Review of Micro cantilever sensors for detecting diseases: Fabrication Methodologies and sensing techniques

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Abstract. Recently Lab on chip devices are widely used for detecting various diseases. Cantilever being used as commonly among variety of sensors used on such chips. This paper presents review of various fabrication methodology and analysis techniques used in sensing diseases using micro-cantilever sensors. The principal aim in detecting diseases using blood sample is to know concentration of antigens or bacteria in sample. This also provides stage of disease in the patient. Various techniques such as ELISA (Enzyme Linked Immunosorbent Assay), Radio-Immuno Assay, X-ray are used for detecting the stages of disease. However, time required in these techniques is very large. To reduce the time in detection, simple micro cantilever Bio-sensor is used widely. For the purpose of detection, cantilevers are coated with antibody to attract the antigens from blood sample which is dropped on cantilever beam. Antigens that get adhered to the surface of cantilever thus develop a surface stress causes bending of cantilever. This redirection of the cantilever can be detected by various strategies and thus we can predict about the concentration of the antibodies in a particular blood sample. This paper exhaustively presents the fabrication methodology and disease detection technique using micro-cantilever.

1. Introduction
This Micro Cantilever Bio-sensor usually uses an array of cantilever beams whose sizes are in range of microns and have an antibody immobilized on the surface of the cantilever beam. For the purpose of sensing the antibody is immobilized on the surface of the cantilever beam. The antigen present in the blood sample dropped on the beam gets attracted or repelled from the antibodies immobilized on the beam. The concentration of antigens to antibody thus leads to the deflection of cantilever beam developing surface stress.[1-2]

Antibodies are used to attract the antigens from the blood sample so that they get adhered to the cantilever beam. As different diseases have different antigens, different antibodies for different diseases have to be used. Antibody varies from disease to disease. A counter acting agent (antibody) is fundamentally a ‘Y’ formed protein that is used to identify foreign objects like bacteria and viruses. Each tip of ‘Y’ has a paratope that is specific for one particular epitope or an antigen.[2-4]

Cantilever sensor consists of simple structure fixed at one end and free at the other end (see figure For increase in sensitivity the structure has different variants (see figure 2, 3, 4). Here the dimensions width, length and thickness are varied to enhance the sensitivity (deflection) for the same loading
conditions. Although the variants increase the sensitivity of the structure, it is difficult to develop with present micro-fabrication techniques. Bulk lithography [5] has presented the capability to produce cantilever with varying thickness. However, the minimum feature size of structure, formed are in order of 100 microns and surface roughness is in order of 10 microns. This restricts its utility as sensor. A Micro Cantilever Bio-sensor has its dimensions usually in the order of few microns ranging from 1 to 100 microns.

![Figure 1. Dimensions of Micro-cantilever](image)

![Figure 2. Front view of Micro Cantilever showing decrease in Thickness](image)

![Figure 3. Top view of Micro Cantilever showing decrease in Width](image)

![Figure 4. Front view of Stepped Cantilever](image)

![Figure 5. Y-shaped protein.](image)

Such a Micro Cantilever beam has a series of different processes that are to be carried out in order to fabricate it. Fabrication process mainly includes the different sub processes like Thermal Oxidation,
Hot Wire Chemical Vapour Deposition (HWCVD) and also Inductively Coupled Plasma Chemical Vapour Deposition (ICPCVD). Once the deflection is obtained on the Micro Cantilever the only task remains is to sense the deflection of the beam. Many different methods have also been developed to measure the deflection of cantilever beam. These methods are mainly Optical Detection Method, Piezo Resistive Method and also Capacitive Method. [6]. This paper reviews these fabrication processes [7-11] and present their merit and demerits. Further paper also presents the different deflection measurement techniques which are used as one of the sensing parameter for determination of disease.

2. Fabrication.
The Fabrication of Micro Cantilever involves different steps of layering as follows:-

2.1 Step i. Selection of Silicon Wafer.
A p-type Silicon Wafer is used as the substrate on which the complete setup of Micro Cantilever Bio sensor is mounted. Very first the selected substrate material is cleaned by a standard process called as RCA (Radio Corporation of America) cleaning. This is done to evacuate organic as well as metallic contaminants. This is done by dipping it in different chemicals like NH$_4$OH , DI water, HCL HF which is followed by subsequent heating and cooling of substrate.[6]

![Figure 6. RCA Cleaned Silicon Wafer](image6.png)

