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A study and analysis of Microcantilever materials for disease detection*

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Abstract

Significant progress on the use of MEMS cantilever sensors to detect the various diseases has surveyed. The Cantilever made in the micrometer size provides an opening to develop a highly sensitive sensor. It detects the biological molecules, chemicals, diseases and explosives. MEMS cantilevers can be produced in abundance at low cost with the material like Silicon, Silicon Nitride and Polymers. This paper has summarized various cantilevers for different diseases into a tabular form. This will enable the researchers to pick up genuine cantilever for right disease by choosing different materials, size and shape. And also it addresses various read out techniques used to detect the different diseases.

Keywords:
Microcantilever, MEMS, Sensor, Resonant Frequency, piezoresistive, piezoelectric and optical lever

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Keywords: Type your keywords here, separated by semicolons ;

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1. Introduction

For the past twenty years, microcantilever was found to be immensely applicable to sense the various diseases with micro samples in the biosensing field [1].A microcantilever is a beam fixed at one end and free at the other end. It is simple MEMS (Micro Electro Mechanical system) component. It is frequently used as Biosensor and chemical sensor to detect many diseases with micro samples. [2]. The characteristics of the microcantilever are more sensitive, fast measurement of mechanical movement, less power consumption, various stimuli can be measured with microcantilever array. The two modes of the operation of the cantilever are static mode and dynamic mode [3]. In static mode, the cantilever bends due to the surface stress [4] by bimolecular reaction [5-10] of the disease molecules on the surface of the cantilever. In dynamic mode [11], the absorption of the disease molecules [12] increases the mass of the cantilever and resonant frequency changes. The extremely sensitive cantilever arrays are used to detect the multiple analytes [13] existing in the micro sample. The sensitivity of the cantilever is improved [14] [15] by using different shapes of the cantilever to detect the disease. Many Researchers have reported about the cantilever based sensor [16]. The current survey concentrates on disease detection using different shapes and materials of microcantilever only.

2. Different read out methods

When the biomolecules falls on the cantilever, it binds with the antibody coated on it. The cantilever bends due to the added biomolecules on the surface, which induces surface stress on it. The deflection of the cantilever can be read by different techniques like optical, piezoresistive, piezoelectric, hard-contact read out and capacitive [17-22].

Optical lever method was novel method [23-24] used to detect minute deflection of the cantilever. The laser beam falls on the free end [25] of the cantilever. The reflected laser light [26] is received by the position sensitive photo detector [27-28]. The received light converted into electric current which determines measure the deflection of the cantilever. The deflection from the cantilever array can also be measured optically [3].In Piezoresistive method [29] of sensing, the cantilever has embedded with piezo resistors like p-doped or n- doped silicon [30-31] to measure the strain induced [32-33]. Silicon gives good piezoelectric effect and most commonly used material.[34-35].The piezo resistors are embedded near the fixed end of the cantilever to measure the stress and achieve maximum sensitivity. [36].When the cantilever bends, the resistance of the piezo resistor change and it can be measured using Wheatstone bridge [37]. This method can sense the deflection of the cantilever in liquids and gas in a better way [38]. This technique is used for static mode and dynamic measurement. The demerit of piezoresistive scheme is less sensitive and produces more noise than optical read out [39].The cantilever plate is acts one of the electrodes of the capacitor. The other parallel electrode kept very near to the cantilever [38]. When the cantilever deflects, the distance between the cantilever and the parallel plate changes .Thus the capacitance is changed and deflection is measured. This method is not applicable for liquids. It is highly sensitive for small measurements and not suitable for big displacements. [40]. The piezoelectric material is integrated on the fixed end of the cantilever. When the cantilever bends, it experiences stress and voltage is generated across the piezo material [23] and vice-versa [38]. The different piezoelectric materials can be embedded into the cantilever are Zinc Oxide, Lead Zirconate Titanate (PZT-2) and Quartz.[41].For accurate measurement the cantilever can be operated in dynamic mode. Thin piezoelectric material unable to hold the voltage developed during the static mode. Hence sufficient thickness of the cantilever should be maintained. In the tunnelling method the cantilever is kept near the counter electrode. The tunnelling current is measured between the counter electrode and the cantilever. The fabrication is very complex to realize a very small gap between the electrode and cantilever [38].The hard contact technique [42] was built on the on-off switch structure [43]. The cantilever 'switches-on' the electrical path as it deflects and touches the counter electrode and 'switches-off' when it arrives to the initial position. It can produce large electrical signals when compared to other methods. The merit of this method is simplified electronics design. Quasi-static deflection measurements cannot use this technique because of switching nature [38].

