Simulation and Analysis of Micro Cantilever Sensor for Enhanced Biosensing of Disease causing Pathogens

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***Abstract*—This paper deals with a biosensor using a micro fabricated array of micromechanical cantilevers. This biosensor is used to detect tuberculosis. The sensor consists of antibody layer immobilized onto gold-coated cantilevers and interacts with antigen. The patient blood sample is placed on the cantilever surface. If the sample contains disease causing antigen, immobilized antibody binds with the antigen. This antigen antibody binding causes increase in surface stress. The addition of mass due to antigen antibody binding involved in this process causes the cantilever to bend. The deflection of these cantilever beams can be detected using various techniques like piezoresistive, piezoelectric or capacitive effects. The detection of pathogens requires an extremely sensitive cantilever. Increasing the sensitivity of a microcantilever biosensor can be done by changing the shape of the cantilever. Intellisuit software is used to analyze the proposed microcantilever with increased sensitivity.**

***Index Terms*— Biosensor, antibodies,Cantilever.**

I. INTRODUCTION

All Tuberculosis (TB) is a disease caused by bacteria called Mycobacterium tuberculosis. The bacteria usually attack the lungs, but they can also damage other parts of the body. One third of the world's population is thought to have been infected with M. tuberculosis, with new infections occurring in about 1% of the population each year. It is very essential to detect Tuberculosis in early stage. The following table 1.shows the various disadvantages of existing diagnostic methods.

Table1.Existing methods for TB diagnosis

TB Diagnostic Test	Time taken	Drawbacks
Tuberculosis skin test based on purified protein derivative(PPD)	48-72 hours	Non Specific
Culture of M.tb bacillus	3 to 8 weeks	Takes long time
RadioImmuno Assay	Less than 2 hours	require labeling,Hazardous
Polymerase Chain Reaction(PCR)	Few hours	Highly sensitive but expensive and technically demanding.
X –ray	1-3 hours	Not suitable for all kinds of TB
Piezoelectric Immunosensor	1-3 hours	in R and D stage
Enzyme linked Immunosorbent assay(ELISA)	2-4 hours	Expensive and technically demanding
Microscopy	Less than 2 hours	Positive only when there is high bacterial load.
Multi-antigen print ImmunoAssay	2-4 hours	Greater number of steps involved.
Microcantilever based diagnostic kit	Less than 1 hour	Ultrasensitive (upto pg),specific,fast, cheap and label free.

II. ENZYME LINKED IMMUNOSORBENT ASSAY (ELISA)

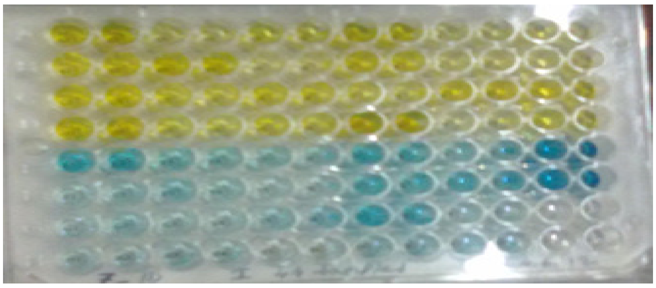

Fig 1.Enzyme linked Immunosorbent assay (ELISA)

Enzyme linked Immunosorbent assay(ELISA) method of detecting Tuberculosis .Fig(1) Elisa wells with strong colour change detects the presence of the disease.

Fig 2 .Enzyme linked Immunosorbent assay (ELISA) reading

Elisa plates are read at 450 nm with 650 nm as the correction wavelength using a ELISA reader Fig (2). These tests are technically demanding and consumes a lot of time.Microcantilever biosensor based diagnostic kit is the fast and sensitive method to detect Tuberculosis.

III. BIOSENSOR

Biosensor Fig. (3) consists of a biological sensing element, a transducer, a signal conditioner, a data processor and a display. The sensing component must produce a signal that is proportional to the concentration of a specific chemical or biological substance. This sensing component takes advantage of the ability of a biomolecule, such as an antibody to specifically recognize the target substance. This biosensor is used to detect tuberculosis.Patients blood sample is placed on the surface of the cantilever. Presence of the disease can be detected by a recognition system. Cantilever immobilized with antibody forms the recognition system. Interaction of antigen antibody takes place if the patient's blood sample contains Tb antigen. This antigen antibody binding is more if the sample contains more antigen. When antigen antibody binding takes place on the surface of the cantilever mechanical or electrical characteristics of the cantilever change. The cantilever reacts to this external stimulus and the product is mechanical stress. The transducer converts this product into a conventional electrical signal. Amplifier amplifies the electrical signal which is processed and displayed. These biosensors are simple portable and are used as a point of care testing device.

