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MEMS based Piezoelectric Sensor System for Virus Detection

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***Abstract* — In this paper we design a novel piezoelectric MEMS sensor for the detection of 100nm size viruses that include HIV and Herpes. A PZT-5A piezoelectric micro cantilever of length 500 µm is used in the model for sensing changes in mechanical vibrations caused by adsorption of virus mass of the order of ng at the tip of cantilever, producing an output signal at different resonant frequencies. A COMSOL model for the MEMS based piezoelectric sensor shows high sensitivity to changes in attached mass at the tip. This would allow the sensor system to be used for detection of specific viruses by incorporating appropriate biomarkers that provide selective binding for such viruses. Design of op-amp based signal processing circuits provides high gain, low noise output. The results strongly indicate the reliability of designed sensor for 100 nm HIV, Herpes viruses.**

***Keywords* — MEMS/NEMS, Cantilever, sensors, COMSOL Multiphysics, Piezoelectric, biomarker, amplifier.**

I. Introduction

The detection of multiple target molecules in a small volume of sample has immediate relevance in the early detection of diseases, such as viruses of the type HIV and Herpes, which fall in the size of 100nm [1]. High frequency nano electromechanical systems (MEMS/NEMS) are being considered as new sensors and devices. The ability to tailor the surface properties with specific biomolecules can be used to create chemically functionalized MEMS/NEMS cantilever for study of physical chemistry, bio molecular biocompatibility and interactions. It may be possible to detect and study pathogen viral binding by observing their effects on the MEMS/NEMS devices [2]. Some of the currently used MEMS sensors include blood pressure sensor, Triglyceride biosensor, sensors for glucose detection and blood cell counter [3-7]. While the design of all these micro or nano sensors are based on various optical methodologies, not much literature is available for detection of such viruses using piezoelectric sensors. The present work describes modeling of a PZT-5A micro-cantilever structure to convert mechanical vibrations to voltage, which can be used as a sensor for virus detection to provide a novel approach for biosensing.

A cantilever when placed in an oscillatory environment produces strain, which in turn produces stress that results in the generation of electric potential across the piezoelectric material. The electrical output attains a peak value if the vibration frequency of the environment matches the resonant frequency of the cantilever, and dies out dramatically when it deviates from the resonant frequency of the device. The sample mass lowers the resonance frequency to a value of the order of few hundreds of Hz [8]. It also increases the amount of deflection, thereby increasing the amount of stress produced at the fixed end [9]. By having a PZT layer at the fixed end of the cantilever, an increase in stress produced results in an increase in the output voltage. Appropriate electrodes and an op-amp circuit can be used for acquiring and amplifying the incoming voltage signal.

Binding of viruses can be done by using various biomarkers which are detection specific. There is range of soluble biomarkers for HIV which depends on markers of immune activation, markers of coagulation, tissue fibrosis and inflammation and markers of enterocyte damage and monocyte activation [10].

A. Design of Piezoelectric Cantilever

The design consists of micro cantilever beam which is anchored at one end and free at the other. The schematic of PZT-5A micro cantilever is as shown in “Fig.1”. A micro cantilever having dimensions 500µm x 100µm x 7µm made of polysilicon is taken as first block for design. The second layer is a 500µm x 100µm x 7µm SiO_2 insulator with a 200µm x 80µm x 4µm pit positioned (200,0,4) to bind maximum number of viruses. At the fixed end, on top of the cantilever, a piezoelectric material PZT-5A having dimensions 50µm x 100µm x 2µm is sandwiched between an upper platinum electrode and a lower platinum electrode. The purpose of platinum electrode is to take out electrical terminals for measuring the generated output electrical voltage. SiO_2 layer is

