ABSTRACT

Recent developments in (MEMS) fabrication techniques have exploited the properties of polymers. Traditional lithographic techniques have been used to create a template in a thick layer of photoresist that can be filled with a heat -or-UV curable polymer and used to cast numerous replicas of Tesla channels in an elastomeric material-poly (dimethylsiloxane) (PDMS). The surface of this replica, and that of a flat slab of PDMS, is oxidized in oxygen plasma and brought into conformal contact to seal tightly.

N-isopropylacrylamide polymers have attracted much interest in the area of scientific research and microfluidic technologies due to their unique thermal response in aqueous medium. To design microactuators of these gels with a high aspect ratio and a strong adhesion to the microchannel, substrates have to be developed. To achieve this, a modification of the simple (NIPA) polymer is needed; therefore, this calls for chemical modification of the (NIPA) material itself and the PDMS.

The integration of autonomous microvalves into complex microfluidic Tesla channel networks is presented. Hydrogel directly grown onto vinyl modified PDMS and in contact with process medium. Thermoelectric element capable of changing the temperature of the system is used to actuate the valve.

A distortable diaphragm at the center coupled to a piezoelectric that is connected to the ports of two channels. The other ends are connected to two small water tanks. Valve operation results in an oscillating or a positive net flow depending on valve status.

Keywords: poly (dimethylsiloxane), poly-N-isopropylacrylamide, temperature-sensitive hydrogel, vinyltrimethoxysilane, piezoelectric materials, SU-8 Photoresist, N-N’methylenbis-acrylamide.

INTRODUCTION

Numerous studies have been conducted on the stimuli-sensitive hydrogels that are able to respond to the changes in environmental conditions such as pH, temperature, ionic strength, and electromagnetic field. Due to their drastic swelling and deswelling in response to environmental stimuli, these polymeric hydrogels have been investigated for many microfluidic and biomedical applications. Among these “intelligent” polymers, temperature-sensitive [1], [2], [3] and pH-[4], [5] hydrogels are the most widely investigated.

Poly (N-isopropylacrylamide); (PNIPAAm) is perhaps the best known of a class of temperature-sensitive polymers. The polymer exhibits a well-defined lower critical solution temperature (LCST) in water. This LCST depends on solvent composition in mixed aqueous solutions of PNIPAAm [6], [7], and that PNIPAAm gels undergo analogous volume transitions in aqueous solvents [8], [9]. Using the volume transition exhibited by this polymer in response to changes in temperature, a highly effective thermally actuated valve based on porous polymer monoliths with poly (NIPAAm) is designed.

Microvalves are a primary component of microfluidic systems. As such, they offer a vehicle to compare and contrast different actuation mechanisms. The major bases for comparison are closing force (pressure range of operation), temperature range, speed, and reliability. The actuation principle employed in this work has been based on the thermal actuation of a hydrogel valve.

The fabrication of hydrogel microvalve consisted of the mold fabrication by photolithography, microchannels by soft lithography, and in situ photopolymerization. Multilayer soft lithography was used as an extension to soft lithography paradigm to build-up a film thickness in a multi-coat process,
using high-speed spin (1000 rpm) for the final coat thus resulting in a considerably more uniform film.

Two routes were explored for preparing gel, one was to grow gel directly from the surface of the channel substrate and the other was to synthesize the hydrogel modified with a silane side group vinyltrimethoxysilane (VTMS). PDMS was first oxidized in plasma, which resulted in the production of –OH group’s surface. The –OH groups were then modified with vinyl silane group. This surface was then introduced into a solution of (NIPA) and N-N’ methylen bis-acrylamide (BIS).

The presented microvalve consists of components with different functions. Flow channels and actuator chamber were generated on a PDMS substrate by photolithographic process. The actuator chamber/channel contains the sensitive hydrogel film. A thermoelectric module (TEM) is integrated in the PDMS. The cover contains the (PZT) diaphragm and closes up the flow structure. The channel geometry and the actuator chamber were generated by soft lithography process. Applied materials were glass wafers, SU-8 photoresist and PDMS.