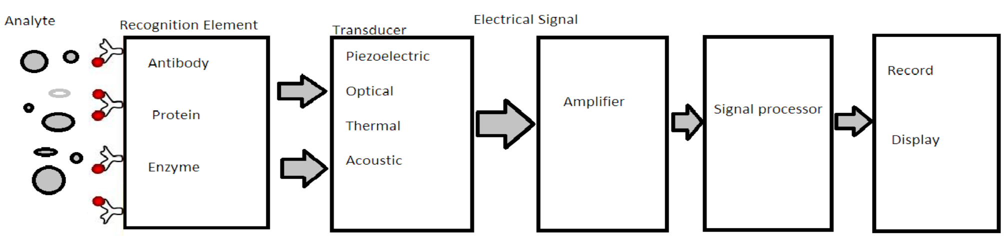

Fig 3. Biosensor

IV. MEMS CANTILEVER

Micro-Electro-Mechanical Systems (MEMS) technology has generated a significant amount of interest in the government and business sectors. This interest is happening due to the potential performance and cost advantages with micro-scale devices fabricated based on a silicon processing technology [1]. MEMS devices utilize numerous transducing mechanisms for both actuation and sensing. The deflection of these cantilevers beam can be detected using various techniques same as the techniques for AFM technology such as optical reflection, piezoresistive, piezoelectric, capacitive, and electron tunneling. This cantilever biosensor device acts as a surface stress sensor where the sensitivity detection of this device is due to adsorption induced variation due to mass loading [2]. Fig (4) shows a biosensor, where a target biochemical species adsorbing on a functionalized surface of the MEMS cantilever beam. These biosensors have the advantage to accurately, quickly and economically detect patients for the presence of various diseases [2].

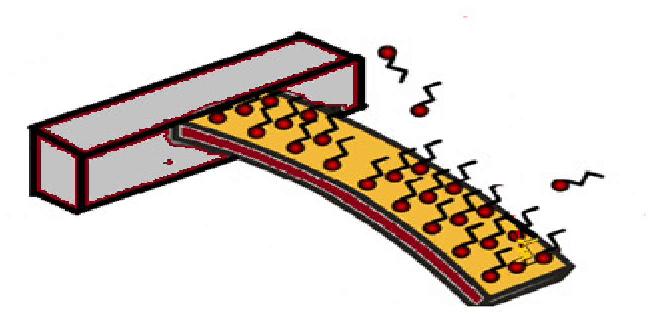

Fig 4. Cantilever Biosensor bending due to antigen antibody binding.

Cantilever beam has one end fixed and other free as shown in Fig (4). The adsorption of biomolecules causes the cantilever to bend. Adsorption onto the sensing element composed of two chemically different surfaces produces a differential stress between the two surfaces and induces bending. The adsorbed layer can attempt to expand or may try to contract know as a compressive surface stress and a tensile surface stress, respectively [3]. A relationship between the cantilever tip displacement δ and the applied surface stress σ can be expressed as [3]; The more material that is adsorbed, the more the microcantilever will deflect [4],[5],[6].

……… (1)

E is the young's modulus of the cantilever material;
ν is Poisson's ratio;
l is the length of cantilever;
t is the cantilever thickness.

Eqn (1) gives the relation between applied surface stress and deflection. There are several advantages to use microcantilevers as sensors like microscale size, ease of constructing many cantilevers in one array ,ability to detect multiple analytes in one solution using one MEMS device shows high sensitivity , selectivity and low power consumption. These cantilevers can be used in air, vacuum and liquid environment. The cantilever's, natural resonant frequency, angular deflection, resistivity, capacitance variation are the properties used to measure the change in the cantilever. The cantilever can be operated in static mode and dynamic mode. The static mode is when the cantilever is not actuated. Any displacement of the cantilever due to intrinsic stress generated on or within the cantilever .When the cantilever is externally actuated causing the cantilever to oscillate at its natural resonant frequency it is operated in dynamic mode. Any change in the load or mass of the cantilever results in a change in this frequency. The change in frequency is measured. Dimensions like length, width and thickness of the cantilever, properties of the material from which it is made , geometric shape are the factors affecting the cantilever. The geometric shape, and material used to fabricate the cantilever determines the cantilever's ability to respond when a force is applied. Displacement caused by either an external load or an intrinsic stress would normally be considered small in the macroscopic systems. In microsystems this displacement is big enough to indicate a change in mass as small as a few nanograms . Deflection results from two mechanisms added mass and surface stress from adsorbed species[7],[8],[9].The relation between stiffness K of a cantilever and length is given by eq (2).