3. Different shapes of Cantilever

The different shapes of the cantilever like rectangular [44-46][32-33], trapezoidal[47], triangular, stepped profile[48], V shaped cantilever[49], T-shaped[50] [51] [52] are used to assess the deflection of the cantilever when the same magnitude of stress applied on it. The sensitivity of the different shapes of the cantilever can be measured and able to detect different diseases. The complex shapes are modeled and simulated using different FEM software. The Software helps us to forecast the complete structure, behavior and analyze the performance of the device before fabrication, which reduces the cost of the MEMS devices.

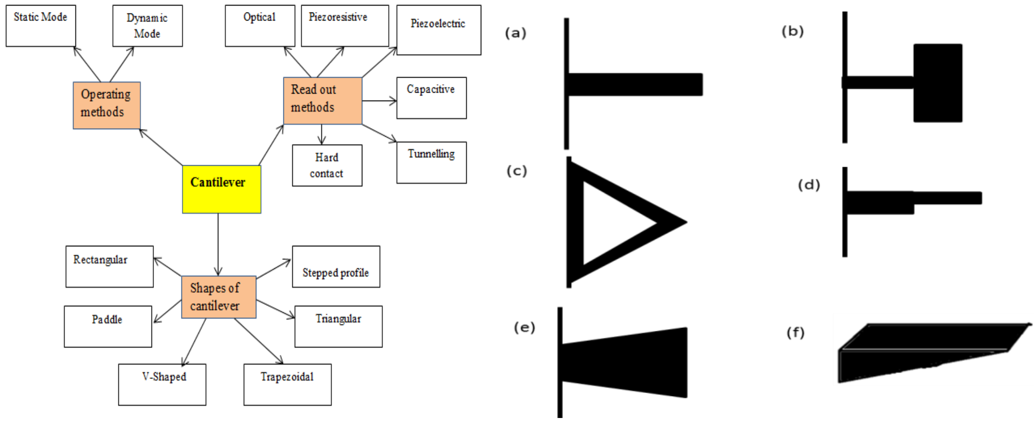

Fig.1. (a) Different Transduction principles of Cantilever ; (b) Different shape types of microcantilever (top view) (a) Rectangular (b) T-shaped (c) V-shaped (d) stepped profile (e) trapezoidal (f) Triangular.

4. Detection of different disease with various materials of cantilever

The productive cantilevers are customarily made of silicon, silicon nitride, silicon oxide, polysilcon. These distinct shapes of cantilever of different materials can detect different disease are given below in table 1

Disease Detected	mode/Read–out Method	Dimension/ Cantilever Material	References
Cancer and cardiac markers	piezoresistive	Gold	[53]Datar. R et al., (2007) [50]Sreevidhya et al (2010)
Acute Myocardial Syndrome	optical	L= 2.5mm / polymer coated with aluminum beams	[54]Ion Stiharu et al.,(2005)
Breast Cancer	piezoelectric	Nickel + PMN-PT	[55]LiNa Loo et al., (2011)
Hepatitis A and C viruses	optical	t=1nm/Electroplated Nickel +t=100nm Gold	[56]Erman Timurdogan et al ., (2011)
Pathogen	resonant shift	L= 180 mm /Silicon Nitride	[57]Weeks B.L. et al., (2002)
Hepatitis B Virus	Piezoresistive	L=150µm/Gold/ Ti Layer	[58]Yu-Jie Huang et al ., (2013)
low density lipoprotein	Piezoresistive	L= 200µm /Silicon +gold	[33]Kalaiarasi A R et al., (2011)
tuberculosis	electrostatic	L=100µm/ Silicon nitride +Gold	[59]Sangeetha P et al., (2013)
Glucose Sensing	Piezoresistive	L=195µm /Polysilicon	[60]Nina Korlina Madzhi et al., (2012)
Cancer	Piezoresistive	T=650nm/SiO_2	[61]Youzheng Zhou et al., (2005)
Bacillus Anthrax, Pseudomonas aeru-ginosa, Coryne Bacterium Diptheria ,	piezoelectric	L=200µm / Silicon+Gold	[62]J. Sakthi Swarrup et al., (2010)

