

**A HYDROGEL-ACTUATED ENVIRONMENTALLY-SENSITIVE MICROVALVE FOR
ACTIVE FLOW CONTROL**

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ABSTRACT

This paper reports on the fabrication and test of a hydrogel-actuated microvalve that responds to changes in the concentration of specific chemical species in an external liquid environment. The microvalve consists of a thin hydrogel, sandwiched between a stiff porous membrane and a flexible silicone rubber diaphragm. Swelling and deswelling of the hydrogel, which results from the diffusion of chemical species through the porous membrane is accompanied by the deflection of the diaphragm and hence closure and opening of the valve intake orifice. A phenylboronic acid based hydrogel was used to construct a smart microvalve that responds to the changes in the glucose and pH concentrations. The fastest response time (for a pH concentration cycle) achieved was 7 minutes using a 30 μm thick hydrogel and a 60 μm thick porous membrane with 0.1 μm pore size and 40% porosity.

Index terms: Microvalve, Microfluidics, Hydrogel, Smart Material, Drug Delivery.

I. INTRODUCTION

Environmentally sensitive hydrogels offer unique opportunities for active flow control in microfluidic systems. These tangled networks of cross-linked polymer chains, immersed in a solvent, manifest a reversible and abrupt swelling and deswelling phase transition in response to the changes in environmental factors such as glucose concentration, pH, electric field, temperature, and light [1-4]. This transition often results in an abrupt volume change (swelling or shrinking) that can be as large as 1000 fold. Because of this property, hydrogels are attractive candidates as components of microactuators operating in aqueous media such as body fluids. For example, the volume phase transition in these materials can be harnessed in smart microfluidic components such as valves [5]. Transient swelling-deswelling behavior of a chemically sensitive hydrogel is limited by the diffusion of chemical species into the hydrogel and by the absorption and expulsion of the solvent (usually water). This results in exceedingly long response times in situations where the diffusion path-length is large. However, in certain microscale applications, the path-lengths become short enough to permit the hydrogels to be used as mechanical actuators with a reasonable response time. Integrating hydrogels with MEMS microfluidic structures such as valves and pumps therefore can provide smart microsystems that respond to various environmental stimuli. Several different approaches have been proposed to accomplish this goal. Hydrogels have been selectively photopolymerized around posts inside silicone microchannels to regulate flow in response to the changes in the flowing solution [6]. Alternatively, hydrogels have been polymerized as a pair of bistrif flaps attached to the walls of a microchannel forming a structure mimicking venous valves [7]. Flow inside a microchannel has also been controlled by the concentration of the solution flowing in an adjacent microchannel [6]. In this case the channels were separated by a silicone rubber membrane, whose deflection by volume changes of the hydrogel placed in one channel produced the opening and closing of an inlet hole in the other channel.

All the aforementioned techniques control the flow in response to the changes in the concentration of a solution inside a microchannel. A recent design intended for drug delivery applications provides

external exposure of the hydrogel through a perforated plate [8]. However, in this device, the hydrogel is manually loaded and the dimensions of the hydrogel cavity (macromachined from methacrylate plates) are large and hence the response time is exceedingly slow (~10 hours response time). In this paper, we describe the fabrication and test of a MEMS-based microvalve capable of responding in a reasonable time (a few minutes, which is adequate for most drug delivery applications) to the changes in the concentration of specific chemical species in an external liquid environment. In our approach, a thin hydrogel is confined in a cavity that communicates with the external solution by diffusion through a stiff porous membrane, Figure 1. The hydrogel's volume change produces deflection of a bossed diaphragm that opens and closes the intake orifice of the valve. We will demonstrate that by appropriate design of the hydrogel-containing cavity and the porous membrane (i.e., its porosity, thickness, and pore size) it is possible to achieve a response time of a few minutes. Applications of this unique approach are obvious in the field of drug delivery microsystems and biotechnology. For example, variants of the present design may prove useful for closed-loop delivery of insulin in response to fluctuations in blood glucose level seen in diabetes. In subsequent sections, we will describe the design (Section II), fabrication (Section III), hydrogel loading (Section IV), and test (Section V) of the glucose/pH-sensitive microvalve.

Some of the results reported in this paper were previously presented at MEMS 2002 and MMB 2002 conferences [9, 10].

II. HYDROGEL-ACTUATED MICROVALVE DESIGN

In this section we outline important design features of the microvalve. Figure 2-a shows the cross-sectional schematic of the designed device. The main body of the microvalve is made out of silicon and contains the bossed flexible diaphragm. A glass plate with inlet and outlet orifices and the porous membrane are attached on either side of the silicon part to complete the valve structure. In the open position (i. e. the hydrogel is shrunken), the liquid enters the inlet and passes through a microchannel defined in the silicon, which fixes the flow rate (or dose rate), before leaving through the outlet. Specific

changes in the chemical environment generate a positive osmotic pressure leading to increased volume of the hydrogel and subsequent deflection of the flexible diaphragm. As the hydrogel swells, the osmotic pressure is partially relaxed and is also opposed by the elasticity of its polymeric network, the stress in the deflected diaphragm, and the hydraulic pressure in the flow channel. When the boss contacts the glass plate, the hydrogel cannot expand any more and the remaining osmotic pressure assures the closure of the valve. In order to fully utilize the generated osmotic pressure, the diaphragm should oppose the hydrogel expansion with a minimum possible force. In the present design a two-component silicone rubber (Nusil MED10-6640) with a Young's modulus of 1.18 MPa was used to fabricate the diaphragm. This product was chosen because of its high tear resistance (42 kN/m) and low pre-polymer solution viscosity necessary to obtain thin layers. With a thickness of 20 μm , a diameter of 1800 μm and a central boss diameter of 500 μm , the diaphragm is expected to provide negligible counter-pressure to the expansion of the hydrogel.

