Research Article

Design of Microcantilever-Based Biosensor with Digital Feedback Control Circuit

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This paper present the design of cantilever-based biosensors with new readout, which hold promises as fast and cheap "point of care" device as well as interesting research tools. The fabrication process and related issues of the cantilever based bio-sensor are discussed. Coventorware simulation is carried out to analyze the device behavior. A fully integrated control circuit has been designed to solve manufacturing challenge which will take care of positioning of the cantilever instead of creating nanometer gap between the electrodes. The control circuit will solve the manufacturing challenge faced by the readout methods where it is essential to maintain precise gap between the electrodes. The circuit can take care of variation obtained due to fabrication process and maintain the precise gap between the electrodes by electrostatic actuation. The control circuit consist of analog and digital modules. The reliability issues of the sensor are also discussed.

1. Introduction

The cantilever-based Bio-MEMS sensor represents one instance from many competing ideas of biosensor technology based on Micro-Electro-Mechanical Systems (MEMS). The advancement of Bio-MEMS from laboratory-scale experiments to applications in the field will require standardization of their components and manufacturing procedures as well as frameworks to evaluate their performance [1, 2]. Identification and quantitative analysis of biological molecules are critical in disease detection and monitoring, drug discovery, and many fundamental problems in molecular biology. The major characteristics of biosensor are that they need to be very specific; they need to be able to detect a specific molecule (a specific antibody e.g.) at very low concentration. This is necessary for two reasons. The response time and cost of detection are reduced if a smaller sample is needed for detection, and more importantly, most diseases can be cured if they are discovered at an early stage [3].

Micro- and Nano-Electro-Mechanical systems (MEMS and NEMS) are designed mostly for detecting and sensing specific bimolecular at very low concentration. The sensing principal varies according to the device, the nature of the analyte molecules, and the precision required. Micrometer-sized cantilever devices can be used as very sensitive and simple biochemical sensors in ambient and aqueous environments. The cantilever structure has a low flexural resistance it responds mechanically to changes in the surface stresses on its surfaces. Even as early as 1909, Stoney observed that the deposition of a tensile film on another material caused a curvature in the composite structure due to residual stresses in the deposited film [4]. Cantilever structures are susceptible to this phenomenon which has been exploited for sensing purposes. Although this process was facilitated by the availability of refined microcantilever readout schemes and microfabricated microcantilever probe, cantilever transducers for specific analytical application are still in their infancy due to the manufacturing issues [5].

The biochemical reaction at the cantilever surface can be monitored as a bending of the cantilever, due to a change in the surface stress. For biorecognition, one cantilever surface is made biosensitive by depositing a sensing layer onto it. Ethir this layer contains the bioreceptors or the bioreceptors are covalently bonded to it. This process is known as functionalization. The reaction between an analyte and its

bioreceptor molecule is unique. The most common forms of bioreceptors used in biosensing are based on proteins, antibody/antigen, or nucleic acid interactions. In particular, chemical or biological reactions on one surface of a microcantilever beam were found to change its surface free energy density or surface tension due to modifications in interactions between neighboring molecules, which then produced a bending moment that deflected the cantilever [6]. Since the cantilever deflection depends on the molecular species and its concentration, by measuring the cantilever deflection the attaching species as well as its concentration can be determined [7].

The deflection of these devices can be detected using various techniques such as optical reflection, piezoresistive, interferometric, piezoelectric, capacitive, and electron tunnelling. The optical method employing low-power LASER and position-sensitive photodetector is the major effective method for detection. Optical detection method required extra hardware for detection and sensing, hence the size of the device is larger [8]. Due to its requirement for costly and highly sophisticated instrumentation and very precise mechanical alignment, it is not suitable for routine low-cost disease diagnosis. The capacitive method does not work in electrolyte solution due to the generation of Faradic current between the capacitive plates and is therefore limited in its sensing applications. The interferometric methods work well for small displacements but are less sensitive in liquids [9, 10]. The electrical detection method which we developed described in Section 2 is more suitable for this purpose since it involved a simpler setup as compared to the former which involved a LASER detection system. The fabrication process of the microcantilever-based biosensor is discussed in Section 3. The device design was done with Coventorware and presented in Section 4.

The main problem in these detection methods is the measurement of deflection which is in nanometers in response to biostress. Manufacturing of such cantilever devices now face the challenge of creating precise gap. The positioning of the cantilever is controlled by the feedback control circuit described in Section 5. The control circuitry will provide the predetermined deflection in the device instead of creating a gap in nanometers between the electrodes during fabrication, which is very difficult using conventional etching process. The control circuit design and its implementation are discussed in Sections 6 and 7. The reliability issues are discussed in Section 8 followed by discussions on results and conclusion.

