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Design, Simulation and Analysis of Cantilever Sensor for in-Vitro LDL Detection

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Abstract: This work is focused on the design, simulation and analysis of microcantilever integrated with piezoresistors in Wheatstone bridge arrangement to detect low density lipoprotein (LDL) in blood, which is responsible for cholesterol accumulation in arteries. This paper uses Finite Element Method (FEM) to obtain the performance of piezoresistive microcantilever sensor to measure surface stress corresponding to the adsorption of LDL molecules. The FEM results are compared with the analytical solutions. The results suggest that the designed sensor can effectively sense LDL molecules as in-Vitro with few micro-litre of blood sample. *Copyright © 2011 IFSA.*

Keywords: Low density lipoprotein, Microcantilever, Piezoresistor, Surface stress, in-Vitro sensing.

1. Introduction

Low density lipoprotein in human blood is said to be the major cause for the formation of atherosclerosis plaque in coronary artery. This plaque causes blockage to flow of blood in the artery and affects the circulation of blood in the artery, and it may lead to heart attack. In this paper a method is investigated to sense the number of LDL molecules in blood as In-vitro method.

To sense the LDL molecules this work uses a microcantilever sensor with piezoresistors in wheat stone bridge arrangement. Microcantilevers are used as sensors in biochemical sensing applications [1-5]. This device can act as a sensor to detect surface stress which is caused due to the adsorption of biomolecule on one side of the functionalized cantilever beam. When a target biomolecule, of interest, is made to bind on the cantilever surface, by specifically functionalizing the cantilever beam, the beam deflects [6]. This deflection is measured either in static mode or in dynamic mode.

In dynamic mode of detection the beam is actuated by means of any one of actuation technique such as electrostatic, piezoelectric etc., the resonant frequency of the beam is measured before and after adsorption of biochemical species. Resonant frequency is given in equation (1)

$$f_0 = \sqrt{\frac{k}{m}}, \tag{1}$$

where k is resonant frequency and m is the mass. If there is an increment in mass, there is a corresponding shift in resonant frequency. Therefore measurement of resonant frequency using appropriate method will indicate the adsorbed mass of biochemical species [7]. But this dynamic method [8] is not suitable in liquid based environments as the liquid offers damping to the vibration of beam and may alter the resonant frequency.

In static deflection measurement method [9], the piezoresistors are integrated with the beam experience a change in strain and resulting changes in resistance (ΔR). The change in resistance can be measured as a voltage in a Wheatstone bridge measurement. [10]. This paper also simulates the performance of a piezoresistive microcantilever with Wheatstone bridge arrangement for the surface stress applied, which [19-23] is equivalent to the stress due to of LDL molecules adsorbed on the cantilever.

2. Device Modeling and Simulation

The cantilever beam is made by silicon nitride. The piezoresistive material is polysilicon which is deposited on the beam. Oxide layer is deposited on the piezoresistor as conformal deposition. So that oxide insulates the cantilever beam and polysilicon from the top layer of gold. The layer dimensions are given in Table 1.

Table 1. Dimension of Layers.

Layer	**Material**	**Length**	**Width**	**Thickness**
Beam	Nitride	200 µm	40 µm	0.5 µm
Piezo	Polysilicon	200 µm	10 µm	0.5 µm
Insulation	Oxide	200 µm	40 µm	1 µm

When the biochemical sample (LDL) is applied to the cantilever sensor, the sample may bind with receptor molecule antiapolipoprotein B [12] which is functionalized on the gold layer. So the gold surface is acted upon either by a compressive or by tensile stress. Due to this stress the beam deflects; and the deflection as given in [13, 14] can be found from equation (2).

$$\frac{1}{R} = \frac{6(1-\nu)}{Et^2}\Delta\sigma, \qquad z = \frac{3l^2(1-\nu)}{Et^2}\Delta\sigma, \tag{2}$$

where R is the Radius of curvature, E is the young's modulus of beam, ν is the Poisson's ratio, t is the thickness of beam, z is the cantilever Displacement, Δσ is the differential Surface stress and *l* is the length of the beam. This equation shows that the deflection and the surface stress are linearly proportional.

In this work a surface stress corresponding to the real life adsorption of LDL molecules in human blood [19-23] is considered. Since the developed surface stress in the cantilever based sensor is easy to analyze. This LDL values are converted into corresponding surface stress as described below. For lower range the level of LDL [19-23] is 1.3 mmol /l in blood, the total number of LDL molecules corresponding to this range in a 10 µl sample is calculated and it is found to be 7.829×10^{15} molecules. Then equivalent surface stress created is found to be 9.5 N/M. Similarly moderate, high and very high ranges of LDL levels have also been considered and the corresponding surface stress is calculated and the values are used for simulation and for analytical calculation.

The FEM simulation is done using CoventorWare. Here the simulation is done to find the response as surface stress in the LDL sensor. The material property which is used in simulation is given in Table 2.

Table 2. Material Properties used for simulation.

