Biosensor for Tuberculosis detection using MEMS device

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Abstract-A biosensor is a device which converts biological activity into quantifiable signal. Biosensors possess several unique features such as compact size, simplicity of use, one-step reagent less analysis, absence of radioactivity, etc. that make them very attractive alternatives to conventional biological sensing techniques. Most conventional microelectromechanical (MEMS) and nanoelectromechanical systems (NEMS) are designed for detecting and sensing. The sensing principle varies according to the device, the nature of the analyte molecules, and the precision required. Capacitance, piezoresistance and resonance frequency are among the sensing principles depending upon the mechanical properties of the device. The paper presents simulation and analysis of microcantilever based biosensor based on capacitive sensing. The biosensor structure is designed and simulated using Coventorware software. This biosensor can be designed as a microdiagnostic kit to detect diseases. This microcantilever based biosensor can detect tuberculosis by immobilizing specific antibodies on the microcantilever. These antibodies are specific to TB antigen 85 complex. When the patient sample containing TB antigen 85 complex is placed on the cantilever, biochemical interactions take place between TB antigens and the antibodies immobilized on the upper surface of the microcantilever. This causes microcantilever to bend and facilitates to detect the presence of Tuberculosis.

Keywords--Microcantilever, Biosensor.

I. INTRODUCTION

MEMS are tiny micromachined systems (measured in microns) that are typically arranged on small chips (less than cm by cm) for different purposes. They are primarily silicon based and manufactured using various etching and deposition techniques. MEMS applications are in inkjet printer heads, airbag deployment sensors, and biomedical sensors (biosensor). In this paper the capacitive sensing aspect of the biosensor using cantilever beam is focused. A patient blood sample will be introduced to the MEMS chip, and the goal will be to identify the mass adsorbed by the chip using capacitive sensing. Direct measurement of such a small amount of mass is difficult, which is why capacitive sensing is utilized to indirectly find the mass adsorbed onto the MEMS device. Biosensors are usually made by immobilizing a biologically-sensitive layer to a appropriate sensing system, which converts the biological response into a measureable and processable electrical signal. The biologically-sensitive materials can be an enzyme, a bacterial cell or other whole cell, an antibody or an antigen etc.

The molecular recognition is done by binding of the respective receptor area and the biological component (or analyte) to be recognized. When biological molecules come into 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. Fig 1 shows the diagram of a biosensor. These biosensors provide an analytically powerful and inexpensive alternative to conventional technologies by enabling the identification of target substances in the presence of a number of interfering species.

II. CANTILEVER BASED BIOSENSORS

Cantilever based biosensors uses mechanical transduction mechanism. It is based on the bending of micro fabricated silicon cantilevers, caused by the adsorption of biomolecules onto the sensor surface. In biosensors applications the displacement of a cantilever can be related to the binding of bio molecules on the surface of the cantilever beam, and is therefore used to compute the strength of these bonds, as well as the presence of specific reagents in the solution under consideration [1,2]. Stoney observed that the deposition of a tensile film on another material caused a curvature in the composite structure due to residual stresses in the deposited film [3]. Piezoresistive, [4, 5] piezoelectric [6, 7], thermal
expansion [8] or capacitive effects [9, 10] are the various method for detection. A major advantage of capacitive detection, is the fact that it offers both electrostatic actuation as well as integrated detection, without the need for an additional position sensing device. In capacitive detection an AC voltage at a frequency much higher than the mechanical bandwidth of the cantilever is applied.

The current output at that frequency is then used to estimate the capacitance, and consequently the cantilever position. This sensing scheme is the simplest position detection scheme available; however, it is widely believed to be less accurate than optical levers or piezoresistive sensing. Cantilevers (springboard) are micromechanical biosensors, microfabricated with the standard silicon technology. Their sizes are in the micrometer or nanometer ranges. The device that we propose is an electrostatically actuated microcantilever for biomolecular recognition. Due to their intrinsic flexibility, together with the availability of techniques designed to monitor bending, cantilevers are very useful in biosensing. This technology is a highly sensitive technique, and a real time method useful for a variety of applications, such as plastic explosive detection using gas biosensors, whole microorganism detection as part of liquid biosensors, or DNA and proteins studies. Functioning principle: Detection of molecular interactions involves the immobilization of antibodies on the cantilever surface for its use as a micromechanical sensor Fig (2). The selection of the biomolecule depends on the intended application. This principle applies whether if the biomolecule to be detected (analyte) will be presented in a liquid or a gas phase. The immobilized molecules provide the cantilever with specificity for the analyte. The specific molecular interactions taking place at the flexible surface of cantilever increase surface tension, forcing the cantilever to bend. This type of surface tension induced by molecular interactions is not generally observed on the surface of common materials. The cantilever senses the tension and bends in response to the free energy changes taking place at its surface.

III. FEATURES OF CANTILEVER BASED BIOSENSORS

Micromechanical cantilevers show great potential as highly sensitive biochemical sensors. Cantilever-based sensing involves the transduction of a bimolecular interaction to a measurable mechanical change in the cantilever resulting from induced surface stresses added mass. When target molecules interact with the sensitized surface of the cantilever, the change in surface stress between the sensitized and passivated surfaces results in a measurable mechanical deflection of the cantilever beam. Recent advances in MEMS promise considerable and realistic potential for the development of innovative and high performance sensing and diagnostic approaches in biomedical field.

IV. DESCRIPTION FOR A SINGLE CANTILEVER

The schematic of a single cantilever sensor is shown in Fig. (3). It consists of two adjacent electrically conductive beams forming the two plates of a capacitor. One of the beams is rigid, while the other referred to as the cantilever and represents the movable part of the structure. Sensor size of a length of 100 um, 35 um wide and 0.5um thick was simulated using Coventerware software.

