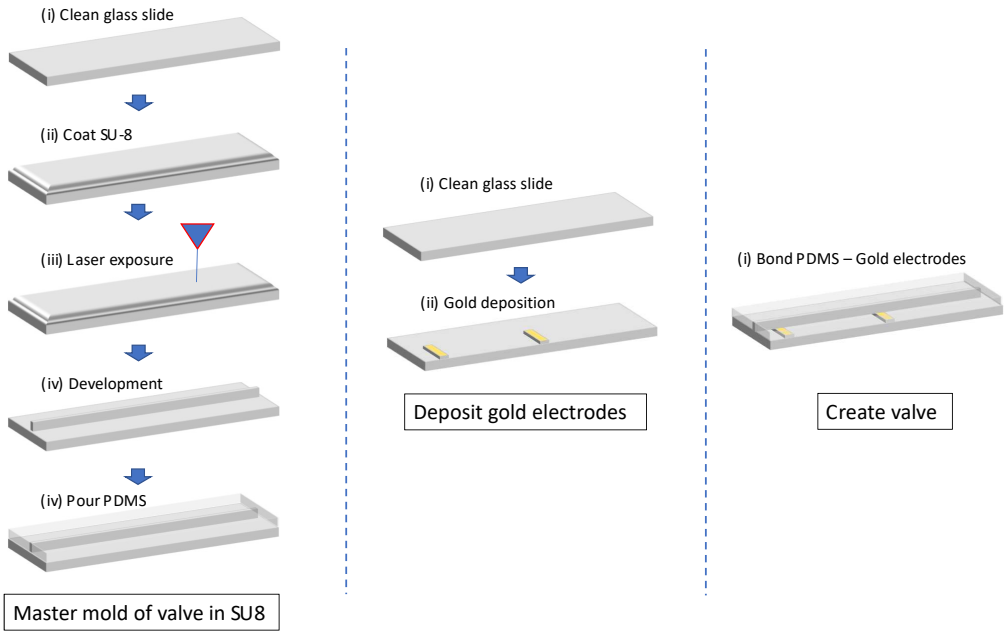

Figure 3.3: Valve Creation Process

3.4 Procedure for creation of microvalve SU-8 mold

Materials: The glass slide used for creating mold and as heating base plate were from AmScope (AmScope, size 25.4x76.2x1mm), Aluminum Metal plate used to place these glass slides was homemade milled piece (size 64X90X4mm), Epoxy-based negative photoresist used was SU-8 2050 from MicroChem (MicroChem Corp., MA, USA), Developer for SU-8 was from MicroChem (MicroChem Corp., MA, USA), Acetone for cleaning was from KMG (KMG, TX, USA), Isopropanol for cleaning was from KMG (KMG, TX, USA), Deionized Water (DI) used was from a deionized water system - Purelab Classic from ELGA LabWater (ELGA LabWater, UK) with resistivity 18.2 MΩ.cm

Equipment: Hot plate used for heating the SU-8 on mold glass slide was Opersder (Opersder 946C), Laser writer used for exposing patterns in photoresist was from Microtech srl (LW405C, Microtech srl, Italy), Rocker platform used to clean the glass slides was from Bellco biotechnology (Bellco biotechnology, NJ, USA), Magnetic stirrer used to clean the glass slides was from Corning (Corning, NY, USA), Spin coater used to spin-coat SU-8 on glass slide was Nilo 4 (Ni-Lo Scientific, Ottawa, Canada)

Design: Design of microvalve was created using AutoCAD Inventor 2019. It was then converted to "cif" file format which is readable by the laser writer. Referring to Figure 3.4, it contains a narrow neck region connected to wider microchannels.

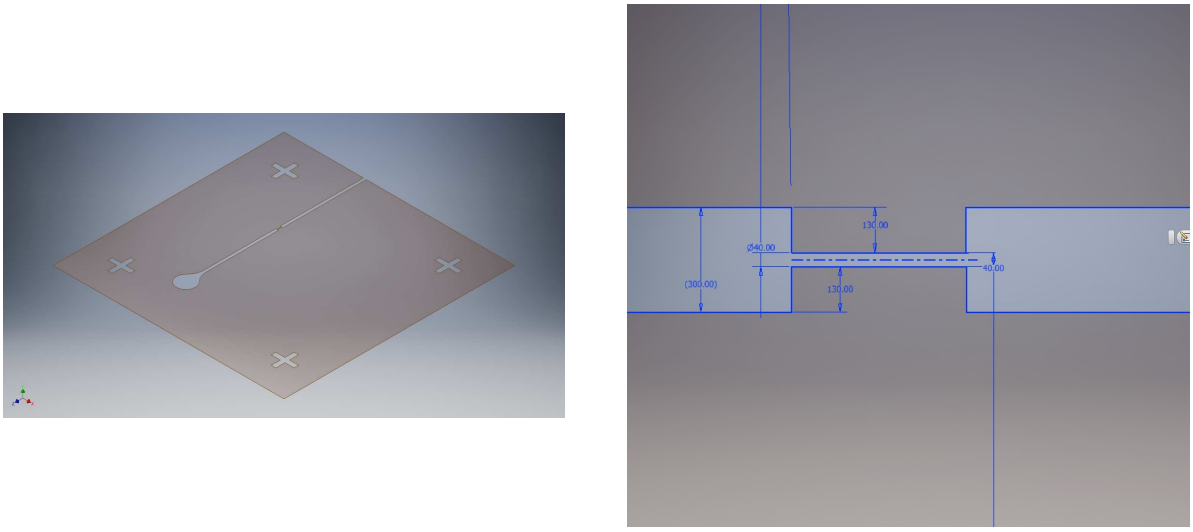

Figure 3.4: SU-8 mold design

Method: Microvalve was created using the following steps in the order as shown -

1. Prepare SU-8 base coat 3.4.2
2. Spin coat SU-8 3.4.3
3. Soft bake 3.4.4
4. Laser Exposure 3.4.5
5. Post Exposure Bake 3.4.6
6. Development 3.4.7
7. Hard Bake (Optional) 3.4.8

3.4.1 Setup for SU-8 valve mold

The equipment setup for preparing SU-8 master mold on glass slide is depicted in Figure 3.5. It involved placing a metal plate on a hot plate, then put a clean glass slide on the aluminum metal plate, and finally using this slide to place the glass slide on which mold needs to be created.

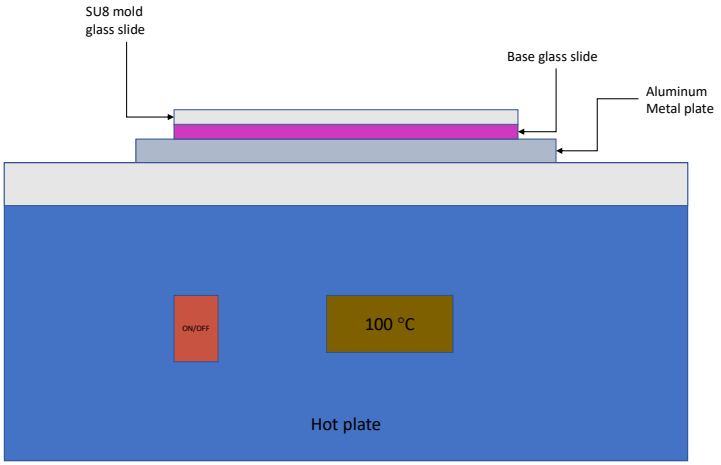

Figure 3.5: SU-8 Valve Mold setup

3.4.2 Prepare SU-8 base coat

The steps to prepare the SU-8 base coat consisted of the following -

1. Washed glass slide using a hand soap under running tap water to remove any organic residues
2. Dried the glass slide using Nitrogen jet
3. Cleaned the glass slide again by putting it in acetone bath and stirred using the magnetic stirrer or by rocking motion on the rocker platform for 10 minutes
4. Rinsed using Acetone, IPA and DI water
5. Removed stains/dirt using kimwipes and acetone

6. Evaporated all liquids on the slide by putting it on the hotplate for 10 min@ 65 °C (Kept it on another clean glass slide)
7. Cooled the slide by taking it off the metal plate for 10 min and placing on a metal plate
8. Dried the glass slide in Nitrogen jet again to remove any remnants
9. Heated the glass slide for 10 min at 65 °C
10. Switched off the hot plate
11. Poured SU-8 directly from its bottle on the prepared, slightly hot glass slide
12. Spread SU-8 using a wooden mixing stick so that no area remain uncovered
13. Cooled SU-8 on the glass slide to room temperature - about 50 min

3.4.3 Spin coat SU-8

The steps to spin-coat SU-8 base coat consisted of the following -

1. Used spin-coater with following settings

Stage 1		Stage 2	
RPM	500	RPM	Final rpm
time	5	time	30
Acceleration	100	Acceleration	300

2. Here, Final rpm = 2000 for 80μm, Final rpm = 3000 for 60μm, and Final rpm = 4000 for 40μm height of valve

3.4.4 Soft bake

The steps to soft bake SU-8 base coat consisted of the following -

1. Step of heating (step 1) followed by cooling (step2) needs to be done 1 time for each 10 μm thickness of SU-8

1.	100 °C	10 min
2.	Cool off on hot plate	40 min

2. So an 80μm height SU-8 needed 8 cycles of heating and cooling to have excellent adhesion on glass

3.4.5 Laser Exposure

The following steps were used on the laser mask writer -

1. Set focus on the top
2. Use settings -

Gain	Energy	Dstep	repeat
36	902 mJ/cm^2	4	2

3. Set focus on the bottom and repeat

3.4.6 Post-Exposure Bake

The steps used to perform post-exposure bake consisted of the following -

1. Immediately after exposure, the glass slide need to be baked directly on the hot plate

1.	70 °C	2 min
2.	95 °	8 min
3.	Cool down on the hot plate	40 min

2. A pattern started emerging after step 1
3. Rested the glass slide for 24 hours to remove residual stress

3.4.7 Development

The steps to develop SU-8 consisted of the following -

1. Sonic cleaned in a flat beaker with SU-8 developer for 1.5 min

2. More sonic cleaning was done if valve area was still unclear for 30 more secs

3. If sonic clean didn't work then glass slide was wrapped in kimwipes, a few drops of SU-8 was added on these kimwipes

4. A cotton swab dipped in SU-8 developer was gently rubbed on this wrapped glass slide along the direction of microchannel especially at the valve area

5. Washed the glass slide with IPA, DI water, and dried using nitrogen jet

6. Repeated steps 2, 3, 4 till valve was clearly seen under a microscope

3.4.8 Hard Bake (Optional)

The steps used to perform hard bake consisted of the following -

1. Heated the glass slide on the hot plate with 7 °C increase for every 1 min

2. On reaching 100 °C, heated it for 3 min

3. Cooled it down at a rate of 5 °C per min till 65 °C

4. At 65 °C, switched off the hot plate to cool the glass slide naturally

3.4.9 SU-8 valve

During development process stage, a lot of molds used to get removed from the glass slide due to low adhesion. To solve this problem, 9 valves of different widths were created on each glass slide of 1" X 3 ". This led to an improved yield of molds per glass slides. Figure 3.6 shows one of the microvalve molds.

