Section A-Research paper
ISSN 2063-5346

Field Programmable Gate Array Based Detection Method in Bio-MEMS Cantilever Array with Electronic Integration

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Abstract

This study presents a novel readout method for cantilever-based biosensors, which has the potential as both a quick and inexpensive "point of care" device and an intriguing research instrument. The cantilever-based micro/nonmanufacturing procedures and associated challenges are described. The expedient's behaviour is analyzed using a COMSOL simulation. An FPGA-based control circuit has been designed to address the complex arrangements of the readout mechanism in the process of encapsulating the instrument. The circuit can compensate for deviations caused by the fabrication process by using electrostatic actuation. The finite element analysis of microcantilever-based biosensing with a feedback-controlled electrical readout mechanism is presented in this study. The resultant deflection concerning voltage and stress is investigated. The feedback control circuit was developed and tested using the Artix-7 FPGA and associated electronic circuitry. As a result, the sensor's dependability challenges are also being studied, and the suggested readout method's performance in design metrics is around 47% greater than typical optical readout methods.

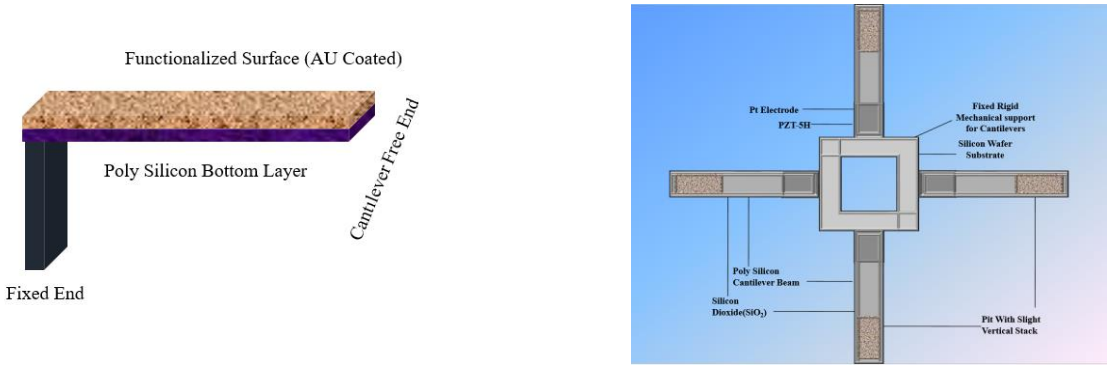
Keywords: MEMS, NEMS, FPGA, Biosensors, Feedback Control

1. Introduction

The cantilever-based Micro-Electro-Mechanical-Systems (MEMS) technology is only one example among a wide range of emerging concepts when it comes to biosensor technology. It is essential to match the components and manufacturing processes of MEMS to go from laboratory studies to field based applications[1]. The discovery of new drugs, the early diagnosis of disease, and other molecular biology challenges all depend on the accurate identification and precise quantification of biological components and their interactions. To be considered a biosensor, it must be very specific and able to detect a specific molecule (a specific antibody, for example) at a low concentration[2]. There are two elucidations for this. First, smaller samples may reduce the time and cost of detection, and more significantly, most illnesses can be treated if they are found at an early stage[3].

MEMS and NEMS are primarily developed for detecting and sensing particular bimolecular at low concentrations[4]. The sensing principle may change depending on the device, sample molecule type, and desired accuracy. When these are utilized as biochemical sensors in atmospheric and aquatic conditions, micrometer-sized cantilever devices are susceptible and straightforward[5]. Because of their relatively low tensile resistance, cantilever structures are mechanically sensitive to variations in surface stresses. Early on, Stoney observed that residual stresses caused the deposition of a tensile film on another material to form a curve in the composite structure. This phenomenon, which has been used for sensing, is particularly vulnerable to cantilever structures[6]. Cantilever based transducers for specialized investigative applications are stagnant in their infancy due to manufacturing challenges, even though this process was assisted by improved microcantilever readout schemes and microfabricated cantilever probes[7]. Due to a change in surface tension, the cantilever bends due to the biochemical reaction on its surface. A sensing layer is deposited onto a cantilever

surface to aid biorecognition and make it biosensitive[8]. The bio receptors are covalently attached to this layer or include them. Functionalization is the term used to describe this process[9]. Bio receptor molecules and analytes respond in distinct ways. Nucleic acid and protein interactions are the most frequently employed biosensor-receptors. Microcantilever beams can be bent by chemical or biological processes that alter the surface tension topside of the cantilever. By measuring cantilever deflection, the molecular species and concentration are both dependent on cantilever deflection[10].



(a) (b)

Figure 1: (a) Basic cantilever structure (b) Aster shaped array cantilever array

The readout techniques including photosensitive reflection, piezoresistive measurement, interferometry, piezoelectric sensors, and electron tunnelling may all be used to monitor the device's deflection[11]. However, it is most beneficial to detect it using a visual approach that utilizes a low-power laser and a position-sensitive camera. As a result of the additional hardware needed for detection and sensing, optical detection devices are more significant[12]. However, it is not ideal for ordinary low-cost ailment diagnostics since it requires expensive and very advanced apparatus and incredibly perfect mechanical alignment. Furthermore, since the faradic current between the capacitive plates prevents them from working in an electrolyte solution, the capacitive technique has only a restricted number of sensing applications and interferometry techniques[13]. While compared with the use of the previous design contains LASER system, the electrical detection method with feedback control mechanism described in section 3 is more suited for this high sensitivity and precision requirements. Section 2 covers literature survey which discusses existing methods and their limitations. Finally, section 4 explains how the device was built with associated electronics. Sections 5 and 6 address the design and execution of the feedback control mechanism. After discussing the dependability difficulties in Section 7, we next analyze the outcomes and concluded section 9.

2. Literature Survey

The critical issue with these detection systems is measuring nanometre-scale deflections in response to stress. Cantilever devices now confront the point of producing a specific deflection cavity in manufacturing. Now this section describes recent detection methods and their limitations.

In Ref. [14], silicon(Si) and diamond MEMS cantilevers are proposed in this work, and silicon cantilevers were sensitized using polymeric coatings to detect analytes. The suggested system's gas cell included detachable connections so that sensors could be swapped simply for cleaning and other purposes. In addition, the suggested device could accommodate up to eight sensors and provide electrical readouts.

In Ref.[15] gas-sensing advancements are discussed. They addressed sensor materials, manufacturing processes, and design restrictions. In Ref. [16], they explored chemical and acoustic gas sensors. This study showed that chemical biosensors are useful for low-concentration molecule detection. Their sensing quality depends on the sensing materials. Their sensing behaviour was also altered by ambient temperature and relative humidity. Inorganic chemo-resistive detectors offer increased susceptibility and can work at standard temperatures. Still, they are temperature reliant and have poor discernment, and are impacted by humidity instabilities. (Carbon Nano Tube)CNT sensors were flexible and had unique chemical groups, but their recovery time was slow. Acoustic type sensors were fast and sensitive but had limited selectivity and were temperature-sensitive[17]. Optical sensors have a long lifespan and great sensitivity, but they are bulky.

