Parylene micro membrane capacitive sensor array for chemical and biological sensing

Srinath Satyanarayana a, Daniel T. McCormick b, Arun Majumdar a, c, *

a Department of Mechanical Engineering, University of California, Berkeley, CA 94720, USA
b Berkeley Sensor and Actuator Center, Department of Electrical Engineering, University of California, Berkeley, CA 94720, USA
c Materials Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA

Received 29 June 2005; accepted 13 October 2005
Available online 21 November 2005

Abstract
The need for high-throughput label-free multiplexed sensors for chemical and biological sensing has increased tremendously in the last decade with new applications in the areas of genetics, diagnostics, drug discovery, as well as security and threat evaluation. Surface stress-based sensors are a relatively new class of sensors that has immense potential to satisfy the demand, and has been investigated extensively in the recent years. In this paper we present the design and fabrication of a novel parylene micro membrane surface stress sensor that exploits the low mechanical stiffness of polymers. The salient features of the sensor are that it: (i) is label-free; (ii) is a universal platform suitable for both chemical and biological sensing; (iii) uses electronic (capacitive detection) readout; (iv) has integrated microfluidics for addressing individual sensors on the chip; (v) is capable of handling both liquid and gas samples; (vi) is made using standard low temperature microfabrication processes (<120 °C); (vii) can readily be scaled and multiplexed. The first generation sensor arrays were fabricated and the sensor response to organic vapors like isopropyl alcohol and toluene were measured.

© 2005 Elsevier B.V. All rights reserved.

Keywords: Parylene; Polymer; Micro membrane; Surface stress sensor; Capacitive; Microfluidics

1. Introduction

Fast, label-free detection of chemical and biological molecules would enable inexpensive and high-throughput testing and diagnosis. Chemical sensing typically deals with gas and vapor molecules like H₂, CO₂, NO₂, explosives like TNT, RDX, toxins like DMMP, etc. In one class of sensors, the changes in electrical and/or mechanical properties caused by adsorption of these chemical species onto specific thin films (polymers, metals, metal oxides, ceramics, etc.) are used for detection [1–5]. In thin film-based systems, the major problems are the lack of selectivity and interference from agents like water vapor which are always present at large concentrations. Secondly, some of these sensors need to be operated at temperatures greater than 200 °C [4,6]. Mass-spectroscopy (MS)-based methods are very accurate, but the equipment is bulky and expensive. The concept of ‘electronic nose’, i.e. a sensor array and principal component analysis (PCA) method, holds a lot of promise for addressing the problem of selectivity [1,5,6]. The more diverse the sensor array in such systems, the greater is its selectivity and resolution. Hence, an accurate high density multiplexed sensor array would be an enabling technology for selective chemical sensing. Biomolecular analyses in mixtures are currently performed in two steps – separation based on differences in mobility or through specific binding with receptor molecules. Separation-based bioassays, such as gel electrophoresis and mass-spectrometry, are often limited by low throughput, lack of quantification, and/or high cost per assay. DNA microarrays, which offer high-throughput bioassay for DNA sequences, have revolutionized the area of genetic research and clinical diagnostics [7]. Though these microarrays have demonstrated excellent sensitivity and range, they require samples to be labeled with a fluorescent tag for detection purposes. The major drawback associated with the process of labeling is sample loss during the steps of labeling and purification, especially when the sample quantity is limited. In the case of molecules like
proteins and small ligands, attaching a label may also result in loss of functionality and/or stability.

Surface stress-based sensors use the free energy change, the underlying concept in any binding reaction, and hence, offer a universal platform for chemical and biological sensing. When bio/chemical reactions occur preferentially on one surface of such a sensor, changes in intermolecular forces create a surface stress that modifies the curvature of the mechanical sensing element. Using microcantilever sensors several researchers have demonstrated the capability of surface stress sensors in detecting a variety of reactions, which include alkanethiol immobilization [8], water vapor adsorption [9], DNA hybridization [10–13], antigen–antibody binding [14] and explosive vapor detection [15]. Changes in surface stress in such reactions were reported to be in the range of 5–50 mJ/m² [10,14,16] or as high as 200 mJ/m² [8] and 900 mJ/m² [13]. All these above sensors used silicon or silicon-based microcantilevers and/or optical beam deflection method for detection. The sensitivity of these sensors is a function of the mechanical stiffness of the sensor element. The use of capacitive sensor readout makes the system viable for miniaturization and multiplexing. In the present work, a parylene micro membrane capacitive sensor array with integrated microfluidics has been demonstrated. Details of the sensor array design, fabrication process and preliminary chemical sensing experiment results are presented in the following sections of this paper.