Tre-ponema pallidum			
myoglobin and creatin kinase-MB	piezoelectric	L=150 µm / silicon nitride, silicon dioxide/platinum , PZT+ Gold	[63]Kyo Seon Hwang et al., (2007)
Cancer	optical	Gold	[64]Hashem Etayash et al., (2015)
tuberculosis	piezoresistive, piezoelectric or capacitive effect	L=100 µm / Silicon nitride+ Gold	[65]Sangeetha P et al., (2014)
HIV virus	Resonant method	L= 150 µm /Silicon di oxide	[66]Gopinath.P.G. et al., (2014)
Cancer (prostate-specific antigen)	piezoelectric	polycrystalline silicon+ Lead Zirconate Titanate+Gold	[67]Raghave Gupta et al., (2015)
C-Reactive Protein	piezoresistive	L=200 µm /Silicon nitride+Gold	[68]Yi-Kuang Yen et al., (2013)
Myoglobin protien	optical	L=190 µm / Silicon nitride+Gold	[69]Grogan C et al., (2002)
prostate-specific antigen (PSA)	optical	L=200 µm /Silicon nitride+Gold	[70]Guanghua Wu et al ., (2001)
C-reactive protein	piezoelectric	L=310 µm / Silicon Nitride/SiO_2/Pt	[71]Jeong Hoon Lee et al., (2004)
prostate specific antigen (PSA) and C-reactive proteins	piezoresistive	PolySilicon +Gold	[72]Kyung Wook Wee et al., (2005)
Liver cancer	Difference between reference and sample cantilever	Silicon+Gold	[73]Xuejuan Chen et al., (2016)
Human papilloma virus	magneto-mechanical	L=500 µm /Silicon+Gold	[74]Hyung Hoon Kim et al ., (2015)
Breast Cancer	piezoresistive	L=260 µm /Polysilicon + Su-8	[75]Hardik J. Pandya et al., (2015)
Triglyceride	enzymatic hydrolysis	L= 200 µm +Polysilicon	[76]Renny Edwin Fernandez et al., (2009)

Table1: List of different diseases, readout techniques and material table

5. Modelling and Simulation

Modeling is the process of gaining a deeper understanding of a system through imitation. Simulation shows how models behave in a particular environment. [77].

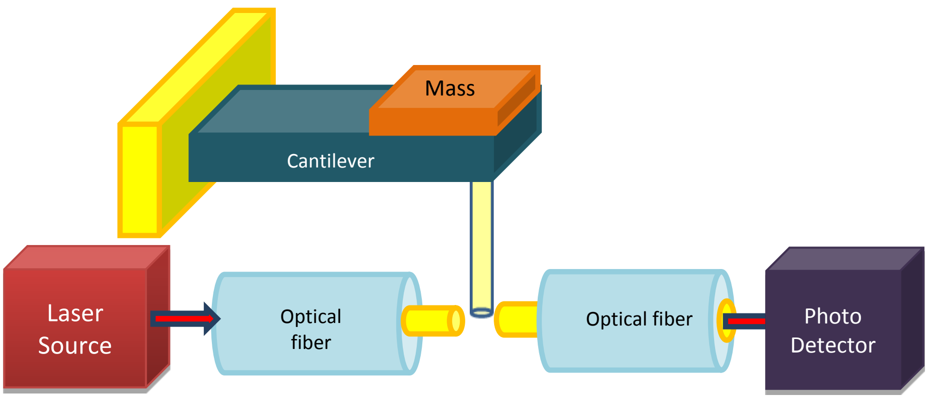

Fig. 2. Block diagram of the Mass detection Optical MEMS Sensor

Ptolemy II is an open-source framework for modelling, simulation, and design of concurrent systems [78]. The Ptolemy models can be built using the graphical environment Vergil. [79]. The main components in Ptolemy are Actors and Directors. The Directors play vital roles in coordination of actions between different Actors. Actors are components written in java language [80] that execute concurrently and communicate data with each other by sending messages via ports. A model was created in the Vergil editor and then simulated and analyzed.

