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Biosensing by Cantilever Resonator for Disease Causing Pathogen Detection

KEYWORDS: biosensors, antigen, antibody, cantilever

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ABSTRACT *Microcantilever biosensors can detect small amounts of materials such as pathogenic bacteria for medical diagnostics. These biosensors can be used as immunobiological detectors for a specific disease. This paper gives a resonant frequency based biosensor using cantilever beam for detection of tuberculosis based on antigen antibody binding events. This binding event is due to the interaction of antibody immobilized on the surface of the cantilever and the antigen 85 complex in the blood sample. Increase in mass due to antigen antibody specific binding can be detected by measuring a resonant frequency shift. Simulation of the resonator was done using HFSS software and the analysis of the cantilever was performed using Matlab.*

INTRODUCTION

The idea of using cantilevers for bio sensing applications has given a new dimension to the field of biosensors [1], [2]. These mechanical cantilever biosensors can be operated in both static and dynamic mode. In the static mode the cantilever is not vibrating and the deflection of the cantilever is produced because of a change in surface stress. In the dynamic mode, the cantilever is made to vibrate and the resonance frequency change occurs due to a change in mass or/ and spring constant of the cantilever. In the decade since its inception, researchers have demonstrated its sensitivity of single base pair mismatch detection in DNA hybridization [3] in static mode, and of single airborne virus particle [4] mass detection in dynamic mode. Until now mass detection using dynamic mode has been developed to work in gaseous environment. Bio-sensing requires the sensor to operate in aqueous environment. However, dynamic mode in a fluid still remains a challenge. The sample is placed on the cantilever surface biological reaction on the surface adds to the oscillator's mass, thus lowering the resonance frequency [5, 6].

BIOSENSOR

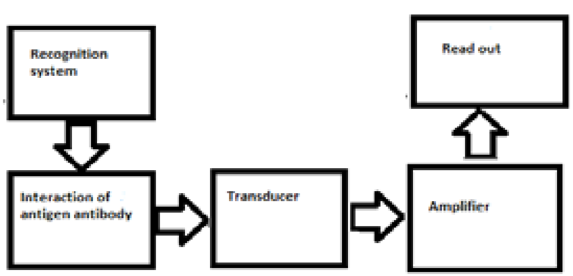

Figure 1: Biosensor

Biosensor (Figure 1) is a device which converts a biological reaction into electrical signal. It consists of detectors which forms the recognition system to detect the target. The transducer converts the biological interaction into electrical signal.This electrical signal is amplified and output is displayed in the readout system. The transduced signal can also be transmitted.Biosensor consists of biologically sensitive material in close conjunction with a device that will convert a biological reaction into electrical signal. The biologically sensitive materials can be an enzyme, a bacterial cell whole cell, an antibody an

antigen the molecular recognition is done by binding of receptor area and the biological component (or analyte) to be recognized. When biological molecules come in contact with the sensing layer there is a change in some parameter associated with the interaction. This change may produce ions, electrons, gases, heat, mass or light. These quantities are converted into electrical signals by the transducers, amplified, processed and displayed in a suitable form .In this biosensor antigen antibody reaction is made use to sense the presence of pathogen causing tuberculosis.

ANTIGEN -ANTIBODY

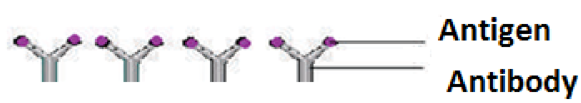

Figure 2: Antigen- Antibody

Antibodies (Figure 2) known as immunoglobulin, (Ig) are proteins that are found in blood or other bodily fluids. Antibodies are used by the immune system of our body to identify and neutralize foreign objects, such as bacteria and viruses. Antibodies are produced by white blood cell called a B cell. The general structure of all antibodies is same, a small region at the tip of the antibody is extremely variable, allowing number of antibodies with slightly different tip structures to exist. This region is known as the hyper variable region. Each of these variants can bind to a different target, known as an antigen. An antigen or immunogen is a substance that prompts the generation of antibodies and can cause an immune response. Antigens are defined as substances that bind to specific antibodies.

CANTILEVER BIOSENSOR

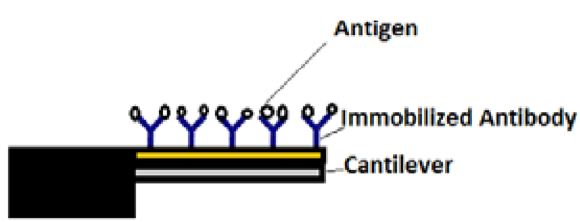

Figure 3: Cantilever Biosensor

Cantilevers(Figure 3) are structures which are fixed at one end and free at the other end .Gold coated cantilevers are immobilized with the specific antibody to detect tuberculosis. Blood sample is placed on the cantilever. The presence of Tb antigen in the blood sample will cause antigen