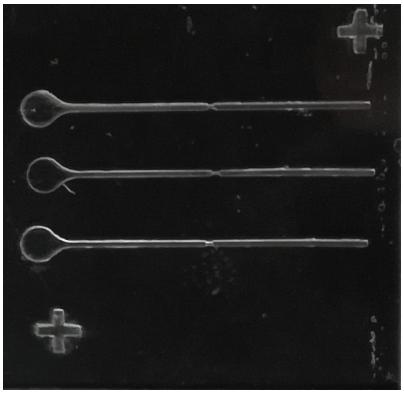

Figure 3.6: SU-8 Valve Mold

3.5 Procedure for preparing acrylic mold for valve

Materials: Acrylic sheet used to create the base and valve mold was a generic sheet of thickness 5.4 mm. To glue these mold together, Superglue (The Original Superglue Corporation, CA, USA) was used.

Equipment: To cut the acrylic sheet, laser engraver from BOSS Laser (LS-1416, BOSS Laser, FL, USA) was used.

Design: Design of acrylic mold was created using AutoCAD Inventor 2019. It was then converted to "dxf" file format and then to "rld" file format which was readable by BOSS laser writer.

Method :

1. The base plate is a rectangular size of 95 mm X 45 mm as shown in Figure 3.7.

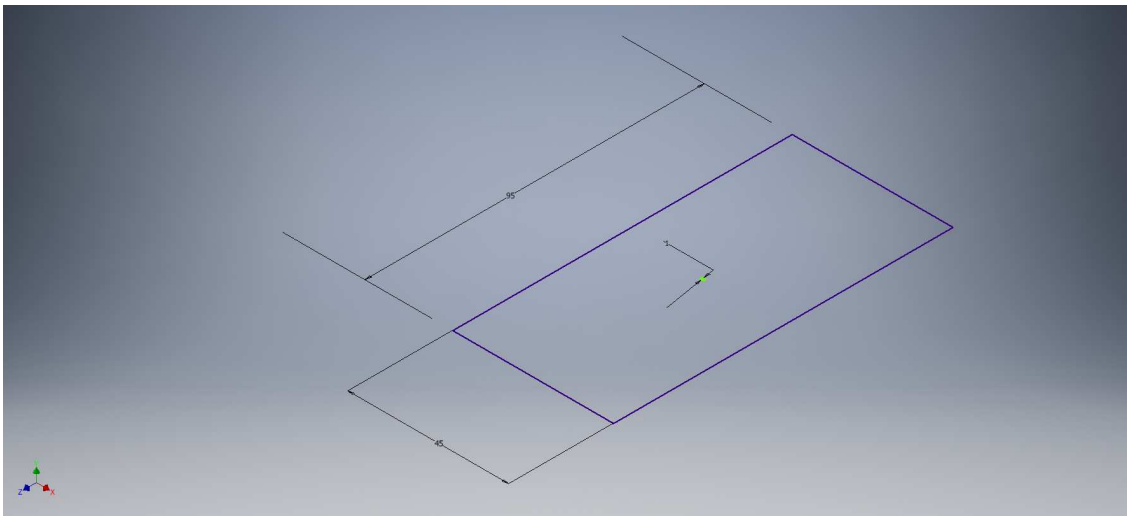

Figure 3.7: Valve Mold Housing Base plate

2. The valve plate is a frame with an outer dimension of 83.5 mm X 33.5 mm and an inner dimension of 76.5 mm X 26.5 mm as shown in Figure 3.8.

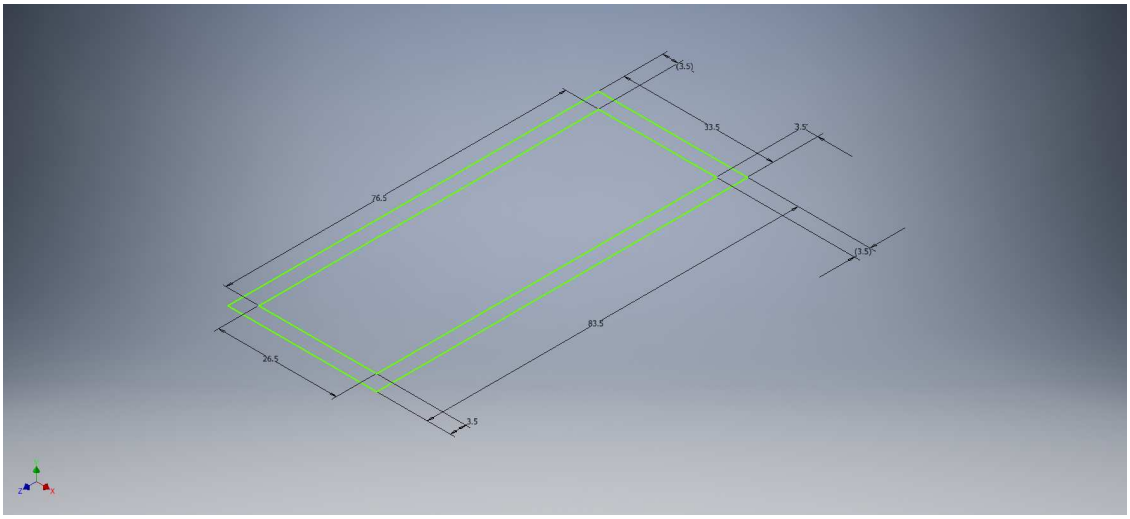

Figure 3.8: Valve Mold Housing Valve plate

3. Used the laser cutter to cut acrylic sheet in size shown in Figures 3.7 and 3.8

4. Pasted valve plate on the base plate

5. Picture of a ready acrylic mold is shown in 3.9

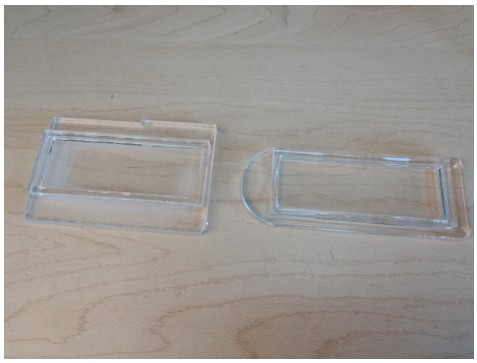

Figure 3.9: Acrylic mold to place SU-8 mold

6. Placed the SU-8 valve mold in acrylic mold so that mold features were facing up as shown in Figure 3.10

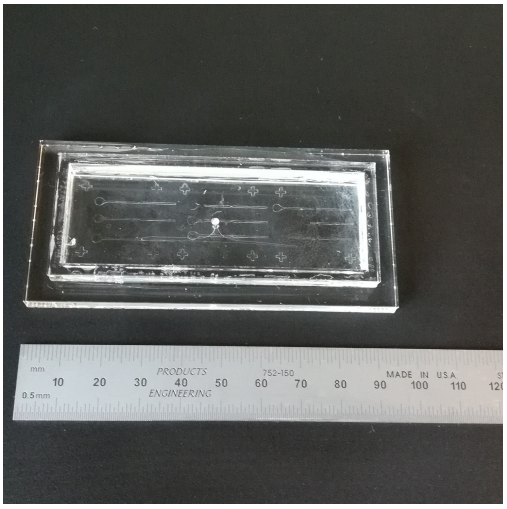

Figure 3.10: SU-8 mold placed in Acryllic mold

3.6 Procedure for creation of electrodes

Materials: Glass slides for electrode were from AmScope (AmScope, size 25.4x76.2x1mm), Positive photoresist S1813 to create electrode mask was from ROHM and HAAS (ROHM and HAAS Electronic materials LLC, MA, USA), S1813 developer - Megaposit MF 26A to develop S1813 was from ROHM and HAAS (ROHM and HAAS Electronic materials LLC, MA, USA), Gold pieces were cut from PAMP Suisse Gold Bar 0.9999 Pure.

Equipment: Hot plate used for heating S1813 on the glass slide was from Opersder (Opersder 946C), Laser writer used to expose patterns in photoresist was from Microtech srl (LW405C, Microtech srl, Italy), Evaporator used to deposit gold on glass slide was from Low-Temperature Lab, Physics Department, Colorado State University (CSU), Sonic cleaner used to clean and develop glass slides was from iSonic (P4810 Ultrasonic Cleaner)

Design: Design of electrode was created using AutoCAD Inventor 2019. It was then converted to "cif" file format which is readable by the laser writer. The design, as shown in Figure 3.11, has gold electrodes along the width of the glass slide. The two leftmost electrodes are for the reservoir. The middle one is for the valve. A set of concentric electrodes at the right end form Working, Reference, and Counter electrodes to perform electrochemical analysis.