2. Microcantilever-Based Biosensor

We propose the new design for detection of biomolecules shown in Figure 1. The cantilever deflection is measured in terms of current flowing through the electrode. The cantilever is placed close to a rectangular-shaped electrode. The cantilever touches the electrode when the surface stress due to interaction between antibody/antigen exceeds the particular limits. By measuring the current the amount of antibody/antigen attached to the cantilever beam surface can be detected. The current is inversely proportional to the
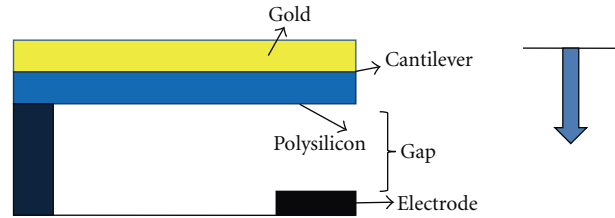

FIGURE 1: Microcantilever-based biosensor.

contact resistance. The contact resistance varies with contact area.

Optimum cantilever size of a length of 100 um, 35 um wide and 0.5 um thick was designed by optimizing parameters such as spring constant, bioinduced stress, and stability in the flow field. The cantilever structure is designed in Coventorware shown in Figure 2(a). On the top side of the cantilever that is, on the sensing side, antibodies are deposited. Specific biomolecular interactions between antibodies and antigen alter the intermolecular interactions within the biolinker layer. As a result, the cantilever is bent as shown in Figure 2(b). The process to fabricate the device is described in Section 3.

3. Fabrication Process and Related Issues

Proposed device can be fabricated by standard surface micromachining process. Fabrication process incorporates four different photomasking levels as shown in Figure 3. These steps are combinations of material deposition and etching techniques used to control the film uniformity, the beam lengths, thickness, and the final gap between substrate and structure. The fabrication process begins with the deposition of an isolation layer on top of the silicon substrate. This process can also utilize the isolation and metallization layers available on a CMOS processed wafer. This step is followed by the deposition and patterning of a doped polysilicon layer, which will serve as the first or bottom electrode. Next, sacrificial layer is deposited on top of the polysilicon layer and patterned; this step is followed by the deposition and patterning of a $0.5\,\mu$m thick polysilicon to create the first layer of the cantilever beam. Polysilicon is used as the structural material. On top of this layer, $0.3\,\mu$m thick gold layer is sputtered and patterned to form the sensing surface. Metal is the top layer of the device and can be used as conductive layer. On this surface, biomolecular interaction takes place and the binding event is transduced into an electric signal.

The adsorption of biomolecules on the surface of the microcantilever changes its surface characteristics and results in its bending. The surface stress is of the order 0.005 N/m–0.5 N/m, which results in bending of the cantilever to the tune of a few tens of nanometer. The major issue for the device fabrication is the creation of the precise gap between the electrodes of this order. During etching process there is variation in thickness of about 10%. This will affect the sensitivity of the device. This problem is common in all the detection methods reported earlier. To improve the sensitivity of the device we have designed the feedback control circuit
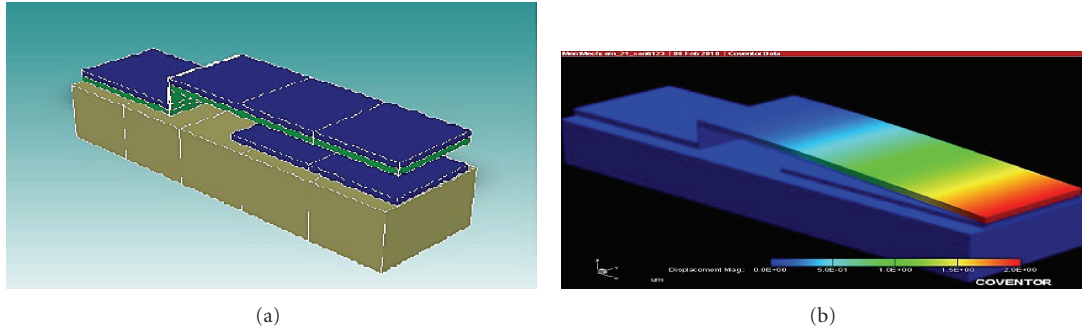
FIGURE 2: (a) Cantilever structure designed in coventorware (initial state). (b) Cantilever bending due to biomolecular interactions (final state).