Another important component of the microvalve is the porous membrane. This membrane must be stiff enough to deflect negligibly under the hydrogel pressure, and this sets limits on how thin the membrane can be. On the other hand, the thickness of the membrane influences the response of the microvalve by defining the diffusion time of the species from the external solution to the hydrogel cavity. The porosity will also effect the response time by defining the rate of diffusion of species into and out of the cavity. The diameter of the pores in the membrane must be small enough to prevent the hydrogel from escaping or protruding into the external environment. The pore diameter also determines the size of the species that can diffuse from the solution to the cavity, so the plate can work as a filter for undesired species such as bacteria or "clogging" proteins. In the present work, aluminum oxide porous membranes (Anopore™), with 100 nm pore diameter and 40% porosity, were used. The pores are straight all along the thickness of the membrane (60 μm).

Dimensions of the hydrogel cavity are another key design factor that is important for proper operation. As was mentioned previously, the response time of the hydrogel depends mostly on its

thickness. Therefore, in order to achieve short response times one needs to use a very thin hydrogel. However, the thinner the hydrogel, the smaller the deflection of the diaphragm it will produce. For the valve to function properly, the deflection of the diaphragm when the hydrogel is swollen should be larger than the initial gap between the boss and the orifice in the glass plate. When the hydrogel is shrunken the deflection should be smaller than the initial gap. To achieve such behavior we can vary three design parameters: 1) the size of the initial gap, 2) the thickness of the hydrogel cavity (defined by the spacers located between the porous membrane and the diaphragm), and 3) the thickness of the hydrogel. Because the thickness of the hydrogel depends on the environment, we will refer to its value at the time of formation, which is equal to the thickness of the mold or cavity where it was polymerized. In the present work, we determined the suitable spacer thickness and gap size for every hydrogel thickness tested. The spacers were made of PDMS (polydimethylsiloxane). This material was chosen based on 1) ease in fabricating spacers with a wide range of thicknesses, 2) the capability to bond PDMS to the silicon piece, which also has a silicone rubber layer covering its surface, and 3) the excellent sealing properties of PDMS, which facilitates the use of a simple technique for loading and curing the hydrogel *in-situ*. For the thinner hydrogels, it was found that the spacer could be avoided, so when placing the porous plate on top of the device the hydrogel was trapped in the cavity formed by the deflection of the diaphragm, as shown in Figure 2-b. Fabrication of the spacer and loading of the hydrogel inside the cavity are explained in the following sections.

III. FABRICATION

Figure 3 shows the fabrication process for the silicon part containing the silicone rubber diaphragm and the flow restrictor. An initial KOH etch on a silicon wafer was used to define: 1) the gap between the boss and the intake orifice, and 2) a microchannel connecting the intake to the output orifice (3-a). A 0.5 μm thick thermal oxide was used as a mask for the KOH etch. Subsequently, the valve seats were defined in the recess using a dry etching step (3-b). A flexible silastic layer was then spin-casted on the

unpolished side of the silicon wafer (3-c). The two component silicone rubber was spun at 1000 rpm for 20 seconds and cured for 30 minutes at room temperature, 45 minutes at 75 °C, and 135 minutes at 150 °C, resulting in a final thickness of 20 μm. Finally, a deep reactive ion etching (RIE) step was used to remove the silicon under the diaphragm and create the central boss (3-d). Both of the dry etch steps were carried out in an inductively coupled plasma etcher (Plasma-Therm SLR series) using a single 16 μm-thick layer of Shipley STR 1075 photoresist as the mask for each etch step. Due to the rough surface topography and long etch time of the final RIE step; the photolithography parameters are critical to obtain a good step coverage in the KOH recess. The photoresist was spun at 1000 rpm for 60 seconds and pre-baked for one minute at 90 °C and for 4 minutes at 110 °C on a hot plate. After exposure and development steps, the wafers were hard-baked for 6 minutes at 120 °C. In order to avoid crack formation, the wafers were cooled down slowly by turning off the hot plate and removing the wafers when the temperature is below 70 °C. The initial KOH step is critical in defining the gap between the boss and the intake orifice. This separation defines the diaphragm deflection required to close the valve. The results presented in this paper were obtained from valves with two different KOH etch depths, 30 and 70 μm. As was mentioned previously, this step also defines a V- or trapezoidally-shaped microchannel (depending on the etch depth) of length 2 mm and width 100 μm, that fixes the flow rate in the microchannel's open state to a predetermined value. The use of microchannels to obtain accurate dose rates has proved to be very reliable [11]. Figure 4 shows the details of the fabricated silicon part with the bossed diaphragm and the microchannel.