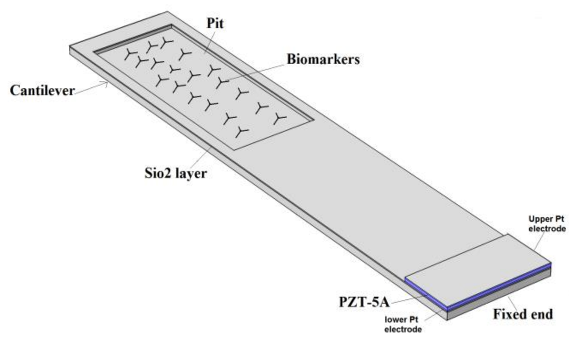

Fig. 1. Schematic of PZT-5A micro cantilever sensor

used to insulate the micro cantilever. Fixed end can be terminated by SiO_2 layer for insulation purpose as there can be attachment of an array of micro cantilever or other micro modules. The cantilever vibrates at different eigen frequencies generated by electromagnetic induction corresponding to natural frequencies of vibration, and the eigenvectors are the shapes of vibrational modes [11]. Beeby et al [12] have provided a practical approach for incorporating electromagnetic induction by developing a silicon-based generator that comprises micro machine paddle, four NeFeB magnets and a wire-wound coil in a device shown in “Fig.2”. Two of the magnets are located within etched recesses in the two Pyrex wafers, which are bonded to each face of the silicon

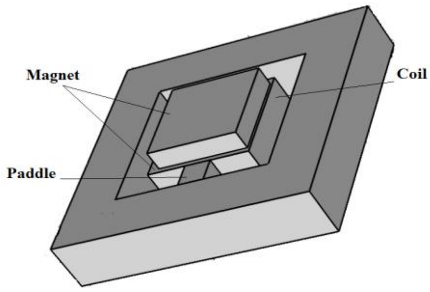

Fig. 2. An electromagnetic generator

wafer. The coil is located on a silicon cantilever paddle, which is designed to vibrate laterally in the plane of the wafer.

B. Equations

The microcantilever can be modeled as a harmonic oscillator with mass “m1” and resonant frequency “fo”. Estimated minimum detectable surface mass loading Δm is given by

$$\Delta m = k\left[\frac{1}{(fo-\Delta f)^2} - \frac{1}{fo^2}\right] \quad (1)$$

Where k is the spring constant and Δf is the frequency shift. This equation assumes that the flexural rigidity is unchanged due to subsequent additional mass loading. Assuming Δf<<fo, first-order expansion of Eq. (1) yields

$$\frac{\Delta m}{\Delta f} = 2m1/fo \quad (2)$$

In Piezoelectric effect, Piezoelectricity means electricity generating from pressure applied over it. The piezoelectric effect can be understood as the electromechanical interactions in crystalline materials with no inversion symmetry. The IEEE standard on piezoelectricity gives different forms of piezoelectric constitutive equations. The form used here is strain-charge form and the equations are as follows:

$$\epsilon = s^E \sigma + d^T E \quad (3)$$
$$D = d\sigma + \epsilon E \quad (4)$$

Where σ = Stress, ϵ=Permittivity, s= Compliance matrix
d = Coupling matrix, D = Electric displacement vector
E = Electric field
The generated voltage from a piezoelectric material can be calculated from the following equation as follows

$$V = S_v * P * D \quad (5)$$

Where V = Piezoelectric generated voltage in volt, P = Pressure in N/m², S_v = Voltage sensitivity of the material in volt-meter/ newton, D = thickness of material in meters.

For one specific mode, taking the voltage sensitivity as 9.2 v-m/N, we have calculated pressure applied due to a 50 ng mass as 21.8 N/m², and using a PZT material thickness of 2μm, we get an output voltage 4.018e-4 volts.
Voltage sensitivity values are provided with the material when received from the manufacturer. Different materials and different geometry cuts give different sensitivities.

C. Simulation using COMSOL

The structure was simulated using MEMS Module of COMSOL Multiphysics having three type of physics added. The different value of resonance frequency was obtained using electromagnetic induction applied 2 volt for oscillation of cantilever. At different Eigen frequencies for different sample mass, a range of generated voltage obtained shown in “Fig.3”. For m=20ng, Table I shows the variation of slice and surface voltage generated from PZT-5A piezoelectric material at different eigen frequencies. The result shown here is for polysilicon cantilever having length and thickness 500 μm and 7 μm respectively which is fixed at one end. The vibration of the cantilever at different frequencies when induced by electromagnetic induction, results in a range of output voltage across the electrodes in the PZT which peaks at positive and negative voltages for up and down direction of cantilever vibration, shown in “Fig 3”.