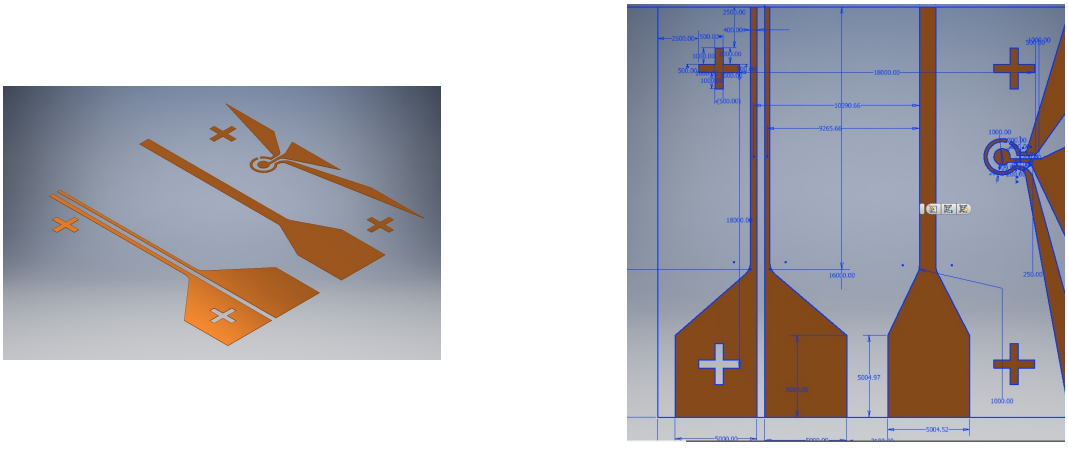

Figure 3.11: Valve electrodes design

Method: The electrodes were created using a two-step process:

1. Preparation of glass slide for gold deposition is detailed in Section 3.6.1
2. Gold deposition on slides is detailed in Section 3.6.2

3.6.1 Preparation of glass slide for gold deposition

The steps for glass slide preparation involved:

1. Cleaned the glass slide first using acetone, then methanol or IPA and finally DI water
2. Evaporated all liquids by placing it on the hot plate for 1 min at 115 °C
3. Cooled it down for 2 min on a metal plate
4. Spin coated S1813 using these settings

Stage 1	
RPM	4000
time	30
Acceleration	800

5. Baked this S1813 coated glass slide on the hot plate for 1 min at 115 °C
6. Cooled it down for 2 min on the metal plate
7. Used the laser writer to write the electrode pattern with laser dose settings at power = 190mJ/cm^2
8. Developed the lasered pattern on glass slide using S1813 developer bath for 40 sec
9. Put glass slide in DI water bath for 1 min
10. Dried the glass slide using Nitrogen jet

3.6.2 Gold deposition on slides

Gold is deposited using a vapor deposition process. The procedure described below pertains to the evaporator available in the Chen lab in the Scott building.

1. Loaded the glass slides prepared in earlier steps on mounting plate upside down in evaporator. Made small pieces of gold and put then in evaporation crucible in the evaporator. Put on the glass dome
2. Put Rough/Backing valve to "Rough"
3. Put Hi vacuum valve and Diffusion pump to OFF
4. Start the rough pump
5. When P1 gauge showed less than 200mTorr, switched Rough/Backing valve to Back
6. On P2 reaching less than 200 mTorr, switched Hi Vaccum valve to ON
7. When P2 shows less than 60mTorr, turned the diffusion pump ON
8. When P1 gauge shows 10 μTorr, started evaporation by turning the current ON
9. After evaporation is done, shut OFF Hi vacuum valve
10. Shut OFF diffusion pump
11. After 30 min shut OFF Rough/Backing valve
12. Shut off mechanical pump
13. Gold-coated slides were taken out and dipped in an acetone bath
14. Placed acetone bath in Sonic cleaner and turned it ON for 1.5 minutes
15. Gold pattern emerged as seen in picture 3.12

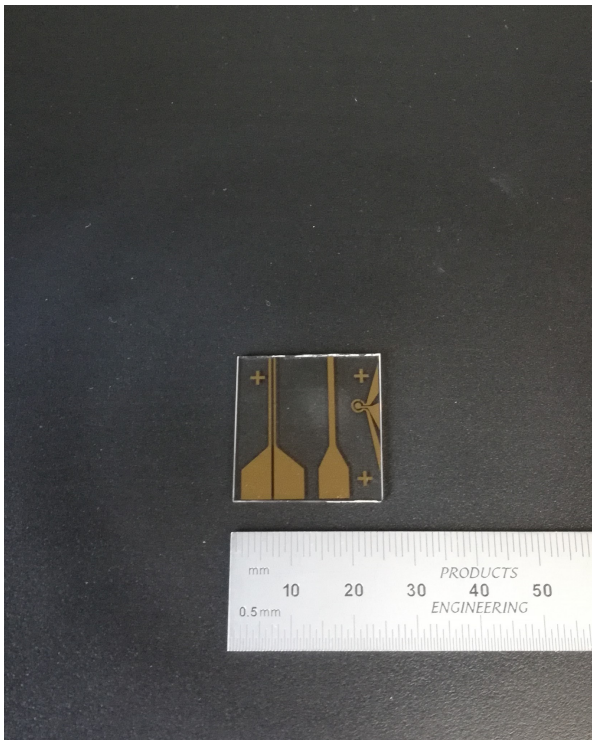

Figure 3.12: Gold Electrodes

3.7 Procedure for preparation of valve in PDMS

Materials: PDMS kit used to create valve was Sylgard 184 silicone elastomer base and curing agent, both from Dow Corning (Dow Corning Corp, MI, USA). A wooden mixing stick from CSU's chemistry stockroom was used to stir and mix the elastomer base and the curing agent in a plastic glass.

Equipment: Degassing the mixture of elastomer base and curing agent was done using vacuum pump from Kozyvacu (TA500, 2 stages, Kozyvacu, WA, USA) and a generic plastic vacuum desiccator. PDMS was baked in convection oven from Breville (Breville, CA, USA)

Method: The steps for preparing microvalve in PDMS involved:

1. Added elastomer curing agent to elastomer base in a ratio of 1:10

2. Mixed them thoroughly by stirring using a mixing stick for about 10 min

3. Degassed for 10 min in desiccator

4. Poured this mixture in the acrylic mold with SU-8 mold in it

5. Baked in the oven at 70 °for 20 min and then 80 °for 1 hour

6. Cooled it in the oven itself for 24 hours. If not cooled in oven then PDMS becomes sticky

7. Used a sharp blade to cut out PDMS valve from the mold. If required, blowed nitrogen gently in the cuts. This removed the valve PDMS without tearing it

8. Placed the valve on a cleaned glass slide

9. A completed valve is shown in Figure 3.13

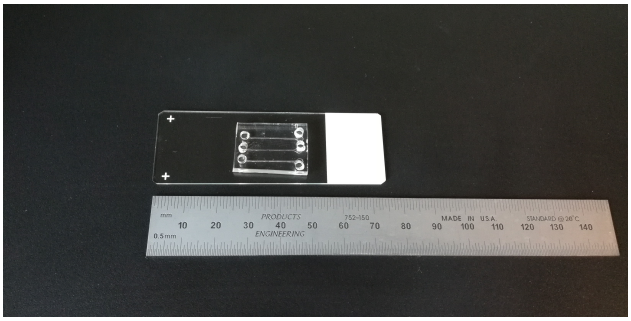

Figure 3.13: PDMS valve

3.8 Procedure for creation of valve assembled on electrodes

Equipment: Oxygen plasma treatment was done in Plasma asher from Technics Inc. (PlanarEtch II Model 750, Technics Inc., CA, USA)

Method: The steps for preparing microvalve assembled on gold electrode glass slide involved:

3.8.1 General procedure

1. Started flow of water in the cooling system of Plasma asher
2. Started oxygen flow to Plasma asher
3. Started the vacuum pump
4. Switched ON the plasma asher
5. Switched ON the digital display for vacuum
6. Kept the gold electrode glass slide in the plasma chamber - electrode side facing up. Closed the lid by unscrewing the pin and simultaneously pressing the cover lid down
7. Vacuum was settled to a value close to 0.25, power = 50, and the pressure on bubble gauge close to 45
8. Toggled oxygen switch to ON. This increased pressure in the chamber. Settled pressure back to the earlier value of close to 0.25, and pressure on the bubble gauge as before at close to 45
9. Started plasma for the required amount of time by throwing generator switch to ON
10. After the time duration, switched OFF plasma but kept oxygen ON for 1 min
11. Kept oxygen ON and switched ON venting for 1 minute
12. Turned back screw to release vacuum - the lid pops up in about 30 sec
13. Waited for 1 min after lid pops up
14. Placed PDMS valve on electrode glass slide ensuring that valve is aligned with the electrode
15. The cleaned surface on electrodes binded with the PDMS surface

16. The valve was now ready for use. One of the completed valves is shown in Figure 3.14

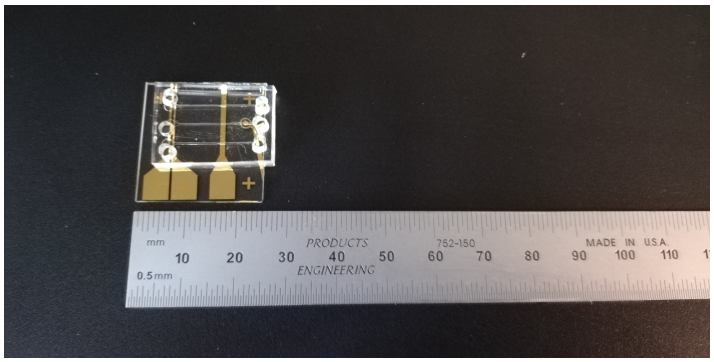

Figure 3.14: PDMS valve assembled

3.9 Testing of the electrically controlled microvalve

Materials: KCl (1M) was prepared by dissolving the required quantity of KCl (Sigma-Aldrich, St. Louis, MO, USA) in DI water. Phosphate Buffered Solution (PBS) was procured from Sigma-Aldrich (Sigma-Aldrich, St. Louis, MO, USA) and used as it is. Gmops, Foetal Buffer Solution (FBS), and Cell culture solution were procured from Equine Reproduction Laboratory (ERL) at Colorado State University. KCl and PBS were dyed using 10 drops of food color.