In Ref. [18] used a piezoresistive microcantilever to detect organic chemicals. The findings demonstrated that piezoresistive microcantilever sensors with organic metal coatings provided reversible detection of methanol and water vapor. Ref. [19] presents cantilever based MEMS for bio-sensing. According to this research, sensitivity may be increased by adopting stiffer, shorter microcantilevers or higher resonance modes. Thick coatings may boost sensitivity but slow reaction time. In Ref. [20], a micromechanical cantilever sensing device was used to detect 2,4-dinitrotoluene. Micro-pre-concentrate was joined directly through the cantilever, increasing its sensitivity to target molecules. The cantilever-based system's sensing performance must be improved.

In Ref. [21], the dynamic reaction of microcantilevers was utilized to determine the composition of a binary combination of ethanol and CO_2. The Eigen frequencies at a given temperature and pressure dropped with increasing ethanol mass percent. Low pressure increased sensitivity. This research showed that microcantilever resonance frequency could better determine mixture composition. In Ref. [22], the author used a MEMS cantilever-based sensor array to determine surface stress effects on MEMS chemical differentiation. The sensor array detects molecular sniff. This work showed that polymer swelling's surface stress on MEMS sensors improved chemical selectivity over stiffness and mass loading effects. The gaseous, such as pentane and ethane, suggesting hypoxia were consistently recognized and distinguished among usual interfering in breath by MEMS cantilever-based sensor array. In this investigation, the MEMS sensor only detected a few molecules.

In Ref. [23], PC and PMMA cantilevers were designed for vapor level sensing. The (QF) quality factor and resonant frequencies (f_o) of these cantilevers vary by pulse mode. Ref. [24] used a MEMS-fabricated piezoelectric microcantilever for molecule sensing. Poly-methyl methacrylate was used to coat the microcantilever for gas sensing. Complex impedance analysis detected a resonant frequency deviation. Increased alcohol vapor concentration shifted the resonance frequency to a lower range. The cantilever's methanol vapor sensitivity was 0.03 KHz/ppm. The sensing performance requires further investigation. In Ref.[25], micro disc resonators detect molecular gas. Such type of sensing was accomplished after applying an analyte-absorbing polymer coating. M-xylene, toluene, and benzene had detection limits of 0.6, 1.2, and 5.3 ppm. Although it has decent sensitivity for molecular, additional enhancement is needed.

In Ref.[26] Uses bimorph microcantilevers to sense biomolecules. In this work, the flexible reaction of cantilevers was measured using the bimetallic effect. The microcantilevers flexed differently as the actuation current rose. The conductivity of the cantilever may alter the device's sensitivity. The suggested microcantilever array sensed molecular vapors. Sensor length did not affect sensitivity. In Ref. [27], a Surface Acoustic Wave(SAW) based MEMS sensor for molecule recognition is designed. The sensor's GHz (Gega Hertz) frequency range provided highest sensitivity. The researchers found the resonant frequency shift by exposing a MEMS device to 100 ppm of dissimilar gases. The researcher observed lowered the resonance frequency for molecular sensing.

In Ref. [28], a nano-enabled MEMS sensor for detecting molecules was described. The sensor had various sensitivity levels due to two operating frequencies 450 and 287 MHz on the same die. In Ref. [29], [30] discusses molecular sensing utilizing polymer-deposited MEMS cantilevers. The cantilever identified lower quantities of octane and toluene. The researcher used biosensing technologies in Refs. [31], [32]to detect molecules in human breath, but they were expensive and not portable.

In Ref.[33],[34] polymer-coated microcantilevers were used to detect benzene, octane, and hexane. The author tested polymer coating sensitivity with polyethylene-vinyl acetate employed for microcantilever molecular sensing investigation. The resulting sensitivity and selectivity characteristics may be used to choose polymer coated MEMS cantilevers for chemical analysis for molecular detection. MOS (Metal Oxide Semiconductor) biomolecule sensors have several commercial uses, but many need constant temperatures.

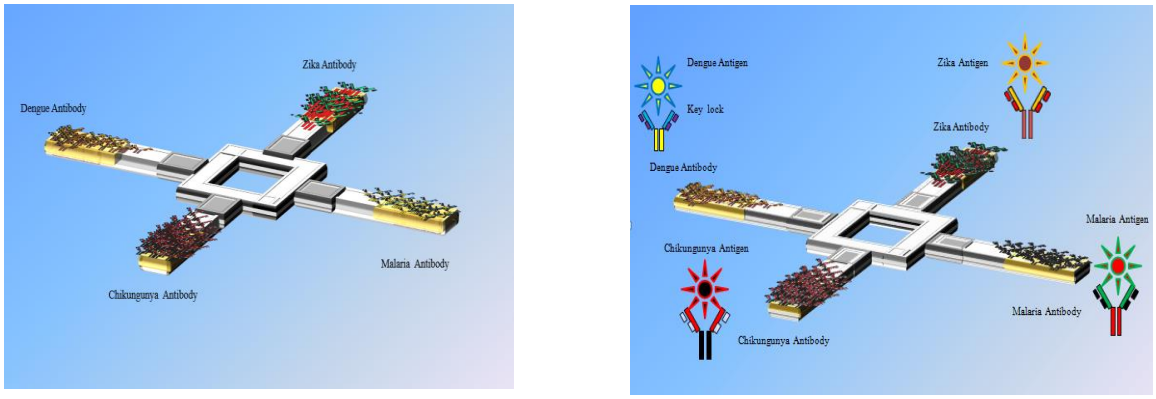
In Ref.[35],[36], [37]researchers studied chemiresistor molecular sensing. Sensors have low detection limits and rapid reactions. The production proved difficult because these devices relied on lower dimensional materials like carbon nanotubes (CNTs) and graphene. In Ref. [38],[39],[40], [41], a microcantilever covered with polyaniline detects vapor level molecules. Higher molecule concentrations also increased deflections. Enhanced polarity increased coated microcantilever sensitivity. All molecular responses were under 2.2ms. Biosensor responses were reasonable, reversible, and fast whereas uncoated and non-functionalized microcantilevers are sensed inadequately.

3. Design and Methodology

This section dealt with introductory concepts of basic MEMS cantilever, cantilever array structure with COMSOL, fabrication process and related issues, feedback control circuit design and implementation in Xilinx and Top Spice, Multisim.