2.2 Step ii. Deposition of Silicon di-oxide (SiO$_2$) layer.
After RCA cleaning Silicon di-oxide (SiO$_2$) is deposited by a method called as Thermal oxidation. A layer of 250 nm of SiO$_2$ is to be deposited by thermal oxidation as shown in the setup diagram as shown below in figure 7. This is done to provide isolation between the upper layers to be deposited and the silicon substrate.[6]

![Figure 7. Thermal Oxidation of silicon wafer.](image7.png)

It consists of wafers arranged horizontally in the heating furnace which contains water vapor. Hydrogen and oxygen gas get heated when it is passed through the heating element. The temperature of silicon wafer is raised to temperature of about 1100°C. The Oxygen reacts with the silicon surface to form Silicon-di-Oxide (SiO$_2$). Thus the layer of Silicon-di-oxide is formed just by oxidizing its upper layer[5]. SiO$_2$ layer formed is shown as in figure 8.
2.3 Step iii. Deposition of Poly Silicon layer:
After deposition of SiO$_2$ the next step is deposition of Polysilicon and it is done by a method called HWCVD (Hot Wire Chemical Vapour Deposition). This is an important layer as it forms a structural part of Micro cantilever. The setup diagram is shown in figure 9. Subsequent to setting the substrate temperature is raised up to 300°C. Here proportion 1:5:10 is set in gas stream controller for SiH$_4$:B$_2$H$_6$:H$_2$.

When these gases pass from the filament that is heated to the temperature of 2100°C, Silane gas gets decomposed to one Si atom and four H atoms. Thus a layer of Polysilicon is formed on the substrate. And when it is continued for further 30 minutes a complete layer of 1 micron is formed as shown in Figure 10. This method is specially used to have small layer deposition which is usually in the order of microns. [12]

2.4 Step iv. Patterning of Polysilicon layer.
The subsequent stage after testimony of Polysilicon layer incorporates patterning of Polysilicon. The patterning is finished by technique called RIE (Reactive Ion Etching). It is a sort of a Dry Etching.
Technique where a material is evacuated, commonly a masked material by presenting it to the barrage or bombardment of ions and is appeared in figure 11.

![Figure 11. Reactive Ion Etching.](image)

In this procedure for Polysilicon scratching we utilize the gas SF$_6$ (Sulfur Hexa-fluoride). The test arrangement comprises of the encased chamber with substrate holder with negative terminal beneath and positive terminal over the substrate. Hexafluoride gas is presented inside the chamber and at the same time a solid RF electromagnetic field of 1500W is connected. This causes the ionization of SF$_6$ particles making SF$_5^+$ particles. Because of enormous potential contrast connected over the posts SF$_5^+$ particles will in general float towards the Silicon substrate. These ions slam into the samples to be etched [13]. As a result the removal of the entire layer takes place and we get the electrode formed from the previous Polysilicon layer as shown in figure 12.

![Figure 12. Patterning of Polysilicon.](image)

2.5 Step v. Deposition of Sacrificial layer.
This layer is stored by the strategy for ICPCVD (Inductively Coupled Plasma Chemical Vapor Deposition). It utilizes the gases like SiH$_4$ and N$_2$O to store the layer of SiO$_2$. In the exploratory arrangement of ICPCVD as appeared in figure 13 the encased chamber has a channel opening that is associated with the gas chamber that contains the gases like SiH$_4$ and N$_2$O. The substrate is put on the substrate holder and is raised to the temperature of 400 °C. At the point when gases enter through the opening RF intensity of around 30 W is connected which causes a chemical reaction between SiH$_4$
and N$_2$O which results into the arrangement of SiO$_2$. This Silicon-di-oxide layer that is created acts just as a conciliatory layer. The designing that is required as appeared in figure 14 is finished by RIE.[14]

![Figure 13. Inductively Coupled Plasma Chemical Vapor Deposition](image13)

![Figure 14. Deposition and Patterning of Sacrificial layer.](image14)

2.6 Step vi. Deposition of Polysilicon layer.
In the wake of patterning of Sacrificial layer, again the Polysilicon layer of thickness 1 micron must be stored as appeared in figure 15. Same HWCVD technique is utilized to deposit Polysilicon.

![Figure 15. Deposition of Polysilicon layer.](image15)
2.8 Step vii. Patterning of Polysilicon and Removal of Sacrificial layer.
The last advance comprises of patterning upper layer and evacuation of Sacrificial layer as appeared in figure 16. Patterning is finished by same RIE strategy while Removal of Sacrificial layer is finished by dunking it in Acetone \((\text{CH}_3\text{CO})_2\) and evaporating. This method is utilized to accomplish total evacuation of Sacrificial layer including all the base corners.