If the length of the cantilever is much bigger than its distance from the bottom plate, the capacitance is given by

\[ C(z) = \frac{A \varepsilon_0}{d - z} \]

Where, \( \varepsilon_0 = 8.85 \times 10^{-12} \text{ As/Vm} \) is the permittivity in vacuum, \( A \) is the area of the plates, \( d \) is the gap between them and \( z \) is the vertical displacement of the cantilever from its rest position. The attractive force, \( Fa \), between the capacitor plates generated by applying a voltage \( V(t) \), can be easily found to be
\[ F_a = \frac{1}{2d^2} \left( 1 - \frac{z}{d} \right)^2 \approx \frac{1}{2d^2} \left( 1 + \frac{2z}{d} \right) V^2(t) \]

Where, the approximation holds when \( z/d \ll 1 \). Fig (4) shows the relationship between oscillation distance and natural frequency. Max oscillation of a cantilever beam occurs at the natural frequency \( \omega_n \) and using (1), by determining the capacitance of the MEMS device the oscillation distance can be found experimentally.

\[
\omega_n = \sqrt{\frac{k}{m}} \text{ or } f_n = \frac{1}{2\pi} \sqrt{\frac{k}{m}} \ldots (1)
\]

Where, \( k \): stiffness constant of cantilever beam (N/m); \( m \): mass (gram); \( \omega_n = 2(\pi)(f_n) \): natural frequency of oscillation of cantilever (rad/sec).

\[ \text{Fig. 4 Oscillation Amplitude vs. Natural Frequency} \]
\( \omega_0 \) is the natural frequency with no mass adsorbed by the MEMS cantilever, and \( \omega_f \) is the natural frequency after mass is adsorbed onto the cantilever.

V. SYSTEM BLOCK DIAGRAM

The procedures for determining natural frequency are as follows. MEMS chip with sample to be adsorbed onto the cantilever beam is made ready. Sample is placed on the MEMS chip which is connected with probes. A small sinusoidal signal is applied to make the cantilever beam oscillate. Maximum capacitance can be determined (this implies maximum amplitude of oscillation). Natural frequency is tracked as biomolecular recognition takes place on the cantilever beam, by adjusting the frequency of the AC voltage input accordingly. Inputs to the system include the voltage wave (amplitude in the millivolts range, frequency in the KHz range), and the biomass that is added to change the natural frequency of the cantilever beam. After measuring the capacitance we can determine oscillation distance which will indirectly tell us the mass of biomass adsorbed onto the beam. Sensor simulation was done using coventorware software. Results show the displacement of the cantilever beam with applied voltage and different modes with frequency.

VI. MICROCANTILEVER BASED DIAGNOSIS OF TUBERCULOSIS

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis the bacteria exist as rods ranging in size from 0.3 to 0.6 millimicrons by 1 to 4 millimicrons straight or slightly curved, occurring singly or in occasional strands. Tuberculosis (TB) is the most infectious disease with one-third of the world population infected, 8 million people developing the active disease and 2 million dying of TB each year. India and China alone account for 3 million cases each year. It is estimated that 4 out of every 1000 persons are suffering from active disease, which in turn decimates nearly 5000 persons every day in India tuberculosis typically attacks the lungs, but can also affect other parts of the body. Diagnosis of TB in the early stages is very important. This MEMS biosensor can be used as a diagnostic tool to detect TB. This microcantilever based biosensor can detect tuberculosis by immobilizing specific antibodies on the microcantilever. An antibody (Ab), also known as an immunoglobulin (Ig), is a large Y-shaped protein produced by B-cells that is used by the immune system to identify and neutralize foreign objects such as bacteria and virus. The antibody recognizes a unique part of the foreign target, called an antigen Fig (6). Each tip of the "Y" of an antibody contains a paratope (a structure analogous to a lock) that is specific for one particular epitope (similarly analogous to a key) on an antigen, allowing these two structures to bind together with precision. Using this binding mechanism, an antibody can tag a microbe or an infected cell for attack by other parts of the immune system, or can neutralize its target directly.

Fig. 5 Block Diagram
The antibodies that are specific to TB antigen 85 complex is coated on the microcantilever. When the patient sample containing TB antigen 85 complex is placed on the cantilever biochemical interactions take place between TB antigens and the antibodies immobilized on the upper surface of the microcantilever. This causes microcantilever to bend and facilitates to detect the presence of Tuberculosis. The paper presents simulation and analysis of microcantilever based biosensor based on capacitive sensing. This system consists of two adjacent electrically conductive beams forming the two plates of a capacitor. One of the beams is rigid, while the other referred to as the cantilever and represents the movable part of the structure. When the cantilever bends due to the stress created by the antigen antibody binding capacitance changes. Increase in mass due to adsorption causes the resonant frequency of the oscillation of cantilever to change, by measuring the capacitance and resonant frequency change we can detect the presence of the disease.

VII. RESULTS

Outputs of biosensors were simulated using Coventorware. Outputs show the cantilever bending due to biomolecular interaction. The software simulations also give different capacitance values. Sensor size of a length of 100 um, 30 um wide and 0.5 um thick was simulated using Coventorware software.
VIII. CONCLUSION

The field of MEMS has experienced an exponential growth. Researches have recently focused on the search for alternative materials to the already traditional silicon based technology. Simulation for an electrostatically actuated microcantilever has been derived based on the idealization of a movable plate capacitor. The biosensor structure is designed and simulated using Coventorware software. This bio sensor can be used to detect Tuberculosis. The Coventorware simulation results are presented and analysed.

REFERENCES

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