A FLUIDIC CHEMICAL AND BIOLOGICAL SENSING MECHANISM WITH HIGH TRANSDUCTION BASED ON DISSOLVABLE MEMBRANES

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ABSTRACT

We demonstrate an elegant chemical and biological sensing mechanism that transduces chemical and biological signals to electrical signals with large intrinsic amplification not requiring complex on-chip microelectronics. The sensing mechanism employs dissolvable membranes separating a fluid chamber from an interdigitated capacitor initially in air. Dissolution of the membrane (here, a hydrogel membrane) in the presence of the target species (here, dithiothreitol) allows the target species to flow into the capacitor bringing about a change in its impedance. Using this mechanism, a simple circuit can generate 2.9V DC output with 2.94V DC supply. No DC power is consumed until the detection of the target species. A range of species can be sensed by defining membranes specific to the target species. The fabrication process is compatible with conventional IC fabrication technologies and is applicable to wireless microsensor networks.

Keywords: biological sensing, chemical sensing, dissolvable membrane, low power, microfluidics

INTRODUCTION

The importance of sensing biological and chemical agents especially to guard against biological attack is well recognized [1]. The design and implementation of an efficient sensing mechanism which can be easily fabricated, portable and cost-effective from a system’s perspective can prove to be a non-trivial engineering problem. Although there has been a considerable effort in this direction, most approaches provide a small electrical output susceptible to noise, parasitics and temperature variation that require complex on-chip microelectronics for signal conditioning. Such schemes are based on complicated electronics and photonics [2, 3], or need macro-scale spectrometry to quantify the output [4, 5].

We demonstrate here an elegant sensing mechanism to transduce chemical and biological signals to electrical signals with large intrinsic amplification. Fig. 1 describes the sensing mechanism. A target-recognition membrane separates the sampling microfluidics and an interdigitated capacitor. The capacitor is initially in air. The membrane becomes porous and dissolves due to the target species, allowing the fluid to flow into the capacitor. This drastically changes its impedance which can be transduced to a large electrical output without complex electronics. Here, we use the selective dissolution of poly(acrylamide) (PAAm)-based disulfide-crosslinked hydrogel membranes by dithiothreitol (DTT) [6] to demonstrate the mechanism.

The approach is universal since a range of species can be sensed by defining membranes specific to the target species. This bio/chemical recognition process, based on molecular-level chemical reaction, is universal and can be highly specific and sensitive [7]. The mechanism eliminates the need for complex on-chip microelectronics. Furthermore, no DC power is consumed until the detection of the target species, thus improving battery life. The fabrication process is based on liquid-phase photopolymerization (LP3) and is compatible with conventional IC-based MEMS technology [8]. The sensor is also applicable to wireless microsensor networks.

FABRICATION

The sensor is fabricated on a Si substrate coated sequentially with 0.40 µm Cr, 20 µm polyimide (PI) 2611 (HD MicroSystems, Parlin, NJ), and 0.05µm Ti, 0.4µm Cu, and 0.05µm Ti. Polyimide is used for insulation while the Cr layer promotes adhesion of polyimide to the underlying Si substrate. Fig. 2 shows the detailed fabrication. The capacitor is formed by electroplating nickel (Ni) using Cu as the seed layer. An
electroplating mold of the interdigitated capacitor electrodes is formed by patterning a 10µm thick AZP-4620 photoresist using a chrome photomask (Mask 1). The Ti layer on top of the Cu layer, which prevents the oxidation of Cu, is removed just before electroplating. Ni is electroplated and the mold is removed. The seed metal layers (Ti/Cu/Ti) underneath the mold are removed, but the capacitor is not released.

Next, the fluidic channels (Mask 2) to direct fluid flow into the capacitor, and the chamber to hold the sampled fluid are photopatterned using liquid-phase photopolymerization (LP3) with an isobornyl acrylate (IBA)-based pre-polymer (poly(IBA)) [8]. (c) A poly(acrylamide) (PAAm)-based hydrogel membrane is also photopatterned using LP3. The width, ‘w’, is an important factor determining the dissolution time of the hydrogel. The capacitor and channels are covered on the top with a transparency sheet having an opening for sampling the incoming fluid. It is glued to the fluidic channels with a 125µm-thick adhesive tape. The bottom surface of the capacitor and connection channel are made hydrophilic through molecular vapor deposition of a silane-based self-assembled monolayer – mPEG-chlorosilane [9]. This, as well as the fluid pressure created by the sample acquisition system, ensures that the fluid gets inside the capacitor following the dissolution of the hydrogel membrane.

![Images of electroplating mold, fluidic channel, and hydrogel membrane]

**Fig 2.** Fabrication process flow. A Si wafer is coated with 20µm-thick polyimide for isolation. Ti/Cu/Ti (0.05µm/0.4µm/0.05µm) is sputtered as a seed layer for subsequent Ni electroplating. (a) A 10µm thick AZP-4620 photoresist is photopatterned to define a mold of the interdigitated capacitor. Ni is electroplated and the mold is removed. (b) The fluidic channels, which direct fluid flow into the capacitor, and the chamber to hold the sampled fluid are photopatterned using liquid-phase photopolymerization (LP3) with an isobornyl acrylate (IBA)-based pre-polymer (poly(IBA)) [8]. (c) A poly(acrylamide) (PAAm)-based hydrogel membrane is also photopatterned using LP3. The width, ‘w’, is an important factor determining the dissolution time of the hydrogel. The capacitor and channels are covered on the top with a transparency sheet having an opening for sampling the incoming fluid. It is glued to the fluidic channels with a 125µm-thick adhesive tape. The bottom surface of the capacitor and connection channel are made hydrophilic through molecular vapor deposition of a silane-based self-assembled monolayer – mPEG-chlorosilane [9]. This, as well as the fluid pressure created by the sample acquisition system, ensures that the fluid gets inside the capacitor following the dissolution of the hydrogel membrane.