The Pyrex[®] glass substrate containing the inlet and outlet orifices, and the spacers to form the hydrogel cavity were fabricated separately and assembled in the last step. The Pyrex glass was ultrasonically drilled to obtain orifices 250 μm in diameter, which are smaller than the diaphragm silicon boss (500 μm in diameter). PDMS spacers of different thicknesses were fabricated with SYLGARD 184 Silicone Elastomer Kit (Dow Corning) following the micro-molding technique described in [12]. The molds were made by patterning SU-8 photoresist on a silicon substrate. After mixing and degassing the two components of the PDMS, the solution was poured on top of the micromolds and clamped between

two thick aluminum plates. A transparency sheet, a glass wafer and a 2 mm rubber layer were placed in-between the uncured PDMS and the top aluminum plate to provide flatness and homogeneous pressure distribution and to facilitate the disassembling of the micromold after curing.

IV. MICROVALVE ASSEMBLY AND HYDROGEL LOADING

In this section, we elaborate on the assembly and hydrogel loading techniques developed for the microvalve. Although these techniques were used for individual devices, with minor modifications, they could be easily adapted for batch fabrication. The silicon substrate and the glass plate containing the inlet-outlet orifices were assembled using a UV curable epoxy (LOCTITE[®] 363). First, a small amount of epoxy was deposited on the silicon piece around the microfluidic (microchannel and inlet-outlet chambers) area. Then, both pieces were brought in contact and a slight pressure was applied. During this operation, the epoxy flowed all over the silicon surface, and no bubbles were observed through the glass plate in the area of glass to silicon contact. The inlet orifice in the glass plate and the diaphragm boss were aligned under an optical microscope. During exposure to UV light, a simple transparency mask was used to avoid curing of the adhesive inside the microfluidic area. The remained non-cured adhesive was rinsed out with acetone through the glass plate orifices. The PDMS spacers were bonded on top of the valve using the technique described in [13]. The PDMS surface on both pieces was activated in oxygen plasma (100 sccm, 100 mTorr and 100 W) for 2 min before they were brought into contact. Methanol was applied between the two pieces to momentarily avoid stiction and allow the alignment. Once methanol was evaporated, the device was baked in the oven at 100 °C for 2 h.

Two different techniques were used to load the microvalve with hydrogel. The first technique was based on curing the hydrogel in a separate mold and manually transferring it into the microvalve. The mold was defined in a silicon wafer by deep RIE etching. It was subsequently filled with pre-gel solution and clamped with a silanized glass plate. Once the gel was polymerized, the mold was open and the hydrogel piece was equilibrated in saline solution before introducing it into the microvalve. The second

technique involved polymerization of the hydrogel *in-situ*. Figure 5 shows a schematic drawing of this technique. Initially, an acetone soluble wax was melt cast under the diaphragm in order to prevent deflection of the diaphragm during loading and curing of the hydrogel. The cavity defined by the spacer was then flooded with the pre-polymer solution and a glass plate having a piece of Teflon tape was placed on top of the device. Teflon tape was used to avoid stiction of the hydrogel to the plate. Subsequently, the structure was clamped in order to remove the excess pre-polymer solution from the surface of the device while allowing it to remain inside the cavity. Finally, the hydrogel was polymerized and the wax was dissolved in acetone. Both loading techniques were successful but for obvious reasons the *in situ* technique is more suitable for batch fabrication. Assembly of the stiff, porous membrane and the connectors was performed with the aid of a silicone-based adhesive. Figure 6 is a photograph of a completely assembled microvalve.

A phenylboronic-acid-based hydrogel was used to load the valve [14]. This hydrogel swells and shrinks in response to changes in both glucose concentration and pH, and is therefore useful both in drug delivery applications, and as a model hydrogel for the present work. Hydrogels were synthesized at room temperature in a 200 mg/ml aqueous solution containing a feed of 18.4 mol% 3-methacrylamidophenylboronic acid (MPBA), 81.5 mol% acrylamide (AAm), and 0.1 mol% N,N'-methylene-bisacrylamide (Bis) solution, with ammonium persulfate and N,N,N',N'-tetramethylethylenediamine (TEMED) as initiators. Figure 7 shows the free swelling characteristics of the hydrogel when exposed to 0.015 M phosphate buffered saline (PBS) solutions of variable pH and glucose concentrations, at room temperature. The diameter of cylindrical pieces of hydrogel that had been polymerized inside capillaries was measured with the help of a microscope (Research Precision Instrument Co., Wayland, MA). As can be seen, linear dimensions of this particular hydrogel increase more than twofold when pH changes from 7 to 10 (i.e., a volume change of more than eight times). The response to change in glucose concentration (at the physiological pH of 7.4) is weaker over the range 0-100 mM. It can be shown that this difference relates to the relative efficiencies of pH change and glucose

concentration in modulating hydrogel charge over the respective ranges of observation. The hydrogel shows maximum sensitivity to glucose in the range of human glucose levels (<3.5 mM for hypoglycemia, ~5 mM for normoglycemia and >7 mM for hyperglycemia).