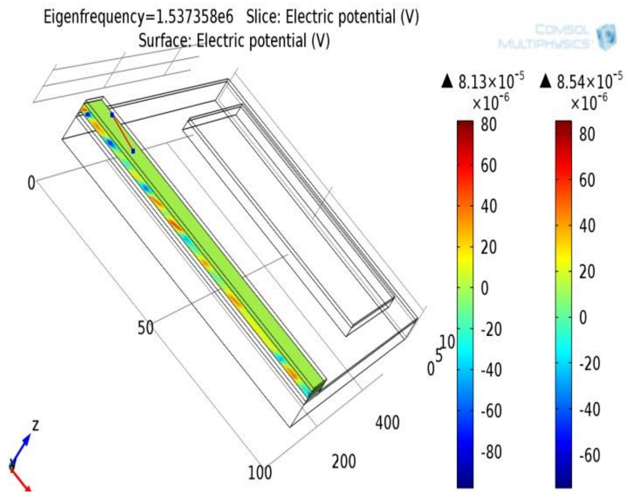

Fig. 3. At Eigen frequency=1.537358e6 Hz

Table I. Different voltage and frequency for m=20 ng.

Frequency (Hz)	Slice Voltage (V)	Surface Voltage (V)
2.573691e5	7.42e-6 to-8.63e-6	6.26e-6 to -8.63e-6
7.379044e5	8.43e-5 to-7.64e-5	6.38e-5 to -6.28e-5
8.054803e5	1.17e-4 to-7.89e-5	8.66e-5 to -9.89e-5
1.350764e6	1.1e-4 to -4.48e-5	8.71e-5 to -7.39e-5
1.537358e6	8.54e-5 to-7.45e-5	8.13e-5 to -7.45e-5

This also shows that in COMSOL it is possible to take a slice voltage along the y-z plane, which is also the direction of displacement of piezoelectric layer in this model. The resulting variation of electric potential with frequency for m=20ng shown in "Fig.4".

The measurement of output is taken in z-direction which is maximum at frequency 1.350764e6 Hz, resulting in a 1.1e-4 to -4.48e-5 volt slice voltage. When a cutline is taken over surface of piezoelectric material, surface voltage can be measured which is 8.71e-5 to -7.39e-5 V in this particular case. Similarly, for different range of frequencies, generated voltage can be easily measured.

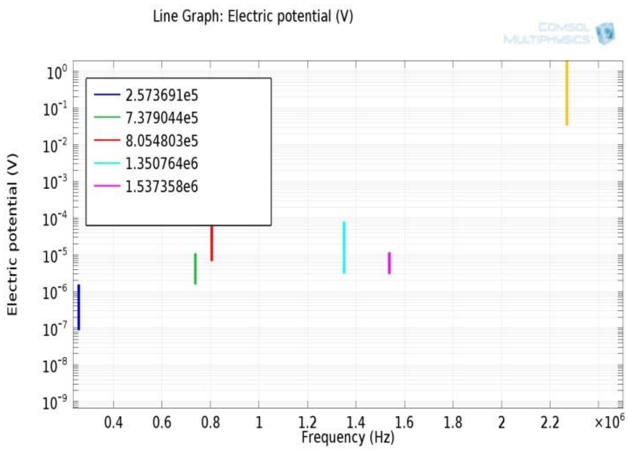

Fig. 4. Variation of electric potential with frequency for m=20ng

The simulation was repeated with sample mass m=30ng and simulation results are shown in "Fig. 5".

The model used in COMSOL for simulation with a 30ng added mass assumes that the resulting vibration is in the downward z axis. The pit taken at the tip of cantilever is assumed to be having all samples mass and can be directly incorporated in the design for fabrication of the sensor.