The block of the MOEMS Sensor is shown in fig 1.The MOEMS Sensor contains a laser source, detector and microcantilever beam connected with slit as shown and co-axial fibers1 and 2. The slit will vary the intensity of light passing through the fiber 2 depending on the force applied to the microcantilever. In the present investigation, we developed software codes for various actors in a software platform called Ptolemy. The various actors are Laser, Photo detector and Mass Actor. The software can be tested [81]by applying various mass on the cantilever.

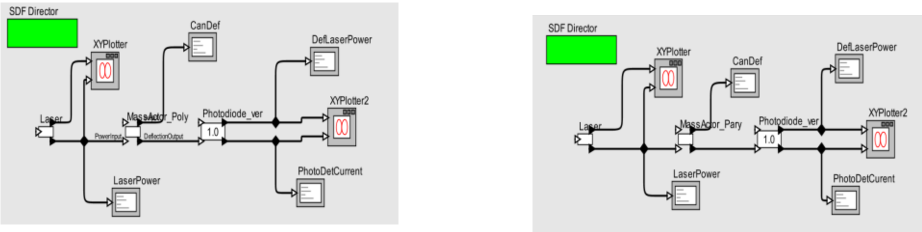

Fig. 3. Model of the Optical MEMS Sensor using Ptolemy II.(a) Polyimide Material ;(b) Parylene Material

6. Results and Discussion

Different actors like laser actor, Force actor and photodetector have been developed and added in Ptolemy framework. The physical functioning of each device has been simulated using these actors. The results have been presented. The MOEMS based macro mass sensor is simulated in Ptolemy II and able to sense the low mass of 50.96µm to 32.72e-3 using Polyimide material as Cantilever and sense the low mass of 30.58e-6to 27.72e-3using Parylene material as Cantilever with the present fiber optic setup. The results are shown in the Fig 3.

Polyimide Optical MEMS Sensor		Parylene Optical MEMS Sensor	
Mass (gms)	Cantilever Deflection	Mass (gms)	Cantilever Deflection
50.96e-6	2.718E-7	30.58e-6	1.9286e-7
5.097e-3	2.719E-5	5.097e-3	3.2143E-5
0.02	1.0875E-4	0.01	6.4286E-5
32.72e-3	1.7454E-4	27.72e-3	1.7486E-4

Table 2: Mass Applied vs. Cantilever deflection of the Two Optical MEMS Sensor using Ptolemy

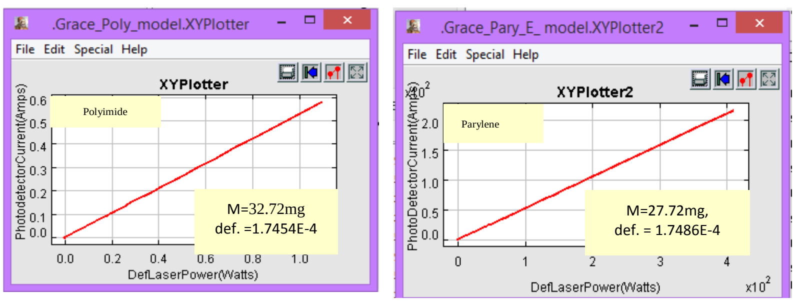

Fig 4: Simulation result of the Optical MEMS Sensor Deflected Laser Power Vs Output Current at the photodetector (a) using Polyimide material ;(b) using Parylene

7. Conclusion

A Significant progress on the present state of MEMS cantilever sensors to detect the various diseases has reviewed. Different materials and dimension used to identify different diseases are summarized and presented in a complete table which focuses on the dimension, material, shape and different disease that were detected through cantilever. In spite of the vast published papers, many important concepts are yet to be explored .They are (1) sensor non-linearity in cantilever disease detection applications(2) testability of sensor response repeatedly(3) enhanced understanding of antigen –antibody binding on the surface of the cantilever (4) enhanced understanding of added mass of the antigens and the surface stress contribution. With the present set up we can sense the low mass of disease detection molecules in the order of 30.58μg using Parylene as cantilever material.

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