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Design and Simulation of MEMS Biosensor for the Detection of Tuberculosis

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Abstract

Background/Objectives: This paper presents the design and simulation of MEMS microcantilever sensor for the identification of *Mycobacterium tuberculosis* in the given blood sample. **Method/Analysis:** The surface of the microcantilever is covered with TB antibodies which are specific to TB antigen 85complex. When the blood sample containing tuberculosis bacteria is placed on it, biochemical reactions occur between TB antigens and the antibodies on the surface of the microcantilever. This gives a deflection to the microcantilever from which TB can be detected. COMSOL Multi Physics is used in the design of micro cantilever. **Findings:** Presently the most general method for diagnosing TB is the sputum smear microscopy in which micro organisms are observed under a microscope. In some of the advanced countries culture methods are used to detect TB. At present TB identification method requires a period of 4 to72 hours and is not so accurate. Hence there is a need of MEMS sensor which offers quick and accurate method to detect *Mycobacterium tuberculosis*. When the patient's blood sample is placed on the microcantilever, the antigen-antibody interaction causes it to bend and the adsorb molecules generates a surface stress on the microcantilever. This stress is created due to the interactions between the molecules and the microcantilever surface. It has been observed that the deflection of the micro cantilever is high for a length of 20μm and for a width of 5μmkeeping the other parameters constant **Application/Improvements:** Using this MEMS bio sensor, tuberculosis disease can be identified very accurately and speedily comparing to existing methods.

Keywords: Antibodies, Deflection, Interaction, Microcantilever, Tuberculosis

1. Introduction

The Bacillus *Mycobacterium tuberculosis* is the cause of Tuberculosis disease[1]. Normally it influences the lungs (pulmonary TB), however it can also show an impact on other organs of the body (extra pulmonary TB). The protein ESAT-6/CFP-10, secreted by the extended region of RDX- 1 is responsible for the virulence and pathogenicity in the host[2]. The ESAT-6 and CFP-10 interact together to form a tight 1:1 complex and they are hydrophobic and Vander-Waals interactions[3].

Tuberculosis (TB) is a global health issue which causes sickness to a large number of individuals every year and ranks next to human immune deficiency virus (HIV) as a main cause of death globally[4]. The number of TB deaths is inadmissibly high, among the assessed 2–3 billion individuals contaminated with *M.tuberculosis*; 5–15 % will develop TB disease. In people infected with HIV, the probability of occurrence of TB is very high. One-third of the world's population is expected to have been infected with M. tuberculosis, with new infections occurring in around 1% of the population every year. Hence it is very important to detect Tuberculosis at an early stage.

The most generally perceived methodology for diagnosing TB is the sputum smear microscopy. In this microorganisms in sputum are observed under a microscope. However, with the advancement of new technologies, several new methods have been developed for TB detection. In some of the countries where most advanced developed laboratories are available, culture method is used to detect TB. At present TB identification method requires minimum of 4 hours to maximum of 72 hours and are not so accurate[5]. Hence there is a requirement of

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MEMS sensor which offer quick and accurate method to detect Mycobacterium Tuberculosis.

2. Principle of Micro Cantilever and Diagnosis of Tuberculosis

Biomolecules and their capacity of interaction between two or more atoms through non-covalent bonding, for example, hydrogen bonding, metal coordination, hydrophobic strengths, Van-der-Waals forces, π-π bonding, halogen bonding, electrostatic and electromagnetic impacts can be examined through their mechanical reaction to external forces. These molecular recognitions can induce surface stress which results in the mechanical bending of solid surfaces like a microcantilever. Similar transduction processes like modification of the lateral tension of a lipid bilayer due to membrane molecule interactions can be observed[6].

In a microcantilever, the surface stress induced by molecular recognitions is converted into nano-mechanical responses. These nano mechanical reactions induce a change in capacitance, piezo resistance or resonance frequency of the microcantilever material. This mechanical bending induced by ligand binding is detected by the monolayer of receptor molecules immobilized on one side of the microcantilever surface. The bending mechanism and antibody immobilization is shown in Figure 1.

The molecular collaborations occurring on the surface of the microcantilever increase surface strain, compelling the microcantilever to bend. The free energy changes[7] taking place on the microcantilever is unique to that particular pair of molecules (for instance antibody-antigen).

The antibodies that are specific to TB antigen 85 complexes are covered on the microcantilever. When the patient's blood sample is placed on the microcantilever the antigen-antibody interaction causes it to bend and facilitates the identification of Tuberculosis. Immunoglobulin (Ig) is a large Y-shaped protein created by B-cells that is used by the immune system to distinguish and kill foreign objects such as bacteria and virus. Immunoglobulins are glycoprotein molecules created by plasma cells (white platelets) which are the basic part of the resistant reaction. They particularly perceive and kill the bacteria or viruses by binding to specific antigens. The antibody immune response is highly complex and exceedingly particular. The diverse immunoglobulin isotypes vary in their organic elements, structure, target specificity and distribution.