3.1 Microcantilever-Based Biosensor

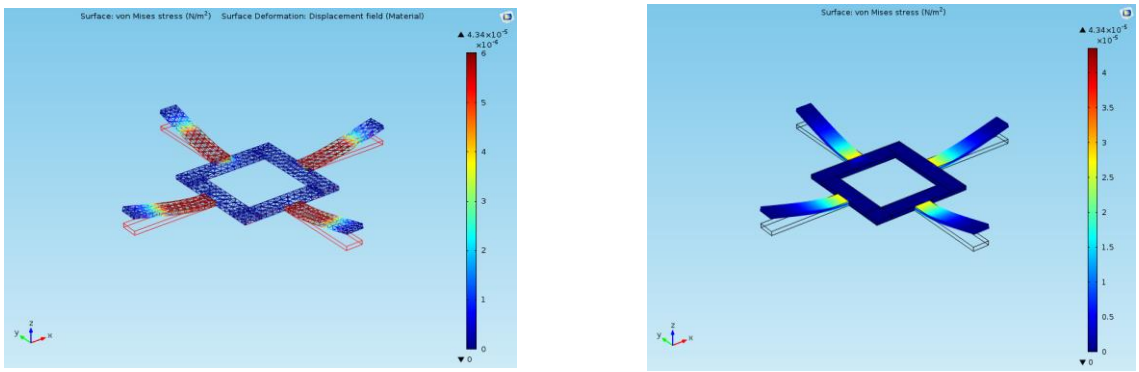
Figure 2 shows our unique biomolecule detection design of array. It is evaluated based on the amount of current that flows through an electrode. An electrode with a rectangular form is positioned near the cantilever. When the surface tension from the antibody-antigen interaction crosses the threshold limits, the cantilever comes into contact with the electrode. The number of antibodies or antigens adhered to the surface cantilever may be determined by calculating the surge current. Contact resistance has a direct impact on the current. Depending on the contact area, resistance changes. The spring constant, bioinduced stress, and flow field stability were optimized to produce a cantilever with an ideal length, width, and thickness of 400um, 250um, and 50 um.



(a) (b)

Figure 2: Proposed Array Cantilever Structure (a) Antibodies are deposited on the cantilever's sensing side (b) Cantilever array representation for simultaneous detection

Figure 3 shows the cantilever structure created in COMSOL (a). Antibodies are deposited on the cantilever's sensing side i.e. top side. The bio-linked layer's intermolecular connections are altered by particular bimolecular interactions between antibodies and antigens. Thus, as seen in Figure 3(b) shows the simulation response of the cantilever for matched antigen antibody reactions.



(a) (b)

Figure 3: Shows the cantilever structure created in COMSOL (a).Superfine meshing finite element analysis (b) Response of cantilever array, when respective antigens are exposed.

3.2. Fabrication process and related Issues

It is possible to manufacture the proposed apparatus using the usual surface micromachining method. A four-level photo masking system in the fabrication process, as illustrated in Figure 4. A combination of

deposition and etching operations is used to assess the film's uniformity, beam geometries, and the crucial gap between the device substrate and structure. The initial stage in production is the deposition of an insulation layer on top of the silicon substrate. On a CMOS-produced wafer, this method may also employ isolation and metallization layers. The first electrode is then formed by depositing and patterning a doped polysilicon layer. The cantilever beam's initial layer is formed by depositing and patterning a sacrificial layer on top of the polysilicon layer, followed by patterning a 0.3µm thick polysilicon layer on top of it. Polysilicon is used to make the structures. To construct the sensor surface, a 0.2µm dense gold (Au) layer is spluttered and patterned on top of this layer. Metal may be used to conduct electricity since it is the device's top layer. The binding of biomolecules to this surface creates electrochemical signals. The microcantilever bends as a consequence of the biomolecules adhering to the surface cantilever. The cantilever bends by a few nanometres when subjected to surface tension of 0.05N/m – 0.5N/m. Creating the correct distance between electrodes is a big challenge for device construction. The etching procedure results in a 10% variance in thickness. This (etching procedure) will alter the device's sensitivity. All of the detection techniques described earlier have the same issue. Here researcher created a feedback control circuit that will take care of the cantilever's placement for the best outcomes. This FCC (Feedback Control Circuit) will address the difficulty of establishing a required gap to significant deflection of the beam. Figure 4 shows a typical manufacturing technique used to construct these cantilevers. Section 4 presents the results of the device simulation analysis.

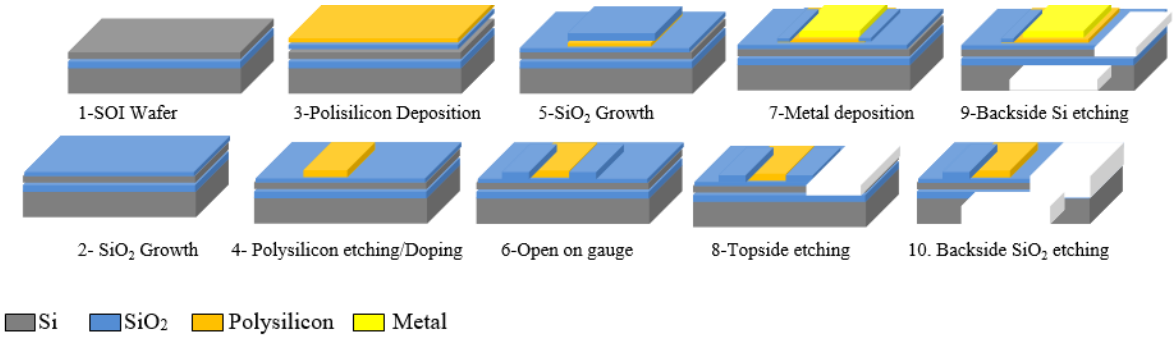


Figure 4: Fabrication Process flow of the Cantilever

3.3. Design and Analysis

COMSOL software is used to design and simulate the cantilever structure. Figure 2 depicts the cantilevers exposing and respective deformation of array cantilevers. Polysilicon is used to make the cantilever, which measures 400x250x50µm. The sensor layer is composed of gold with a thickness of 0.2µm.

The cantilever construction was designed in COMSOL using the following steps:

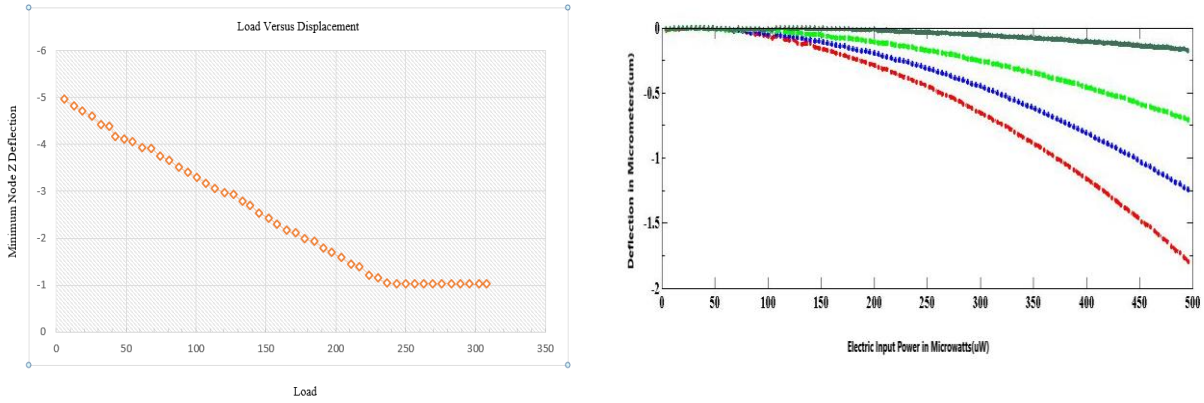
(a) Establishing a procedure (a succession of deposit and etch stages of various materials), (b) constructing a mask layout to build a model of that procedure; and (c) using the previous two stages, creating a solid model.

