Micromechanical cantilever as an ultrasensitive pH microsensor

R. Bashir[a]

School of Electrical and Computer Engineering, Department of Biomedical Engineering, and NSF Program on Therapeutic and Diagnostic Devices, Purdue University, W. Lafayette, Indiana 47907-1283

J. Z. Hilt

NSF Program on Therapeutic and Diagnostic Devices, and Biomaterials and Drug Delivery Laboratories, School of Chemical Engineering, Purdue University, W. Lafayette, Indiana 47907-1283

O. Elibol and A. Gupta

School of Electrical and Computer Engineering, Purdue University, W. Lafayette, Indiana 47907-1283

N. A. Peppas[b]

Department of Biomedical Engineering, NSF Program on Therapeutic and Diagnostic Devices and Biomaterials and Drug Delivery Laboratories, School of Chemical Engineering, Purdue University, W. Lafayette, Indiana 47907-1283

We report on a pH sensor with ultrahigh sensitivity based on a microcantilever structure with a lithographically-defined crosslinked copolymeric hydrogel. Silicon-on-insulator wafers were used to fabricate cantilevers on which a polymer consisting of poly(methacrylic acid) (PMAA) with poly(ethylene glycol) dimethacrylate was patterned using free-radical UV polymerization. As the pH around the cantilever was increased above the pK_a of PMAA, the polymer network expanded and resulted in a reversible change in surface stress causing the microcantilever to bend. Excellent mechanical amplification of polymer swelling as a function of pH change within the dynamic range was obtained, with a maximum deflection sensitivity of $1 \text{ nm}/5 \times 10^{-5} \, \Delta\text{pH}$. © *2002 American Institute of Physics.* [DOI: 10.1063/1.1514825]

The use of microelectromechanical systems can result in microfluidic devices, lab-on-a-chip, and related sensors with very high sensitivity, in addition to reducing the total time to result for chemical and biological analysis. The low cost due to wafer-scale manufacturing and the reduction in sample size due to miniaturized sensors are also very attractive. A key parameter to measure in most biochemical and biological processes is the change in pH in very small volumes. These pH changes are created by release of H^+ ions by trans-membrane pumps, by-products of chemical reactions, and other processes. The microscale detection of changes in pH has been reported in literature and examples include using ion-sensitive field-effect transistors (ISFETs),[1–3] potentiometric metal oxide electrodes,[4–6] light addressable potentiometric sensor (LAPS),[7] and scanning probe potentiometer (SPP).[8] ISFET structures with SnO_2/Al- or Ta_2O_5-gate have demonstrated a linear pH sensitivity of approximately 58 mV/pH in a concentration range between pH 2 and 10.[2,3] Iridium oxide has been the most widely applied solid-state metal oxide for pH sensing[5] and iridium oxide-based pH electrode with a sensitivity of approximately 60 mV/pH and with extremely high stability have been demonstrated.[6] The LAPS device measures an alternating photocurrent through an electrolyte-nitride-semiconductor structure in reverse bias, while the silicon is illuminated with a modulated laser beam.[7] Again, sensitivities in the range of 40–60mV/pH have been demonstrated. The SPP, which integrates the LAPS onto a cantilever structure, demonstrated a sensitivity of 0.01pH units, limited by the rms noise of 500 μV.[8]

Microcantilevers utilize a unique sensing mechanism since they provide mechanical amplification of a signal due to change in the surface properties. The surface of the microcantilever requires functionalization to provide for selective detection of an analyte or environmental condition. For example, thiolated single-stranded DNA were used to form a self-assembled monolayer (SAM) on a gold-coated microcantilever, and then these modified microcantilevers were used to detect complementary DNA strands.[9] In other work, polymer coated microcantilevers were used to successfully detect the selective absorption of organic solvents.[10] These hydrogels[11] can be micropatterned and in the work presented here, we integrate the ability of hydrogels to actuate in response to changes in pH to create highly sensitive microcantilever pH sensors. The photolithography process also allows for multiple applications of different polymers on different cantilevers on the same chip. When compared with other micro-scale techniques such as LAPS or SPP, the sensitivity is increased by at least two orders of magnitude.