Deposition of silane-modified hydrogel on surface has been done and demonstrated by preparing a gel labeled with a pyrene molecule. This sample has been placed on the PDMS surface after it has been exposed to the plasma and it was subjected to a detector and a lamplight with a wavelength of 337 nm to excite the pyrene only. The spectrum of the pyrene was seen which indicates that gel has been chemically linked to surface.

Gels of desired shapes were prepared by using appropriate mold in which gelation took place. The linear swelling ratio (α) of the gel was determined by measuring the volume of the gel on preparation (V₀) and after swelling (V). The volume of gel was obtained from the measured thickness (t). (α) is defined by the cubic root of the ratio (V/V₀).

The hydrogel samples were analyzed by a Fourier transform infrared spectroscopy (FT-IR) in the region of (3500 – 1000 cm⁻¹). The functional vibrations of C=O, N-H, CH₃ and the Si-OH groups were determined and results suggested that the (NIPAAm) is grown from the surface of the (PDMS) after treating it in the plasma and modifying the (PNIPAAm) with the (VTMS).

**EXPERIMENTAL**

**Materials**

All materials mentioned here are purchased from (Sigma –Aldrich, Mo) unless otherwise stated. N-Isopropylacrylamide (NIPAAm) from Fisher Scientific, N-N’ methylen bis –acrylamide (BIS) a cross linking agent, 2-2’-Azobisisobutyronitrile (AIBN) a radical initiator, Vinyltrimethoxysilane 98% (VTMS), Tetrahydrofuran (THF), Diethyl ether Anhydrous, 1,4 Dioxane and 4,4’ Azobis (4 Cyanovaleric acid). Hexane and Methanol obtained from (Chemistry Lab., URI). Silicon wafers (4” diameter) SST Lab., URI. Dow Corning Sylgard 184(PDMS), PDMS hardener, SU-8 2100 photoresist, SU-8 developer solution, Methanol, Acetone and DI water from Microchem Corp. Newton, MA. Photomask of the desired channel was created on a Solid Work program and was printed out on a transparent paper using a high-resolution emulsion printer at the SST lab, URI. Thermoelectric module (TEM) purchased from Te-Tech. Michigan, UV lamp (200 watts) Zeiss, West Germany. Scanning Electron Microscopy (SEM) from SST Lab., URI. Fourier Transform Infra Red (FT-IR) from the Chemistry Dept., URI.

**HYDROGEL PREPARATION**

The fabrication of hydrogel microvalves consists of two steps: fabrication of microchannels and in situ polymerization. For the 2-D microvalve, microchannels with a depth of 260 μm were fabricated by spin- coating photoresist (SU-8 2100, Microchem Corporation, Newton, MA) on a 4 inch silicon wafer at 500 rpm for 10 seconds then ramped up to 1000 rpm for 30 seconds followed by a pre-bake at 65 °C for 7 minutes and a soft-bake at 95 °C for 60 minutes. This procedure is repeated 3 times, each time a layer of 260 μm is obtained. UV lithography (400 mJ/cm² at 365 nm) for 3 minutes. A post-expose bake at 95 °C for 15 minutes, and development for 20 minutes. The photomask of the desired channel was created, and then the silicon wafer was cleaned using methanol, acetone and DI water. The substrate was dried with N₂ and was completely dry and clean.

Different routes for assembling the hydrogel in the channels have been adopted in this research. The first approach was to prepare the hydrogel by free radical polymerization and to place a small piece within the channel. This technique has several drawbacks, such as the exact placement in the tiny channels calls for skill labor and induces more technical difficulties, another issue is how to keep the gel in place so it doesn’t move or be washed away and plug the channel or the issue of uniformity of swelling and deswelling is not clearly foreseen.

There are two other routes which were explored for preparing the gel, one of which is to grow the gel directly from the surface of the channel substrate
(PDMS) and the other is to synthesize the hydrogel modified with a silane side group e.g. Vinyltrimethoxysilane 98%(VTMS) that links to the oxidized PDMS film. The former route is carried out by first oxidizing the PDMS slab in the plasma which will result in the production of surface –OH groups that are then modified with vinylsilane group. This surface will then be introduced into a solution of the NIPA and BIS. Reaction will proceed and hydrogel will be directly grown onto the surface of PDMS. Refer to Figure 1 & 2. This approach was demonstrated and hydrogel was grown onto the PDMS slab.

