Automated Detection of Tuberculosis Based on Cantilever Biosensor

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Abstract. Mycobacterium Tuberculosis is one of the most hazardous disease. Universally millions of people are suffering from this dangerous disease. Number of detection techniques are available, but due to its complex structure this infectious disease not get diagnose easily and within time. To prevent spreading the bacteria and to stop mortality there is a huge requirement to build an automated and easy technique which can detect tuberculosis at a developing phase. The purpose of the article is to design and simulate the cantilever biosensor for detection of tuberculosis. Micro cantilever biosensor are designed with cylindrical and rectangular shape with silicon substrate. The cantilever surface is coated with antibodies and when patient sample is placed on it, the antigen-antibody gets binds together. When targeted antigen-antibody binds together stress generated and it forms deflection. The displacement achieved by Cylindrical-shape was 2.06 $\times$ 10^6 μm and rectangular-shape was 1.2 $\times$ 10^{26} μm for 100N load force correlates to 28.228 $\times$ 10^{-24} kg weight of antigen. From both the model maximum displacement were recorded and considered the rectangular-shape model as the leading model for tuberculosis detection.

Keywords: Tuberculosis · Cantilever · Biosensor · Simulation · MEMS · Antigen · Antibody

1 Introduction

All around the world Mycobacterium Tuberculosis is one of the hazardous disease [1]. Every year millions of people are suffering from this infectious disease [2, 3]. It comes under the top ten syndromes around the world. Tuberculosis is caused by Mycobacterium Tuberculosis. Tuberculosis classified into Pulmonary Tuberculosis and Extra-Pulmonary Tuberculosis. When Tuberculosis bacteria affect to the lungs organs it is called as Pulmonary Tuberculosis and when it affects to other part of the body rather than lungs it is called as Extra-Pulmonary Tuberculosis [4, 5]. It is also called as airborne disease due to its bacteria get released into the air and people get infection through these bacteria [6]. Tuberculosis is very dangerous disease, if patient not get proper treatment within time, the disease may converted to drug resistant tuberculosis which increases the chance of mortality. For getting proper treatment the disease should get diagnose at an early stage.

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For this purpose there is a necessity to developed proper diagnosis method, which can diagnose this disease easily and within time. Most of the detection methods have been developed by many researchers. But these methods are insensitive and take lot of time for diagnose the disease. Some methods are laboratory based and some methods are very expensive. Laboratory based methods required proper sample and collection of sample is very tedious job. Laboratory based methods used very heavy and expensive equipment [7, 8]. So researchers are tried to developed biosensor based diagnosed methods. Because various fields used sensor based technologies. In medical field also, to detect various disease biosensors are used. Biosensor sense the biological sensing elements with physicochemical transducer [9]. Work of biosensor is based on antigen-antibodies. Based on the signal transducer the biosensors are categorised as piezo-electric quartz crystal, electrochemical, magneto elastic, breathalyser sensor [10]. Due to its stability and sensitivity biosensor plays a vital role in the medical field. But most of the biosensors are at the developmental stage due to complicated structure of TB bacteria. The objective of the paper is to designed and simulate the Bio-MEMS cantilever sensor for detection of tuberculosis. Cylindrical and Rectangular shapes were used to design Cantilever sensor and analysed the displacement of cantilever for both the shapes and find the best model for quick detection of tuberculosis.

2 Bio-Mems Cantilever Sensor

In the medical field, Micro Electro-Mechanical system plays a vital role to diagnose the molecules. Biosensor consist of a biological diagnose system known as bio-receptor and a transducer. Transducer convert into an electrical signal when bio-receptor and analyte interact with each other. The most common techniques used by transducer are electrical, optical and mechanical detection. The biosensor used bio-receptors which are based on interaction of antigen-antibody.