Afterward, the solid model is partitioned into meshable and nonmeshable sections. Only the cantilever meshes (Super Fine Meshing) are used to minimize the computational burden on the model. Finally, the model was subjected to boundary conditions (force, voltage). The cantilever is deflected by the interaction of antibodies with antigens, resulting in surface tension. Fig. 4 shows the stress analysis over 0.005 N/m to 0.5 N/m.

Using a step size of 5, the x-axis in fig. 4 depicts a load range of 1– 350Kda, representing a stress range of 0.005 N/m–0.5N/m. The y-axis's minimum node displacement is shown in micrometres. We intend to employ electrostatic actuation to establish the appropriate spacing. The cantilever's response to the applied voltage is calculated in the following study. In Figure 5, the voltage applied is changed between 1 and 3 volts, and the deflection is shown. The Minz represents the deflection in micrometres seen in fig. 5 on the y-axis. It is possible to establish the necessary spacing between the electrodes using electrostatic actuation. Hardware must deliver the voltage needed to generate the specified electrode spacing for deflection.

At the cantilever free end, Miranji katta et al [19] found that myoglobin protein injection resulted in maximum surface stress of 0.5N/m, and the cantilever deflection was 0.9µm at that point. There is a rise in cantilever deflection and contact between the beam and electrodes. The current flowing through the electrode, measured,

rises when the contact resistance, or resistance between the electrodes, decreases. This variation in current will limit the change in apparent surface stress.

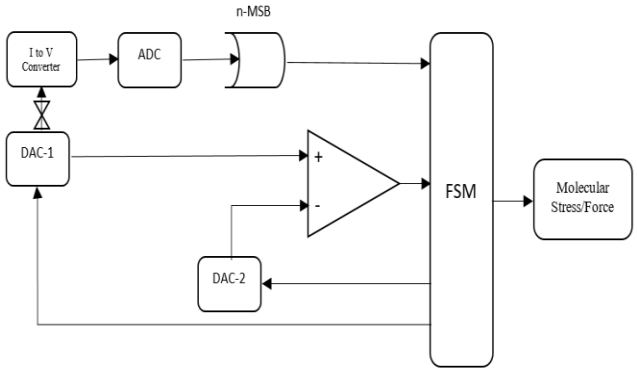


(a) (b)

Figure 5: Cantilever response (a) Deflection of cantilever beam with respect to parametric load (b) Deflection of cantilever beam with respect to input Electrostatic input power.

3.4. Feedback Control Circuit

In this set-up, there is a distance of 2 m between the electrodes. So, putting a voltage between the surface of the cantilever and the bottom electrode will make the cantilever bend in the right way to keep the right distance between the electrodes. Figure 6 shows the control circuitry that is used to figure out where to put the cantilever. DAC 2 gives the reference voltage to the comparator so that the finite-state machine can create the right gap between the electrodes (FSM). Once the exact location of the cantilever is known, the FSM will move on to the next stage, which involves adding biological molecules to the surface of a functionalized cantilever. This part talks about how the circuit is made. Since the bottom electrode is not touching the cantilever when there is no voltage, no current flows through the cantilever-based sensor. Because the current-to-voltage (I to V) converter output is zero, the analog-to-digital (A to D) converter output is also zero. (ADC). Digital outputs use the OR gate as an input. All of the inputs to the OR gate are set to zero, so the output is also zero. Figure 7 shows how this logic state is handled by a Finite State Machine (FSM) (Output of OR Gate). The FSM makes the supply voltage go up or down depending on the logic state of the input, which is "1" when there is current and "0" when there is none. If there is no current, the counter will go up by one (State 0). Then, DAC1 changes it into an analogue voltage, which is sent to the cantilever sensor. When a high voltage is used, the electrodes and cantilevers move closer to each other. When the current flows through the cantilever and the electrode, the voltage across the cantilever goes up (State 1).



(a)

Figure 6: (a) Basic Block Diagram of feedback control circuit (FCC)

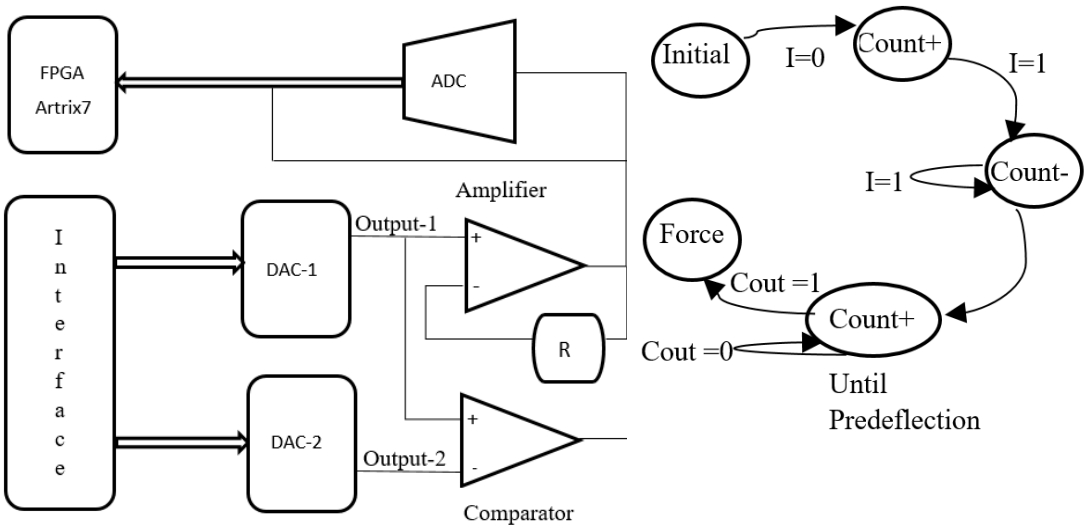
Electrostatic forces prevail over stress forces at a particular voltage. This voltage determines how much the system will bend when the gap closes because it is no longer stable. Adding one step of voltage to the cantilever closes the gap and brings the cantilever into contact with the bottom electrodes. The cantilever starts moving with the flow of the water. An I to V converter makes the equivalent voltage, and an ADC turns that

voltage into a digital value. If at least one of an OR gate's inputs is "1," the output will also be "1." After getting a "1" as an input, the FSM moves on to the next step, which is to use the counter and DAC1 to lower the voltage at the cantilever. At the end, the cantilever will go back to where it started, and the current will be gone. Again, the noise will go away if you use MSBs for the ADC output instead of 2 or 3 LSBs.