V. TEST RESULTS AND DISCUSSION

Before assembling and testing the complete microvalve, some preliminary tests were performed in order to characterize the individual components. First, the mechanical behavior of the silicone diaphragm was evaluated. The silicon piece containing the diaphragm was mounted in a fixture that permits the application of pressure to one side while allowing the deflection to be observed under the microscope on the opposite side. Deflections of up to 100 μm were observed with less than 1 kPa applied pressure, which confirms that the diaphragm will not oppose much force to the hydrogel expansion. A second characterization test was performed in order to measure the diaphragm deflection produced by the hydrogel. In these experiments, the hydrogel was cured *in-situ* using PDMS spacers of various thicknesses. A partially assembled valve (without the glass plate) was then mounted in a fixture that permits the wetting of the porous membrane side in a solution while observing the deflection with a microscope on the opposite side. The deflection was recorded while changing the pH of the solution from 7.4 to 10, Figure 8. As expected, the time for the hydrogel to reach a steady volume after a change in the pH is shorter for thinner hydrogels. It can be observed that for pH 7.4 the deflections are negative, i.e., the diaphragm deflects inwards. We associate this phenomenon to the fact that the hydrogel volume at the shrunken state is smaller than the volume at the time of formation, i. e. than the volume of the cavity. It is also apparent that the hydrogel sticks to the internal surfaces of the cavity, including the diaphragm and the porous membrane surfaces, hence pulling the diaphragm inwards when the hydrogel is in its shrunken state.

Subsequent to initial tests on individual components, we tested the performance of a partially assembled microvalve (without the hydrogel and porous membrane) under a pneumatic pressure. The

assembly was mounted in a fixture that permits the application of a pneumatic pressure to the diaphragm external side, while measuring the flow from the inlet to the outlet. The flow-through liquid was de-ionized water from a water column whose constant height (60 cm) set the hydraulic pressure at the inlet at 5.9 ± 0.2 kPa (the error value has been added to account for the variations of the water level in the reservoir as it was emptied by the flow and manually refilled every few minutes). In the open state, the pressure at the inlet slightly decreased due to the flow resistance of the tubing, the valve connectors and the inlet orifice in the glass plate. Using the Hagen-Poiseuille law [11] this resistance was estimated to be $2.28 \text{ Pa}/\mu\text{l}/\text{min}$ (producing 0.32 kPa of pressure drop for a flow of $140 \mu\text{l}/\text{min}$). Flow rate was calculated from the velocity of an air bubble injected in a capillary of known diameter connected to the outlet. Figure 9 shows the result of the flow rate measurements versus applied pneumatic pressure. The pressure needed to close the valve is approximately the pressure at the inlet as was expected. The hysteresis observed in the closing and opening cycle is caused by the unequal surfaces seen by the liquid pushing the diaphragm on the inner side in the closed and open states. However, the ratio of pressures at the closing and opening points (1:3) is smaller than the ratio of the mentioned areas (1:16). This is due to the fact that part of the force applied to the diaphragm by the external pressure is transferred to the substrate through the stretched perimeter, so that the valve opens when the inlet pressure overcomes the rest of the force transferred to the boss. The hysteresis behavior seen in the pneumatic tests may not translate directly to the case where membrane deflection and valve closure is due to swelling of the hydrogel, since the latter is an elastic material instead of a gas.

It is interesting to note that when the boss closes the inlet orifice, the pressure at the inlet chamber equilibrates to atmosphere through the microchannel. This produces an additional differential pressure across the membrane that helps closing the valve more tightly. No leakage flow was detected in the closed state. At the open state the flow rate is about $140 \mu\text{l}/\text{min}$. The theoretical flow rate calculated for the V-shaped microchannel at 5.9 kPa, however, is $62 \mu\text{l}/\text{min}$ [11]. We associate this discrepancy with the flow of liquid through the gap left between the glass and the silicon piece after the epoxy UV-curing and development steps during the assembly process. Although this gap is much thinner than the

microchannel depth, it turns out to be much wider (1 mm) and shorter (1 mm), and thus contributes considerably to the total flow. The feature in the transparency mask used to avoid curing the glue inside the microfluidic area was defined larger than the mentioned area (~0.5 mm in all directions) in order to facilitate alignment, which was performed manually. If an accurate and repetitive flow rate at the open state is desired, the assembling process should be improved by using a better alignment system and providing a better glue thickness control. This will also contribute to obtain a more repetitive gap between boss and inlet orifice, which is augmented by the epoxy gap.

A schematic drawing of the experimental setup used to test the complete microvalve in liquid environment is shown in Figure 10. The inlet pressure generation and flow rate measurement were performed in the same way as for the previous experiment. The valve was alternatively immersed in solutions of different analyte concentrations allowing them to fully open and close before switching from one solution to the other. A magnetic stirrer was used to assure homogeneity of the solution. Table 1 summarizes the results obtained from different hydrogel thickness, porous plates, and solutions (pH and glucose). For the test of response to glucose, the valve was immersed alternately in solutions with 0 mM and 20 mM glucose concentration. For pH response, the valve was immersed alternately in two phosphate saline solutions with pH 7.4 and 10 (adjusted adding NaOH). Figure 11 shows the response of the valve to changes in glucose concentration when a 70 μm thick hydrogel was used. The flow rate at the open state is again much larger than expected due to the lack of control of the effective microchannel cross-sectional area, as mentioned above. The response times shown in Table 1 were calculated as the interval between a concentration change to the point when 50% of full-scale flow rate was reached. The fastest response (7 min) corresponds to the thinnest hydrogel (30 μm), and a change in the pH.