Equipment: DC potential was generated using a power supply from Tektronix (Keithley 2230-30-1 Triple channel DC supply, Tektronix Inc., OR, USA). Live video was captured using a generic USB microscope. XY axis movement mount used to position valve under the microscope was generic. Acrylic platform to place and elevate valve assembly was homemade - made by cutting

and stacking acrylic sheet pieces. Logic Terminals to connect the gold electrodes to power supply were generic. Pipette to insert the fluid was generic.

3.9.1 Test setup

Figure 3.15 shows the connections made. The negative terminal was connected to valve electrode and positive to reservoir electrode.

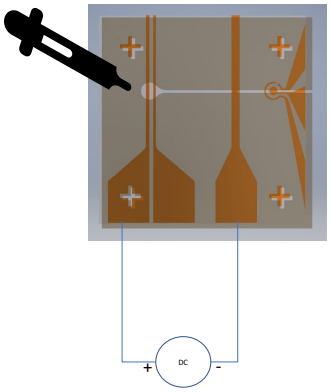

Figure 3.15: Circuit for testing of valve

The valve was placed on an acrylic elevation platform which is on a precision XY axis movement table. The screws on the XY movement table were adjusted to bring the valve under the lens of a USB microscope. Figure 3.16 shows the test setup. The USB microscope was connected to a laptop which allowed a live view and recording of the valve during the test process.

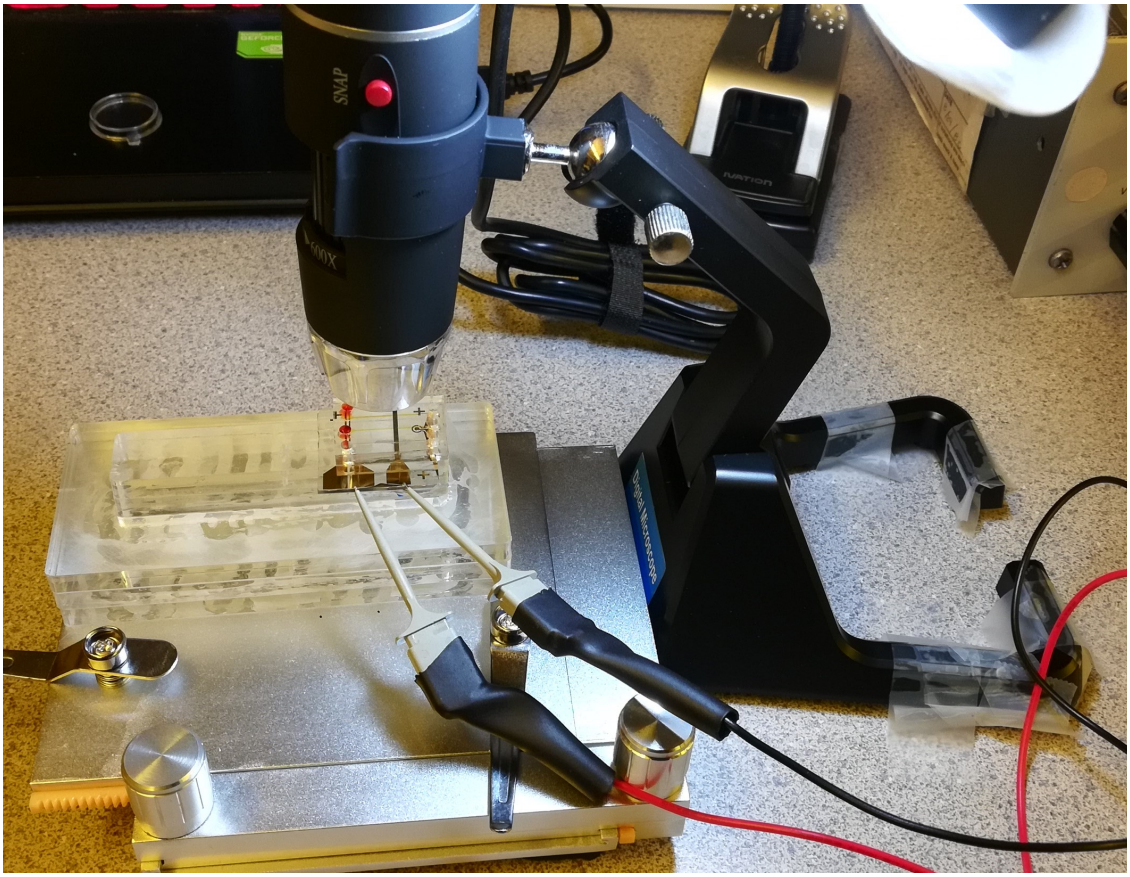

Figure 3.16: Valve Testing Setup

3.9.2 Testing procedure

Using the setup discussed in the previous section for each variant of valve, experiments were conducted using KCl, Phosphate Buffer solution (PBS), GMOPS, Cell culture, and 10pc Foetal Buffer Solution. During the tests, it was found that plasma treatment was needed to obtain correct valve action. Retention probability for each micro-channel width and the voltage at which the valve functioned correctly with the corresponding microchannel width were studied during the experiments. At least 6 tests were conducted for each type of test. The following subsections describe the procedures used during the experiments to find the correct amount of plasma treatment, liquid retention probability, and the minimum voltage needed for the valves to work.

3.9.3 Procedure to find plasma treatment duration time needed that gets the valve action

1. Did plasma treatment on gold electrodes for duration 30 seconds, 1 min, 2.5 min, and 5 min
2. Inserted fluid at the reservoir chamber using a pipette
3. Applied potential at valve with respect to reservoir electrode in steps of -0.1 V
4. Checked through live video, if the liquid moved beyond the valve on the application of potential

3.9.4 Procedure to find Retention probability for each width

1. Did the plasma treatment on gold electrodes for the time period found in Section 3.9.3
2. Inserted fluid at the reservoir chamber using a pipette
3. Fluid started flowing towards the valve due to hydrophilic glass
4. Checked and noted if the flow stops at the valve for each valve width

3.9.5 Procedure to find the voltage at which valve worked and corresponding valve width

1. Did the plasma treatment on gold electrodes for the time period found in Section 3.9.3
2. Applied potential at valve with respect to reservoir electrode in steps of -0.1 V
3. Checked if liquid moves at each voltage step

Chapter 4

Results and Observations

4.1 Results

Experiments were conducted for all models of valves using 1M KCl, Phosphate Buffer solution (PBS), GMOPS, Cell culture and 10pc Foetal Buffer Solution. The results from the experiments can be summarized in the following categories: 1) retention probability, i.e. the proportion of times the valves acted correctly out of the total number of attempts; 2) plasma treatment time, i.e. the time needed to get the valves act correctly with a minimum voltage; 3) the minimum voltage at which the valves acted correctly with its corresponding micro-channel width. Also, the shelf life of valves was tested by keeping the valves in storage for different time durations.

4.1.1 Results with KCL

Plasma Treatment time - It was found that 5 minutes of plasma treatment was enough to get valve working.

Retention probability - As seen in Figure 4.1 and 4.2, the ability to retain the fluid at the valve site was found to be maximum when valve's micro-channel is at 100 μm width and either 80μm and 60μm height.

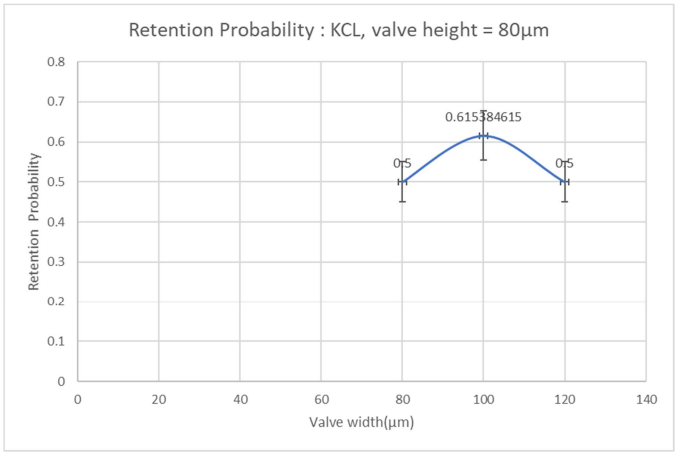

Figure 4.1: Retention Probability KCl with valve height = 80um

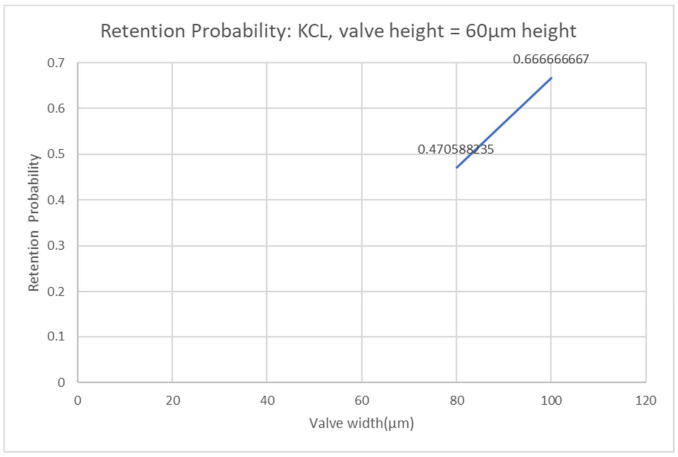

Figure 4.2: Retention Probability KCl with valve height = 60um

Valve activation DC voltage - Figure 4.3 shows a plot of average valve actuation voltages vs valve width. The average DC activation voltage was found to be 1.5 V for valves with 100 μm

width and 80μm height. The average DC activation voltage to be 1.9V for valves with 100μm width and 60μm height