2. Design

2.1. Conceptual design

The conceptual design of the parylene micro membrane sensor is illustrated in Fig. 1. The sensor element consists of a thin parylene membrane that is fixed on all four sides and is suspended over a metal pad patterned over a substrate. A part of the membrane surface is coated with a thin metal layer which acts as the flexible electrode for capacitance sensing with the metal pad as the second electrode. A part of the membrane surface, in this case the top electrode, is also modified to selectively attach probe molecules to the surface. When selective chemical/biological reactions occur between the target and probe molecules on the sensor surface, the changes in the intermolecular forces induce a surface stress change which causes the membrane to change curvature and deflect as shown in Fig. 2. The sensor deflection changes the effective gap between the two electrodes and changes the capacitance. The deflection (curvature change) of the membrane is a function of the type and kinetics of the surface reaction, and by measuring the capacitance change one can obtain the details about the reaction.

2.2. Sensor design

Of the several polymers used in microfabrication, parylene was chosen for making the flexible membrane because of its biocompatibility, room temperature deposition, relatively stress-free nature of the deposited films and ease in patterning. A thin film of gold was used to make the top electrode as it can also work as a scaffold for probe molecule immobilization via gold-thiol chemistry. Chromium was used to make the bottom electrode
based on process sequence compatibility. Quartz was chosen as the substrate for fabrication of the sensor because of its excellent dielectric properties.

The objective of the design process is to maximize the sensor signal, i.e. the capacitance change for a given surface stress change, while all other constraints imposed by fabrication processes, microfluidics, and chip size are satisfied. The capacitance change is a function of the sensor deflection, the gap between the electrodes \(g_s\) and the electrode sizes \((c_s, g_c)\).

The sensor deflection is a function of the mechanical stiffness of the gold–polymer composite membrane. From basic membrane/beam theory, it is well known that the membrane stiffness for surface stress loading is directly proportionate to \((l_m/l_p)^3\), where \(l_m\) is the membrane length and \(l_p\) is the membrane thickness. The gold layer on the top of the membrane, which is essential for functionalization and electrical detection, increases the membrane stiffness and, hence, should be as thin as possible. Based on prior experience with parylene processing and cantilever sensor design, the membrane thickness \(t_p\) and the gold thickness \(t_m\) were set at 500 nm and 25 nm (with a 5 nm chrome adhesion layer), respectively. A smaller air-gap \(g_s\) between the capacitor electrodes increases the nominal capacitance and also makes the device more sensitive. However, very small gaps cause adhesion of the sensor membrane to the bottom electrode during the release process (see Section 3). The optimal value for \(g_s\) was found to be 2 \(\mu\)m by trial and error.

The design variables that are available for optimization are the capacitor electrode sizes \((c_s, g_c)\) and the membrane size \(l_m\). For a given membrane size, maximum capacitance is obtained when the electrode size is as large as the membrane size. Since the membrane configuration is similar to the double-clamped beam configuration (membrane is clamped on all four sides unlike the double-clamped beam), it was expected that the sensor response would be zero when the membrane size is same as the gold electrode size, i.e. \(g_s = l_m\) and that there would exist an optimum gold coverage ratio \(g_s/l_m\). Unlike the case of the double-clamped configuration, analytical solutions for membrane deflection arising from surface stress changes for partially covered membranes do not exist. Consequently, finite element (FE) analysis was used to determine the optimal gold coverage ratio for the membrane configuration.