A number of factors need to be considered in future efforts to optimize the temporal response of the valve. It is convenient to consider the opening or closing of the valve in response to an external change in glucose level as resulting from three processes, recognizing that these processes will overlap in time to some degree. First, a change in external glucose concentration leads to influx or outflow of glucose

through the rigid porous membrane. At quasi-steady-state, which should be rapidly achieved in thin membranes, flux will be inversely proportional to membrane thickness, and will increase with membrane porosity. Second, glucose must diffuse through the gel and (reversibly) bind to pendant PBA groups. Assuming that the binding reaction is relatively fast compared to diffusion through the thickness of the gel (a reasonable assumption in many diffusion-reaction systems), the characteristic time of this step should scale as the square of the gel's thickness [15-20]. Third, the gel's volume must change in response to the chemomechanical stresses, which develop according to the new charge environment and transport of ions in and out of the gel, sometimes with the assistance of body buffers [17-20]. Taken by itself, the swelling or deswelling process, which entails transport of water into or out of the gel, also has a characteristic time that scales with the square of gel thickness [15-19].

As the hydrogel swells or deswells, the boss moves across the gap, either closing or opening the channel. These mechanical processes complicate the simple picture just presented. When the valve is open, swelling of the gel is opposed primarily by the pressure of the flowing stream, and the time taken to close the gap should decrease with original gap distance. Upon closure, swelling pressure will continue to grow until the gel reaches chemomechanical equilibrium, and during this phase the annular part of the PDMS diaphragm will stretch further and bulge into the inlet chamber. Reopening of the gap, then, will not occur until the swelling pressure of the gel drops below the opening pressure. The amount of swelling "overpressure" developed will depend on both the chemical composition of the gel and the geometry of the overall device structure.

Taken together, these arguments suggest that response time can be altered in a number of ways, but a delicate interaction between the gel's chemo-mechanics and various geometric parameters (membrane thickness, membrane porosity, hydrogel thickness, gap distance) must be taken into consideration. Despite the complexity, we may conclude that by reducing the thicknesses of the hydrogel, the response time can be reduced. It should be mentioned, however, that we observed a decrease in the yield and reliability of the valves along with the hydrogel thickness reduction. The valves loaded with a 30 μm -thick hydrogel showed very asymmetrical opening/closing times and stopped functioning after a few

cycles. In these valves the hydrogel thickness is about two orders of magnitude smaller than its diameter, which is equal to the diaphragm diameter (1800 μm). This may lead to poor mechanical stability. Due to its deformability, the hydrogel can be squeezed out of the boss area towards the flexible rubber area where it finds less opposition to swelling, and stresses produced may lead to breakage of the gel. Thus, in order to further reduce the thickness of the hydrogel a new design with a smaller diaphragm diameter should be considered.

One may think intuitively that reduction of thickness and diameter of the hydrogel will lead to valves with a smaller pressure capability. Nevertheless, the osmotic pressure developed within the hydrogel does not depend on its dimensions. Yet, the absolute volume change, and hence, the diaphragm deflection, will decrease proportionally with the hydrogels dimensions, so a smaller closing gap will be necessary. This will make more difficult the “tuning” of the valve for closing at the desired glucose level. A smaller gap will also limit the liquid flow-rate attainable for a given inlet pressure due to an increase of flow resistance. Another possible limitation to the reduction of dimensions would be an increase in the stiffness of the diaphragm. However, due to the low Young’s modulus of the silicone rubber, there is still a considerable margin for diameter reduction before this becomes a problem. For example, according to the plate theory [21] if the bossed membrane dimensions are reduced five times (keeping the membrane thickness of 20 μm); a deflection of 9 μm is obtained with only 1 kPa applied pressure. On the other hand reduction of dimensions can help to prevent diaphragm tear during assembly and operation of the valve, which was one of the main causes of failure. Another possible way to decrease the valve response time would be using a faster hydrogel. For example, it has been shown that hydrogels with lower degree of cross-linking or with porous structures exhibit faster responses [22], although at the expenses of a lower swelling pressure.

VI. CONCLUSIONS

In this paper, we have reported on the design, fabrication, and testing of a smart hydrogel-based microvalve for active flow control in microfluidic systems. An environmentally sensitive hydrogel was sandwiched between a stiff porous membrane and a flexible silicone rubber diaphragm. Exposure to an external variable environment (e.g., different glucose concentrations, pH) resulted in a reversible swelling-deswelling of the hydrogel, deflection of the silicone diaphragm, and opening/closing of the valve intake orifice. We demonstrated that reasonable response times can be achieved by reducing the hydrogel thickness. An opening response time as low as 7 minutes was obtained using a 30 μm hydrogel in response to a sudden pH change. As indicated initially, a primary potential application of the responsive hydrogel-controlled microvalve will be glucose-sensitive, closed loop control of insulin delivery in the treatment of diabetes. Because of the critical nature of the insulin response, the simple valve structure described here may have to be augmented with features that guarantee, for example, a limit in the amount of insulin delivered during a pulse. Moreover, in the present implementation, rise and fall in glucose concentration leads to closing and opening of the microfluidic valve, respectively. For insulin delivery, the opposite response is desired. While reversal of valve “polarity” might be achieved by mechanical redesign of the valve, it may be simpler to design hydrogels that shrink instead of swell with increasing glucose concentration [14].

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Figure 1: Schematic drawing of the valve basic structure and working principle.

Figure 2: Schematic drawing of the microvalve cross-section a) with spacer, b) without spacer (thinner hydrogel).

Figure 3: Fabrication process of the silicon piece.

Figure 4: Photograph of the microvalve silicon part. The dimensions of the silicon chip are 10×10 mm. The “active” fluidic area is 5×3 mm.

