



Design and Simulation of a Micromachined Glucose Sensor

Shahrouz Khorouji Shabestari

Department of Electrical Engineering

Urmia MEMS Lab.

June 2004

A thesis submitted to the University of Urmia for the degree of Master of
Science in the Faculty of Engineering

Supervisor: Dr. Ebrahim Abbaspour Sani

Co-supervisor: Dr. Khalil Farhadi

۹۲۷۱۳

In the Name of God

Who is in Our Hearts

93713

Urmia University

Title

Design and Simulation of a Micromachined Glucose Sensor

by

Shahrouz Khorouji Shabestari

The Advisory Committee certifies that this thesis complies with Urmia University's regulations and meets the accepted standards for the degree of Master of Science. The rank of the thesis is Excellent with grade: 19.1.

ADVISORY COMMITTEE:

Dr. Ebrahim Abbaspour Sani



Chair

Dr. Khalil Farhadi



Dr. Sattar Mirza Koochaki

Dr. Behbood Mashoufi



Dr. Abdollah Khoei



Signature

Name

To My Parents

And Dear Brother
Amir

Acknowledgements

At the beginning I thank to my God to this scientific success, and I have great thanks to my father, mother and brother, who help me all the time in my life.

I am thankful to my advisors, Dr. Ebrahim Abbaspour Sani and Dr. Khalil Farhadi because of their great helps in my thesis.

I also have special thanks to my teacher Dr. Hadidi.

I would like to thank Mr. Ramin Rahmani because of his help in CFD simulations.

I have thanks to Dr. Pourabbas, Dr. Galichi and Dr. Razavi in Sahand University, for their helps in blood flow analysis.

My thanks also go to all my friends in Urmia MEMS Lab. And Urmia Microelectronic Research Center specially Mr. Oskooi, Mr. Jalili, Mr. Nasirzadeh, Mr. Gadami, Mr. Zare, Mr. Anasari, Mr. Aminolroaya and Mrs. Masoom. I wish them all success in their life and education.

Table of Contents

Chapter 1: An Introduction to MEMS Applications.....	1
1.1 Introduction.....	1
1.2 Medical Applications of MEMS.....	3
1.3 Application in Diabetic Treatment.....	5
1.4 The Objective of Present Work.....	5
Chapter 2: Glucose Detection Methods.....	2
2.1 Introduction.....	7
2.2 Photometric Sensors.....	7
2.3 Amperometric Sensors.....	9
2.4 pH Sensitive Sensors.....	11
2.5 Electro Microbalance Sensors.....	12
2.6 Molecularly Imprinted Polymers (MIP) Based Sensors.....	13
Chapter 3: MIP method.....	15
3.1 MIP Method.....	15
3.1.1 Sensor preparation.....	17
3.1.2 Electron transfer through polymeric film.....	18

3.1.3 Direct detection of glucose.....	20
3.2 Calculation of Glucose-iPPD Interaction Parameters.....	22
3.2.1 Verification of the imprinting effect.....	22
3.2.2 Analytical performances.....	23
3.2.3 Glucose-iPPD interactions.....	23
Chapter 4: Blood Flow in Microchannels.....	15
4.1 The Equation of Continuity.....	27
4.2 The Equation of Motion.....	28
4.3 The Navier-Stokes Equation for an Incompressible Flow.....	28
4.4 Flow at Low Reynolds Number.....	29
Chapter 5: Sensor Design.....	34
5.1 Design of the Electrode Area.....	36
5.2 Sensitivity Calculation for Sensor.....	39
5.3 Simulation of Capacitance Variation.....	43
5.4 Microneedle Design.....	45
5.4.1 Determination of Needle Length.....	45
5.4.2 Design of the Inner Diameter.....	46
5.4.3 Micro Needle Strength.....	51
Chapter 6: Fabrication Process.....	60
Chapter 7: Conclusion.....	70
References.....	75

List of Figures

Figure 2.1: Near-infrared glucose sensor implanted in the body. Its readings transmitted via radio waves to a small display unit on the wrist.