To diagnose the disease through biosensor antigen-antibodies are required. ESAT-6 and CFP-10 are two main antigens which are used for diagnosis purposed, since these antigens are the sources of tuberculosis. For tuberculosis 6KDa and 11KDa are the molecular weight of ESAT-6 antigen and Anti-ESAT-6 antibodies. The total molecular load is 17KDa, since the value of 1 KDa is near about 1.661×10^{-24} kg, thus considering the value of 1KDa, the total molecular weight of ESAT-6 antigen and Anti-ESAT-6 antibody is 28.228×10^{-24} kg [11]. The surface force range are 10N to 100N for interaction of antigen-antibody whereas the intermolecular force is 10N which generated by single antigen-antibody interaction [12]. Thus the 28.228×10^{-24} kg is the load of 10 antigens. The intermolecular force is estimated by considering the interactions of 10 antigen-antibodies and it applied on the surface of cantilever and demonstrates the value of deformation [13].

A bio-sensing design were produced by cantilever when interaction of biomolecular combined with a micro cantilever platform. The vibrational frequency or variations in cantilever bending can be identify by micro cantilever sensor. The structure of micromechanical and electromechanical sensor associated by micro cantilever sensor [14, 15]. With the collaboration of antigen-antibodies, the stress generated on sensitive aspect of cantilever, which generated displacement on one side of cantilever, as one edge of it is fixed and other edge is free for displacement. The specific antibody is immobilised on the top surface of cantilever, since when sample of patient is drop on it and if sample contain specific elements it binds with antibodies which generated stress on the surface and micro cantilever gets deflected. These defection of cantilever is estimated for 10N to 100N load force and consider the model which generated maximum displacement as a best model for detection of tuberculosis.

3 Experimental Details

The model of micro cantilever biosensor has been made on 3D design where static constraint are applied at one end and hanging free at the other end in COMSOL Multiphysics. The solid mechanics model under structural mechanics the MEMS module were designed. 10N to 100N force were applied to get maximum displacement. The equation for the force in sample is:

$$F_A = {}^{F_{tot}}\!/_{A} \tag{1}$$

Where, F_A is force per unit area, F_{tot} is total force and A is area of the surface.

The value for Young's modulus = 170 Pa and Poisson's ratio = 0.44 was deliberated for all the models when load force applied to the sample. Thus when the surface generated stress due to interaction of antigen antibody it forms the deflection [16].

Cylindrical shape and Rectangular shapes of Cantilever has been designed with different dimensions as shown in Table 1 and Table 2 respectively, and the surface of cantilever are made with Silicon material, to analyse the deflection of cantilever by applying same force. To find the maximum displacement, the sensitivity of both the shapes were analysed and the maximum displacement model were consider as a best model for detection of tuberculosis.

Micro cantilever biosensor based on the organisation of Micromechanical and Electromechanical sensor for detection of tuberculosis has been design and simulated in COMSOL Multiphysics. One side of cantilever is used as a static constraint and other side is free for displacement. On the surface of cantilever load force has been applied which is correlates to the weight of ESAT-6 antigen, due to this weight cantilever gets deflects. When the stress generated on the surface of cantilever it produced deflection. Deflection of cantilever is measured using the equation as

$$Deflection = {}^{PL^3}\!/_{3EI} \tag{2}$$

Where, P is applied load, L is length, E is young's modulus and I is moment of inertia.

Table 1. Dimension of Cylindrical shape geometry

Shape	Dimension	Magnitude
Cylindrical	Radius	1 μm
	Height	1 μm

Table 2. Dimension of Rectangular shape geometry

Shape	Parts	Dimension	Magnitude
Rectangular	Cantilever	Width	5
		Depth	80
		Height	1
	Sample Compartment	Width	20
		Depth	40
		Height	2
	Fixed End	Width	40
		Depth	10
		Height	5

Moment of inertia is measured using the equation as

$$I = {BD^2}/{12} \tag{3}$$

Where, B is breadth and D is thickness.