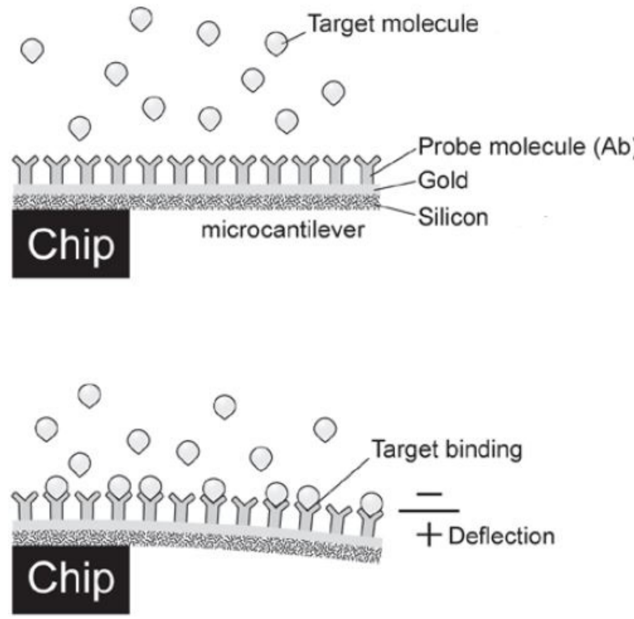

Figure 1. Immobilization of antibodies on the cantilever Surface and bending of cantilever after biomolecular recognition.

Therefore, the assessment of the immunoglobulin isotype can give profitable understanding into the complex humeral resistant response. The antibody identifies a remarkable part of the foreign target, called an antigen. The tip of the "Y" of an antibody contains a lock like structure called paratope that is particular for a specific epitope, a key-like structure of an antigen[8]. The coupling component of paratope and epitope tag a microorganism or an infected cell and kill its target directly.

3. Analytical Analysis

The microcantilever can be used as a mass sensor which detects minimal changes of a massattached to the surface. Many factors like young's modulus, spring constant, Poisson's ratio, stress etc are taken into consideration for the microcantilever that is used in the measurement. Since the thickness of the beam is very less, the rotational inertia and shear deformation can be neglected.

The adsorb molecules generates a surface stress on the microcantilever. This stress is created due to the interactions between the molecules and the microcantilever surface. The relation between surface stress (σ), introduced due to analyte adsorption and deflection (d) of the beam can be expounded by Stoney's equation.

$$d = \frac{3\sigma(1-\vartheta)}{E}\left(\frac{L}{t}\right)^2$$

Where

E is young's modulus

ϑ is Poisson's ratio.

L is the length of the microcantilever

tis the thickness of the microcantilever

Young's modulus and Poisson's ratio are material dependent, surface stress changes based on the amount of analyte placed on the sensor and the deflection of the beam varies in accordance with the changes in the length and thickness of the microcantilever beam. Deflection can be calculated for various lengths by making width constant and vice-versa. The mass induced can be detected by the shift in frequency in dynamic mode. Resonant frequency shift can be found by the following equation

$$f = \frac{1}{2\pi}\sqrt{\frac{E}{\rho}\frac{t}{L^2}}$$

Where

f is fundamental resonant frequency

E young's modulus

ρ density of the material

4. Model Description and Simulation of Micro Cantilever

Simulation plays a vital role in designing of any sensor which helps to analyze the sensor in all aspects. The modeling and simulation of physics-based problems require advanced numerical methods and a powerful integrated environment like COMSOL Multiphysics. COMSOL software provides a platform to perform analysis on different physics streams. COMSOL simulation includes selecting physics, defining geometry, and materials, setting up physics, meshing, and analysis of results. Based on the defined mode of the microcantilever the structural mechanics is selected.

The microcantilever is a simple mechanical structure clamped at one end. By coating a specific sensing element on the surface of the microcantilever it can be used as a sensor. The microcantilever contains length of 100μm, width of 20μm and contains apolysilicon layer and gold layer of thicknesses 0.5μm and 0.2μm respectively that are coated over the microcantilever. A basic microcantilever model is shown in the Figure 2. *A tetrahedral mesh is applied to the model that is* shown in *Figure* 3. Surface stress generated by the adsorb molecules will bend the microcantilever. The deformed structure is shown in Figure 4.

Polysilicon layer helps to avoid non-specific interactions and gold layer enables the immobilization of antibodies and helps in the detection of microcantilever beam deflection by Surface Plasmon resonance. The total surface stress generated on the microcantilever is proportional to the number of analyte molecules attaching to the gold layer.