Property	Unit	Poly Silicon	Oxide	Gold
Young's Modulus	MPa	1.65e5	7.0e4	7.72e4
Poisson ratio	-	2.3e-01	1.7e-1	4.2e-1
Density	Kg/µm^3	2.23e-15	2.1e-15	1.9e-14
CTE	1/k	3.5e-6	0.35e-6	1.42e-5
Thermal Conductivity	pW/µm.K	5e7	1.42e6	3e8
Specific Heat	pJ/kg.K	1.0e14	7.1e-14	1.28e14
Electrical conductivity	pS/ µm	7e10	-	3.4e13

3. Results and Discussion

The proposed sensor model was created in CoventorWare which is a MEMS simulation tool. The material properties used for simulation is given in Table 2. The model which is shown in Fig. 1 is varied with a surface stress. The surface stress which is applied here is the stress corresponding to the practical values of LDL levels [19-23] for low medium, high and very high ranges. As described in section II the practical values of LDL for low medium, high and very high levels have been converted into corresponding surface stress and the stress is used in simulation.

Fig. 2 shows the surface stress corresponding to practical LDL levels and their displacement. In order to validate the simulation results, theoretical calculations have been done using equation 2. The maximum error between both the values is around 50 %.

The difference between the analytical and FEM results may due to the thickness of the layers which is presented in the sensor is not considered in Stoney's equation. But the trends of both the responses are found to be same as in Fig. 2. If the applied stress increases then the displacement increases linearly as in equation (3).

The change in resistance [16] is given by the equation (3)

$$\frac{\Delta R}{R} = \frac{3 \beta \pi_L (1 - \nu)}{t} \Delta \sigma \tag{3}$$

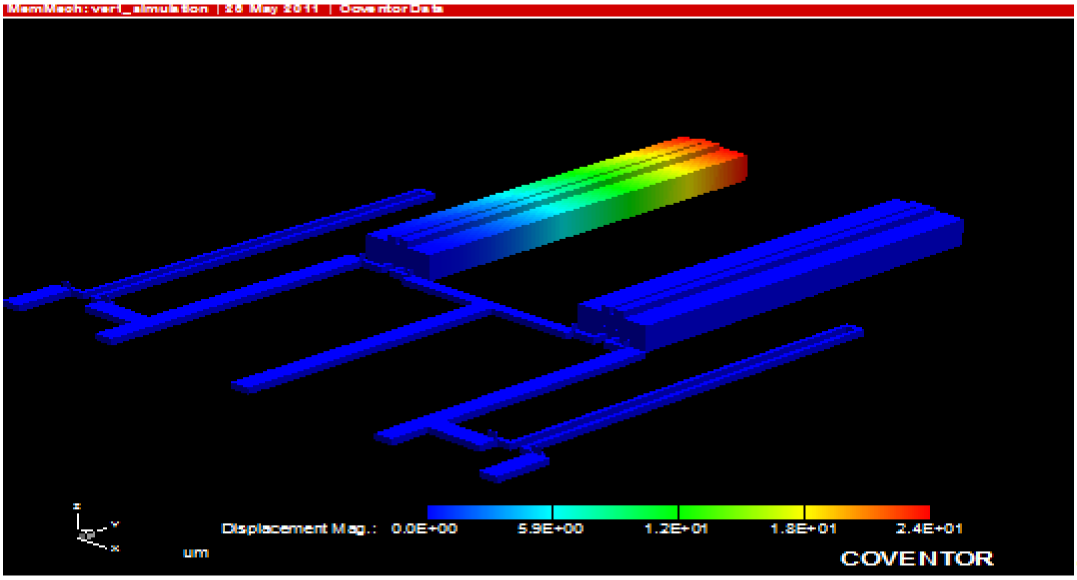

Fig. 1. Surface stress simulation.

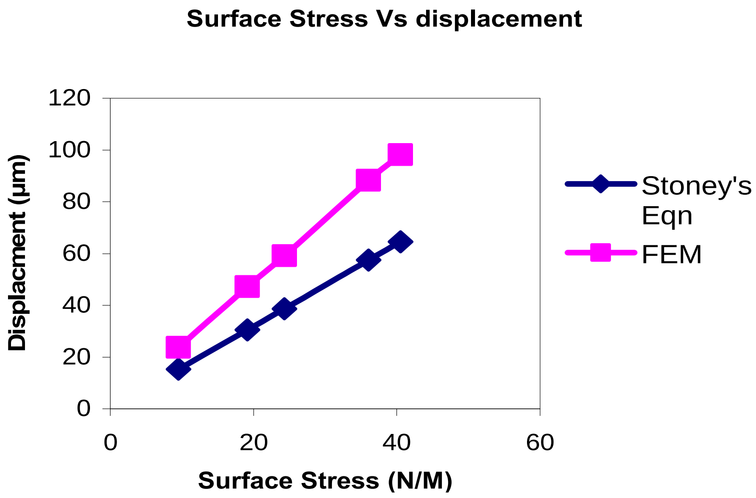

Fig. 2. Displacement as a function of Surface stress which is equivalent to LDL levels.

where π_L is the piezoresistive coefficient of piezoresistor, β is a factor that is adjusted for the thickness of the piezoresistor [17]. The change in resistance (sensitivity-ΔR/R) calculated analytically from equation (3) are compared with the values obtained from FEM simulations are given in Fig. 3. The trends of both the curves are same even the error between them are 28 %. The surface stress sensitivity is found to be 4.5 N/M.