Figure 5: Hydrogel loading technique.

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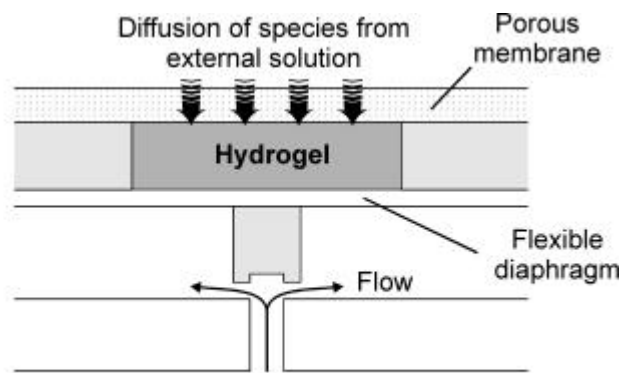
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Table 1. Response times of several tested valves.

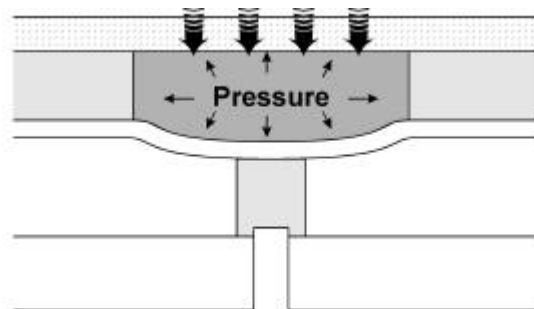
Table 1. Response times of several tested valves.

<i>Hydrogel Thickness (μm)</i>	<i>Spacer Thickness (μm)</i>	<i>Gap size (μm)</i>	<i>Analyte</i>	<i>Opening Time</i>	<i>Closing Time</i>
500	500 ^(a)	70	Glucose	4 h and 15 min	4 h and 20 min
70	50	70	Glucose	32 min	18 min
70	50	70	pH	16 min	18 min
30	No spacer	30	pH	7 min	13 min

(a) This spacer was made with a 500 μm glass plate ultrasonically machined

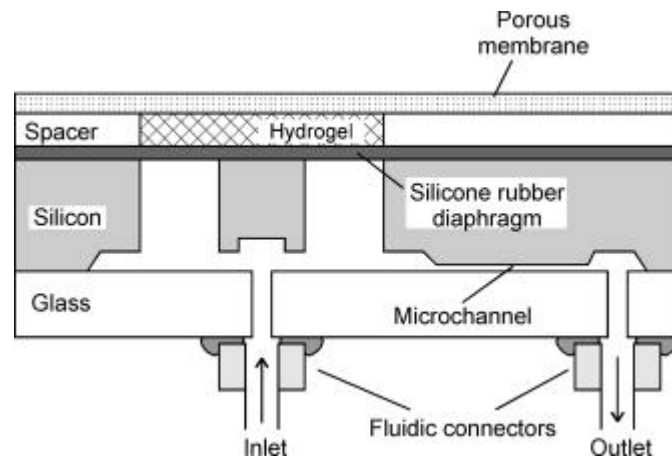


(a)

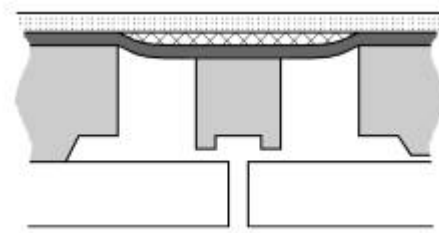


(b)

Figure 1: Schematic drawing of the valve cross-section and working principle.



(a)



(b)

Figure 2: Schematic drawing of the microvalve cross-section a) with spacer, b) without spacer (thinner hydrogel).

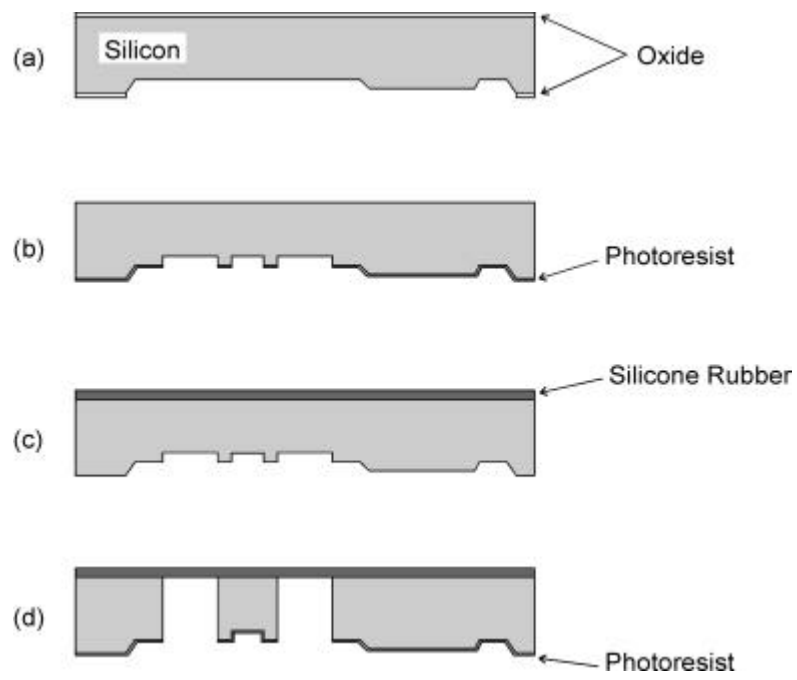


Figure 3: Fabrication process of the silicon piece.