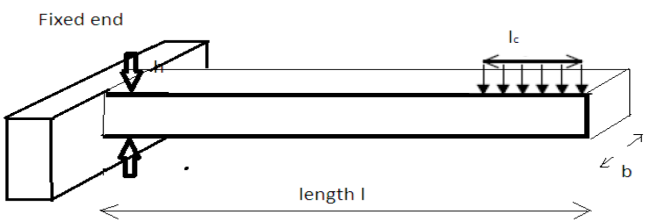

Fig 5. Cantilever Biosensor

…….(2)

Where λ= lc / l
E is the young's modulus of the cantilever material;
l is the length of cantilever;
b is the width of cantilever;
h is the thickness of cantilever;

lc is the length over which equal distributed transverse load is applied Fig(5) .Spring constant 'K' is an important parameter for the mechanical operation of sensor. Spring constant is governed by the length of beam and young's modulus. Spring constant of a beam is also called as beam stiffness. The stiffness reduces if the length of the cantilever is increased Fig (6) .Deflection of the cantilever can be can improve by changing width and thickness. Spring constant increases with increase in beam width and thickness Fig(7),Fig(8).

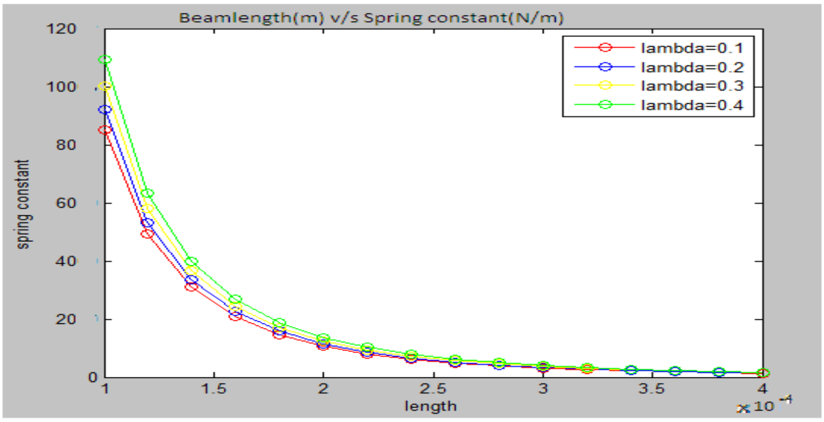

Fig 6. Cantilever length variation with spring constant

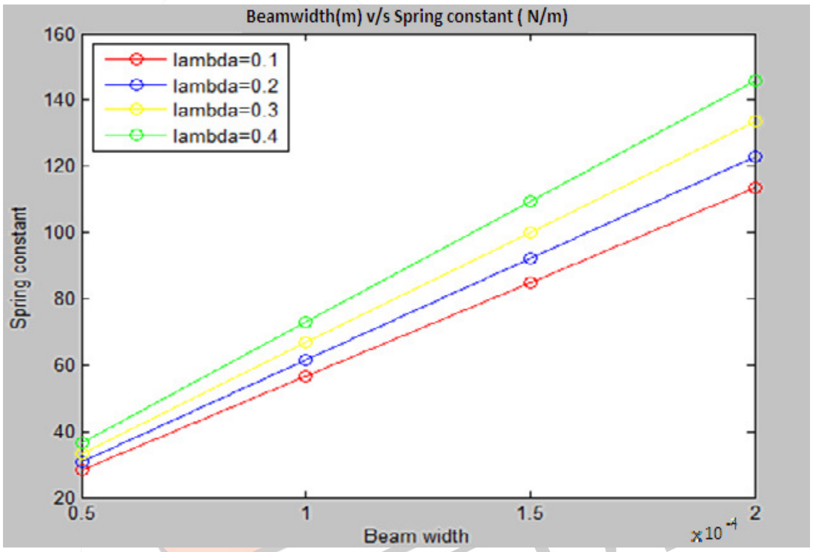

Fig 7. Cantilever width variation with spring constant

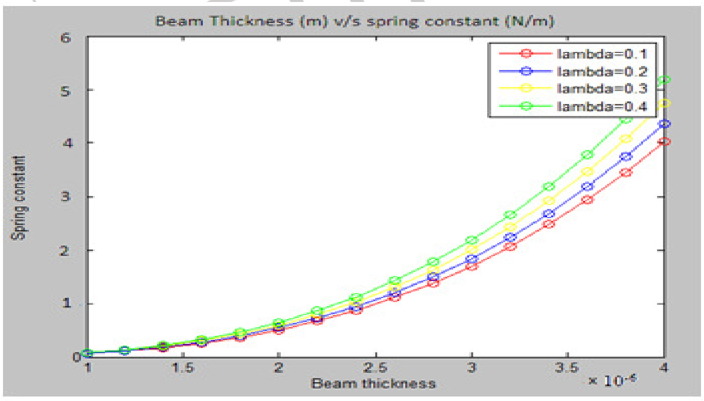

Fig 8. Cantilever Thickness variation with spring constant

V. SENSITIVITY OF MICROCANTILEVERS

Intermolecular forces that result from adsorption of biomolecules can bend a micromachined cantilever and enable detection of nucleic acids and proteins without any prior labeling of target molecules.[10],[11], the reliability of the signal resulting from the molecular binding reaction is improved by monitoring the relative, or differential bending[11],[12].Cantilever simulated in this paper has a length of 100 µm, width of 30 µm and thickness of 1 µm. Cantilever sensitivity depends on its ability to convert biomolecular recognition into deflection. Fig(9) shows the magnitude of displacement of rectangular