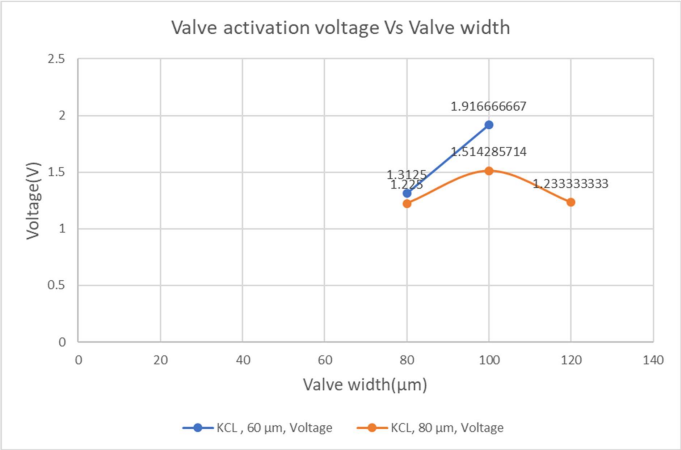

Figure 4.3: KCL valve activation voltage

4.1.2 Results with PBS

Since valves with 80 μm height had all three widths, i.e. 80 μm, 100 μm, 120 μm, available, it was used in all remaining testing.

Plasma Treatment time - It was found that 1 minute of plasma treatment was enough to obtain the correct valve actions.

Retention probability - As seen in Figure 4.4, retention at valve was found to be maximum in 120 μm width valve.

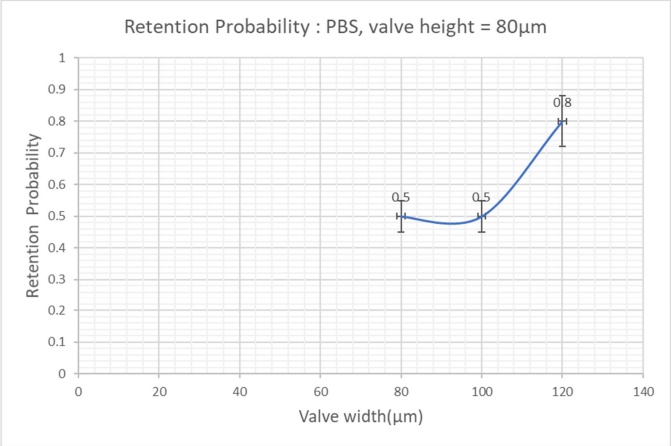

Figure 4.4: PBS Retention Probability

Valve activation DC voltage - Average DC activation voltage was found to be 1.25V for valves with 120 μm width valve and 80μm height.

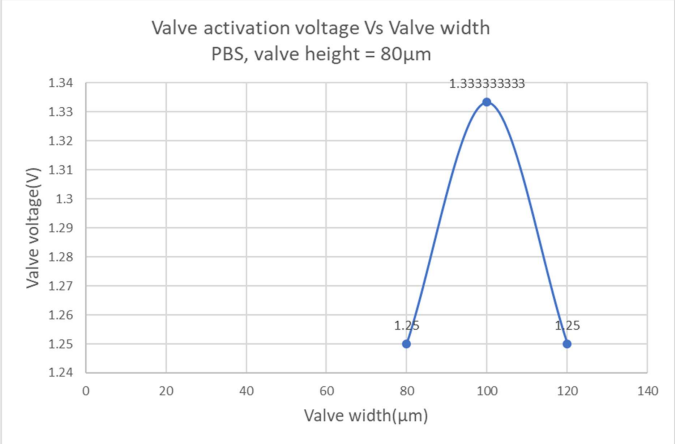

Figure 4.5: PBS Valve activation voltage

4.1.3 Results with GMOPS

Retention probability - Retention probability was found to be very less with these valves for GMOPS, as seen in Figure 4.6. This was with a little treatment of 30 secs. Any less treatment and fluid won't move in glass part of micro-channels.

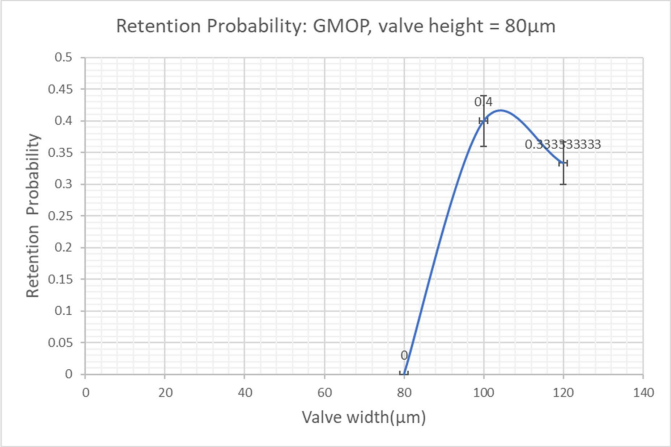

Figure 4.6: GMOPS Retention probability

4.1.4 Results with Cell Culture

Retention probability - Similar to GMOPS, the retention probability was found to be lower for Cell Culture. Figure 4.6 shows the plot of the retention probability vs the microvalve width.

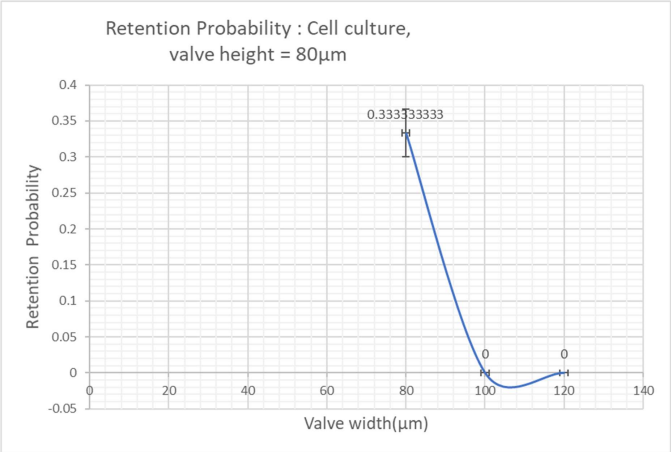

Figure 4.7: Cell Culture Retention probability

4.1.5 Results with 10pc FBS

Retention probability - With 10pc FBS retention probability was found to be zero, i.e. valve couldn't stop the fluid at all.

4.1.6 Shelf life

Shelf life was tested by using a valve after 1 day of plasma treatment. No movement even along the microchannel between reservoir and valve was seen indicating loss of hydrophilicity in the glass.

4.2 Observations

1. It was found that each type of analyte was stopped by different widths depending on the viscosity of the fluid as found by earlier researchers.

2. Potential to mobilize was found to be matching with other researchers (~1V) [185]. A very low voltage compared to EWOD.

3. Fluid could be retained for an unlimited amount of time if no potential was applied at the valve. Though it would eventually cause reduction at the valve electrode of the carbonaceous compound on the gold and block the fluid making valve less effective over time.

4. Reusability of the valve was not found to be good. Once the fluid is released, the wetted part couldn't be dewetted, and hence it couldn't stop the fluid flow.

5. With 40 μm microchannel width, the valves could not stop the target fluids.

Chapter 5

Conclusion and Future work

5.1 Conclusions

Electrically controlled hydrophobicity based microvalve can be used for fluids with a viscosity similar to water. The valve width needs to 100 μm; the height needs to be 80 μm, and microchannel width needs to be 300 μm. These valves can operate at a DC activation voltage of around 1V. It is vital that the gold electrode surface at the valve site be very clean. It is recommended to get such a clean surface using plasma cleaning. However, the lack of shelf life, i.e. need to do in situ preparation, does not make this technology useful for portable LOC devices that are field deployable. In this thesis, the fabrication process of high profile SU-8 structures on glass is presented. This makes it possible to use simpler and cheaper materials such as glass on gold compared to others who have used sophisticated materials, coatings, and micro-structures. In addition, testing of hydrophobic valve with different materials was done, unlike earlier attempts which used only KCl [185].

5.2 Improvement suggestions for future work

1. After plasma treatment keep the valve assemblies in an air-tight container. This might help to retain the valve's hydrophobic effect.

2. Find a way to clean gold using chemical methods for lower cost.

3. It is found that prolonged application of voltage potentials causes electrolysis because the electrode is exposed to the target fluid. A solution would be to apply a pulsed DC potential only till fluid passes the valve region. The amount of time to apply the pulse would depend on the concentration and type of fluid used.

4. In the process of creating SU-8 microvalve mold, it is recommended to use a programmable hot plate that heats and cools as per a set protocol. This would improve turn-around time and reduce human intervention.

5.3 Improvement suggestions in creating direct electro-wetting valves

1. It may be advantageous to use gold micropillar structure to modulate the hydrophobicity of the valve region [189]. It was found that this reduces the contact angle on gold leading to better effectiveness in stopping fluid flow. Also, switching speed increased with this change. Both of these benefits were obtained at the same potential applied as a smooth valve. A simulation framework for such surface patterning is available [190].

2. Instead of using solid-liquid-air systems as in the device presented in this thesis, try to use a solid-liquid-liquid system. In such a system, working fluid is immersed in another medium such as oil [191]. The solid-liquid-liquid systems can be more robust, i.e. they exhibit a substantial contact angle variation, have excellent reversibility and very less contact angle hysteresis.

3. It may be worth trying to make use of perfluorodecanethiol to create a hydrophobic valve, print electrodes using an inkjet printer and create microchannels on a PET film using UV-nano imprint lithography. This would make fabrication easier [192] and amenable to mass-production.