Figure 2.2: Polarization of light in a defined direction and detecting it with special filters.

Figure 2.3: Calibration curve for Kim's sensor.

Figure 2.4: whole amperometric glucose sensor structure.

Figure 2.5: The calibration curve of pH sensitive Sensor (Alexandre A. Shual'ga).

Figure 2.6: Calibration curve for Yin's sensor.

Figure 2.7: Separate extended ENFET measurement circuit with instrumentation amplifier LT167

Figure 3.1: A scheme for imprinting modification of *o*-PD on the gold electrode surface.

Figure 3.2: Cyclic Voltametric responses recorded in an $\text{Fe}(\text{CN})_6^{3-}$ solution when the measuring electrode was: (a) bare gold, (b) gold modified with polymeric layer, (c) as in (b) with additional modification with 1-dodecanethiol. All scans were performed in aqueous $10 \text{ mmol l}^{-1} \text{ K}_3 \text{ Fe}(\text{CN})_6 + 1.0 \text{ mol l}^{-1} \text{ KCl}$ solution. Scan rate: 100 mV s^{-1} .

Figure 3.3. Impedance spectra of gold electrode obtained for various conditions in $10 \text{ mmol l}^{-1} \text{ Tris} + 100 \text{ mmol l}^{-1} \text{ NaCl}$ buffer solution (pH 7.14). Curve (a): Impedance spectrum for the bare gold electrode surface. Curve (b): Spectrum after electro polymerization of *o*-PD. Curve (c): Spectrum after subsequent modification with 1-dodecanethiol. Amplitude, 10 mV ; d.c. potential, 0 V .

Figure 3.4: Impedance response for the molecularly imprinted *o*-PD gold electrode in $10 \text{ mmol l}^{-1} \text{ Tris} + 100 \text{ mmol l}^{-1} \text{ NaCl}$ buffer solution (pH 7.14) (a), and in a solution containing an appropriate concentration of glucose, 5 (b), 10 (c), 15 (d) and 20 mmol l^{-1} (e).

Figure 3.5: The calibration plot for glucose. Experimental conditions are same as those in Fig. 3.3. The capacitance was obtained at a frequency of 10 Hz from Fig. 3.3.

Figure 3.6: (a) QCM response of an iPPD-based sensor to glucose injection. (b) calibration curve for the sensor.

Figure 3.7: Scatchard plot relevant to calibration curve in Fig. 3.5b

Figure 4.1: Schematic of whole sensor. A) out view. B) inner view from AB cross section

Figure 4.2: The force dF on a small surface element dS , exerted by the fluid on the positive side [40].

Figure 4.3: Comparison of present results with the literature. The curves are not supposed to be identical as they are measured on different samples [40].

Figure 4.4: The figure shows the viscosity for different blood constitutive equations, which have been derived from different blood samples. The plotted Walburn and Schneck and Power Law (Blood) model are the default models in the CFD-ACE+ package [40].

Figure 5.1: filled chamber (a), electrical model of the filled chamber(b), simplified model of chamber(c).

Figure 5.2: Whetstone bridge to detect the capacitance variation

Figure 5.3: Output voltage diagram for different C_d values.

Figure 5.4: a) capacitor plate, shows the filled and empty sites. b) simple model of capacitance

Figure 5.5: Comparing our sketched model with the Chang's measurement.

Figure 5.6: Linear estimation of our model in the human blood glucose concentration range.

Figure 5.7: Linearization error in the range of human blood glucose concentration range.

Figure 5.8: Voltage variation around the two plates of capacitor.

Figure 5.9: Electric field around the plates of capacitor. A) whole capacitor. B) Zoomed on the left corner.

Figure 5.10: Variation of an ideal capacitor (stream line) and our simulated capacitor (cross) versus permittivity.