P type < 100 > wafer high resistivity RCA cleaning

Thermal oxidation wet 100 nm

Doped polysilicon deposition

Patterning bottom electrode-mask 1

Deposit and pattern sacrificial layer-mask 2

Deposit polysilicon

Polysilicon patterning-mask 3

Metal deposition gold sputtering

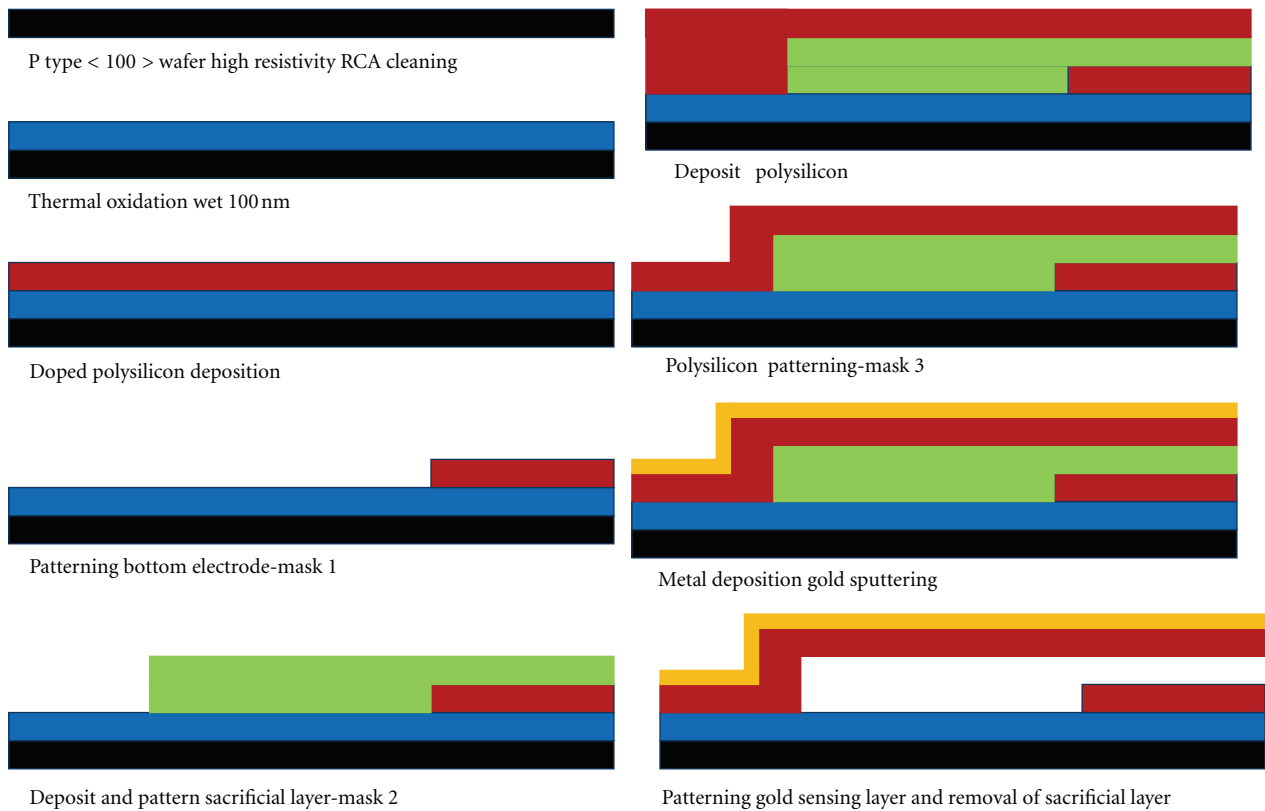Patterning gold sensing layer and removal of sacrificial layer

FIGURE 3: Fabrication steps of microcantilever-based biosensor.

which will take care of positioning of cantilever for optimized results. This feedback control circuit will solve the problem of creating a gap which is in nanometers. We will fabricate the device having 2 μm gap between the electrodes. Which will easily created by conventional fabrication process describe in Figure 3. The device design using above steps is done in Coventorware. Analysis of the device simulation is carried and presented in Section 4.

4. Design and Analysis

The cantilever structure is designed and simulation is carried out using Coventorware software. The corresponding deflection with respect to stress and voltage is studied. The cantilever under study is shown in Figure 2. The cantilever is of polysilicon having dimension $100 * 35 * 0.5 \mu$m. The gold is used as sensing layer having thickness 0.3 um.

The following steps were employed to design the cantilever structure in Coventorware:

(1) defining a process, that is, a series of deposit, etch steps of different materials on a silicon substrate specifying an appropriate mask;

(2) designing a mask layout to generate a model;
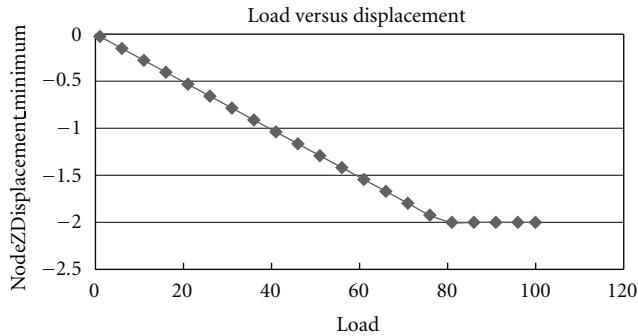
(3) generating a solid model using the above two steps.

Load versus displacement

FIGURE 4: Load versus deflection(NodeZDisplacement_minimum).
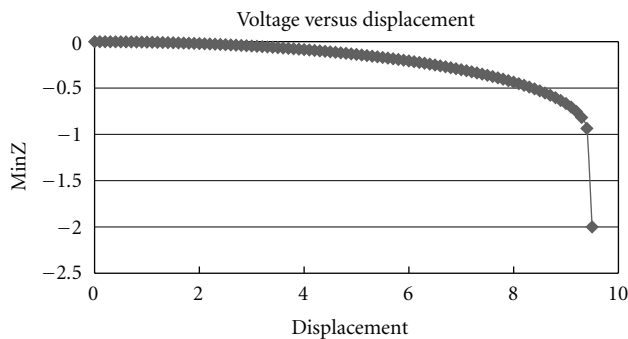
Voltage versus displacement

FIGURE 5: Voltage versus deflection(MinZ) (0 volt–10 volt).