![Figure 1. Surface modification for growing of film onto surface.](image1)

The proposed advantages of this procedure of growing gel directly onto surface are that we can expect more uniform swelling and shrinkage. Also the hydrogel will be anchored into place so it will not move down the channel since the movement may block the channel.

![Figure 2. Uniform Film of Hydrogel Grown from Surface](image2)

**DESIGN OF THE HYDROGEL VALVE ON TESLA-TYPE CHANNELS**

The synthesized crosslinked polymer was tested in a hydrogel Tesla-type channels. The liquid flows directly through the “gel-actuator”. Changing the temperature of the liquid above and below the lower critical solution temperature “LCST” stimulates the swelling/deswelling of the gel film. The presented microvalve consists of components with different functions Figure (3): Flow channels and actuator chamber were generated on a PDMS substrate by a photolithographic process. The actuator chamber or the actuator channel contains the sensitive hydrogel film. A thermoelectric module (TEM) is integrated in the PDMS substrate. The cover closes up the flow structure and protects them. The valve chamber is filled with a monolithic film of PNIPAAm of 2 mm x 2 mm x 520 μm in the dry state. The microvalve is consisting of a channel structure support made of PDMS, an Aluminum substrate at the bottom permanently attached to the PDMS for mechanical stability. The channel geometry and the actuator chamber are generated by soft lithography process. Applied materials were Si wafers, Su-8 2100 photo resist and PDMS. Thermoelectric module (TEM) is used for valve actuation.

**RESULTS AND DISCUSSION**

Valving operation

The hydrogel actuator was directly placed in the flow channel and remains in contact with the process medium. The actuator swells by absorption of the medium. In the normal case the medium temperature...
is below the $T_c$ and the hydrogel seals the flow channel completely (“normally closed” function). The operation of the valve was achieved by a thermoelectric module (TEM). To open the valve the gel actuator was warmed above $T_c$ with the thermoelectric module. The hydrogel actuator deswells and allows the fluid to flow through the channel.

Temperature within the channels was controlled by 5 x 3.4 mm thermoelectric element (Standard single-stage thermoelectric cooler, Te-Tech industries, Inc.; Michigan). The thermoelectrical element was attached to a rectangular-shaped cavity etched at the outside of the PDMS in the area located beneath the location of the valve, and the thickness of the PDMS wall was reduced to $\mu$ m range. The aluminum plate was firmly attached to the lower PDMS layer to ensure good physical contact between the surface of the PDMS layer and the thermoelectrical element, as required to obtain rapid changes in the temperature.

The opening and closing functions were actuated by varying the temperature between 10 and 65 °C. Although the actuation itself can be achieved at temperatures much closer to the LCST of poly(NIPAAm) at 32 °C, this much broader range was used to rapidly cool or heat the bulk of material of the chip to achieve the desired rapid temperature change within the channel.

The valving function of the gel was tested. The substrate was heated to 65 °C to induce gel collapse. When the external heating is removed, the gel swells and closes the valve. Gel collapses and releases most of its water in 26 seconds. Once the gel returns to room temperature, the gel becomes hydrophilic and regains its shape via diffusion after 2 minutes. The temperature within the channels is controlled by thermoelectrical element. Since PDMS is a poor thermal conductor, square-shaped cavities able to accommodate thermoelectrical element were etched at the outside of the channel layer in the area located beneath the location to reduce the thickness of the PDMS wall.

The most fundamental property of a gel is the swelling ratio, which is usually determined by measuring the volume of the gel on preparation ($v_0$) and after swelling ($v$). Measuring the volume of the gel with high accuracy under strictly specified condition is not easy because we have to measure the volume of the gel without taking it out of the solvent in a temperature-controlled bath [10]. The easiest way to match this purpose is to use a gel of
symmetrical shape and measure its characteristic length e.g. diameter (d) or thickness (t) in this case. The volume of the gel is obtained from the measured thickness (t) as

\[ v = v_0 \left( \frac{t}{t_0} \right)^3 \]  

Where: \( v_0 \) is the volume of the gel on preparation, \( t_0 \) is the thickness when the gel was formed, i.e. the inner height of the mold used to prepare the gel. \( v \) and \( t \) are the volume and thickness of the gel after swelling. It should be noted that this method is valid only when the gel swells or shrinks homogeneously and isotropically [10].