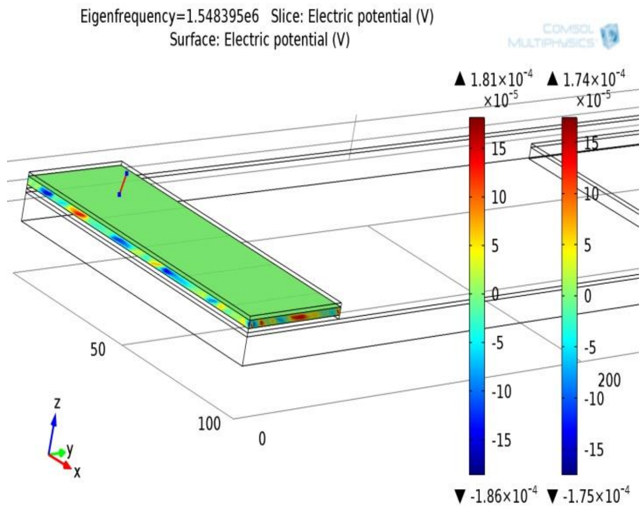

Fig. 5. At Eigen frequency=1.548395e6 Hz for m=30ng.

Using similar dimensions for the cantilever for m=30ng as was used in the design for m=20 ng, we obtained a maximum output in the range 3.5e-5 to 3.2e-5 volt slice voltage at a frequency of 1.361611e6 Hz. The surface voltage at frequency 1.361611e6 Hz is 3.5e-5 to -2.8e-5 volt. At different frequencies, output voltages are shown in Table II.

The variation of voltage with frequency is taken as an output graph shown in "Fig.6".

Table II. Different voltage and displacement for m=30ng.

Frequency(Hz)	Slice Voltage(V)	Surface Voltage(V)
2.593551e5	1.11e-6 to -9.18e-7	1.69e-6 to -1.01e-6
7.438926e5	9.09e-6 to -1.36e-5	1.02e-5 to -1.05e-5
8.110246e5	1.94e-5 to -1.63e-5	1.88e-5 to-2.74e-5
1.361611e6	3.5e-5 to -3.2e-5	3.5e-5 to -2.86e-5

In these simulations, different Eigen frequencies are taken which is obtained by Eigen frequency analysis in COMSOL Multiphysics by adding Eigen frequency study which is integrated with three physical features, namely as Solid mechanics, Piezoelectric and Electromagnetic induction (emi).

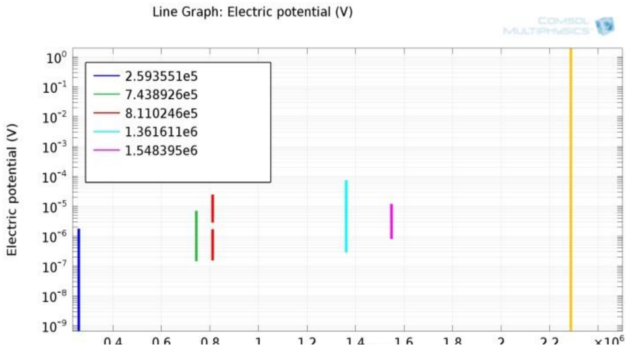

Fig. 6. Variation of electric potential with frequency for m=30ng.

Next simulation is done for m=40 ng in the same way except of added mass which is 40 ng in this case. Simulating the design at five Eigen frequencies, the maximum slice voltage is 1.44e-4to -1.34e-4 volts at 1.559679e6 Hz. The surface voltage is also maximum at this frequency. The variation of voltage with frequency and total displacement for particular frequency is shown in "Fig.7".

The "Terminal" feature in COMSOL has been used for measuring the output signal which can be charge, current and voltage from the electrode domain. The electrode platinum is used which is placed above and below the piezoelectric material. So for measuring of output signal electrodes are assigned as terminal to connect with output circuitry. Meshing can be taken as user controlled based on the requirement for achieving optimum results. The Thin layers of the order of nm require very high attention as meshing edge get dislocated/misaligned. So, for very thin edges, by changing the tolerance value from 1e-6 to 1e-12, meshing can be done with extra precisely.

At five different frequencies, slice and surface output voltages are shown in table II. The output graph is plotted which is logarithmic for variation of output electric voltage with frequencies.