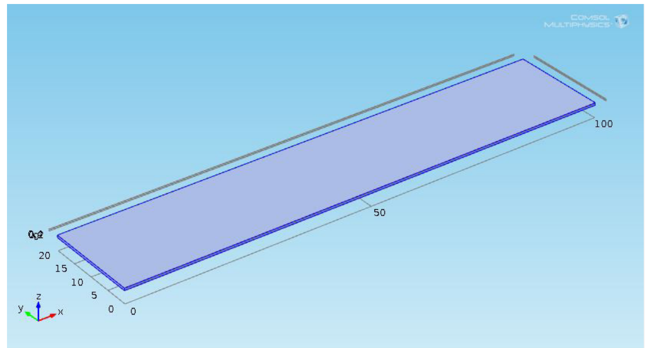

Figure 2. Basic microcantilever Beam.

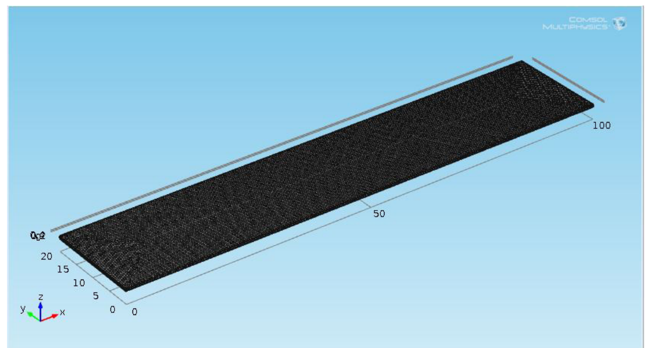

Figure 3. Mesh Model.

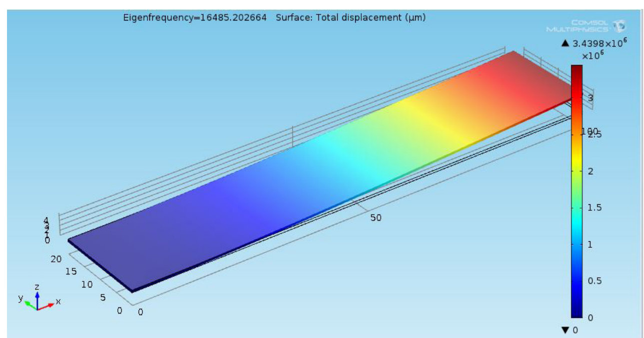

Figure 4. Deformed Shape.

5. Results

The simulation of the MEMS sensor is done in COMSOL Multiphysics. The model is analyzed by varying different parameters. For various parameters, changes in deflection are observed which are shown in Figures 5. [a, b, c, d, f].

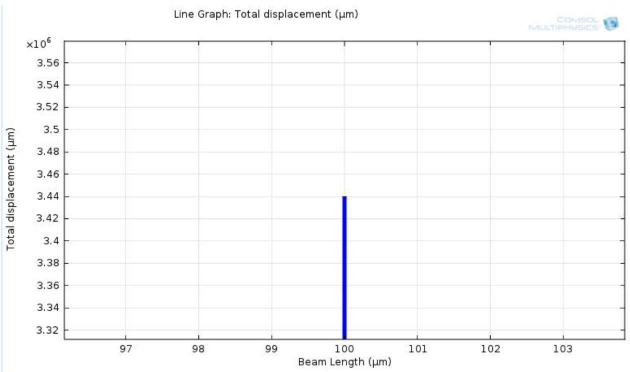

Figure 5a. Beam length (100 μm) vs. total displacement.

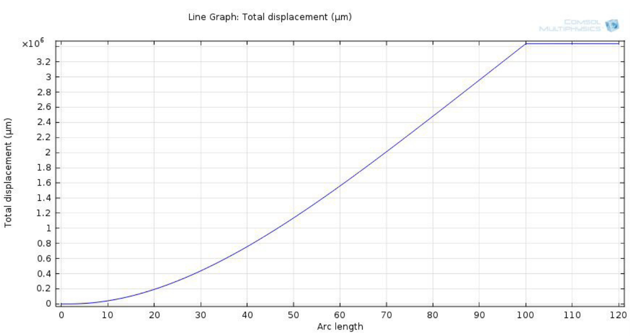

Figure 5b. Arc length vs.total displacement (for 100 μm * 20 μm * 0.7 μm).