The solid model so obtained is then appropriately partitioned into meshable and nonmeshable parts. To reduce the computational load only the active part of the model (cantilever) is meshed. Boundary conditions (force, voltage) were applied to the mesh model.

The MemMech and CoSolve module in Coventorware is used to carry out the simulation.

Surface stress is generated due to interaction of antibodies with antigen which deflects the cantilever. Stress analysis for the value 0.005 N/m–0.5 N/m is observed and shown in Figure 4.

In Figure 4 x-axis represent the load varied from 1–100 which corresponds to the stress value 0.005 N/m–0.5 N/m with step size 5. The NodeZDisplacement_minimum represented on the y axis is in micrometer. We propose the use of electrostatic actuation to achieve the desired gap between two electrodes. Following analysis is done to understand the behavior of cantilever with applied voltage. The applied voltage is varied between 1 volt–10 volt and the corresponding deflection is observed which is shown in Figure 5. The Minz on y-axis represent the deflection in Figure 5 which is in micrometer.

This experiment shows that after 9 volt the beam and electrode are in contact. The desired gap between the electrodes can be achieved by electrostatic actuation. The necessary hardware is required to design which will supply the voltage to achieve the desired gap between the electrodes.

Arntz et al. [11] reported that a maximum surface stress of 0.05 N/m is generated upon injection of $50\,\mu g\,mL-1(\sim 2.5\,\mu M)$ myoglobin protein onto the functionalized silicon

cantilever and produced a maximum deflection of $0.9\,\mu m$ at cantilever free end. When the surface stress exceeds the particular limit the cantilever deflection increases and the beam and the electrodes are in contact. Contact resistance decreases with increase in contact area and hence the current flowing through the electrode increases which is monitored. This change in current will determine the change in the surface stress.

We have designed the feedback control circuit which will create a precise gap between electrodes for accurate measurements, which is discussed in Section 5.

5. Feedback Control Circuit

In this design the distance between the electrodes is kept as $2\,\mu m$. The predeflection of the cantilever required to maintain the precise gap between the electrodes can be obtained by applying the voltage between the cantilever surface and bottom electrode. The positioning of the cantilever is decided by control circuitry shown in Figure 6. The finite state machine (FSM) will provide the reference voltage through DAC 2 to the comparator to achieve the desired gap between the electrodes. Once the positioning of the cantilever is decided, FSM will switch to next state indicating the application of biomolecules on the functionalized cantilever surface for the biosensor application. The simulation result of the control circuit is presented in our previous paper [12].

5.1. Circuit Description. The circuit operates as follows; initially applied voltage is zero and the cantilever and bottom electrode are not in contact hence the current through the cantilever-based sensor is zero. The output of current to voltage (I to V) convertor is zero, which gives zero digital output from analog to digital converter (ADC). Digital output is applied as input to OR gate. As all the inputs of OR gate are at logic zero the output of OR gate is zero. This logic state (Output of OR Gate) is input to the Finite State Machine (FSM) shown in Figure 7. The FSM has been designed to provide (increment/decrement) operation of supply voltage depending on the input logic state, which is "1" when there is current and "0" when there is no current. Initially there is no current (State 0); it will increment the counter. This counter value is then converted into analog voltage by digital-to-analog converter (DAC1) and applied to the cantilever sensor. Due to the applied voltage, the cantilever gets deflected and gap between cantilever and electrode decreases. Due to this process the voltage across the cantilever increases till the current starts flowing through the cantilever and the electrode (State 1).