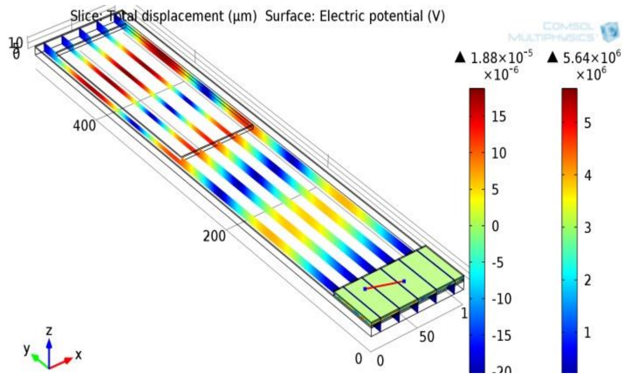

Fig. 7. Variation of frequency and displacement along slice in y-z direction for m=40ng.

Table III. Different voltage and displacement for m=40ng.

Frequency (Hz)	Slice Voltage(V)	Surface Voltage(V)
2.613873e5	1.55e-5 to -1.97e-5	1.88e-5 to -2.18e-5
7.500366e5	1.2e-4 to -1.18e-4	1.42e-4 to -1.44e-4
8.166838e5	7.36e-5 to -6.93e-5	6.17e-5 to -7.11e-5
1.372725e6	4.78e-5 to -2.84e-5	3.14e-5 to -5.16e-5
1.559679e6	1.44e-4 to -1.34e-4	1.52e-4 to -1.64e-4

The output graph shown in "Fig.8" verifies the results of Table III. The result for three cases m=20 ng, m=30 ng and m=40 ng can be compared with the help of Tables I, II and III.

The results obtained from COMSOL suggest that as the sample mass get increased from 20 ng to 40 ng, the output voltage also increases from microvolts to millivolts which can be easily monitored for virus detection purpose. This sensor when fabricated using the COMSOL modeled results with super fine meshing having very low value of tolerance increases the accuracy of the model and provides a much improved response. Generally, semiconductor controlled meshing is done but for fabrication specific model, user controlled meshing should be done.

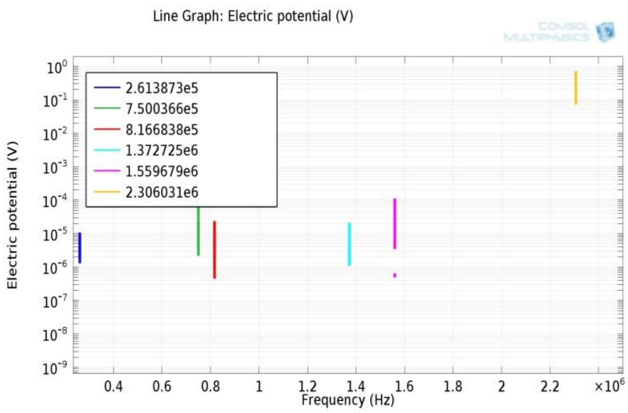

Fig. 8. Variation of electric potential with frequency for m=40 ng.

D. Output Circuit

The output from the piezoelectric sensor can be easily taken by using op-amp amplifier circuit [13] shown in "Fig.9" which comprises of C_F, C_C, C_P and R_F components. The piezoelectric sensor typically has very high output impedance, and this can pose some difficulty when measuring this output with a voltmeter having an input impedance on the order of several MΩ, much lower than the output impedance of the sensor. This calls for the use of a signal conditioning system the primary purpose of which is to provide a signal with low output impedance while simultaneously presenting a very high input impedance to the piezoelectric sensor.

The amplifier can be used for amplifying voltage output where voltage generated by the sensor is transferred onto a feedback capacitance,C_F. It reflects that once value of C_F is known and fixed, then calibration factor is also fixed. Time constant (R_F. C_F) can be selected to give the required dynamic frequency range.