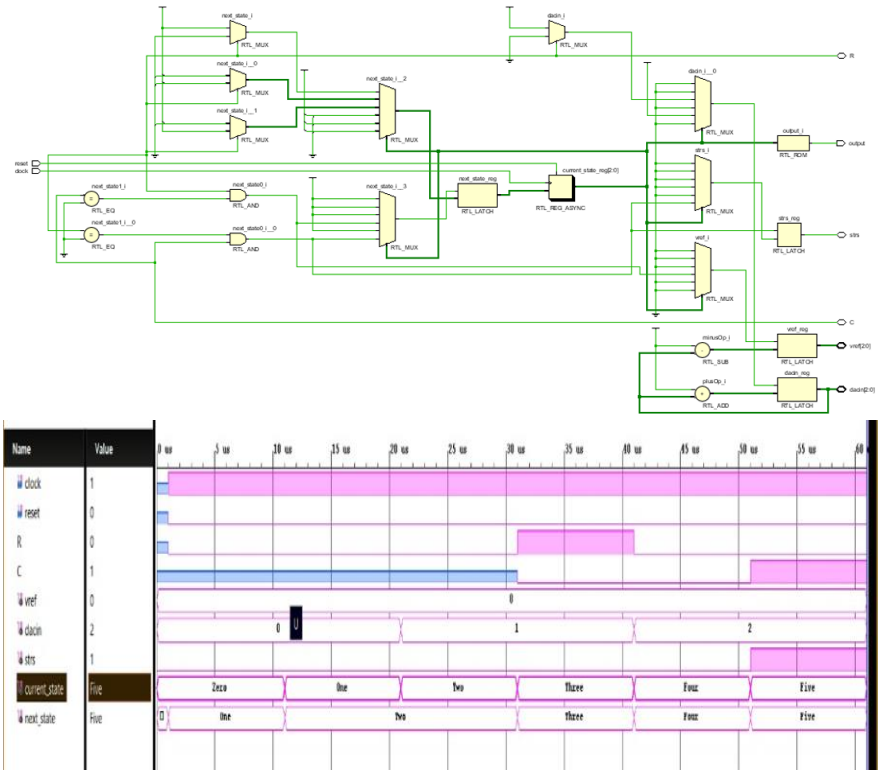
Since then, FSM has determined the deflection reference voltage and assigned it to DAC2 as one of its inputs, making it available to the comparator. Comparator 2 takes DAC1's output as its second input. As a result, the FSM receives an input of logic "0" and increases the voltage once again until we reach the corresponding voltage level of deflection. FSM: As a result, the cantilever is correctly positioned. We can now precisely control the distance between the cantilever and the bottom electrode. Previously, this was impossible. With a modest amount of tension, the space between the sensor and the display closes, allowing electricity to pass through. Force/stress will be shown on the cantilever beam now that FSM has switched to force (function of antigen attached to the cantilever surface). The cantilever begins to bend and comes into contact with the bottom electrode due to its tension. Stress increases the region of contact between the cantilever and the electrodes. The contact area grows, and this current is measured as a result. The antigen concentration on the cantilever surface is inversely related to the current flow rate.

4. Results and Experimental Validation Using Test Circuit

Miranji Katta et al. [11] data were utilized as a starting point for the cantilever design. The injection of NS1 protein onto the functionalized cantilever results in a maximum surface stress of 0.5N/m. In our design, the electrode-to-cantilever separation was originally chosen at 2m. The cantilever initially does not make contact with the bottom electrode, and the voltage across the cantilever is zero (state 0). When the output voltage of DAC1 is 3 volts, the cantilever and bottom electrode make direct contact with the current that has begun to flow (State 1). The predeflection value is 0.5 volts when the cantilever is not in contact with the electrode. Despite the little tension (on the order of 0.05 N/m) on the cantilever surface, current will flow through it when it comes into contact with the bottom electrode owing to electrostatic actuation (in this example, 3 volts is decided by FSM). The amount of antigen stuck to the beam surface is related to the magnitude of the current produced by an increase in the stress value. If the device is properly calibrated, the biosensor output current may be calibrated to detect the amount of antigen attached to the functionalized cantilever surface. The amount of biomolecules on the screen affects how much current is flowing through the sensor.



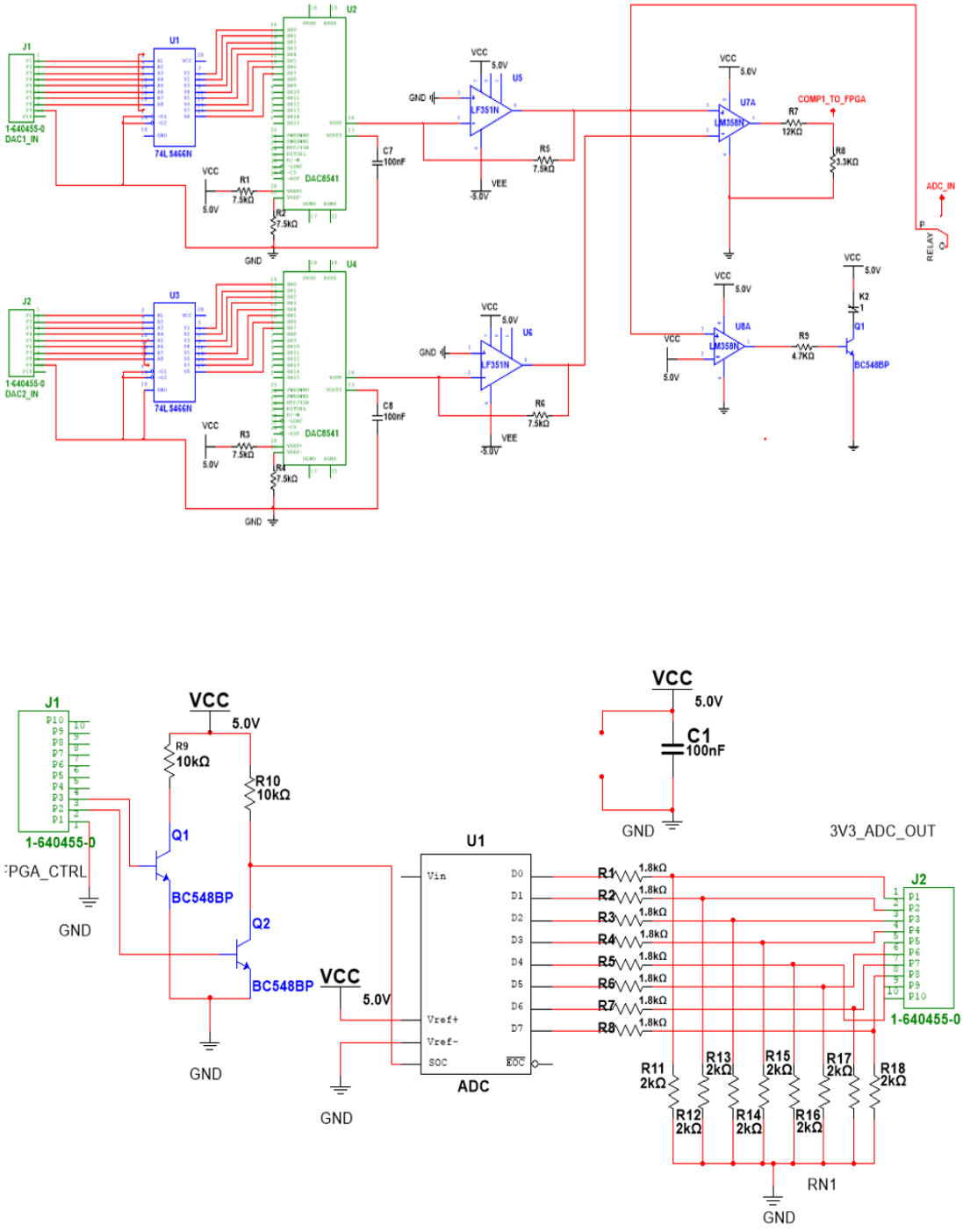
(a) (b)