Figure 5.11: Cross section of human skin [46]

Figure 5.12: 2D simulation for micro needle with a diameter and length of $10\mu\text{m}$ and 3mm respectively. Velocity vectors are shown in the figure their colors differ according to their amplitude.

Figure 5.13: Blood average velocity for microneedle with various diameters. Length of the microneedle is 3mm .

Figure 5.14: Variation of blood average velocity in the microneedle versus length of needle. Width of the microneedle is $30\mu\text{m}$.

Figure 5.15: The symmetry of B and H is shown.

Figure 5.16: Stress distribution at bending mode for microneedle with 40 μ m inner diameter and 30 μ m wall thickness and applied force of 0.07N. Simulation is done by ANSYS 5.4 software.

Figure 5.17: Stress distribution at buckling mode for microneedle with 40 μ m inner diameter and 30 μ m wall thickness and applied force of 0.3N. Simulation is done by ANSYS 5.4 software.

Figure 5.18: Stress distribution in the skin and along the needle during the insertion of the needle into the skin. (Before insertion)

Figure 5.19: Stress distribution in the skin and along the needle during the insertion of the needle into the skin. (after 100 μ m insertion)

Figure 5.20: Stress distribution in the skin and along the needle. Force is applied to the back side of the needle and needle has a deviation degree of 15° from orthogonal axis.

Figure 6.1: Fabrication process steps.

Figure 6.2: Mask 1.

Figure 6.3: Mask 2.

Figure 6.4: Mask 3.

Figure 6.5: Mask 4.

Figure 6.6: Mask 5.

List of Tables

Table 4.1: several models that have been proposed to show non Newtonian behavioral of blood [41].

Table 4.2: Parameters for simple power law constitutive equations [40].

Table 5.1: primary considered at sensor designing procedure.

Table 5.2: Glucose concentration range in human blood.

Table 5.3: Blood velocity and net flow rate in micro channels with different diameters

Table 5.4: Max. stress in the microneedle for applied bending force of 0.07N and inner diameter of 40 μ m, with different wall thickness.

Table 5.5: Mechanical characteristics of polysilicon and human skin.

Table 7.1: Comparing the parameters of this work to other non-micromachined previous works

Table 7.2: Comparing the parameters of this work to other micromachined previous works

Abstract

A micromachined blood glucose concentration sensor for medical application is designed and simulated. The proposed sensor is based on Molecularly Imprinted Polymers (MIP) method. Sensor structure includes a reaction chamber, electrodes, and a microneedle. The glucose concentration is measured by impedancemetry which is a well known method in electrochemically measuring systems.

Several glucose detection methods are described and their opportunities in micromachining technology are studied. Then MIP method is introduced as the best method for glucose measurement procedure. Its advantages are high sensitivity, high durability, high selectivity, enzyme free structure and reaction free measuring procedure. The blood flow in microchannels was simulated by FLUENT 5.2 software. Microneedle strength was simulated by ANSYS 5.4 software.

The overall microneedle dimensions were designed and determined. These designed parameters include length of the microneedle, electrode area, inner diameter of the microneedle and its wall thickness.

A model was proposed for sensor sensitivity versus glucose concentration, and an electrical model of sensor was sketched. Sensor has a precision of about 10mg/dL.

A detection circuit was designed for measuring the capacitance variation. This circuit provides a sensitivity of 10mV/nF, which resulted a total sensitivity of 1.5mV/unit for the sensor, where unit equals to 10mg/dL.

Finally fabrication steps were proposed and the appropriate masks were designed. It must be mentioned that, MIP based glucose micromachined sensor has not been developed yet.

The proposed sensor has: 1) Better measuring method compared to previous micromachined sensor. 2) Small area (6mm^2) which is suitable for batch processing. 3) small response time and 4) High sensitivity.

Chapter 1

An Introduction to MEMS^{*}

Applications

1.1 Introduction

The use of silicon micro sensors is increasing at high rates since micromachining has become a more or less mature technology. These sensors are used in great numbers, specially in automobiles, process control, in the medical field and for scientific instrumentation. Market studies in the past years (mid nineties) have predicted an enormous increase in the need of these sensors. Recent predictions on market volumes of microcomponents are in the range of US \$ 100 billion annually in Europe alone [1].