To analyse the deflection cylindrical and rectangular shape with silicon material were design and simulated with load force 10N to 100N. Figure 1 shows cylindrical model with load 10N to 100N. Similarly Fig. 2 shows rectangular model with load 10N to 100N.

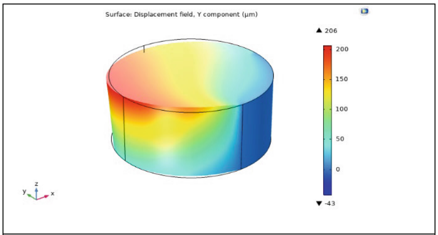
4 Result and Discussion

As shown in above Fig. 1 and Fig. 2, due to collaboration of antigen-antibodies stress generated on the surface of cylindrical and rectangular shape of cantilever and it produced displacement for load force of 10N to 100N and these displacement were explored as shown in table 3.

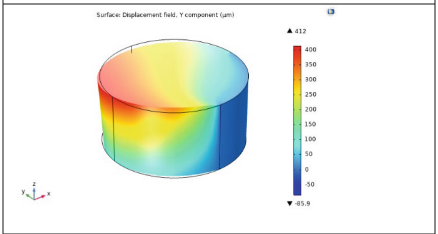
Thus, due to stress displacement generated on the surface of cantilever. The displacement of cylindrical and rectangular shape were analyzed for 10N to 100N as shown in Fig. 3 and Fig. 4.

After analysis it has been observed that, for load force of 100N of both the model it generated highest displacement as compare to lower load. For 100N load of Cylindrical shape produced $2.06 \times 10^6 \mu$m and for same load force rectangular shape produced 1.71×10^{28} µm. After analysing both the models it has been noted that rectangular shape model of cantilever generated highest displacement as 1.71×10^{28} µm for 100N load force. Thus rectangular shape model of cantilever is consider as a best model for tuberculosis detection.

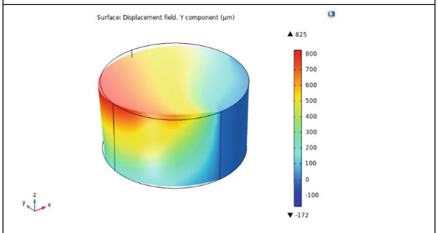
After comparing various biosensors the proposed system that is Micro cantilever biosensor produced an effective result in detection of tuberculosis. As mention in introduction section various biosensors are available for detection. But these biosensors have



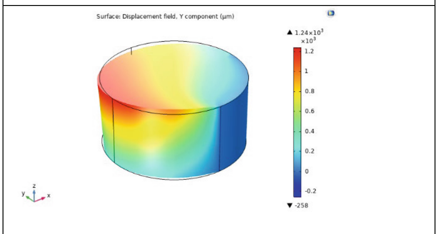
For 10N load force the cantilever displacement was obtained as 206μm.



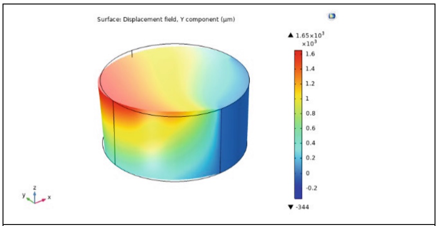
For 20N load force the cantilever displacement was obtained as 412μm.



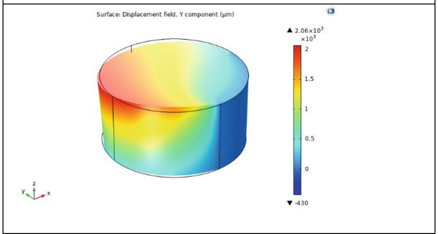
For 40N load force the cantilever displacement was obtained as 825μm.



For 60N load force the cantilever displacement was obtained as 1.24 x 10^6μm.