(c) (d)

Figure 7: (a) FPGA Implementation with associated electronics (b)State diagram of Finite State Machine (C)RTL schematic of FSM implemented in Xilinx 14.5 with Verilog (d) Simulation results of FSM

Analog and digital components make up the feedback control circuit and they are implemented in Multisim Simulation software shown in figure 8. The FPGA platform is used to create a digital circuit, whereas a Multisim is used to implement an analog one. Figure 8 shows the analog and digital systems we've interconnected. The cantilever sensor is represented by a 3-volt relay in our test circuit. The cantilever beam used in the COMSOL analysis passes a current through the device electrode.

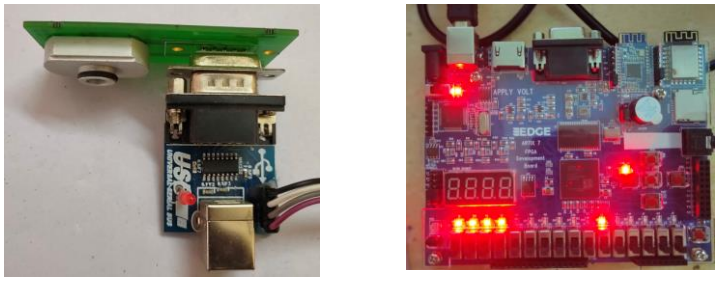


(a)

Figure 8. Analog circuit implementation (a) JTAG connection with Digital to Analog Converter and Operational amplifier (b) ADC (Analog to Digital Converter) interface with FPGA board and associated electronic components.

The system was built using RTL coding in Verilog for the FSM. The FSM will compute the prestressing voltage, but it may vary if the dimensions of the cantilever change. FSM will begin by increasing the voltage until the cantilever and bottom electrode make contact. The voltage will then be lowered. When this voltage is determined, the cantilever stores that value, which may vary depending on the size of the cantilever. So, the FSM in the control circuit can control the effect that uncertainty in the dimensions has on the preloading voltage.

Analog Module on Printed Circuit Board (PCB). Figures 10(a) and 10 demonstrate the analog module's circuit diagram (b). The digital module on ARTRIX-7 FPGA Kit is used to interact with the PCB-implemented circuit. The test circuit is used to verify the findings.



(a) (b)

Environmental setup for experimentation(Power Analysis)

Total On-Chip Power	2.587mW
Junction Temperature	37.6°C
Thermal Margin	47.6°C
Thermal Resistance(Θ_{JA})	4.9°C/W
Dynamic Power	2.510mW
Static Power	0.77mW

Figure 9. Fabricated Cantilever with Serial Port Converter in order to interface with FPGA Board (a) Cantilever sensor integrated module (b) FPGA Artix-7 board with FSM implementation

Design metrics*	Voltage(V)	Current (I)	Avg.Power (Both Static and Dynamic)	Performance (Response time)
Ref. [43]	12V	1.2A	2W	2min
Proposed Method	3V	500mA	2.587mW	1.2min

* Along with size, performance, cost (not data available for above reference hence considered only above parameters to calculate average performance)

With respect to above data proposed method performance is 47% greater than existing most recent references.

5. Aspects of Cantilever-Based Sensor Reliability

The amount of heat produced by the electrodes is determined by the current that flows through them, the characteristics of the contact surfaces, and any other physical characteristics of the electrodes. As a consequence of this, the mechanical and electrical properties of the contacts may be negatively impacted, which may result in welding or melting, which is a significant concern with regard to the dependability of the product [43-44]. It is necessary to investigate the ETM (electro-thermal-mechanical) effects in order to cut down on the Joule heat impacts that are placed on the sensor contact zones. One approach to limiting the amount of Joule heat produced is to restrict the amount of current that flows through the cantilever. To do this, the design of the sensor will need to be modified. It is possible to place a resistor in series with the supply voltage in order to lower the amount of current that is flowing through the contact interface as well as the amount of current that is flowing through the contacts. This model makes the accurate prediction that the fusing current of the polysilicon contacts in our design is 3.3×10^{-3}. A current-limiting resistor with a value of 10K that is connected in series with the supply voltage serves to isolate the cantilever. As a result, the fusing current limit is not exceeded by the maximum current of 0.98 mA that will flow through the contacts.

The installation of a current limiting resistor protects the cantilever. However, the sensor's sensitivity will be drastically reduced by this resistor. This means that a large change in the stress-induced contact resistance, which results in a 250µA relative change in the measurement current, makes it exceptionally difficult to detect the analyte accurately with the recommended values. However, current may be measured with a precision of 1 ppm or lower using currently available operational amplifiers and equipment. In addition, circuit-topology techniques like current fold back and differential current measurements could be used in order to boost

sensitivity without jeopardising the cantilever's level of security. However, these methods have not been shown to be effective.