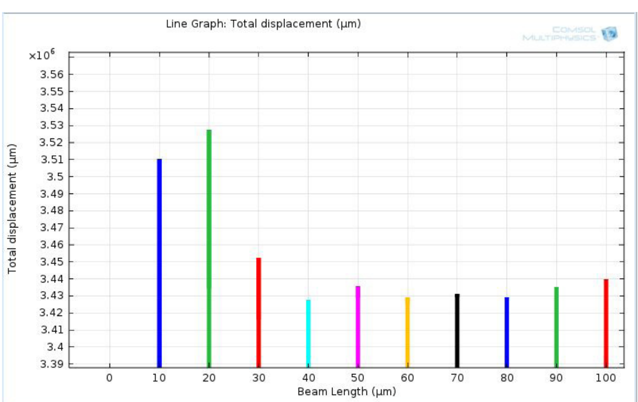

Figure 5c. Beam length vs.total displacement (for varying beam length of range 10 μm to 100 μm at constant beam width and thickness).

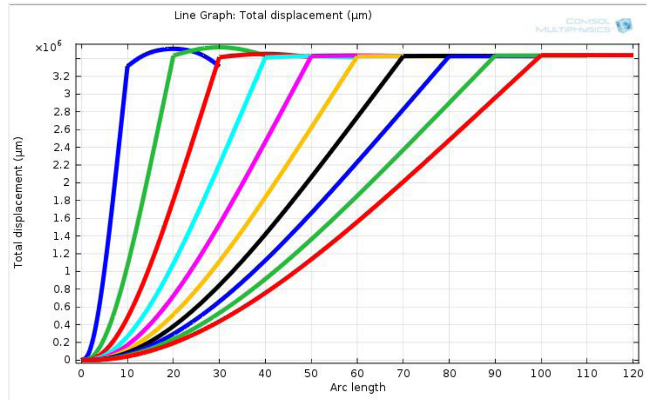

Figure 5d. Arc length vs.total displacement (for varying beam length of range 10 μm to 100 μm at constant width and thickness).

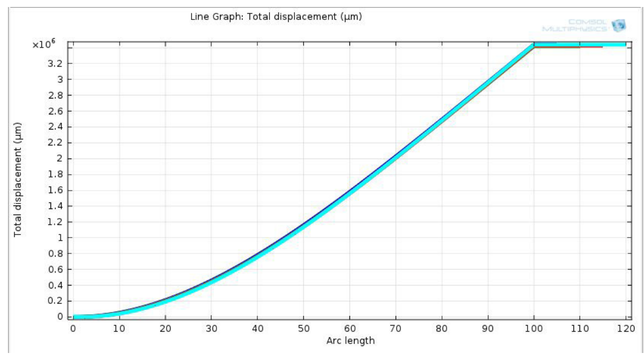

Figure 5e. Arc length vs. total displacement (for varyingbeam width of range 5 μm to 20 μm at constant length andthickness).

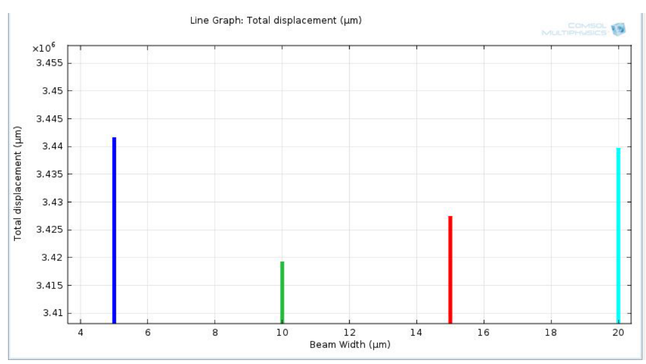

Figure 5f. Beam width vs.total displacement (for beam width of range 10 μm to 100 μm).

Table-1 shows the displacement of the beam for various lengths at constant width and thickness. Table-2 shows the displacement of the beam for various widths at constant length and thickness.

Table 1. Beam length vs. total displacement (at constant beam width and thickness)

Beam Length [µm]	Total Displacement [µm]
10	3.510
20	3.530
30	3.450
40	3.425
50	3.435
60	3.428
70	3.432
80	3.428
90	3.435
100	3.440

Table 2. Beam width vs. total displacement (at constant beam length and thickness)

Beam Width [µm]	Total Displacement [µm]
5	3.440
10	3.420
15	3.430
20	3.438

6. Conclusion

The design of MEMS Biosensor for the detection of t*uberculosis* has been presented. Unlike the available traditional TB detection methods, this sensor makes the analysis and detection of the Tuberculosis very easy and accurate.

At constant width and thickness it is observed that the deflection of the microcantilever is high for the length of 20µm and at constant length and thickness it is observed that the deflection of the microcantilever is high for the width of 5µm. Hence the sensor gives more accurate results either at length of 20µm or at a width of 5µm, keeping other parameters constant. But the stability and sensitivity of the microcantilever does not only depend on length or width or any other single parameter. Hence one should select optimum dimensions to get more accuracy. Hence from the above results, the accuracy of the sensor is high when length is 20µm and width is 5µm. The thickness depends on the number of layers like polysilicon, gold, etc required to be coated in a particular application.

7. References

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