At certain voltage, the electrostatic forces overcome the stress forces. The system becomes unstable, and the gap collapses this voltage decides the level of predeflection. In our case the predeflection voltage is that applied voltage levels to the cantilever, if we increment it by one step the gap collapses and the cantilever and the bottom electrodes are in contact. The current starts flowing through the cantilever. The equivalent voltage will get generated through I to V convertor and is converted to digital value through ADC. As there will
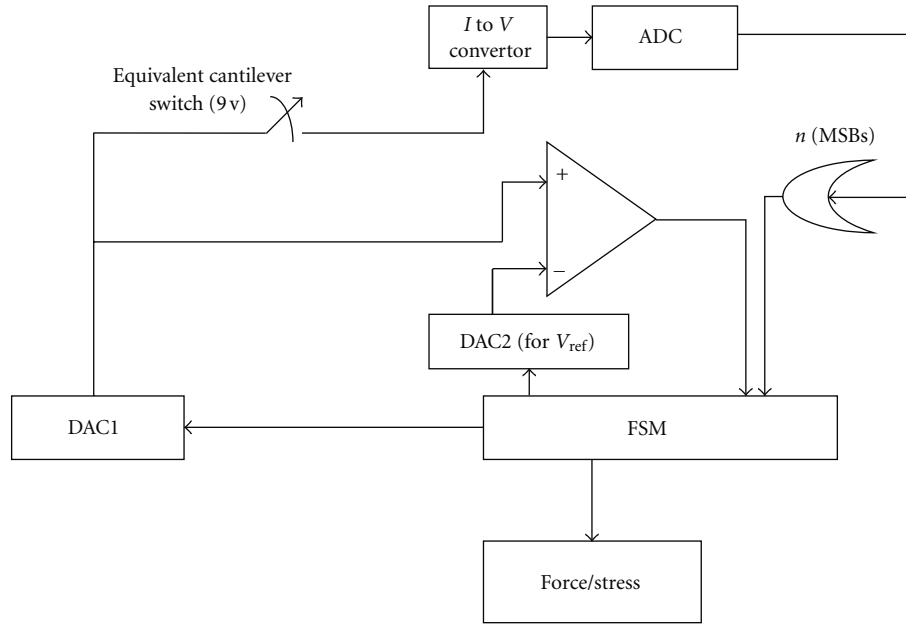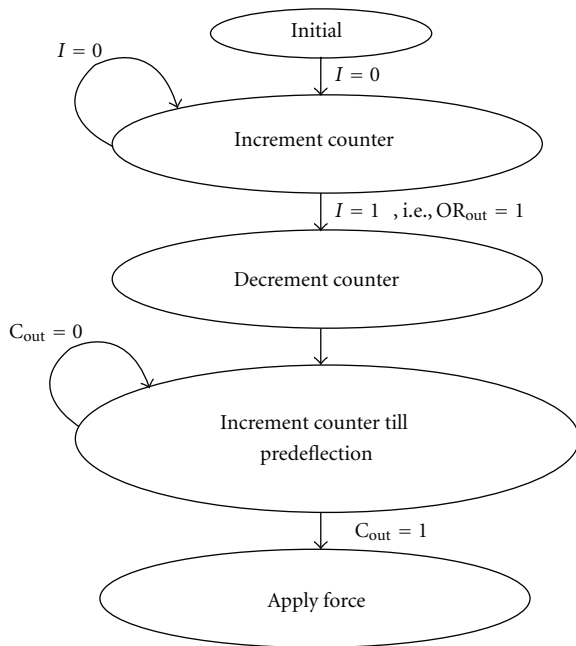
FIGURE 6: Feedback control circuit.

FIGURE 7: State diagram for FSM.

be at least one of the input of OR gate is at logic level "1", output of OR gate will be "1".

FSM will get input as logic "1", and it enters into the next state; now it will decrement the voltage at the cantilever through counter and DAC1. The cantilever will regain its original position; the current will reduce to zero. To avoid the noise we have to use MSBs of ADC output ignoring 2 or 3 LSBs.

Now, the predeflection reference voltage is decided by FSM and applied as one of the inputs to the comparator through DAC2. Second input to the comparator will be the output of DAC1. Now, FSM gets input as logic "0" and again it will increase the voltage till we get the equivalent voltage level of predeflection. Thus the positioning of the cantilever is achieved. Now we are able to achieve the precise gap between the cantilever and bottom electrode. With small applied stress the gap collapse and current start flowing through the sensor which will be monitored on the display.

FSM will switch to force/stress and will display that now to apply stress on cantilever beam (function of antigen attached to the cantilever surface). Due to this stress developed on cantilever, it starts bending and is in contact with the bottom electrode. The contact area between cantilever and electrode increases as stress increases. As the contact area increased the current increases and this current is monitored. The value of current is proportional to the amount of antigen attached to the Cantilever surface.

The system has been implemented by RTL coding in Verilog for the FSM. The FSM will calculate the prestressing voltage which may vary because of change in dimensions of the cantilever. FSM will first increment the voltage till we get contact between the cantilever and bottom electrode. Once this voltage is known it will store that value, which may be different for different dimensions of the cantilever. Thus the effect of uncertainty in dimensions on the prestressing voltage can be handled by the FSM in the control circuit.