Hydrogels have been used for a variety of applications where environmental sensitivity is needed.[12] By controlling the functional groups along their backbone chains, hydrogels can be made sensitive to environmental conditions, such as temperature, pH, or ionic strength.[13] These hydrogels have been micropatterned for application in creating surfaces with regions of different physico-chemical properties.[14–16] In addition, micropatterned hydrogels within a microchannel have been used as a valve that can sense a pH change and actuate for use in microdevice applications.[17]

[a] Electronic mail: bashir@ecn.purdue.edu
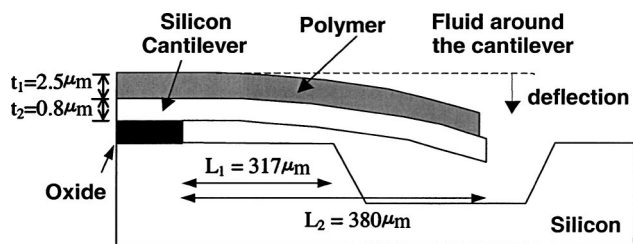[b] Electronic mail: peppas@ecn.purdue.edu

FIG. 1. Cross-sectional schematic of the cantilever/polymer structure with the various dimensions.

In our work, surface micromachined cantilevers were fabricated using commercially available SOI wafers with a 1 μm silicon layer and 1 μm oxide layer. A 0.3 μm oxide was grown and photoresist mask was used to anisotropically etch the oxide, silicon, and the buried oxide layers. A 0.1 μm oxide was grown on the sidewall of the SOI layer, and a dry anisotropic etch was used to remove the oxide from the substrate exposed silicon surface, while leaving it on the sidewalls of the SOI layer. Tetramethylammonium (TMAH) was used to etch the silicon substrate and to release the cantilever/oxide composite structure. The wafers were immersed in buffered hydrofluoric acid to etch off all the oxide and release the silicon cantilevers. The wafers containing cantilevers were soaked in a 10 wt % acetone solution of γ-methacryloxypropyl trimethoxysilane, an organosilane coupling agent, which forms a SAM on the native silicon dioxide surface and presents methacrylate pendant groups that react and bond covalently with the polymer film. Next, the hydrogel was defined on the cantilevers. The monomer mixtures were prepared with a mole ratio of 80:20 methacrylic acid:poly(ethylene glycol) 200 dimethacrylate. The mixture also contained 10 wt % 2,2-dimethoxy-2-phenyl acetophenone (DMPA) as the initiator for the UV free radical polymerization. The monomer mixture was spin-coated at 2000 rpm for 30 s onto the silicon samples containing microcantilevers. The sample was exposed in a Karl Suss MJB3 UV400 mask aligner to UV light with an intensity of 23.0 mW/cm^2 for 1 min and then allowed to soak in deionized distilled water for greater than 24 h to remove any unreacted monomer. Figure 1 shows a final drawn cross section of the device. Figure 2 shows an optical image of the cantilever/polymer structure in the dry state. The TMAH etch resulted in a pillar of silicon underneath part of the cantilever. The thickness of the polymer film patterned on the microcantilevers was determined to be approximately 2.5 μm using profilometry and the thickness of the silicon cantilevers was measured using scanning electron microscopy to be about 800 nm.

After patterning the hydrogel onto microcantilevers, equilibrium bending studies were conducted as shown in Fig. 3. The silicon wafer, containing the microcantilevers patterned with polymer, was placed in a petri dish that was filled with a buffer solution composed of a mixture of 0.1 M citric acid and 0.2 M disodiumphosphate. The petri dish with sample was placed onto the optical microscope stage and a 60$\times$ water immersion objective was used to observe the sample. The sample was allowed to equilibrate at a given pH for 10 min, and the deflection of the cantilever was measured by adjusting the focus plane from the edge of the cantilever well to the tip of the cantilever. The pH of the solution was adjusted by changing the ratio of citric acid and disodium phosphate and measured using a handheld pH meter with micro-pH probe. The measurement results are shown in Fig. 3, where the solid line shows the measured deflection of the cantilever versus pH and the dotted line shows the calculated curve from an analytical model. The behavior of the cantilever structure is complicated but a simplified model can be used if the cantilever structure is examined as a composite beam with no slip at the interface.[18] The model was modified to incorporate the pillar structure into the equations. The polymer expansion is described by its swelling ratio (defined as the ratio of volume of swollen polymer sample to volume of dry polymer sample), which is a function of pH. The swelling ratio of the polymer was measured, as described earlier,[19] and the results were incorporated in the model. The modulus of elasticity of the polymer is known to decrease with increasing pH, but for the first order model developed here, it was assumed to be a constant used to fit the modeled data to the experimental results. A value of 85 MPa was used.[20] It is also important to note that the thickness (and hence the cross-sectional area) of the polymer will increase with pH, but was assumed at the measured value of 2.5 μm. The modeled deflection, with these assumptions, is in fact rather close to the experimental results as shown by the dotted line in Fig. 3. This could be due to compensating effects of the modulus and the thickness, in relating the force to the strain. The inset in Fig. 3 shows the vertical deflection of the cantilever/polymer structure at pH 7 as obtained by the analytical equations. More detailed experiments and modeling is in progress to understand the effect of modulus and thickness variation with pH.
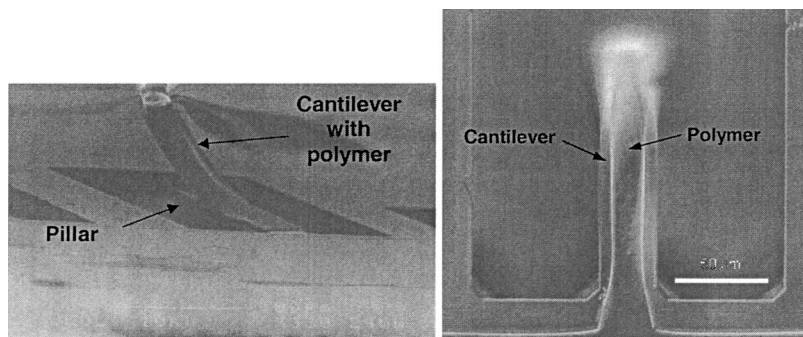