4. Another way to make these valves better is to make use of electrogates. Electrogates take the form of a micro trench etched in the bottom of valve area with a metal coating on the contours of the trench. Fluid stops at this gate due to Gibbs' pinning criterion [149] [193]. On the application of a potential between valve and fluid, the flow starts again.

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Appendix A

Microfluidic pumps

Micropumps move fluids from one place to another in a microfluidic device by pumping action. They are either mechanical or non-mechanical. Mechanical micro-pumps use physical constructs - A motion of mechanical parts pushes liquids directly [194]. They have matured over time and can flow a variety of liquids. Non-mechanical pumps rely on the electric or magnetic field and use the property of the fluid to control the liquid - a limited way. A few types of micropumps are reviewed here to give an idea of their working principle.

The **Electrokinetic** phenomenon has been tried [13], [14], [15]. It requires the creation of high voltage, reducing its use in personal/implantable devices. Also, individual control needs to be provided for each fluid reservoir to minimize leakage. This complicates the control hardware and software.

Traveling-Wave pump consists of a channel with a vibrating ceiling made of piezoelectric actuator array [195]. When a sinusoidal wave with a phase difference between the elements in the array is applied, a travelling wave motion is generated in the ceiling. This pushes fluid in the forward direction. Flow velocity is proportional to the resonant frequency. This principle of the travelling wave has also been applied using magnets with improved flow rate at lesser voltage [196]. Though attractive for portable adoption these designs are bulky and need further refinement. Overcoming this limitation is electric field travelling wave pump [197]. It consists of a planar array of gold electrodes on one side of the channel. Each electrode is applied with a square-wave voltage waveform phase shifted with the electrode on its side. Fluid velocity was found to be approximately proportional to the square of the voltage applied. This pumping is found to be less powerful and hence useful if the displacement required is small.

Thermal Capillary Pumping [198] drives discrete drops of fluids in a channel. Each individual drop is moved by changing the pressure at the liquid-air interface (capillary pressure) of each drop. This is achieved by heating the liquid-air interface at one end using micro-fabricated thermal

elements along the walls of micro-channel. This localized heating decreases the surface tension and increases capillary pressure at that end, drawing the drop in the direction of lower pressure. This is portable, but the effect of heating is different on each fluid and may change the measured parameter of the fluid under consideration.

Piezoelectric Pump [199] is made of two glass plates with a silicon wafer in between. The upper glass plate has inlet and outlet ports. The space between the top glass and middle silicon wafer creates a pressure chamber with silicon wafer acting as a diaphragm. A mesa structure mounted on a piezoelectric actuator is positioned onto this silicon diaphragm from the top. Voltage is applied to the piezoelectric element, causing the mesa structure to press on the silicon diaphragm due to piezoelectric effect. Cutting-off voltage contracts the piezo element causing silicon diaphragm to regain its shape. This alternate movement creates a suction of fluid in the chamber.

Electrochemistry has also been tried to move liquids [200]. In this approach, electrodes are placed at two ends of channels between which flow is desired. Redox-active surfactants species are generated at one end and consumed at another end. This creates a gradient of concentration which changes the surface tension and hence the capillary force between the ends of two channels. This change in capillary force leads to the movement of species from one end to another of channel. This method heavily depends on the chemistry of fluids under consideration and not applicable universally.

Appendix B

Python GUI for electroanalytical chemistry - BlissSTAT

BlissSTAT forms the backend of a system shown in Figure 1.1. Figure B.1 shows a more detailed view of the backend part. It reads data from the electroanalytical experiment (such as Potentiometry and Voltammetry) from a serial port and transforms it into a more readable graphical form. BlissSTAT is a framework as well, in which analysis of waveform can be done.

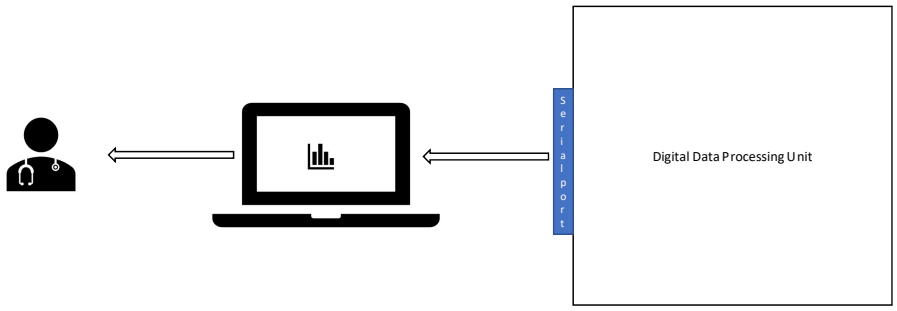

Figure B.1: BlissSTAT block diagram

B.1 How to start BlissSTAT

Steps at a high level (Steps 1, 2 required only once)

- Step 1: Install python
- Step 2: Get the “BlissStat” python script
- Step 3: Run the script

Step 1

- Install python from https://www.anaconda.com/download/
- Make sure that python is in PATH variable

Step 2

- Copy/Checkout/clone the “BlissStat” code in a directory by doing either –
  - Copy from a known location – e.g., Download the code from a Cloud drive
  - Clone from the git repository by running git clone <url>

Step 3

- Start a command prompt of python in Anaconda or Windows
- cd <the directory where BlissStat code is copied>
- Type “python bliss_stat_gui.py" at the command prompt without the quotes

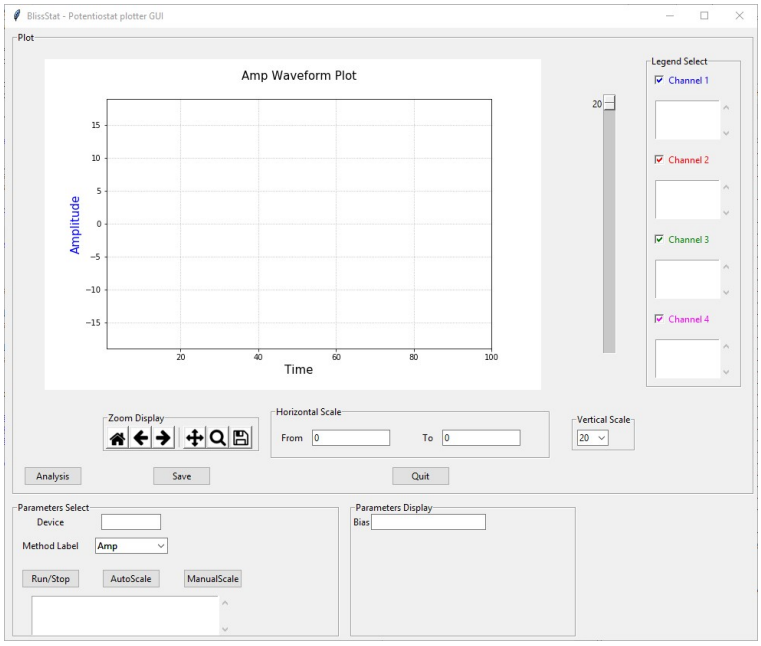

Figure B.2: BlissSTAT start screen

- Screen, as seen in Figure B.2 would be seen

B.2 Components of BlissSTAT GUI

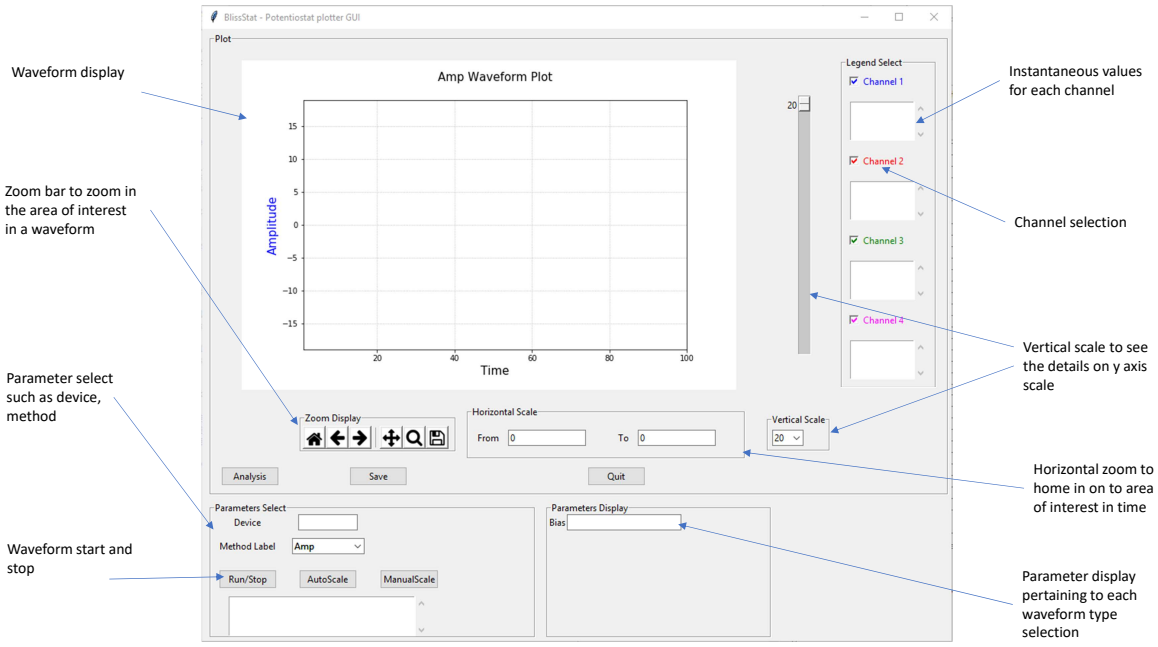

Figure B.3: BlissSTAT GUI controls

Components of BlissSTAT GUI are as shown in Figure B.3

B.3 How to use BlissSTAT

- On clicking “Run” a real-time display of incoming values starts as shown in Figure B.4

