REAL-TIME GLUCOSE SENSING USING A MEMS-BASED BI-MATERIAL DEFLECTING MEMBRANE

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INTRODUCTION

Self-monitoring of blood glucose has become an important and critical tool for effective management of diabetes. A closed-loop, real-time sensing and dispensing system, however, has been elusive. We describe here, a novel MEMS-based sensor intended to measure, in real-time, the concentration of glucose in a solution. The device utilizes a bi-material membrane with a functional hydrogel layer that swells reversibly, and in proportion to, the presence of glucose. The hydrogel is composed of 2-hydroxyethyl methacrylate (HEMA) functionalized with 3-acrylamidophenylboronic acid (AAPBA) groups as the glucose-sensitive moiety. Phenylboronic acid (PBA) derivatives interact with glucose by forming a charged complex, causing the hydrogel to swell by solvent intake \cite{1}.

The HEMA hydrogel is bonded to a PDMS layer to form a circular membrane suspended over a cylindrical cavity that contains the device electronics. The membrane deflects in proportion to the glucose concentration. Signal transduction is performed using a capacitance sensor, where one half of the capacitor is adhered to the PDMS and the other to the base of the cylindrical cavity. The presence or variation in the concentration of glucose is observed as a change in capacitance of the device \cite{2}.

EXPERIMENTAL METHODS

The device is fabricated using standard microfabrication techniques. A Single-Crystal-Silicon (SCS) wafer is fabricated into a die; this die is then placed into a tetramethyl ammonium hydroxide (TMAH) bath for anisotropic etching \cite{3} of the SCS to thin the wafer where the polymer membrane will reside. Si islands are then patterned from the bottom side of the die using PR, followed by coating the top surface with an intermediate PDMS layer. In the final step the last few microns of Si below the polymer membrane are removed using a XeF\textsubscript{2} vapor etch \cite{4}, leaving released islands of Si attached to the PDMS membrane. The XeF\textsubscript{2} vapor phase etch method prevents damage to the polymer membrane while releasing the Si island. The glucose-sensitive hydrogel monomer is then spread onto the PDMS membrane and UV-polymerized.

Prior to device integration, a suite of experiments were performed to study the swelling behavior of the AAPBA functionalized-HEMA hydrogel. This was done to determine the membrane deflection behavior at various and controllable cross-link densities. These studies were conducted to enable precise control, and then design, of the system response. Two types of samples were tested, hydrogel cylinders and laminated beams. Hydrogel samples were cast as cylinders in a Teflon mold and adhered to a glass slide. The monomer recipe was poured into the Teflon mold, sandwiched by a silane-treated glass slide and UV-polymerized to form cylinders. Upon polymerization, the hydrogel cylinders adhered to the silane treated glass slides due to the reaction between the methacrylate groups in the monomer and the complementary methacrylate groups in the silane-treated glass slide. This created an array of cylinders decorating the surface of the slide. The hydrogel decorated slide was then immersed into a polystyrene culture dish containing a buffered glucose solution. After allowing the sample to equilibrate for around 15 minutes, the diameters of the free ends of the hydrogel cylinders were measured using a caliper. The same procedure was repeated for solutions containing varying concentrations of glucose.

A similar procedure was employed to make hydrogel/PDMS beams to determine the deflection behavior of the laminate. Beam dimensions were controlled using a Teflon mold machined to the desired beam depth. Bi-layer beams of PDMS/HEMA were formed using a two step procedure: (1) PDMS beams were cast in the Teflon mold by pouring a pre-polymer mix into the mold cavities, the mix was degassed and heated to 100°C for 4 hours to form the PDMS beams. (2) The beams were removed from the mold, the mold cleaned with acetone,
then filled with a HEMA monomer mixture. Once filled with the HEMA monomer solution, the polymerized PDMS beams were superimposed onto the mold, and illuminated for 30 minutes with a UV-lamp to polymerize the HEMA.

XeF\textsubscript{2} etching experiments were performed using an in-house vapor phase setup to enable precise control of etch-rates for controlled release of the Si-island adhered to the bi-layer membranes. Samples, 3cm square, were diced from a Si wafer to determine the etch-rate. Exactly half the top surface of the samples was covered by a thermally grown SiO\textsubscript{2} layer. The step height between the oxide layer and the Si wafer was measured before and after etching to determine the etch-rate.

RESULTS AND DISCUSSION

Hydrogel swelling experiments were performed to determine the extent of swelling for different monomer recipes with varying amounts of crosslinker.

Figure 1 plots the change in diameters of three different recipes of hydrogel when immersed in solutions of increasing glucose concentration. The recipe identified as HAX-0 (0-volume% cross-linker) exhibits the maximum amount of swelling, HAX-5 (0.5-volume% cross-linker) exhibits intermediate swelling and HAX-10 (1.0-volume% cross-linker) swells the least. These results follow the expected trend i.e. a lower cross-link density allows the poly-HEMA to expand more.

The incorporation of the bi-layer polymer membrane into a device constrains the microfabrication of the Si-based component. The release step of the Si-island attached to the deflecting membrane cannot be performed using conventional ‘high-energy’ techniques such as DRIE, or halogen-based plasma techniques like SF\textsubscript{6} RIE etc. These techniques were found to melt the polymer. As a result, we utilized the ‘low-energy’ technique of XeF\textsubscript{2} vapor-phase etching using an in-house XeF\textsubscript{2} vapor-phase etching system.

In order to calibrate the etching system experiments were performed to determine the etch rates for different pulse durations. The samples were prepared as described earlier and etched in the vapor-phase setup at varying pulse durations. The chamber was purged with ultra-pure N\textsubscript{2} gas between pulses to completely eliminate any moisture. Subsequent etching of the samples was performed by introducing XeF\textsubscript{2} gas emanating from sublimation of pellets housed in an auxiliary receptacle. The pressure of XeF\textsubscript{2} was maintained at around 1 Torr for each of the pulse durations shown in Figure 2. The data points indicate that etch rates increase with decreasing pulse durations.

CONCLUSIONS

A HEMA polymer, which swells in the presence of glucose, can be used in a laminated membrane and incorporated into a MEMS device to measure, in real-time, the concentration of glucose in solution. Design of such a device requires careful experiments to determine the swelling behavior of the HEMA, as well as the composite response of a laminated system. We have shown that the swelling can be controlled by changing the cross-link density. Incorporation of the polymer into a device requires a novel fabrication approach utilizing XeF\textsubscript{2} vapor phase etching. Current experiments are aimed at establishing a theoretical model to predict the mechanical properties of a HEMA/PDMS bi-layer system.

REFERENCES