FIG. 2. (a) Angled scanning electron micrograph and (b) a top view optical image of the cantilever/polymer structure in the dry state. The cantilever is bent upwards and hence the tip region is out of focus in (b). The cantilever is 0.8 μm thick and the polymer is 2.5 μm thick. [The polymer is charging up when viewed in the SEM and hence appears slightly distorted at the top in (a).]

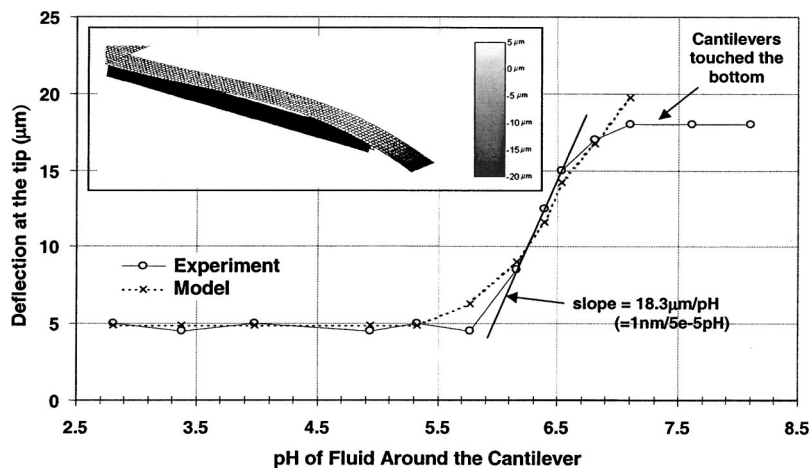FIG. 3. Equilibrium cantilever deflection as a function of pH around the polymer. The solid line is experimental results and a sensitivity of 5×10^{-4} pH for a 10 nm bending deflection resolution can be obtained. The dotted line is obtained with the cantilever and polymer modeled as a composite beam with no slip at the boundary. Small deflections with respect to the length are assumed. Polymer elastic modulus of 85 MPa is used to fit the model to experiments. The inset shows three-dimensional plot of the deflection of the cantilever/polymer at pH=7.0, obtained from the model.

At low pH, the cantilever is bent downwards since the hydrogel is swelled due to the liquid around it, when compared to the dry state. As the pH is increased above 5.7, the polymer swells rapidly and eventually the cantilever touches the bottom of the well. Between pH of about 5.9 and 6.5 (dynamic range of the sensor), the slope of the deflection at the tip versus pH curve, and hence the sensitivity, is maximum at about 18.3 μm/pH. If an optical laser-based deflection measurement system is used, such as the one used in conventional atomic force microscope, where deflections of 1 nm can be easily detected, the above number translates to a sensitivity of 5×10^{-5} pH for a 1 nm bending detection resolution. The sensitivity would be 5×10^{-4} pH for a 10 nm bending deflection resolution. These sensitivities are among the highest reported for any micro-scale pH detectors. This value is two to three orders of magnitude better than prior reported methods. The dynamic range could also be tailored for specific applications by changing the composition of the polymer.

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