Commercially available FE analysis software ANSYS® was used and the details of the FE model are listed in Table 1. The FE model included the sensor, electrodes, substrates and the air-gap. In most commercially available FE analysis software, there is no direct method to apply a surface stress load. Hence, a new method for applying surface stress load via an equivalent temperature load was developed. The equivalent temperature load \(\Delta T\) for a surface stress load \(\sigma_s\) was evaluated using Eq. (1) and the coefficient of thermal expansion (CTE) of all the materials except the gold layer was set to zero for the analysis.

\[
\Delta T = \frac{\alpha}{E} \frac{\Delta \sigma}{\Delta T} \quad (1)
\]

A compressive surface stress of 10 mN/m², which is typical of biological reactions \([10,12,16]\), was used in the FE analysis. The membrane size \(l_m\) used for the FE analysis was 300 \(\mu\)m (chosen based on sizes of typical microcantilever surface stress sensors \([8,14,16]\)). The bottom electrode size \(c_s\) was chosen to be smaller than the top electrode size \(c_c\) in order to confine the electric field lines to the air-gap below the gold electrode. This ensures that the effect of the materials on the top of the gold electrode, which change with different samples being tested, on the sensor capacitance is minimized. Hence, for a given \(g_s\), \(c_s\) was set to 10 \(\mu\)m smaller than \(g_s\).

Once the mechanical deflection of the sensor membrane for the surface stress loading was evaluated, the FE mesh was morphed to incorporate the deflections into the model geometry and the new capacitance of the sensor at its new deformed shape was calculated. The sensor deflection (at the center of the membrane) and absolute capacitance change are plotted against the gold coverage ratio \(g_s/l_m\) in Fig. 3. The compressive stress causes the membrane to deflect away from the air-gap as shown in Fig. 2 and this results in a decrease in sensor capacitance. It is also seen from Fig. 3 that the sensor deflection has a maximum at \(g_s/l_m \approx 0.7\) and the capacitance change has a maximum at \(g_s/l_m \approx 0.8\). Based on the FE analysis three different values for \(g_s/l_m\) between 0.6 and 0.75 were chosen (Note: during the initial design, optical interferometry was also being explored as one of the detection methods and the sensor signal for this method would be the highest at maximum deflection and hence, sensor deflection was also taken into account while selecting the \(g_s/l_m\) values for the first generation fabrication).

![Diagram](image-url)
For large scale multiplexing, it is desirable to have a large number of sensors on a single chip/wafer. Consequently, the sizes of individual sensors have to be as small as possible. However, the nominal capacitance of the sensor decreases as a square of the sensor electrode size. Measuring very small capacitances with high resolution requires the use of sophisticated circuits and proper isolation techniques. Using the different circuits that are available for capacitance measurement, a 0.1 fF capacitance change over a nominal capacitance of $\sim 1$ pF can be measured without any sophisticated techniques [20,21]. Using the optimal $g_s/l_m$ ratios and simple capacitance calculations, three different membrane sizes ($l_m = 200, 300$ and $400$) were chosen for the first generation fabrication.

The final configuration of the sensor and the dimensions of the sensor elements are shown in Fig. 4 and Table 2, respectively. Additional micro-channels connecting the capacitor air-gap and the ambient as shown in Fig. 4 were included to help in the fabrication process (see Section 3). A second metal (Al) was used to make the interconnect lines for the top electrode because the 25 nm evaporated gold film is not continuous across the 2 $\mu$m step due to air-gap.

### 2.3. Microfluidic design

Microfluidics is essential for individually addressing the different sensors in the array, and also for isolating the air-gap from the samples being tested. Fig. 5 shows the design of a fluid cell with two sensors. Liquid can be injected or removed through one of the two I/O port by a micropipette. Two I/O fluid cells have been shown to be better than one I/O cells in preventing bubble entrapment in the chamber as they provide an exit path for the air during the filling process [16]. The microfluidic chip is made out of quartz because it is optically transparent and also has excellent dielectric properties. The dimensions of the microfluidic cell are constrained by the chip size and the isotropic nature of the etching process used for fabrication. The fluid chamber in the current design was a 1.7 mm square ($f_s$) with a height of 0.25 mm ($f_d$) and each I/O was a 0.6 mm square ($s$) as illustrated in Fig. 5.