6. Details of Implementation

For the design of cantilever, parameters reported by Arntz et al. [11] were used as a reference. A maximum surface stress of 0.05 N/m is generated upon injection of
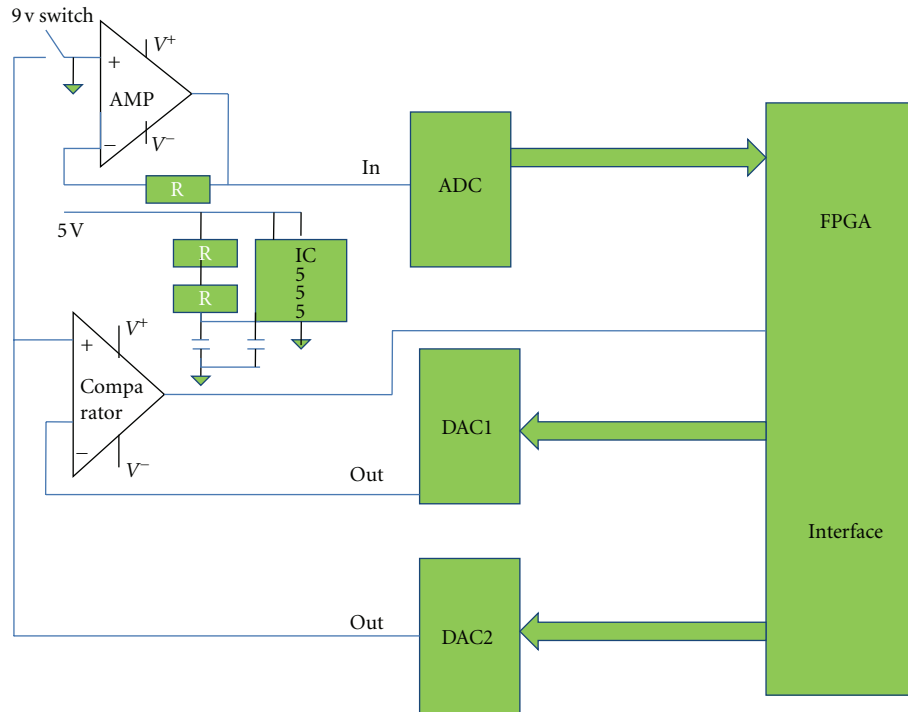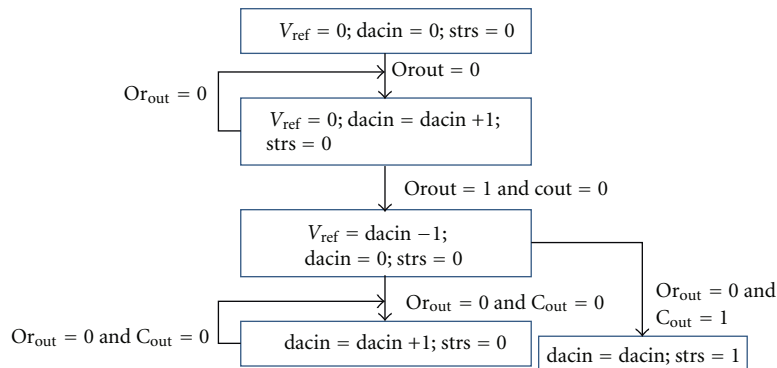
FIGURE 8: Interfacing analog module with FPGA.

FIGURE 9: Finite state machine.

$50 \, \mu\text{g mL} - 1 (\sim 2.5 \, \mu\text{M})$ myoglobin protein onto the functionalized cantilever [11].

In our design initial gap between the electrode and cantilever is $2 \, \mu\text{m}$. Initially cantilever is not in contact with bottom electrode, value of the current is zero (state 0) and FSM starts incrementing the voltage across the cantilever. When the output of DAC1 is 9 volt the cantilever and bottom electrode are in contact with the current that started flowing (State 1). The required predeflection value is 8 volt where the cantilever is not in contact with electrode. Due to positioning of the cantilever by electrostatic actuation (in this case it is 8 volt which is determined by FSM), even though the stress developed on the cantilever surface is very small (of the order of 0.05 N/m) the current will flow through the cantilever as it is in contact with bottom electrode. If the stress value increase further the magnitude of current will

further increase which is proportional to the amount of antigen attached to the beam surface. If we calibrate the device the output current of the biosensor will detect the amount of antigen attached to the functionalised cantilever surface. The current across sensor increases with increase in concentration of biomolecules which is to be monitored on the display.

7. Result and Experimental Validation Using Test Circuit

The feedback control circuit consists of analog and digital modules. A digital circuit is implemented using FPGA platform and analog circuit implemented on PCB. We have interfaced both analog and digital systems shown in Figure 8. We have used 9 volt relay in the test circuit for

(a)

(b)