**Table 1. Physical dimensions**

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<th>Capacitor dimensions</th>
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<tr>
<td>Gap between fingers</td>
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<td>Finger width</td>
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<td>Finger height</td>
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<td>Total area</td>
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<td>Capacitance in air</td>
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<td>Number of fingers</td>
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<th>Hydrogel membrane dimensions</th>
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<td>Length (l in Fig. 2c)</td>
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<td>Height (into paper)</td>
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**Table 1** lists the dimensions of the capacitor and hydrogel membranes.
EXPERIMENTAL RESULTS AND DISCUSSION

Functional testing on the capacitor was done using a Karl Suss PM5 probe station and HP4284A LCR meter. Following functionality testing, the capacitor was connected to a DC power supply and an external 470kΩ resistor as shown in Fig. 6(b). The DC output voltage across the resistor was monitored on an oscilloscope.

The target species (here, DTT in Tris buffer of pH 7.4) was flown into the sensor, following which the membrane became porous and dissolved. The dissolution is a complicated multi-step process [6]. The dissolution time depends on two important factors: the width of the hydrogel membrane (Fig. 2(c)) and C_{DTT}. Fig. 4 shows the dissolution time of the hydrogel membrane as a function of C_{DTT}. Fig. 5 shows the dissolution of a membrane over time.

The sampling fluid (Tris buffer pH 7.4) is slightly conductive. Hence, following the dissolution of the hydrogel membrane, the capacitor impedance changes from C=7.5pF to R_c roughly 1kΩ (DC), which can be easily sensed with a circuit (Fig. 6(b-c)). With a DC supply voltage of 2.94V, an output of 2.9V (DC) was obtained. Until the presence and detection of the target species, no DC power is consumed. The output voltage is approximately the same regardless of the input DTT concentration (C_{DTT}) (Fig. 6(a)) since the external voltage dividing resistor (Fig. 6(b-c)) is much larger than R_c at concerned C_{DTT}. Thus, theoretically, the chemical to electrical transduction (V_{out}/C_{DTT}) is infinity, as long as the sensing membrane becomes porous and allows fluid to flow from the sampling chamber to the capacitor.

A scheme to estimate the concentration of the target species has also been proposed. The concentration of the target species cannot be determined by employing a single membrane since the instant at which the target species enters the fluid chamber is random. Hence multiple (here, two) juxtaposed hydrogel membranes of different widths (200µm and 600µm) are used. Due to the difference in widths, these membranes have different dissolution times although exposed to the same concentration of the target species. As shown in Fig. 3, the membranes are placed symmetrically with respect to the sample acquisition point to ensure that the fluid reaches both the membranes at approximately the same instant.

An output signal is obtained from the circuit of Fig. 6(b) following dissolution of each membrane. Hence using two membranes with individual dissolution characteristics, two output signals are obtained. These signals are separated in time by a duration equal to the difference in dissolution times of the two membranes. The concentration can be estimated based on this time difference. For example, referring to Fig. 4, the 200µm wide membrane becomes porous in 843s, whereas the 600µm wide membrane becomes porous in 2058s. Hence two output signals separated by a time duration of 2058-843=1215s are obtained. From the same figure, it can be seen that the concentration is 0.5M, which is the estimated concentration of the target species.

CONCLUSION

We have demonstrated a chemical and biological sensing mechanism based on dissolvable membranes, which provides a large electrical output. No DC power is consumed until the detection of the target species. This bio/chemical sensing mechanism is applicable to wireless microsensor networks. Issues like noise, parasitics, temperature variation, power consumption, and cost are greatly alleviated. The sensing mechanism is also universal: a single sensor structure can serve to...
Fig 5. Images showing the dissolution of a PAAm-based hydrogel membrane in the presence of DTT at various instants of time. The hydrogel width is 600µm and the DTT concentration is 1M. (a) At t=61s after flowing in DTT, there is no visible change in the hydrogel. (b) At t=1200s there is a visible change in the hydrogel. (c) At t=1802s the hydrogel is completely dissolved and the fluid flows into the capacitor.

Fig 6. Sensing the impedance change due to the target species. (a) With a supply voltage of 2.94V, the output is 2.9V DC. This output voltage is approximately the same regardless of the input concentration since the external voltage dividing resistor R0 shown in (c) is much larger than Rc with input DTT concentration (CDTT) of concern. The chemical to electrical transduction (Vout/CDTT) is thus theoretically infinity as long as the membrane becomes porous and allows fluid to flow to the capacitor. (b) The circuit before flowing in the fluid. 'C' is the sensing capacitor (shown in Fig. 1). 'Rc' is an external resistor. (c) 'C' in (b) is transformed to a resistor Rc due to the flow of the slightly conductive fluid into the capacitor by the dissolution of the hydrogel membrane.

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REFERENCES