The linear swelling ratio (\( \alpha \)) is the most fundamental property of a gel and is defined by the following equation:

\[ \alpha = \left( \frac{v}{v_0} \right)^{1/3} \]  

Where \( v \) and \( v_0 \) are the same terms as defined above, and \( \alpha \) is the swelling ratio. Hence, we can calculate the corresponding gel volumes after heating it at different temperature ranges, and then plot the linear swelling ratio (\( \alpha \)) versus the temperature range as indicated in Figure 6 (a).

The volume of the gel at the preparation (\( v_0 \)) and the thickness (\( t_0 \)) were measured. The dimensions of the gel at different temperatures were taken and the results were recorded. Similarly, the rest of the volumes were calculated at different temperature values and recorded.

![Swelling curve of a rectangular-shaped poly-NIPAAm hydrogel](image)

Figure 6:  
(a) Degree of swelling (\( \alpha \)) of PNIPAAm as a function of temperature calculated with [eq. (2)]  
(b) Temperature and the relative volume (\( \frac{v}{v_0} \)) curve.

The swelling ratio of PNIPAAm hydrogels at different temperatures, as shown in Figure 6 (a), illustrates the LCST behaviors of the conventional PNIPAAm hydrogels. As the temperature increases, the swelling ratio of the hydrogel decreases; particularly at a temperature below the LCST. The patterned hydrogels swelled in cold water up to 10 times in height compared to their dry state.

The swelling ratio (ratio of film thickness in the swollen state (\( t \)) and dry film thickness (\( t_0 \)) in dependence on the temperature is shown in Figure 6 (a). With a decreased crosslinking density the swelling ratio at low temperatures increased [11]. By raising the temperature above \( T_c \), gel collapses to nearly the same swelling ratio. The swelling behavior determines actuator performance; therefore it is the basic property for actuator design. Swelling rate is inversely proportional to the square of the characteristic dimensions of the gel [12]; hence it is essential to reduce the gel size dramatically.

**SCANNING ELECTRON MICROSCOPY (SEM) OF (PNIPAAM) HYDROGELS**

The surface morphology of the hydrogels was studied using scanning electron microscope (Jeol, JSM-5900 LV, Japan). Specimens of the freeze-dried gels were glued to the brass holders prior to the SEM examination. (SEM) has been shown previously [13], [14] to be the method of choice to search for the presence of large-scale demixing structures and to characterize gel structures on the micrometer scale. These images were taken at 500 X and 1000 X magnification respectively. The bar at the bottom of each picture indicates a length of 50 and 100 \( \mu \)m respectively. The porous gels are characterized by
scanning electron microscopy (SEM) after critical point drying.

The structure of the gels depends on the type of monomer and surfactant concentration and can be varied systematically to result in different pore morphologies with different pore sizes [15]. Hydrogels obtained from lower percentages of crosslinking agent in water, showed a porous structure and their swelling and deswelling rate was increased in comparison to hydrogel prepared in methanol with the addition of VTMS. Deswelling may even be further enhanced, depending on the pore size. Accordingly, it is also important to analyze the effect of the pore size on deswelling. In addition, the mechanical characteristics of the hydrogel should be kept intact even for porous hydrogels.

The formation of pores in/on hydrogels seemed to increase the apparent surface area in the hydrogels for the release of water molecules from the hydrogel [16]. Figure (8) shows the SEM photos of the surface structure of the freeze-dried samples. The internal structure of the gels is also investigated. It is found that the internal structure of hydrogels is similar to that of their surface [17]. In a comparison of these micrographs, it can be observed that compared to the 5-mol % NIPAAm gel in water, the VTMS-modified PNIPAAm gels showed less porous network structures because they were more cross-linked.