![Figure 16. Patterning and removal of sacrificial layer.](image)

3. Measuring the deflection of Micro-cantilever.
The capacity to delicately distinguish the physical changes coming about because of stresses connected is a basic part of any micro scale mechanical optical location sensor. By knowing the deflection of Micro Cantilever we can guess the amount of antigens that are immobilized on the cantilever beam from the blood sample. The methods to detect the deflection of Micro Cantilever Bio sensor are :

a) Optical detection method.
b) Piezo Resistive Transducer.
c) Capacitive Transducer.

3.1. Optical Detection Method.
Optical Detection method utilized for estimating the diversion of miniaturized scale cantilever essentially utilizes the low power laser and Photo Sensitive Detector (PSD). At the point when light is episode on the cantilever bar by the laser diode, it gets reflected toward PSD due to gold covering present on the outside of the cantilever as appeared in figure 17. This situation of light on PSD is noted down.[15]

![Figure 17. Reflection of light when Cantilever is undeflected.](image)
At the point when the cantilever is deflected because of the surface burdens built up the situation of light on PSD changes which is appeared in figure 18. The distinction between two positions is only the deflection of Micro Cantilever. This sort of diversion location gadget utilizes Laser diode as well as Photo Sensitive Detector, it makes the framework progressively cumbersome and furthermore cost of the entire arrangement of framework is more. In this manner, this estimating method has turned out to be out of date.[15]

![Figure 18](image)

**Figure 18.** Reflection of light when Cantilever is deflected.

### 3.2. Piezo Resistive Transducer.

Creation of the Micro Cantilever including Piezoresistive transducer is somewhat unique in relation to that of standard Micro Cantilevers. The Micro Cantilever comprises of a Structural layer, Piezoresistive layer and an Antibody layer as appeared in figure 19.

![Figure 19](image)

**Figure 19.** Schematic cross-section of the measurement cantilever.

Alongside the customary basic layer of SU8 polymer it likewise comprises of Piezoresistive layer as appeared in above figure. A twin-cantilever structure in a single chomp, the residue was seen as where one is the reference and other is the measurement cantilever as showed up in figure 20. Simply the measurement cantilever will be secured with bio-identifying particles. Subsequently just measurement cantilever will be diverted because of stress created because of antigens. This redirection is contrasted and the undeflected reference Micro Cantilever and the difference in deflection is determined. Measurement of diversion utilizing Piezoresistive transducer includes the electrical circuit as appeared in figure 21. The two resistors indicated are only the reference and measurement cantilevers separately.[16]
Two Piezoresistors are related to equal expansion between centers X and Y, and are continued with sine waves drivers, that are 180° stage isolated for each Piezoresistor. The voltage divider center point A sets at 0mV if the resistors are undefined. Due to \((\delta R)\) changes in the estimation cantilever in diverted conditions, a little AC voltage appears at the center point A. This signal is intensified and associated with the signal contribution of a lock in Amplifier (LIA), in light of the fact that the significance of the sign at A degrees from nanovolts up to two or three microvolts and thus it ought to be enhanced. The yield of LIA is a DC voltage which is relative to the block assortment \((\delta R)\) which is with respect to avoidance in the measurement cantilever.[16]

### 3.3. Capacitive Transducer.

The Capacitive technique depends on the rule that when the cantilever diversion happens because of the adsorption of the analyte, the Capacitance of a plane Capacitor is changed. The figure 22 proposes...
the plan of Micro-cantilever and fixed shaft. The contraption showed in the figure works for a couple of stages, and the amount of portable and fixed electrodes may be extended for further stages. The capacitance between the versatile and fixed electrodes change as the column diverts on the usage of bio molecule. The adjustment in capacitance is subsequently transuded as the proportion of deflection. [17-19]

Figure 22. Bio-MEMS cantilever device

4. Conclusion.
Micro Cantilevers have been demonstrated helpful to determine the illness to have a less time when contrasted with different procedures. Its creation is an impressive huge procedure that includes distinctive sub procedures like RCA cleaning, warm oxidation, HW-CVD, ICP-CVD and Reactive Ion Etching. Out of the considerable number of strategies for estimating the deflection of cantilever Piezo Resistive technique is for the mostly utilized because of its precision.

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