6. Conclusion

Researchers have recommended using microcantilevers to identify diseases like Arbo-virus originated or cardiac infractions more often than not. The majority of the concepts depend on an optical reading mechanism, which is time consuming and challenging to implement portable and precise instrument in real time environment. Here we implemented more precise, encapsulated electronic instrument that outputs a current-based electrical signal that's direct to measure. A brand-new way of reading data is being developed. There is a demonstration and analysis of the COMSOL, Multisim, Xilinx, Top spice simulation findings. The design of a microcantilever-based biosensor control circuit has been completed to overcome a common problem in all readout methods: the difficulty of manufacturing. The structure of the feedback control circuit includes analog and digital components. When the input logic state changes, the control voltage across the cantilever may be incremented or decremented. For the manufacturing process variation, the FSM determines the predeflection voltage level. Control circuit FSM can deal with the impact of dimensional ambiguity on prestressing voltage. Experimentation using the Artrix-7 FPGA Kit and the test circuit confirms the findings. High-voltage applications might harm the polysilicon cantilever because of the joules heating effect. A current-limiting resistor is placed in series with the control voltage to protect the cantilever from damage. This may diminish the sensitivity. Using an accurate current to voltage converter or other architecture might enhance the readings. The suggested readout method's performance in design metrics is around 47% greater than typical optical readout methods.

Acknowledgements: As part of the research was conducted at the Centre for Nanoscale Engineering (CeNSE) at the Indian Institute of Science, Bangalore, which is funded by the Ministry of Electronics and Information Technology (MeitY), I would like to express my sincere gratitude to the INUP (Indian Nano User Program) members. As a special note of thanks, I'd like to thank the Nanosniff and NMR Spectroscopy for Pharma and Biotech Research Centre at the Indian Institute of Technology, Mumbai, for their help and technical support during our research.

Statements and Declarations:

- **Funding details:** No funding was received to assist with the preparation of this manuscript and no funding was received for conducting this study, No funds, grants, or other support was received.

- **Competing Interests:** The authors have no competing interests to declare that are relevant to the content of this article.

Data availability:

- The histology Images supporting Figures (1)-(3) are available in https://www.sciencedirect.com/science/article/pii/S2214180421000180. Figure (5) to (7) are available as supplementary data of current research up on request willing to provide. The source code developed in Xilinx tool for FPGA implementation is also provided as supplementary data for this research paper. Data available in tables (1) and (2) and associated supplementary data is provided.

  Code availability
- The code is available from the corresponding author by request

References:

[1] N. Maheshwari, G. Chatterjee, and V. R. Rao, “A Technology Overview and Applications of Bio-MEMS,” p. 21.

[2] Miranji Katta and Sandanalakshmi R, “A Technology Overview and Future Scope of Bio-Mems in Tropical Disease Detection: Review,” *IJET*, vol. 7, no. 3.12, Art. no. 3.12, Jul. 2018, doi: 10.14419/ijet.v7i3.12.16446.

[3] Y. Saylan, Ö. Erdem, S. Ünal, and A. Denizli, "An Alternative Medical Diagnosis Method: Biosensors for Virus Detection," *Biosensors*, vol. 9, no. 2, Art. no. 2, May 2019, doi: 10.3390/bios9020065.

[4] J. Ali, J. Najeeb, M. Asim Ali, M. Farhan Aslam, and A. Raza, "Biosensors: Their Fundamentals, Designs, Types and Most Recent Impactful Applications: A Review," *Journal of Biosensors & Bioelectronics*, vol. 08, no. 01, Art. no. 01, 2017, doi: 10.4172/2155-6210.1000235.

[5] Chun-Hao Chen *et al.*, "A Wireless Bio-MEMS Sensor for C-Reactive Protein Detection Based on Nanomechanics," *IEEE Transactions on Biomedical Engineering*, vol. 56, no. 2, Art. no. 2, Feb. 2009, doi: 10.1109/TBME.2008.2003262.

[6] Yu-Jie Huang *et al.*, "A CMOS Cantilever-Based Label-Free DNA SoC With Improved Sensitivity for Hepatitis B Virus Detection," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 7, no. 6, Art. no. 6, Dec. 2013, doi: 10.1109/TBCAS.2013.2247761.

[7] S. Wang, J. Wang, Y. Zhu, J. Yang, and F. Yang, "A new device for liver cancer biomarker detection with high accuracy," *Sensing and Bio-Sensing Research*, vol. 4, pp. 40–45, Jun. 2015, doi: 10.1016/j.sbsr.2014.10.002.

[8] K. Navakul, C. Warakulwit, P. Yenchitsomanus, A. Panya, P. A. Lieberzeit, and C. Sangma, "A novel method for dengue virus detection and antibody screening using a graphene-polymer based electrochemical biosensor," *Nanomedicine: Nanotechnology, Biology and Medicine*, vol. 13, no. 2, Art. no. 2, Feb. 2017, doi: 10.1016/j.nano.2016.08.009.

[9] W.-H. Chu, M. Mehregany, and R. L. Mullen, "Analysis of tip deflection and force of a bimetallic cantilever microactuator," *J. Micromech. Microeng.*, vol. 3, no. 1, Art. no. 1, Mar. 1993, doi: 10.1088/0960-1317/3/1/002.

[10] R. Bashir, "BioMEMS: state-of-the-art in detection, opportunities and prospects," *Advanced Drug Delivery Reviews*, vol. 56, no. 11, Art. no. 11, Sep. 2004, doi: 10.1016/j.addr.2004.03.002.

[11] G. L. Cote, R. M. Lec, and M. V. Pishko, "Emerging biomedical sensing technologies and their applications," *IEEE Sensors Journal*, vol. 3, no. 3, Art. no. 3, Jun. 2003, doi: 10.1109/JSEN.2003.814656.

[12] M. A. Saeed, S. M. Khan, N. Ahmed, M. U. Khan, and A. Rehman, "Design and analysis of capacitance based Bio-MEMS cantilever sensor for tuberculosis detection," in *2016 International Conference on Intelligent Systems Engineering (ICISE)*, Islamabad, Pakistan, Jan. 2016, pp. 175–180. doi: 10.1109/INTELSE.2016.7475116.

[13] X. Li *et al.*, "Integrated MEMS/NEMS Resonant Cantilevers for Ultrasensitive Biological Detection," *Journal of Sensors*, vol. 2009, pp. 1–10, 2009, doi: 10.1155/2009/637874.

[14] H. Mathur, V. Agarwal, and K. Sengar, "Finite Element Analysis of MEMS based Piezoresistive Diamond Thin Film Cantilever Pressure Sensor," vol. 04, no. 02, Art. no. 02.

[15] G. Ciuti, L. Ricotti, A. Menciassi, and P. Dario, "MEMS Sensor Technologies for Human Centred Applications in Healthcare, Physical Activities, Safety and Environmental Sensing: A Review on Research Activities in Italy," *Sensors*, vol. 15, no. 3, Art. no. 3, Mar. 2015, doi: 10.3390/s150306441.

[16] M. Katta, R. Sandanalakshmi, M. Narendra Kumar, and Ch. Jaya Prakash, "Static and Dynamic Analysis of Carbon Nano Tube Cantilever for Nano Electro Mechanical Systems Based Applications," *j comput theor nanosci*, vol. 17, no. 5, Art. no. 5, May 2020, doi: 10.1166/jctn.2020.8862.