Images taken during the SEM tests are presented below:

![SEM Photos](image1)

![SEM Photos](image2)

Figure 8: Scanning Electron Microscopy Graphs for NIPAAm gels made with different crosslinking agent (BIS) %ages in ethanol & water.(a): 1 mol % ethanol, 500X (b): 1 mol % ethanol, 1000X. (c): 10 mol % ethanol, 500X(d): 10 mol % ethanol, 1000X. (e) 1 mol % water, 500X (f) 1 mol % water, 1000X (g) 5 mol % water, 500X (h) 5 mol % water, 1000X (i) 10 mol % water, 500X (j) 10 mol % water, 1000X (k) 5 mol % VTMS, 1000X. The length of the bar is 50 μm for 500X & 10 μm for 1000X.

FORTIER TRANSFORM INFRARED SPECTROSCOPY (FT-IR)

In order to do the FT-IR measurements, the hydrogel samples were analyzed by FT-IR (NEXUS 670, USA) in the region of (3500 – 1000 cm⁻¹). Before the measurement, the originally swollen hydrogel sample (PNIPAAm) were kept at room temperature for 48 h and then dried.

The FT-IR spectra of the PDMS, the PDMS in plasma then in VTMS, PDMS with NIPAAm and NIPAAm that have been dried, are shown in figures (9). The FT-IR spectra of all the above-mentioned samples are dissimilar in their peaks. There exists a typical amide I band (≈ 1650 cm⁻¹), consisting of the C=O stretch of the NIPAAm grown from the PDMS surface, and the amide II band (≈ 3300 cm⁻¹), including N-H vibration in each spectrum. One can also observe two typical bands of C-H vibration with the nearly same intensity at (≈ 2950 and ≈ 2900 cm⁻¹) in each spectrum, which belongs to the divided bands of the symmetric-CH (CH₃)₂ group in the NIPAAm. On the other hand, for the spectra of PDMS in plasma and then PDMS plus
VTMS, one can see the Si-OH (silanol bond) stretch positioned at \(( \cong 3500 \text{ cm}^{-1} )\).

These findings suggest that the PNIPAAm is grown from the surface of the PDMS after treating the PDMS in the plasma and modifying the PNIPAAm with VTMS.

![Figure (9): (a) FT-IR stack-up for all samples. (b) FT-IR stack-up for all samples (blown-up).](image_url)

**SUMMARY**

The silane-modified hydrogel has been physically deposited onto PDMS surface; thus eliminating the need for the hexamethyldisiloxane (HMDS). The integration of a microfluidic device to create a compact valving system was achieved by incorporating the valve layer, the rectifier layer and the PZT layer all on one chip and thus a modified design of a miniaturized valve is realized.

The PNIPAAm valve fabricated using multilayer soft lithography can be used as a temperature-actuated valve; these robust valves respond very quickly to the external stimulus and keep their performance in numerous “open-close” cycles. The presented microvalve can be used in microfluidic processors due to their capability of miniaturization combined with other advantages like a small dead volume, simple setup, and the integrability into microsystems, the particle tolerance and the leakage free behavior.

The hydrogel actuator showed a good chemical and long-term resistance. Only concentrated acids and bases affect the hydrogel stability. Limitation of the hydrogel actuator is that the switching behavior is a diffusion-controlled process which means that hydrogel-based microvalves can not be used in high dynamic applications, another limitation results from the fact that hydrogels need direct contact with the process medium as the swelling agent to operate. The process medium in this case has to be aqueous solutions because (LCST) behavior of temperature sensitive hydrogel in other solvents is not known. Serious malfunction might occur if the process medium is not properly chosen.

The (FTIR) studies were carried out to elucidate and investigate the physical link of hydrogel to the (PDMS) surface. In Figure 9 we see the C=O stretching frequency which proofs that this carbon double bond came only from NIPAA confirming that the PNIPA is physically attached to the (PDMS) surface after treatment with the (VTMS) and the (NIPA). Via modification of the hydrogel chemistry and/or microvalve dimensions, it should be possible to further improve the response time.

**REFERENCES**