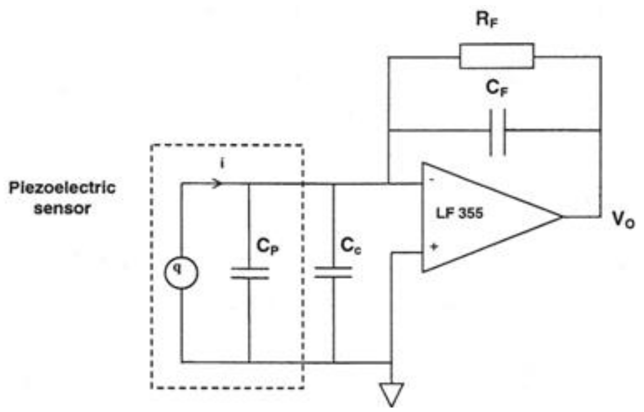

Fig. 9. Op-amp amplifier for output signal

E. Specific Biomarkers

Application of a specific biomarker can be incorporated in the designed sensor to provide specific binding to targeted viruses. The cantilever surface can be chemically modified with dextran matrix over thin gold layer film over which biomarker is attached. The interaction is made in hydrophilic environment. Other matrix can be used to attach specific type of molecules. The specificity of surface is determined by the molecule attached to it. One binding partner is attached to the surface of sensor and other is injected in continuous flow of solution. "Fig.10" shows the various design blocks for signal conditioning circuit and biomarkers [14]. In this study, biomarkers for 100nm size virus as HIV & Herpes are suggested.

For HIV, plasma citrulline appears to be a quantitative biomarker of small bowel mass. Table IV shows some of soluble biomarkers [15] for HIV.

Table IIII. Various biomarkers for HIV

Markers of immune activation	Markers of coagulation, tissue fibrosis and inflammation	Markers of enterocyte, microbial translocation and monocyte activation
IFNγ	D-dimer	I-FABP
RANTES	Fibrinogen	LPS
MIP-1β	hsCRP	sCD14
A-SAA	Hyaluronic acid	Scd163
IP-10	IL-6	

For Herpes virus, 8-OHdG and CSF tau can be used as biomarkers for HHV-6 infection detection but depends upon severity. CSF tau protein is considered as useful biomarkers that might help to diagnose HHV-6 encephalopathy [16].

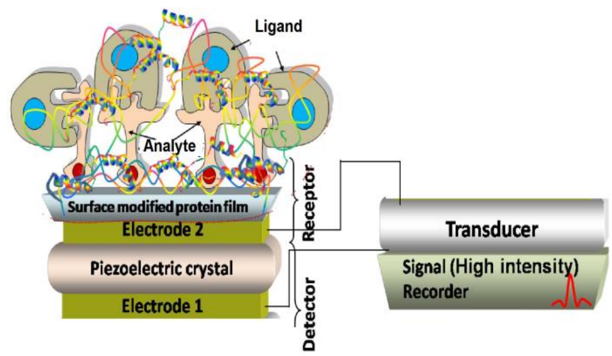

Fig. 10. Various design blocks with biomarkers

F. Sensitivity

We have calculated the sensitivity of response by treating the viruses to have a spherical structure of diameter 100 nm. At the tip of cantilever, a pit having dimensions 200µm x 80µm x 4µm is considered in our design, for binding of ligand and analyte. The mass of herpes virus [17] is in the range of (54-92)e+06 dalton. Accordingly the calculations of the maximum and minimum number of viruses are done based on the above data. The maximum number of viruses that can attach in pit is accordingly 122.24e+06, corresponding to a mass of 18.64 ng while the minimum mass is 10.4 ng. A PZT-5A based sensor shows high sensitivity and better power handling capability since low driving voltage is adequate for resonator actuation which expedites the integration with CMOS circuits [18]. In this, if size of pit is increased or different pattern like zigzag is taken then more number of binding will take place which will result in more mass holding capability. Further use of a pit of different shape like star, rectangular, octagon etc. sensitivity of cantilever can be enhanced.

III. CONCLUSION

A novel MEMS/NEMS PZT-5A cantilever integrated with $Si/SiO_2/Pt/PZT\text{-}5A/Pt$ multilayer has been modeled and designed using COMSOL Multiphysics for detection of viruses of size 100nm. A sample mass of 20ng, 30ng and 40ng at the tip has been found to generate piezo electric voltage in the range of microvolt to milivolts at different eigen frequencies. Since the maximum number of viruses that can bind to a pit surface of given dimensions, depends on the nature of the virus, the generated piezo electric voltage has been associated with the detection of a particular virus. Such a system designed with the proposed signal conditioning circuit and different biomarker layers to provide an output signal can thus be used as a bio sensor.The results show a strong possibilty of the sensor to be realised as 100nm virus detector.

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