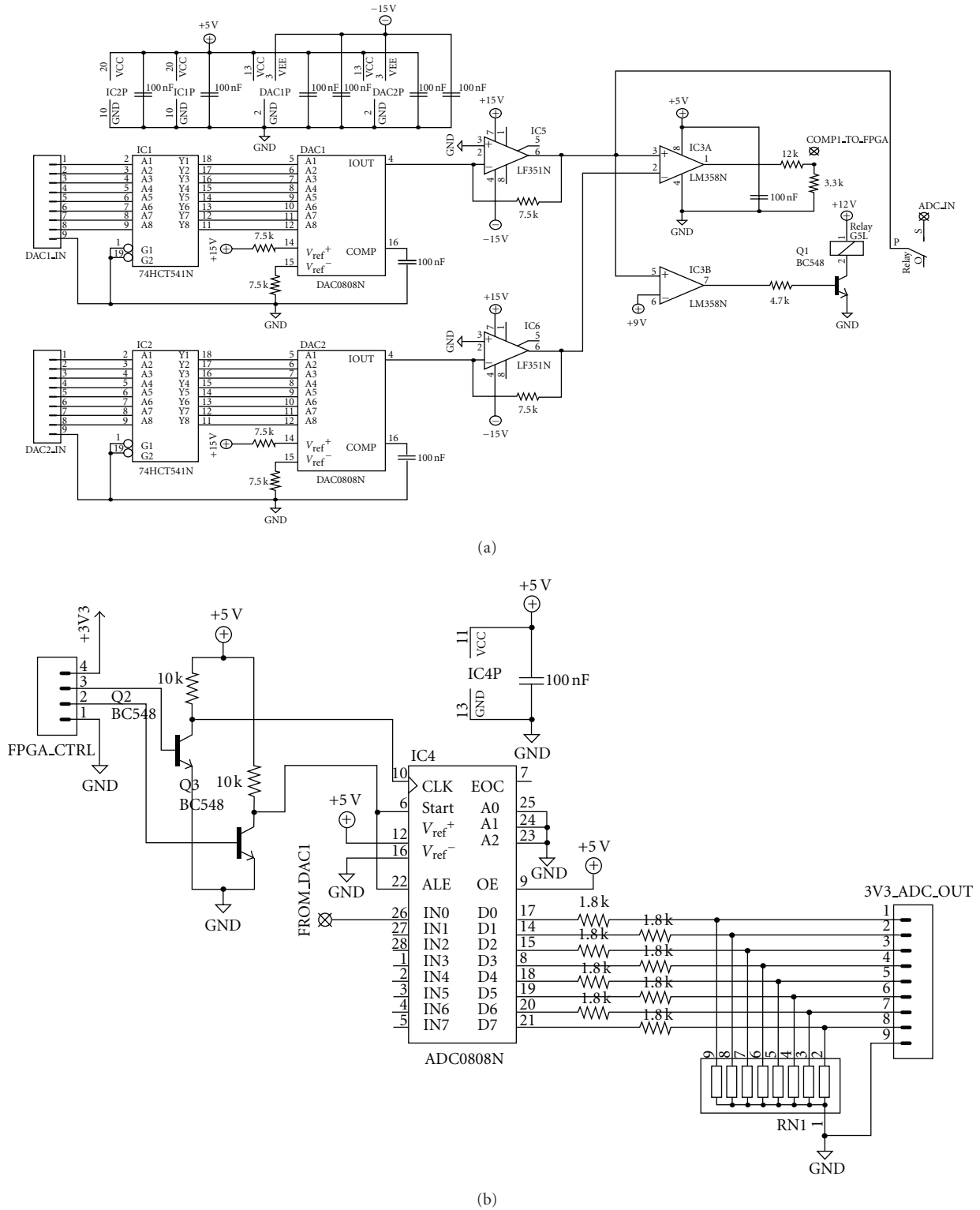Figure 10: (a) Analog modules developed on PCB. (b) Analog modules developed on PCB.

the representation of cantilever sensor. (In Coventorware analysis, the cantilever beam touches the electrode at the 9 volt and current flows through it.)

7.1. Digital Module on FPGA.

Figure 9 shows the state diagram for FSM which consists of 4 steps to carry out incrementing and decrementing voltage across cantilever beam.

The code for the design is written in Verilog language and the synthesis results are verified using Xilinx ISE 9.2i.

7.2. Analog Module on PCB. The circuit diagram for the analog module is shown in Figures 10(a) and 10(b). The circuit is implemented on PCB and interfaced with SPARTAN-II FPGA Kit on which digital module is implemented. The results are verified using the test circuit.

8. Reliability Issues of the Cantilever-Based Sensor

In this work the electrostatic actuation is used to achieve the desired gap between the electrodes in the cantilever-based sensor. Coventorware simulation results shown in Figure 5 indicates, that above 9 volt the contact is achieved, the contact area is around $816.67 \, \mu m^2$, and the contact resistance is 3.33 Ω. Above 9 volt current is around 3 Amp and flows through the cantilever which is sufficient to damage the poly-to-poly-contact due to electro-thermo-mechanical (ETM) effects due to Joule heat generated at the contact areas. This heat is due to the current through the electrodes, characteristics of the contact interfaces, and other physical parameters of electrodes. It significantly raises temperature of the contacts, thus affecting the mechanical and electrical properties of the contacts, which may lead to welding or melting causing a major reliability issue. It is necessary to study the ETM effects to minimize the Joule heat effects on the contact areas, thus improving performance of the sensor [13, 14]. One of the ways to reduce Joule heat is by limiting the current through the cantilever. In order to do so, the design of the sensor should be optimized. In order to minimize the current through the contact interface, a resistor can be placed in series with the supply voltage thus reducing the current flowing through the contacts.

Fusing currents of different kinds of wire were investigated by W. H. Preece [13, 15], who developed the formula

$$I = a^* d^{3/2}, \tag{1}$$

where I is fusing current in amperes, d is diameter of the wire in inches, and a is a material-dependent constant.

The fusing current calculated with this model, for the polysilicon contacts in our design, is around 3.3 mA. The current-limiting resistor of 10 KΩ is added in series with the supply voltage for limiting the current to protect the cantilever. The maximum 1.5 mA current will pass through the contacts, which is below the fusing current limit.

The insertion of a limiting resistor will avoid the damage of the cantilever. However, this resistor will reduce the sensitivity of sensor substantially. With the proposed values (3.3 Ω contact resistance and 10 kΩ limiting resistor), a huge variation of the contact area (and thus contact resistance) induced by the stress (say from 3.3 Ω to 1.5 Ω) only results in a 1.5/10003.3 or 150 ppm relative variation of the measurement current, thus making an accurate measurement of the analyte extremely challenging. Although with available opamps/instruments it is possible to measure current with 1 ppm resolution and below [16]. To improve the sensitivity of the device, the different circuit-topology-like current fold-back technique, differential current measurements may be used which will protect the cantilever without compromising for the sensitivity. These methods are under investigation.