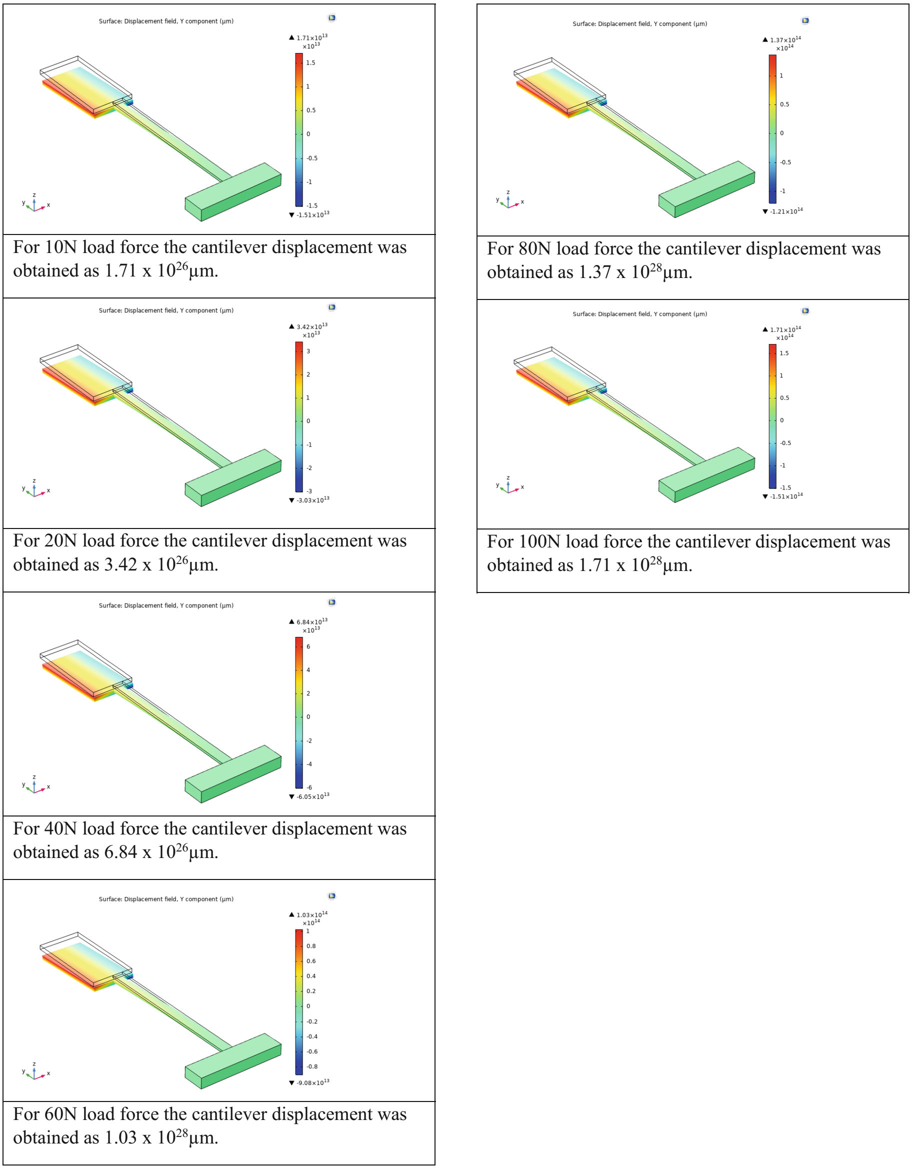


For 80N load force the cantilever displacement was obtained as 1.65 x 10^6μm.



For 100N load force the cantilever displacement was obtained as 2.06 x 10^6μm.

Fig. 1. Cylindrical Shape Model with load 10N to 100N.



For 10N load force the cantilever displacement was obtained as 1.71 x 10^{26}µm.

For 20N load force the cantilever displacement was obtained as 3.42 x 10^{26}µm.

For 40N load force the cantilever displacement was obtained as 6.84 x 10^{26}µm.