Since the sensor membrane is fixed on all four sides, the air-gap between the capacitor electrodes, i.e. the gap between the membrane and the bottom electrode is isolated from the fluid.
cell. The gap, however, is open to atmosphere via a separate micro-channel and an opening in the cover chip (see Fig. 5). This configuration prevents pressure fluctuations during the membrane deflection by allowing the air to move in and out of the gap. These micro-channels also provide an access path for removal of the sacrificial layer during fabrication (see Section 3). The fluid cells enable selective functionalization of the different sensors on a single chip with different probe molecules. Each fluid cell has two sensor membranes to enable common mode rejection, where, one of the sensors could be passivated to prevent reactions from taking place on its surface. Common mode rejection helps in eliminating the effects of phenomena like surface tension, ionic double layer and other factors that can increase noise when sensing in a fluid medium.

The membrane sensors with their microfluidic chambers were arranged in a 2-D array on the chip to achieve a high spatial density as this design is truly scalable to contain several sensors in a single chip. In the first generation fabrication run, a $3 \times 3$ array of sensor unit cells (each with two devices) was implemented on a $1 \text{ cm}^2$ die size.

2.4. Sensing electronics

Two different circuit topologies were designed for single ended and differential capacitance measurement, respectively. The single-ended measurement circuit is primarily designed for chemical sensing in an array format where extremely high common mode rejection may not be required. The differential measurement circuit is more appropriately suited for sensing in liquid environments, where common mode rejection is very important for obtaining a good signal-to-noise ratio. In both circuits a low-level high frequency measurement signal is applied to the driven node of the device. The signal on the sensing node of the device is detected and buffered; synchronous demodulation and filtering provides an output signal corresponding to the capacitance of the device. Additional information on the capacitance measurement techniques may be found in [22].

3. Fabrication

The polymer membrane sensor array was fabricated using surface and bulk micromachining technology. The process consisted of six masking steps for the sensor chip and two masking steps for the microfluidics chip. The six masking steps for the sensor chip are: (i) bottom electrode patterning; (ii) spacer patterning; (iii) parylene patterning to expose bottom contact pads; (iv) Al interconnect patterning; (v) Au film patterning; (vi) parylene patterning for device release. The two masking steps for the microfluidic chip are: (i) front side I/O patterning and (ii) back side chamber patterning. The fabrication steps with corresponding substrate cross-sections in the device process sequence in illustrated in Fig. 6.

The process started with a flat, 100 mm diameter Quartz wafer. The surfaces of the substrate were cleaned with Piranha solution ($3:1 \text{ H}_2\text{SO}_4:\text{H}_2\text{O}_2$) before the first step. A 150 nm chrome layer was evaporated using an E-Beam evaporator (Edwards EEB) and patterned to form the capacitor bottom electrode, interconnect lines, and contact pads. A 150 nm chrome layer was also evaporated on the reverse side of the quartz wafers to make them opaque for automatic handling in the processing equipment. A 2 $\mu$m sacrificial photosensitive (PR) layer was spun-coated and patterned on the chrome electrode to form the spacer layer. Next, the substrate was coated with $\approx 500$ nm thick parylene-N layer (Note: the parylene deposition equipment (Speciality Coating Systems, Model 2010) is designed such that the final film thickness is controlled by the amount of raw material used). Prior to parylene deposition, the surface was treated with an organo-silane layer (A-
174: gamma-methacryloxypropyltrimethoxysilane) to facilitate parylene adhesion. This silane layer was formed by a vapor phase deposition technique as described in ref. [23]. A 150 nm thick aluminum film was sputtered and patterned to form the interconnect lines and contact pads for the top electrode. Next, a 25 nm gold film with a 5 nm chrome adhesion layer was thermally evaporated and patterned to form the top electrode of the capacitor in the sensor. Prior to aluminum and gold evaporation, the substrate was treated with oxygen plasma (Technics PE-IIA Plasma Etcher, power 50 W, 30 s) to enhance adhesion between parylene and the metal layers [24]. The process sequence was designed such that the gold film was evaporated last to keep the gold surface as clean as possible for good surface reaction. Parylene was then etched away in selected areas on the substrate using oxygen plasma (Technics PE-IIA Plasma Etcher, power 300 W, 6 min) to provide access to the sacrificial photo-resist layer. The wafer was then diced into 1 cm square chips for further processing. The protective PR layer used during the dicing process was washed off using acetone and the chip was dried with a N₂ stream.