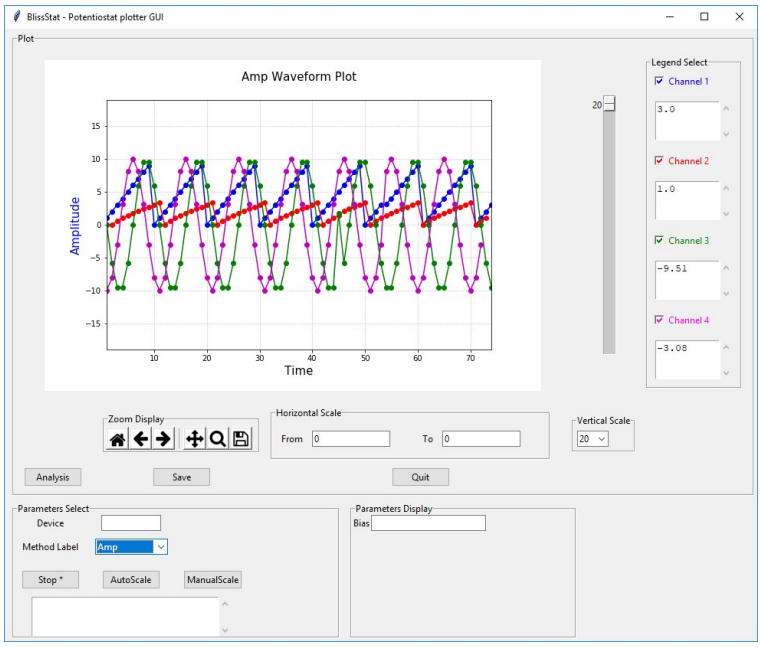

Figure B.4: BlissSTAT run started

- An appropriate channel can be selected for viewing by checking/unchecking the checkbox for each channel as shown in Figure B.5

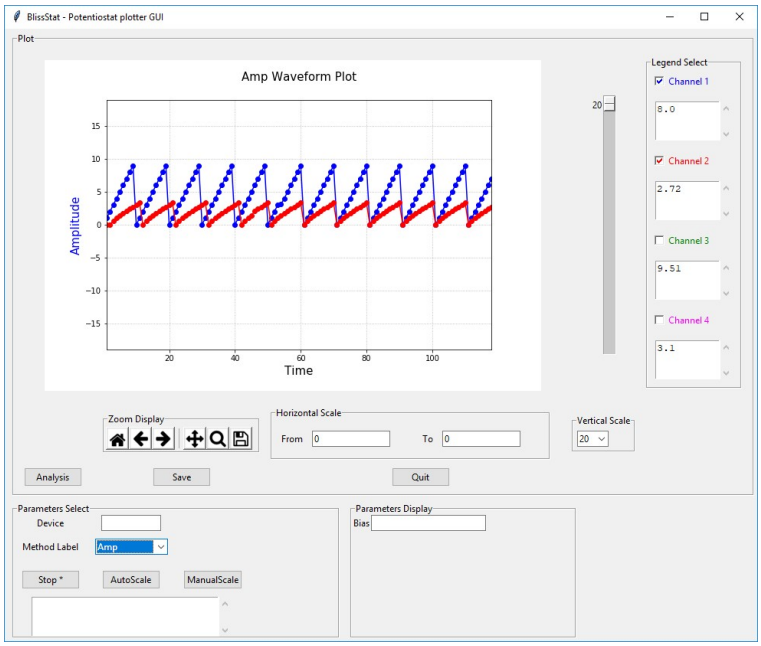

Figure B.5: Select channel

- Click on the zoom button and then select the area to zoom as shown in Figure B.6

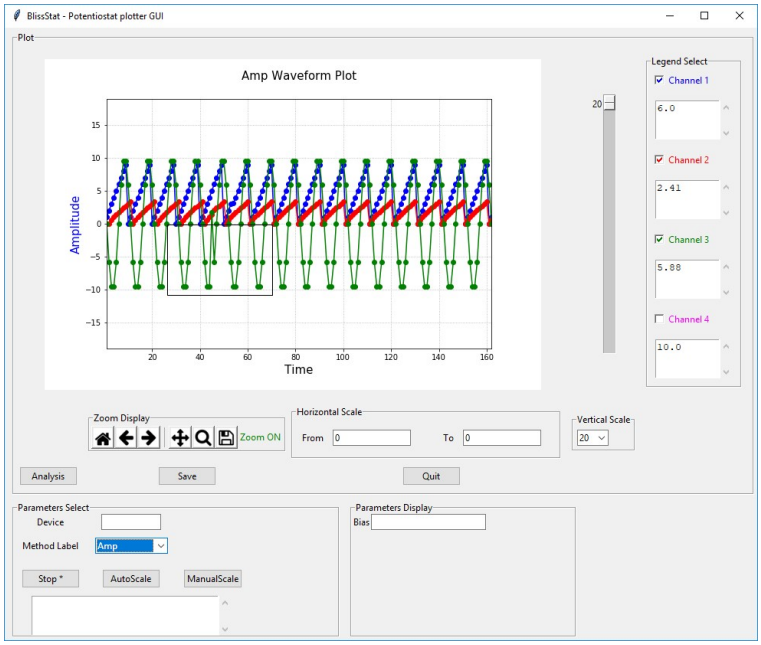

Figure B.6: Zoom select

- The selected area gets zoomed to show a magnified view as shown in Figure B.7

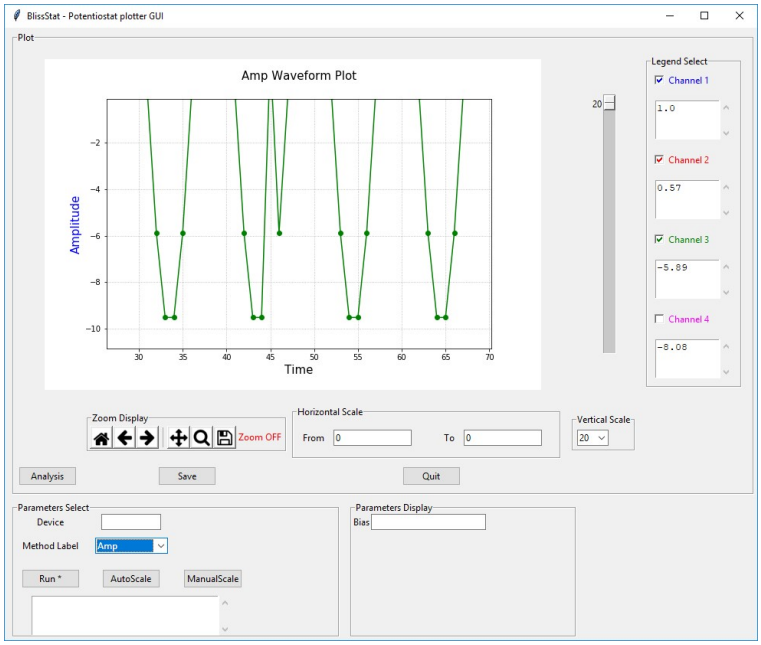

Figure B.7: Zoomed

- An area can be panned by selecting pan button and then dragging cursor in the area as shown in Figure B.8

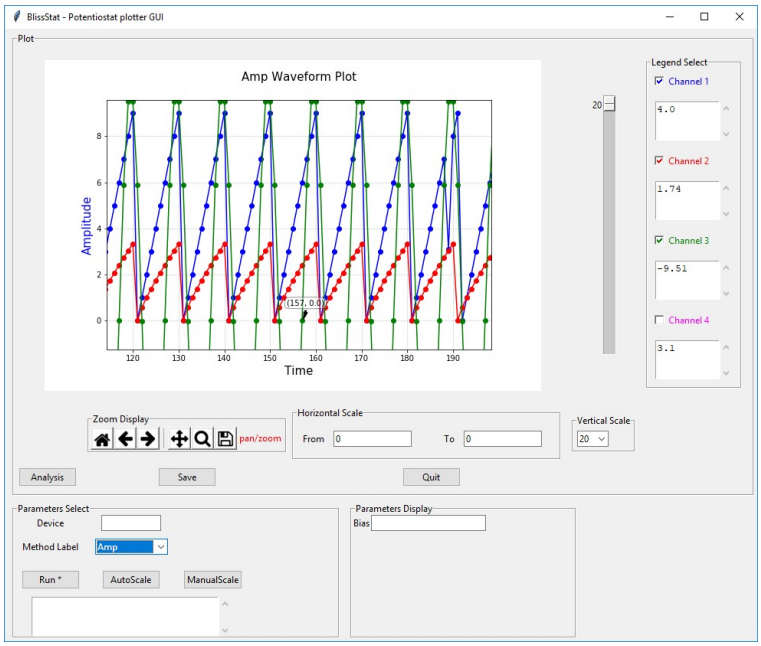

Figure B.8: Panned

- An area of interest can be jumped to by entering values in the horizontal scale as shown in Figure B.9