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antibody binding. The cantilever biosensor transduces the antigen antibody reaction into mechanical response which can be detected using different methods. Previous methods used for the detection of molecular binding,[7–10]chemical reactions,[11] and specific bimolecular interactions[12] have been based on static deflection of microfabricated cantilever beams[13,14] as used in scanning force microscopy[15].In these approaches, adsorption of target analytes to surfaces were used to induce mechanical stress thereby inducing cantilever bending.[16,17].Through various detection mechanisms,[18] the mechanical signal is transduced into either an optical or electrical signal, and deflections are related to imposed forces resulting from the adsorbed material. Microcantilever biosensors depend on their deflection to indicate sensing. This paper shows the simulation of electrostatically actuated microcantilever .The microcantilever is made to resonate any change in mass on the cantilever will cause a shift in frequency.

A relationship between the cantilever tip displacement δ and the applied surface stress σ can be expressed as [19]; The more material that is adsorbed, the more the microcantilever will deflect [20],[21],[22].

$$\delta = \frac{3\sigma(1-\nu)}{E}\left[\frac{l}{t}\right]^2 \qquad \text{......... (1)}$$

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.

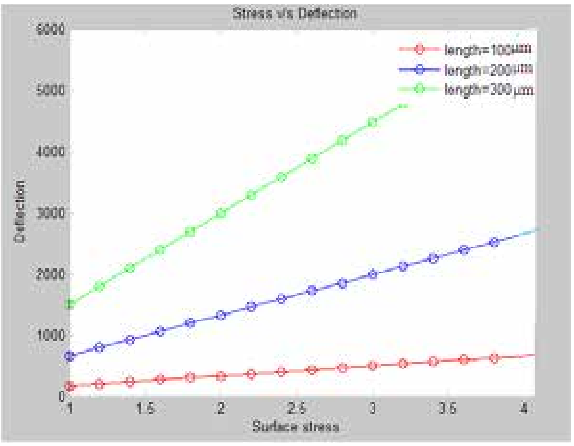

Figure 4: Plot of stress and deflection

Length of the cantilever, properties of the material from which it is made, geometric shape are the factors affecting the cantilever. These factors determine the ability of the cantilever to respond when a force is applied. In macro systems displacement caused by external load or stress is negligible but in micro systems this displacement is large to show a change in mass. Figure 4, shows the variation of stress with deflection of the cantilever. As the length increases there is more deflection for the same stress.

CANTILEVER RESONATOR

Figure 5: Cantilever resonator simulation

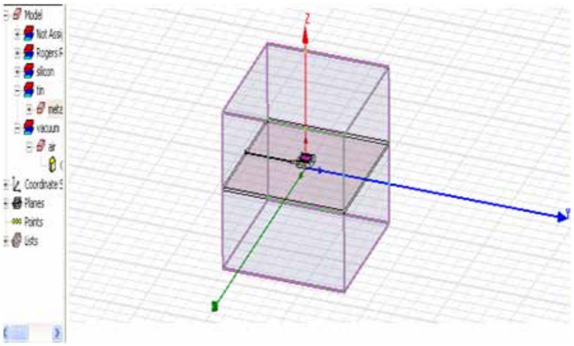

Figure 5 shows the simulation of resonator cantilever biosensor using HFSS software.Cantilever is electrostatically activated and made to resonate. Figure 6 shows the 3D polar plot of the resonator showing maximum amplitude at a particular frequency.

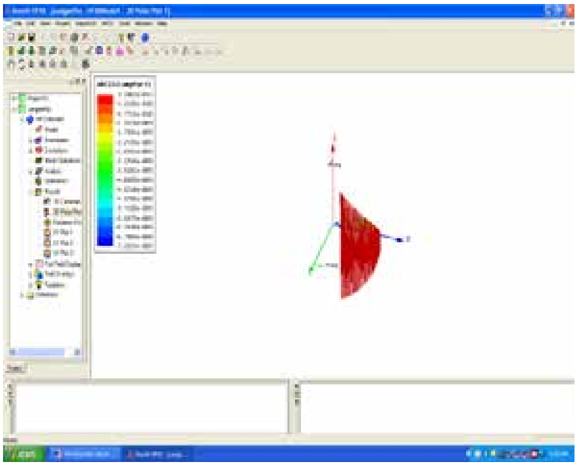

Figure 6: 3D Polar plot

CONCLUSIONS

The simulations and analysis of cantilever biosensor have been done. The cantilevers have been electrostatically excited into mechanical resonance and the resonance frequency has been detected. Antibody specific toTb has to be immobilized on the cantilever surface. Patient blood sample is placed on the cantilever .The sample containing Tb antigen will bind with the antibody. This antigen antibody binding will cause a shift in resonant frequency. The frequency shift is proportional to antigen antibody binding. This biosensor can be used as diagnostic device to detect the presence of tuberculosis.

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