A microfluidic chip processing also started with a flat, 100 mm diameter quartz wafer. A 0.3 μm thick film of polysilicon was deposited and patterned on both sides of the wafer as a mask for the HF (49% solution) etching process. After the quartz etching, the wafer was diced into 7.8 mm squares. The cover chips were then bonded individually to sensor chips using a room-temperature adhesive transfer bonding process described in ref. [25]. The bonded chips were soaked in acetone for 36 h to dissolve and remove the PR spacer layer. The acetone solution was changed regularly to facilitate complete removal of PR. Acetone was then removed from the air-gap using critical point drying (CPD) to avoid stiction problems due to surface tension during solvent removal. Occasionally, a few membranes were partially stuck to the substrate, but applying a small vacuum after CPD helped in releasing them completely. Fig. 7 shows some optical micrographs of the fabricated sensor chip.

4. Experiment results and discussion

4.1. Thermal testing

Thermal characterization of the sensor was performed to evaluate sensor performance and also to test if the membranes were fully released from the substrate. The thermal test chip did not have the microfluidic cover bonded to it. For the temperature test, an adjustable temperature stage was built to maintain the sensor chip at a constant temperature. A commercially available PID controller (Wavelength Electronics, Model LFI3751; temperature resolution of 0.01 K) with adjustable set-points was used to control the stage temperature. Thermal grease (Lakeshore Inc.) was used at the interface between the chip and the stage to ensure good contact. The sensor capacitance during the temperature test was measured using a HP 4284 LCR meter with an excitation voltage of 50 mV at 100 kHz. The plot of normalized sensor capacitance versus temperature for a fully released membrane and a fixed membrane (no air-gap) of size 300 μm are shown in Fig. 8. The parasitic capacitance from the interconnect lines and the bond pads was measured to be 30 fF and was subtracted from all measurements during post-processing. The thermal response of released membrane capacitor was −2.0 fF/K, which corresponds to a 1.25% decrease, whereas, for the fixed membrane capacitor (no air-gap), it was −0.5 fF/K, which corresponds to 0.031% decrease. These values clearly indicate that the sensor is released.

The measured sensor capacitance of 1.558 pF (sensor size, 300 μm) for the fixed membrane device compares well with the value 1.667 pF estimated from the standard parallel plate capacitor equation. For the fully released membrane device, the measured value of 0.127 pF is lower than the value 0.191 pF, obtained from FE model. This lower value may be due to the actual air-gap being greater than the designed value of 2 μm. Secondly, in the FE model the air-gap is a constant over the entire device whereas in the actual device, it is not due to resid-
ual stresses in the thin films. The measured trend of decreasing capacitance with increasing temperature also agrees well with the prediction from FE analysis.

4.2. Chemical sensing experiment

4.2.1. Chip preparation

For preliminary experiments, three alkane thiol coatings with different functional end groups (MUA: SH–(CH_2)_10–COOH, MUO: SH–(CH_2)_11–OH, DOT: SH–(CH_2)_11–CH_3) were chosen as the sensor coating layers. The thiol molecules bind strongly to the gold layer on top of the flexible polymer membrane via the SH group. The test chip had the microfluidic cover bonded to it, and this enabled selective functionalization of the different membranes on the chip as shown in Fig. 9. Ethanolic solutions (5 mM) of these thiols were injected into the microfluidic cells using a micropipette and the membranes were incubated in the thiol solutions for 10 min for coating formation. Once the sensor membranes were functionalized, the entire chip was washed in ethanol to remove the non-specifically bound thiol molecules. The chip was then soaked in acetone to dissolve the sacrificial photo-resist layer and released as described in Section 3.