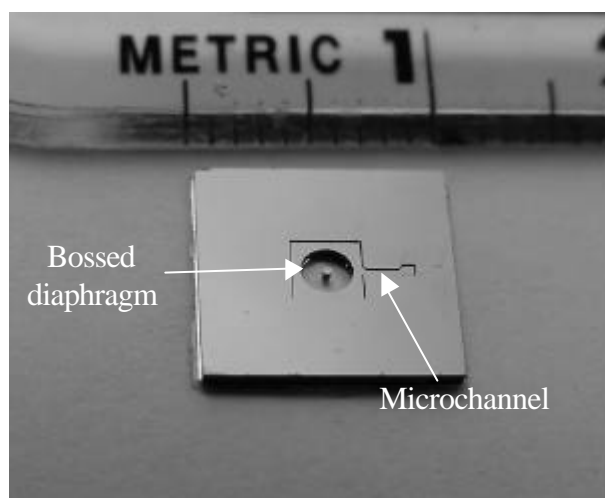


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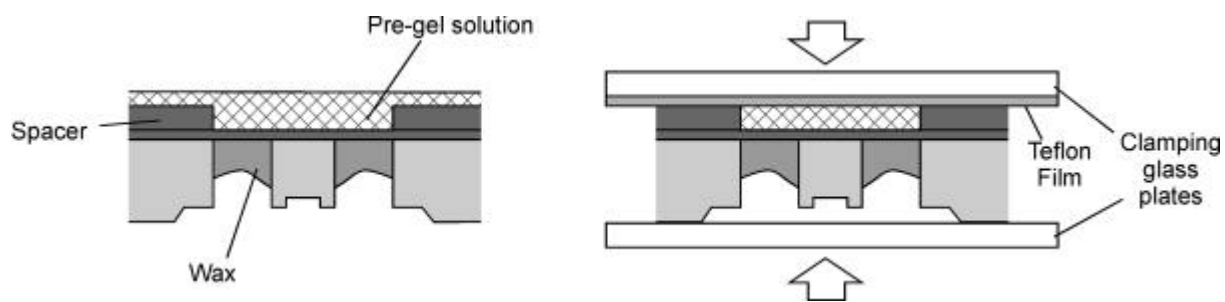


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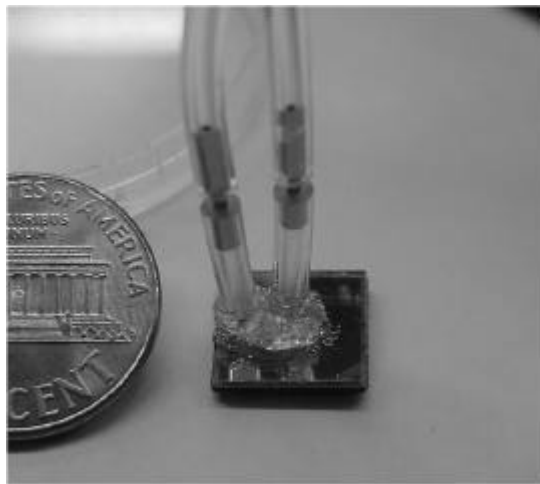
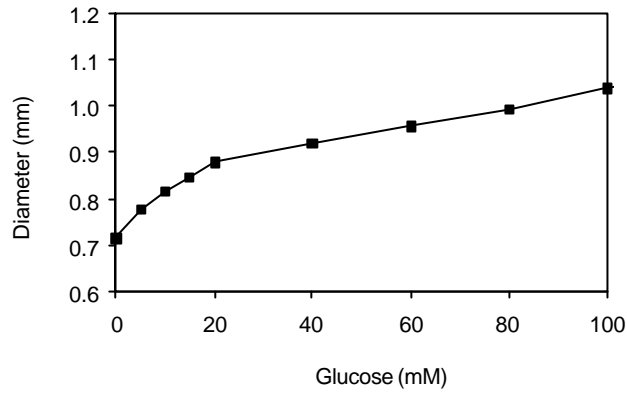
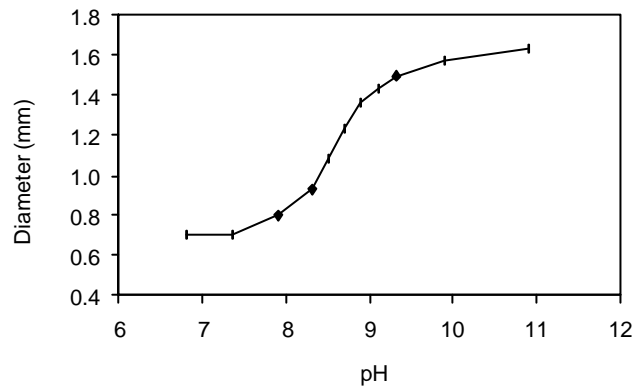


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(a)



(b)