cantilever. Deflection can be improved by reducing stiffness. Cantilever Stiffness decreases with increase in length. The length of the cantilever cannot be increased so much because it will also increase the size of the biosensor and the device miniaturization will be lost. Reducing the thickness will have fabrication problems. Hence we can improve the sensitivity by changing the shape of the cantilever .This new shape is obtained by having a rectangular opening at the anchor point thereby reducing the stiffness at the anchor point Fig(10).Increasing sensitivity will only require a simple read out system. Increasing sensitivity is essential for reducing the cost of these biosensors and also helps in enhanced biosensing of disease causing pathogens. Fig (11) shows that for the same stress the deflection is improved.

VI. RESULTS

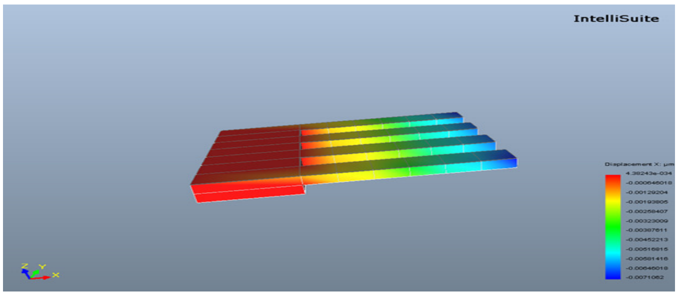

Fig 9.Rectangular Cantilever Biosensor

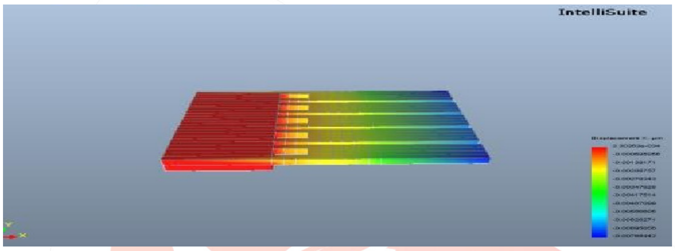

Fig 10. Cantilever Biosensor with hole at the anchor point

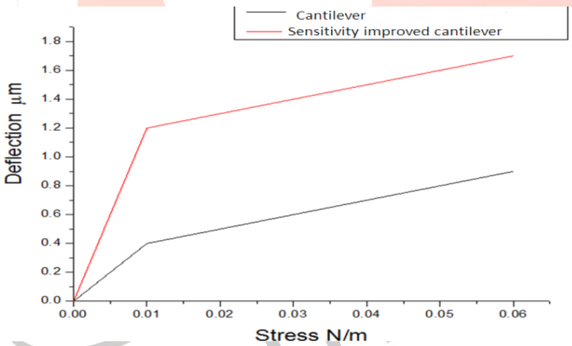

Fig 11. Cantilever stress variation with deflection

VII. CONCLUSION

Simulations of cantilever sensor with enhanced biosensing were done using Intellisuit software. Analysis of various cantilever parameters was performed using Matlab software. A table summarizing the existing method for tuberculosis detection is given. This biosensor can be used to detect the presence of the disease and is a good method than the existing ones.An array of cantilevers can be fabricated and with the same sample several diseases can be detected at the same time. These biosensors can be used as point of care testing devices.

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