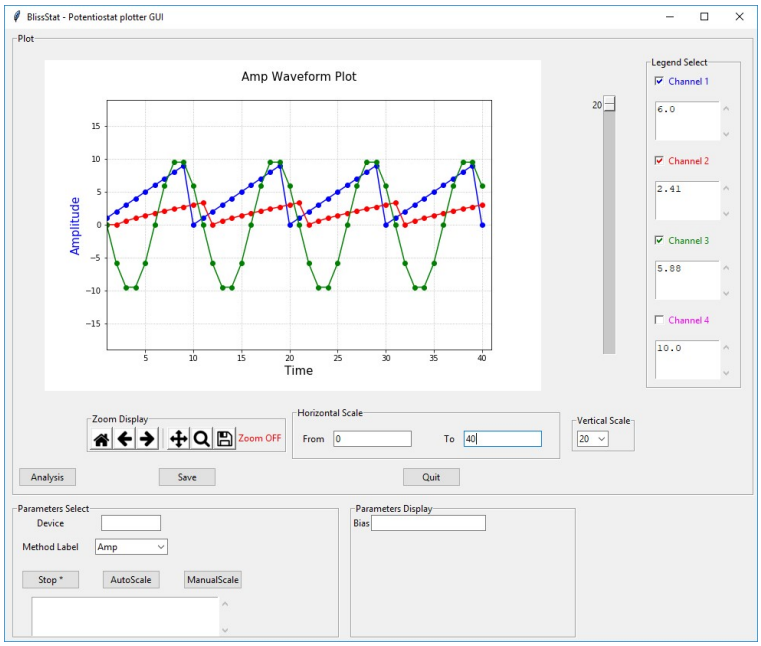

Figure B.9: Horizontal scale

- Vertical axis can be scaled by selecting appropriate scale in vertical scale dropbox as seen in Figure B.10

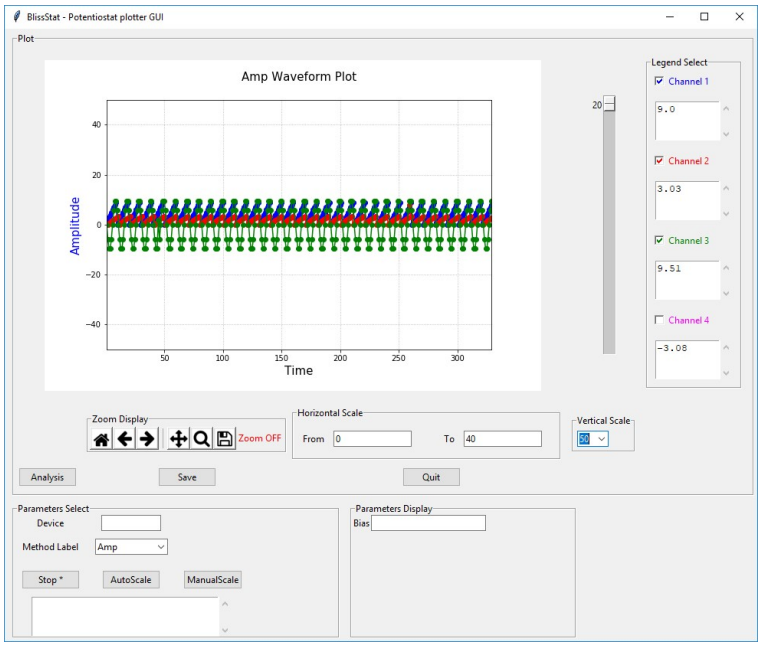

Figure B.10: Vertical scale - direct entry

- Vertical scale can be selected using the slider as well as shown in Figure B.11

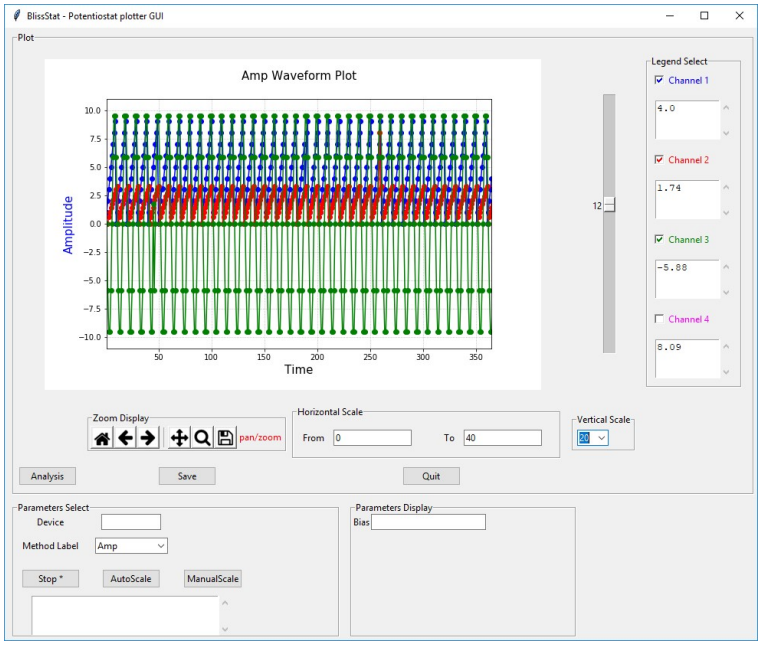

Figure B.11: Vertical scale - using the slider

- Clicking “Stop” or "Save", stops the experiment and data is saved in file with the name mentioned in the dialog box as seen in Figure B.12

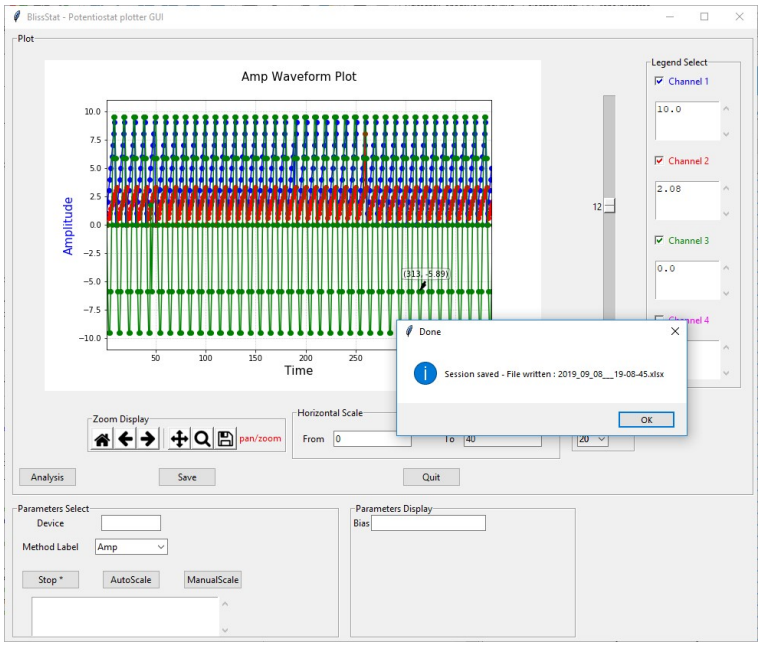

Figure B.12: BlissSTAT data saved

B.4 Design of BlissSTAT

- BlissSTAT has two modes - Measure and Analyze. In Measure mode, it acts like an oscilloscope. In Analyze mode, it can be used to do various operations (unimplemented in current code) such as curve smoothing, Find peak, Integrate, Differentiate et al.

- BlissSTAT uses **Tkinter**, a standard GUI package available in Python that uses **Tk** as its backend to provide a cross-platform widget toolkit. It gives basic widgets such as button, menu, canvas, text, frame, label, etc. that can be used to create complex GUIs. It is available on Linux, Mac and Windows. It offers a native look and feel on all these platforms. Various widgets are provided by Tkinter, which can be instantiated and configured using methods provided for each of them. Events are passed to widgets. On receiving such events widget's handler is called. **Matplotlib** objects are used for plotting data values.

- Main entities in BlissSTAT are shown in Figure B.13. They are -

  - Thread objects: Serial_read(), and RealTimeDataCollector()

  - Thread: RealTimePloter()

- Serial_read() thread reads the data from a serial port and adds it in a queue

- RealTimeDataCollector() reads this serial data from the queue and sends them to the data buffer of each channel

- RealTimePloter() plots this data buffer on "canvas" object

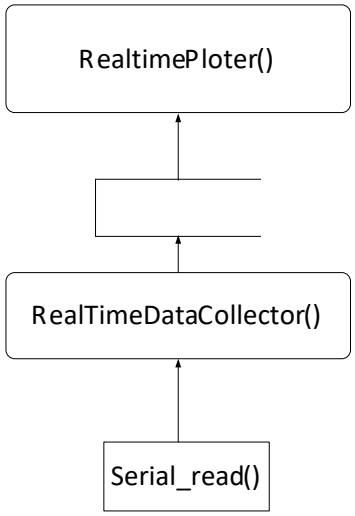

Figure B.13: BlissSTAT Data Flow Diagram

Description of other functions -

- OnMethodSelection - selects the method and updates other GUI elements as per method selected
- OnRunButtonClick - Creates a Microsoft Excel sheet to put the received data. Starts the "RealTimeDataCollector"
- OnSaveButtonClick - Suspends threads and saves data accumulated in a Microsoft Excel file
- zoombar_button_press_callback - Callback to enter in zoom mode using the base class functionality
- zoombar_button_release_callback - Callback to do zoom operation using the base class functionality and switch OFF zoom after mouse release

- PotentioStatNavigationToolbar2Tk - Overridden class to suppress some of the toolbar items, overridden home(), zoom(), set_message_color()
- update_annot - Provide custom updates to the annotations
- hover - gets called when motion is seen on the "canvas" object
- OnManualVerticalScaleSelection - Changes the vertical scale to user-provided value
- OnManualHorizonatalScaleSelection - changes the horizontal scale to user-provided value and redraw the "canvas" object
- Quit - destroys the main window and stops all the threads

B.5 Extending BlissSTAT

Functions to change for extending BlissSTAT -

- OnMethodSelection - To add new methods
- OnAnalysisMeasureButtonClick (Future use) - Start analysis mode
- OnAutoscaleButtonClick (Future use) Start auto-scaling mode if in manual scaling mode is ON
- OnManualscaleButtonClick (Future use) Start the Manual scaling method if auto-scaling is ON
- OnSmoothButtonClick (Future use) - Smoothen curve in analysis mode
- OnFind_peakButtonClick (Future use) - Find peak in analysis mode
- OnIntegralButtonClick (Future use) - Find integration in analysis mode
- OnDifferentiateButtonClick (Future use) - Find differentiation in analysis mode
- OnCkt_fitButtonClick (Future use) - Find circuit fit in analysis mode