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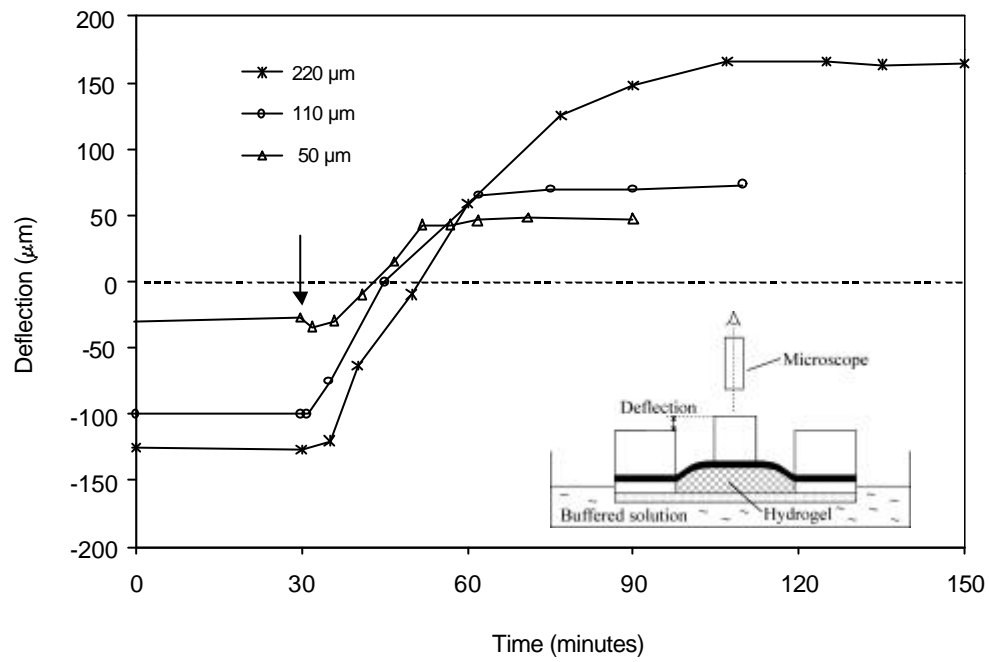


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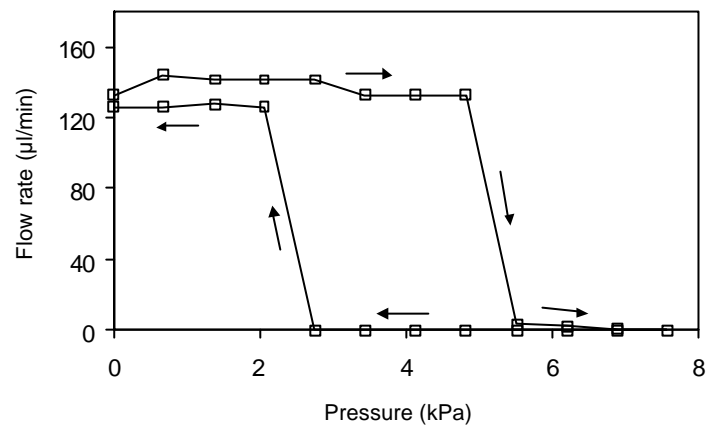


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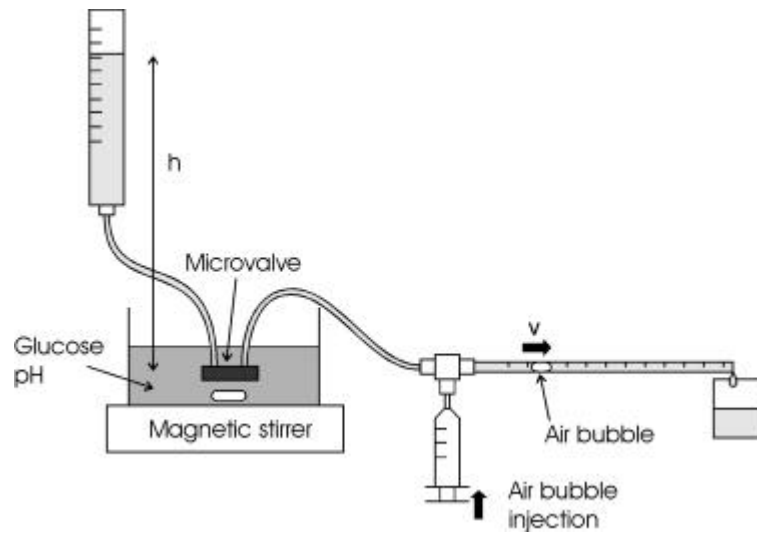


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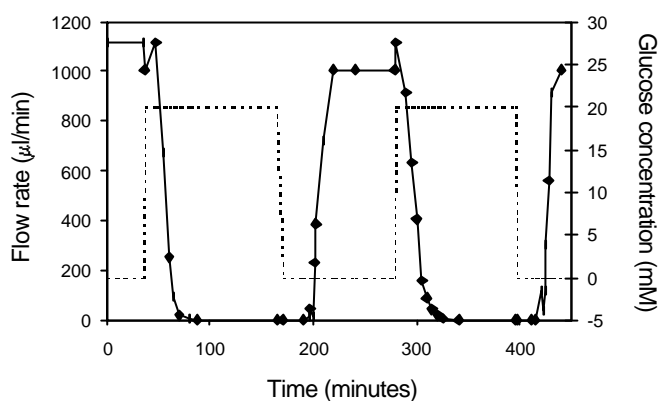


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