The production price for these sensors has dropped well below one dollar per piece. This dramatic development is due in first instance to the way microsensors are fabricated. The technology derives from integrated circuit fabrication technology where the production price per piece is roughly reciprocal to the number of fabrication units. This

*Micro Electro Mechanical Systems

production method is called “ batch processing “ where a large number of components are made at the same time. Basically silicon is machined using etching techniques, thin film deposition and wafer bonding. This fabrication method is now known as “ silicon micromachining “. Silicon micromachining has become reliable, which is a second important reason for the commercial success of microsensors.

In many technical systems there is a strong trend for miniaturization. This trend results on one hand from the fact that small components and systems perform differently: small systems can perform actions, large systems can not (example: minimal invasive surgery). In many cases a miniaturization makes the system more convenient (e.g.: GSM telephone). On the other hand technology derived from IC fabrication processes allows the production of miniature components in large volumes for low prices (e.g.: pressure sensors for automobile applications, ink jet printers) [1].

Micromachining is very complex and not developed to a standard technology. The process space is still largely unexplored. When designing a microsystem, the fabrication process of the system must be designed, too. Thus system design and process design are integrated in a single design process. Microsystems designers, there fore, must have a large number of skills and a rather broad experience. This is a quite different from IC design and processing. For IC processes, there are strict and clear design rules which guide the circuit designer, and he does not have to worry how the circuit is actually made. Microsystems designer must be able to design both the system and the fabrication process.

Usually Microsystems have complex functions. The functions have roots in different physical domains. For a sensor this is clear, a sensor must transmit a signal from a particular domain (chemical, mechanical, thermal) to the electrical domain. A sensor designer must of course know the domains to which the sensor has ports. As an example, in a pressure sensor a membrane is deformed and the deformation is the measure for the pressure. The sensor designer must know the mechanical properties of membranes. The deflection of the membrane can be measured for example by optical interferometry. In this case the designer must know optics as well. The designer must know how to treat his (usually) small electrical signal, how to amplify it, how to realize the interfaces to a computer, so he must have knowledge of electronics, too. Therefore, sensor designers are

Jackes of all trades. In practice, they have to work in groups of engineers of different colors, and understand enough of other disciplines in order to be able to communicate.

The use of lithographic and other fabrication technologies to create miniaturized sensors, actuators and structures has become increasingly popular in many areas of science and engineering. In order to fabricate such devices, the addition, subtraction, modification and patterning of materials are typically done using techniques originally developed for the integrated circuit industry. In the late 1960's, researchers began to appreciate the fact that silicon and other semiconductors could be used to fabricate not only discrete and integrated electronic circuits, but also transducers and other devices with new properties due to the materials used and their miniature size[2]. The term micromachining broadly refers to the use of lithographic and other precision techniques to carry out such fabrication.

The interdisciplinary nature of both micromachining techniques and their application can and does lead to exciting synergies. Use of these technologies has result in an unprecedented range of devices that can be employed in applications through either displacement of macroscopic competitors or by enabling functions that are otherwise impossible. It is the latter case where the use of micromachining can be most effective in creating new capabilities and products [2].

In many cases, the use of these miniaturization technologies confers advantages beyond the obvious decreases in physical volume and weight, such as increased performance and reliability, and decrease cost. We also must say that miniaturizing of some systems wont be a modification. In other hand it is impossible to miniaturize all systems. For example when miniaturizing clinical diagnostic instruments, in many cases the sample volumes required to obtain statistically valid samples of bacteria or viruses are many times larger than the microstructures themselves. (Potentially reducing throughput if they must routed through microfluidic devices).

1.2 Medical Applications of MEMS

Much is expected for application of micromachine technology in the medical field. Recently, less invasive diagnosis and treatment that harms the body less and gives the