For 60N load force the cantilever displacement was obtained as 1.03 x 10^{28}µm.

For 80N load force the cantilever displacement was obtained as 1.37 x 10^{28}µm.

For 100N load force the cantilever displacement was obtained as 1.71 x 10^{28}µm.

Fig. 2. Rectangular Shape Model with load 10N to 100N.

some limitations such as piezoelectric quartz crystal biosensor is fast, label free but the temperature, density and electrical conductivity of the sample may influence the output. Optical biosensor is rapid sensitive specific but it required complex pre-treatments steps. Electrochemical biosensor is sensitive, label free but low managing ability for complex clinical samples. Most of the biosensors required sample purification and sophisticated

Table 3. Displacement of Cylindrical Model and Rectangular Model

Load	Displacement(μm)	
	Cylindrical Model	Rectangular Model
10	206	1.71×10^{26}
20	412	3.42×10^{26}
40	825	6.84×10^{26}
60	1.24×10^{6}	1.03×10^{28}
80	1.65×10^{6}	1.37×10^{28}
100	2.06×10^{6}	1.71×10^{28}

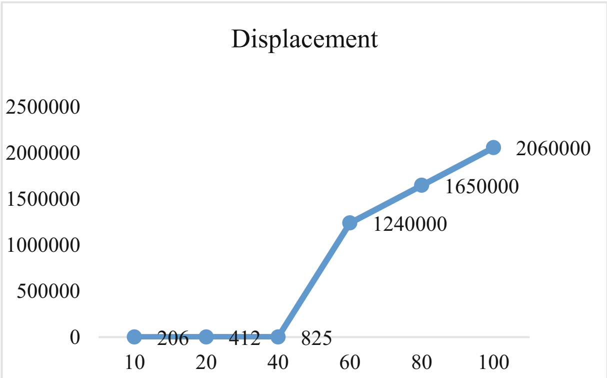


Fig. 3. Displacement of cylindrical shape for 10N to 100N

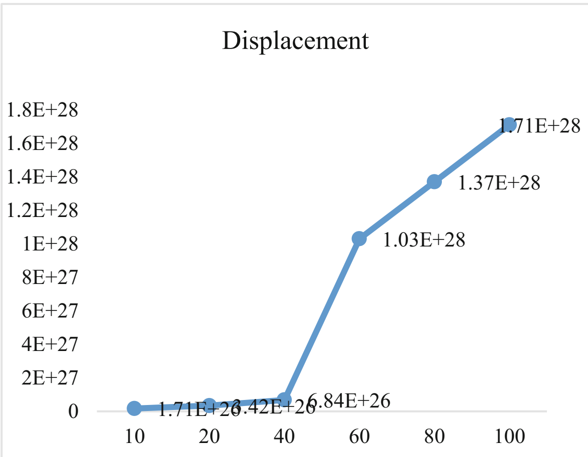


Fig. 4. Displacement of rectangular shape for 10N to 100N

instruments [8]. Whereas our proposed system is a promising tool for directly recognizing bio-molecular collaboration as mention in experiment section.

Conclusion

Mycobacterium tuberculosis is comes under the top ten disease in the world. It is very dangerous disease due to which every year millions of people get infected. Its structure is very complicated, hence tuberculosis bacteria not get diagnose easily. There is a huge need to developed simple detection technique. The purpose of this research is to designed and simulate cantilever biosensor based on MEMS structure. Two models of cylindrical and rectangular shapes cantilever sensor with silicon material were designed and simulated in COMSOL Multiphysics. Various load force were applied to cantilever surface and analysed the displacement for 10N to 100N. From both the models rectangular shape cantilever for 100N load force generates highest displacement as 1.71×10^{28} μm. Therefore, rectangular shape cantilever is consider as a best model for detection of tuberculosis. Since before developing the actual model, simulation helps us to forecast the complete structure and estimate the device performance, which reduced the cost and time.

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