The beam tip is displaced for 1µm to 5µm to find the change in resistance. From Fig. 4 it is clear that Beam tip displacement and the corresponding sensitivity are linearly proportional.

A piezoresistive cantilever sensor has been designed and the surface stress which is equivalent to the adsorption of LDL molecules corresponding to the practical levels as been applied and the response of the designed sensor is observed. The displacement and change in resistance (ΔR/R) are found analytically which are in good agreement with FEM results.

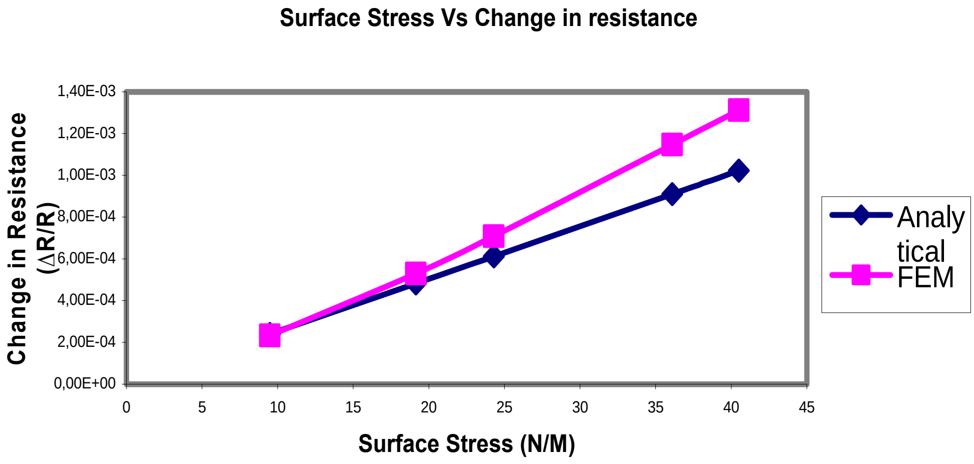

Fig. 3. Sensitivity as a function of surface stress.

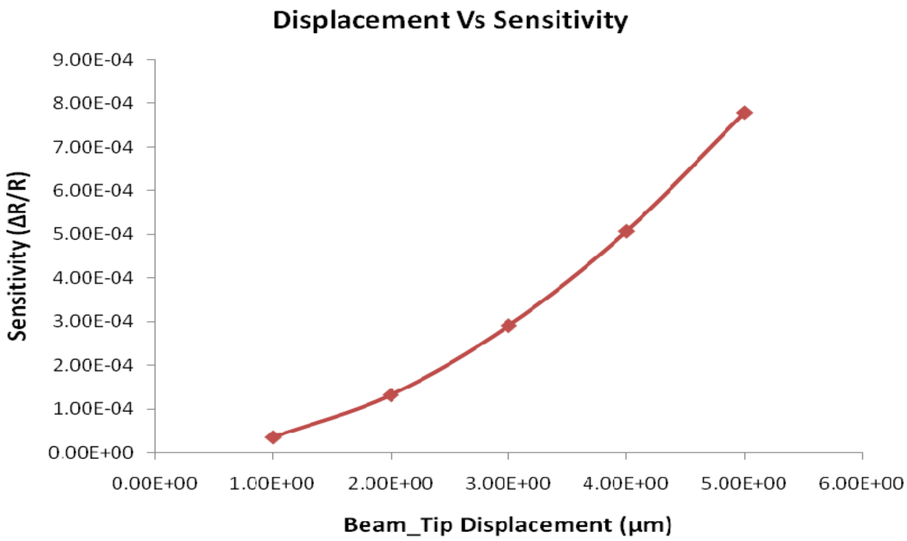

Fig. 4. Sensitivity as a function of Beam tip Displacement.

4. Conclusion

In this paper deflection and sensitivity (ΔR/R) of a piezoresistive cantilever with Wheatstone bridge arrangement responding to a surface stress corresponding to the practical values of LDL levels for low, medium, high and very high cases has been found and compared with analytical results. Both are showing the same trends. This sensor is expected to work effectively as LDL sensor with AAB as receptor to specifically bind LDL. The sensor effectively measures the surface stress which is equivalent to the actual LDL molecules binding. Hence this sensor can be used as a LDL sensor as in-Vitro, with few micro-litre of blood sample. This study guides the design and simulation of piezoresistive microcantilever sensor to detect LDL.

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