A MEMS AFFINITY GLUCOSE SENSOR USING PERMITTIVITY MEASUREMENTS

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ABSTRACT

We present a MEMS affinity glucose sensor using permittivity measurements. This device employs a biocompatible glucose-specific polymer as the sensing solution. By introducing the polymer solution between two electrodes, the permittivity of the polymer solution can be measured from the capacitance changes induced by glucose binding. We characterize the frequency-dependent complex permittivity and the specificity of our device. This glucose sensor has potential use in implantable, stable, long-term, continuous glucose monitoring for diabetes management.

KEYWORDS: MEMS, Affinity glucose sensor, dielectric, permittivity

INTRODUCTION

Continuous glucose monitoring (CGM) is extremely useful for diabetes management. Currently, electrochemical detection using partially subcutaneously implanted enzymatic electrodes is the prevailing CGM technique, but is susceptible to biofouling, which causes large drifts that hinder long-term operation. In contrast, affinity-binding-based glucose detection offers accuracies unaffected by biofouling, and is highly attractive for long-term, stable CGM. Unfortunately, both conventional and microscale affinity glucose sensors currently require transduction methods (e.g. volume expansion [1], impedance [2] and viscosity measurements [3]) that may not be amenable to reliable and optimized in-vivo glucose monitoring. To address this issue, we present a proof-of-concept demonstration of a novel transduction method for continuous glucose monitoring, utilizing affinity binding-induced permittivity changes of a biocompatible polymer solution. This method uses a pair of fixed electrodes with no mechanical moving parts, and detects glucose-induced permittivity changes by capacitive measurements. As such, the method can potentially lead to a completely implanted, wireless affinity sensor that is maximally miniaturized and highly reliable CGM for continuous glucose monitoring.

DESIGN

Our permittivity -based affinity glucose detection method employs a solution of a biocompatible glucose-specific polymer poly(acrylamide-ran-3-acrylamidophenylboronic acid) (PAA-*ran*-PAAPBA) [4] which contains phenylboronic acid moieties that specifically bind to glucose. The polymer solution is bound between two parallel-plate electrodes imposed with an AC electric field, which causes the polarization of the polymer manifested as a permittivity. Glucose binding causes the polymer to crosslink, thereby changing the polymer's polarization behavior and hence permittivity. Thus, measuring the capacitance between the electrodes allows determination of glucose concentration. Implementing this principle, our

proof-of-concept device (Figure 1) consists of a pair of parallel-assembled glass coverslips each coated with a thin-film copper electrode. The gap between the electrodes, defined by a photoresist spacer layer, is filled with PAA-*ran*-PAAPBA solution mixed with glucose (Figure 2).

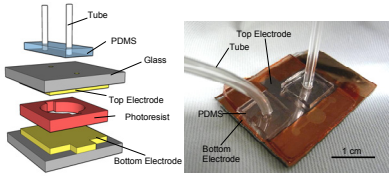

Figure 1. a) Glucose sensor design. Two electrode-covered coverslips are assembled with a photoresist spacer layer. The gap between electrodes is filled with a polymer solution. b) Image of a fabricated device.

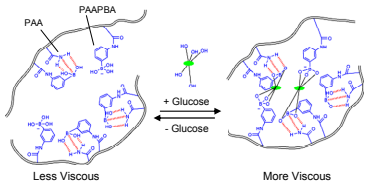

Figure 2. Composition and sensing mechanism of the biocompatible, glucose-sensitive polymer PAA-ran-PAAPBA.

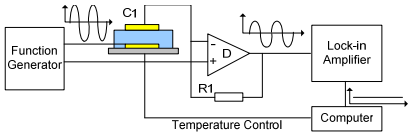

Figure 3. Experiment setup. The output voltage was proportional to the ratio to the sensor capacitance C1 and the resistor R1.

EXPERIMENT

To fabricate the device, copper electrodes were first deposited and patterned on two glass slides. AZ P4620 photoresist was then spin-coated on both slides to prevent the direct contact between polymer solution and the electrodes. Another photoresist layer was then coated and patterned on one of the glass slide to create a chamber for introduction of the polymer solution. Finally, these two glass slides were aligned and glued together by photoresist reflowing.

The capacitance between the electrodes was measured using a capacitance/voltage transformation circuit (Figure 3). The imaginary part of the output voltage, which was proportional to the polymer solution's complex permittivity, was then obtained. We first investigated the specificity of our device by measuring polymer solution premixed with glucose and fructose. The device was then characterized by obtaining the frequency-dependent complex permittivity of the polymer solution at various physiological-relevant glucose concentrations. In addition, the device response to glucose solution (free of polymer) was also demonstrated. Finally, the device stability was assessed over a extended measuring period of about 10 hours to evaluate the device's potential suitability for long-term, stable CGM applications.

RESULTS AND DISCUSSION

First, we investigated the device response (at 10 kHz) to varying glucose and fructose concentrations (Figure 4). As the glucose concentration varied from 0 to 360 mg/dL, the complex voltage amplitude of the circuit decreased monotonically by 10% from 0.149 to 0.135 V while showing virtually no response to fructose, suggesting glucose-specific detection. Next, we investigated the device at additional frequencies (Figure 5). Strong frequency dependence of the device complex permittivity was observed, indicating a frequency-dependent polymer polarization. At any given frequency, the imaginary part of the capacitive circuit output consistently increased with glucose concentration. Measurements with polymer-free glucose solutions showed no response to glucose concentration changes, indicating that the

polymer was critical for dielectrically based glucose detection (Figure 6). Finally, measurements of a polymer solution with 90 mg/dL glucose over 10 hours showed a minimal signal drift of 9 ppm/hr (Figure 7), suggesting an excellent stability, ideal for long-term CGM applications.

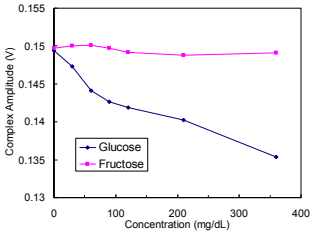

Figure 4. Sensor response (at 10 kHz) at varying concentrations of glucose and fructose (an unspecific analyte).

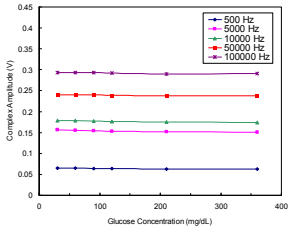

Figure 6. Sensor response to pure glucose solutions (free of polymer) at varying concentrations.

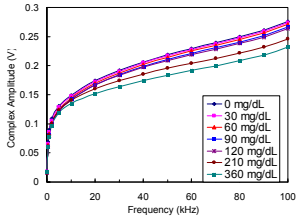

Figure 5. Frequency-dependent capacitance changes of the polymer at various glucose concentrations.

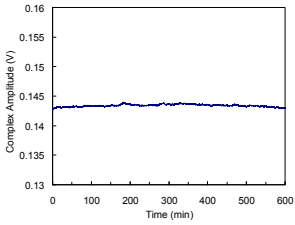

Figure 7. Drift of the sensor at 10 kHz

CONCLUSIONS

We presented an affinity glucose sensor that is based on capacitive measurements of glucose-induced changes in the permittivity of the polymer PAA-*ran*-PAAPBA. The specificity and frequency-dependence of device response were investigated. In addition, the significance of the polymer in dielectric measurements and the stability of the device were demonstrated. This device holds potential to enable long-term and reliable CGM applications.

ACKNOWLEDGEMENTS

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