9. Conclusion

In the literature most of the microcantilevers are being proposed for disease detection such as cancer and heart infraction. Most of the designs rely on optical readout method which is bit complex and difficult to fabricate. We have designed simpler device, which gives electrical signal in terms of current and can be measured easily. New readout method is designed. The Coventorware simulation results are presented and analysed. A fully integrated control circuit for microcantilever-based biosensor has been designed to solve manufacturing challenge which is common in all readout methods. The feedback control circuit is design which is composed of analog and digital modules. Finite state machine is designed to provide increment and decrement operation of the control voltage across cantilever depending on the input logic state. Predeflection voltage level is decided by FSM which will take care of variation obtained due to fabrication process. The effect of dimensional uncertainty on the prestressing voltage can be handled by the FSM in the control circuit. The results are experimentally validated using the test circuit and SPARTAN-II FPGA Kit. The precise gap between electrodes is adjusted by electrostatic actuation. In the polysilicon cantilever due to the joules heating effect cantilever may get damage with high-voltage application. To protect the cantilever from the damage, the current-limiting resistor is connected in series with the control voltage which may reduce the sensitivity. The measurements could be improved by using the precise current to voltage convertor or other topology.

References

[1] S. Kumar, R. P. Bajpai, and L. M. Bharadwaj, "Lab-on-a-chip based on BioMEMS," in *Proceedings of the International Conference on Intelligent Sensing and Information Processing (ICISIP '04)*, pp. 222–226, January 2004.

[2] K. C. Cheung and P. Renaud, "BioMEMS in medicine: diagnostic and therapeutic systems," in *Proceedings of the IEEE European Solid-State Device Research Conference (ESSDERC '05)*, pp. 345–349, Grenoble, France, September 2005.

[3] M. Nardstrom, "Biosensors and BioMEMS-from doctor's office to the crime Lab," Sensor technologies, Tiny Detective, June 9, 2005.

[4] G. G. Stoney, "The tension of metallic film deposited by electrolysis," *Proceedings of Royal Society of London A*, vol. 82, pp. 172–175, 1909.

[5] M. Sepaniak, P. Datskos, and N. Lavrik, "Microcantilever transducers: a new approach in sensor technology," *Analytical Chemistry*, vol. 74, no. 21, pp. 568A–575A, 2002.

[6] M. Z. Ansari and C. Cho, "Design and analysis of a high sensitive microcantilever biosensor for biomedical applications," in *Proceedings of the IEEE International Conference on BioMedical Engineering and Informatics*, pp. 593–597, May 2008.

[7] D. Klaitabtim and A. Tuantranont, "Design consideration and finite element modeling of MEMS cantilever for nano-biosensor applications," in *Proceedings of the IEEE Conference on Nanotechnology*, pp. 489–492, Nagoya, Japan, July 2005.

[8] C.-H. Chen, R.-Z. Hwang, L.-S. Huang et al., "A wireless Bio-MEMS sensor for C-reactive protein detection based on nanomechanics," in *Proceedings of the IEEE International Solid-State Circuits Conference (ISSCC '06)*, 2006, Session 30, Silicon For Biology, 30.6.

[9] A. M. Moulin, S. J. O'Shea, and M. E. Welland, "Microcantilever-based biosensors," *Ultramicroscopy*, vol. 82, no. 1–4, pp. 23–31, 2000.

[10] N. V. Lavrik, C. A. Tipple, M. J. Sepaniak, and D. Datskos, "Gold nano-structures for transduction of biomolecular interactions into micrometer scale movements," *Biomedical Microdevices*, vol. 3, no. 1, pp. 35–44, 2001.

[11] Y. Arntz, J. D. Seelig, H. P. Lang et al., "Label-free protein assay based on a nanomechanical cantilever array," *Nanotechnology*, vol. 14, no. 1, pp. 86–90, 2003.

[12] R. Jumbadkar and J. Kalambe, "Design and simulation of feedback controller for biosensor," in *Proceedings of the International Conference on VLSI, Communication & Instrumentation (ICVCI '11)*, 2011.

[13] D. Brooks, "Fusing CurrentWhen Traces Melt Without a Trace," Printed Circuit Design, a Miller Freeman publication, December, 1998.

[14] B. D. Jensen, L. L.-W. Chow, K. Huang, K. Saitou, J. L. Volakis, and K. Kurabayashi, "Effect of nanoscale heating on electrical transport in RF MEMS switch contacts," *Journal of Microelectromechanical Systems*, vol. 14, no. 5, pp. 935–946, 2005.

[15] D. G. Fink and H. W. Beaty, *Standard Handbook for Electrical Engineers*, McGraw Hill, 15th edition, 2007.

[16] "4200 SCS Semiconductor Characterization System Technical Data by Keithley," Series 2400 Single-Channel SourceMeter Instruments by Keithley.

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