4.2.2. Experiment setup and procedure

The sensor capacitance was measured using a HP 4284 LCR meter with an excitation voltage of 100 mV at 1 MHz in a probe station. The sensor capacitance was continuously sampled at 1 Hz using a National Instruments GPIB-USB interface using Matlab©. The probe station was purged continuously with a slow N_2 flow. The chip was placed in the probe station and the cover was closed as shown in Fig. 10. Once a stable baseline capacitance reading was obtained, the vapor source, a glass Petri-dish with the liquid was carefully placed inside through the small opening as shown in Fig. 10. The system was then allowed to equilibrate and when the sensor capacitance reached a stable value, the Petri-dish was removed carefully and the sensor was allowed to equilibrate again. The ambient temperature inside the probe station chamber was monitored via a thermocouple as illustrated in Fig. 10 and the temperature variation in the probe station chamber was within 0.1 K during the experiment. This experiment was repeated for different vapor sources with a 1 h purge time between experiments. The parasitic capacitance from the interconnect lines and the bond pads, which was measured to be 30 fF, was subtracted from all measurements during post processing.

4.2.3. Results

The normalized capacitance change on exposure to IPA and toluene vapors for the different thiol coated sensors are shown in Figs. 11 and 12, respectively. In both these experiments, the decrease in capacitance indicates that the membrane deflected as shown in Fig. 2. The nominal sensor capacitances of these devices are listed in Table 3. From the IPA response it can be seen that the hydroxyl terminated thiol device (MUO) showed the maximum capacitance change (1.5% decrease in sensor capacitance) whereas the capacitance changes in the carboxyl (MUA) and methyl (DOT) terminated thiol devices were similar and lower than the MUO device. The sensor response to toluene
Fig. 11. Normalized capacitance vs. time on exposure to IPA vapor for sensor membranes coated with different thiol molecules.

Fig. 12. Normalized capacitance vs. time on exposure to toluene vapor for sensor membranes coated with different thiol molecules.

Table 3

<table>
<thead>
<tr>
<th>Sensor coating</th>
<th>Nominal capacitance (pF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MUA</td>
<td>0.154</td>
</tr>
<tr>
<td>DOT</td>
<td>0.151</td>
</tr>
<tr>
<td>MUO</td>
<td>0.152</td>
</tr>
<tr>
<td>Control</td>
<td>1.585</td>
</tr>
</tbody>
</table>

IPA vapor was much higher (7% decrease in sensor capacitance compared to 1.5% seen in IPA response) and the trend was opposite to what was observed in the IPA response. The capacitance change in the MUA and DOT devices were comparable and these were higher than the capacitance change in the MUO device. The capacitance change for the control device, the fixed membrane capacitor, was near zero for both IPA and toluene exposure as seen in Figs. 11 and 12.

The reasons for the observed measurement trends in sensor capacitance for IPA and toluene exposure are not fully understood yet. Further experiments with controlled vapor concentration and multiplexed readout are required for better understanding of the system and such a chemical sensing chamber with a dedicated capacitance measurement circuit board and electrical and vapor interconnects is in process of fabrication.

5. Summary

A new surface stress sensor array that exploits the low stiffness of polymeric materials has been designed, fabricated and tested for chemical sensing applications. This is the first demonstration of a parylene membrane-based surface stress sensor array with integrated microfluidics and electronic readout. Thermal characteristics of the sensors were measured and the sensor response was found to be 2 fF/K for a 300 μm membrane device. For the chemical sensing experiment, three alkanethiol coatings with different functional end groups (–COOH, –CH3 and –OH) were tested as sensor coating layers. The sensor array was selectively functionalized and the responses to IPA and toluene vapors were measured. The IPA vapor exposure produced a smaller capacitance change (~1.5% decrease in sensor capacitance) and the sensor with the hydroxyl thiol coating gave a larger signal when compared to the carboxyl and methyl thiol coated sensors. For the toluene vapor exposure, the observed capacitance change was much higher (7% decrease in sensor capacitance) and the observed trend was opposite to what was seen in the IPA experiment, i.e. the sensor with the hydroxyl thiol coating produced a smaller signal when compared to the carboxyl and methyl thiol coated sensors.

A dedicated circuit board and a controlled chemical sensing chamber have been designed for multiplexed readout of several sensors and are in the process of fabrication. In the near future, multiplexed chemical sensing experiments with controlled environment and bio experiments like DNA immobilization and hybridization will be investigated for demonstrating the capabilities of this new sensing platform.

Acknowledgments

The authors would like to thank Veljko Milanovic and Min Yue for useful discussions and help with device fabrication and the Microfabrication Laboratory, UC Berkeley for providing fabrication facilities.

References