[17] P. Saccomandi, E. Schena, C. Oddo, L. Zollo, S. Silvestri, and E. Guglielmelli, "Microfabricated Tactile Sensors for Biomedical Applications: A Review," *Biosensors*, vol. 4, no. 4, Art. no. 4, Nov. 2014, doi: 10.3390/bios4040422.

[18] P. Antunes *et al.*, "Quantification of NS1 dengue biomarker in serum via optomagnetic nanocluster detection," *Sci Rep*, vol. 5, no. 1, Art. no. 1, Dec. 2015, doi: 10.1038/srep16145.

[19] M. Katta and R. Sandanalakshmi, "Simultaneous tropical disease identification with PZT-5H piezoelectric material including molecular mass biosensor microcantilever collection," *Sensing and Bio-Sensing Research*, vol. 32, p. 100413, Jun. 2021, doi: 10.1016/j.sbsr.2021.100413.

[20] J. Yang, J. Xu, W. Wu, M. Bertke, H. S. Wasisto, and E. Peiner, "Piezoresistive Silicon Cantilever Covered by ZnO Nanorods for Humidity Sensing," *Procedia Engineering*, vol. 168, pp. 1114–1117, 2016, doi: 10.1016/j.proeng.2016.11.361.

[21] M. J. Wadas *et al.*, "Detection of Traumatic Brain Injury Protein Biomarkers With Resonant Microsystems," *IEEE Sensors Letters*, vol. 1, no. 6, Art. no. 6, Dec. 2017, doi: 10.1109/LSENS.2017.2768514.

[22] G. Imamura, K. Shiba, and G. Yoshikawa, "Finite Element Analysis on Nanomechanical Detection of Small Particles: Toward Virus Detection," *Front. Microbiol.*, vol. 7, Apr. 2016, doi: 10.3389/fmicb.2016.00488.

[23] M. Nordström *et al.*, "SU-8 Cantilevers for Bio/chemical Sensing; Fabrication, Characterisation and Development of Novel Read-out Methods," *Sensors*, vol. 8, no. 3, Art. no. 3, Mar. 2008, doi: 10.3390/s8031595.

[24] Miranji Katta, JayaPrakash Ch, NarendraKumar M, Surendra babu Velagaleti, and Mohana vamsi krishna A, "Comparative analysis of lead-free piezoelectric material for ultrasonic glucose sensing applications," *JARDCS*, vol. 11, no. 2-Special Issue, Art. no. 2-Special Issue, Apr. 2019.

[25] A. Gupta, D. Akin, and R. Bashir, "Single virus particle mass detection using microresonators with nanoscale thickness," *Applied Physics Letters*, vol. 84, no. 11, Art. no. 11, Mar. 2004, doi: 10.1063/1.1667011.

[26] P. Sangeetha and D. A. V. Juliet, "MEMS Cantilever Based Immunosensors for Biomolecular Recognition," vol. 2, no. 1, Art. no. 1.

[27] D. Ramos, J. Mertens, M. Calleja, and J. Tamayo, "Study of the origin of bending induced by bimetallic effect on microcantilever," *Sensors*, vol. 7, no. 9, Art. no. 9, Sep. 2007, doi: 10.3390/s7091757.

[28] R. Mukhopadhyay, V. V. Sumbayev, M. Lorentzen, J. Kjems, P. A. Andreasen, and F. Besenbacher, "Cantilever Sensor for Nanomechanical Detection of Specific Protein Conformations," *Nano Letters*, vol. 5, no. 12, Art. no. 12, Dec. 2005, doi: 10.1021/nl051449z.

[29] M. Katta and K. Lavanya, "SIMULATION APPROACH TO DESIGN HIGH SENSITIVE NEMS BASED SENSOR FOR MOLECULAR BIO- SENSING APPLICATIONS," *Clinical Medicine*, vol. 08, no. 03, Art. no. 03, 2021.

[30] P. Sangeetha and D. A. V. Juliet, "Simulation and Analysis of Micro Cantilever Sensor for Enhanced Biosensing of Disease causing Pathogens," p. 6, 2014.

[31] D. K. Parsediya, J. Singh, and P. K. Kankar, "Simulation and Analysis of Highly Sensitive MEMS Cantilever Designs for 'in vivo Label Free' Biosensing," *Procedia Technology*, vol. 14, pp. 85–92, 2014, doi: 10.1016/j.protcy.2014.08.012.

[32] L.-H. Cheng *et al.*, "USING A CMOS-BIOMEMS CANTILEVER SENSOR FOR ORCHID VIRUS DETECTION," p. 3.

[33] . K., J. Rahul, and R. Kumar, "Micro-cantilevered MEMS Biosensor for Detection of Malaria Protozoan Parasites," *J Appl. Comput. Appl. Mech.*, no. Online First, Art. no. Online First, Feb. 2019, doi: 10.22059/jcamech.2019.276035.362.

[34] Y. Chen *et al.*, "Field-Effect Transistor Biosensor for Rapid Detection of Ebola Antigen," *Scientific Reports*, vol. 7, no. 1, Art. no. 1, Dec. 2017, doi: 10.1038/s41598-017-11387-7.

[35] N. E. Tsakoumis, A. P. E. York, D. Chen, and M. Rønning, "Catalyst characterisation techniques and reaction cells operating at realistic conditions; towards acquisition of kinetically relevant information," *Catal. Sci. Technol.*, vol. 5, no. 11, Art. no. 11, 2015, doi: 10.1039/C5CY00269A.

[36] S. Gupta, K. Ramesh, S. Ahmed, and V. Kakkar, "Lab-on-Chip Technology: A Review on Design Trends and Future Scope in Biomedical Applications," *International Journal of Bio-Science and Bio-Technology*, vol. 8, no. 5, Art. no. 5, Oct. 2016, doi: 10.14257/ijbsbt.2016.8.5.28.

[37] Y. Yanagida, "MEMS/NEMS-based Devices for Bio-measurements," *Electrochemistry*, vol. 85, no. 9, Art. no. 9, 2017, doi: 10.5796/electrochemistry.85.572.

[38] . K., J. Rahul, and R. Kumar, "Micro-cantilevered MEMS Biosensor for Detection of Malaria Protozoan Parasites," *J Appl. Comput. Appl. Mech.*, no. Online First, Art. no. Online First, Feb. 2019, doi: 10.22059/jcamech.2019.276035.362.

[39] "Micro- and Nanosensors for Medical and Biological Measurement," *Sensors and Materials*, p. 275, 2012, doi: 10.18494/SAM.2012.793.

[40] L. Fu, S. Li, K. Zhang, I.-H. Chen, Valery. Petrenko, and Z. Cheng, "Magnetostrictive Microcantilever as an Advanced Transducer for Biosensors," *Sensors*, vol. 7, no. 11, Art. no. 11, Nov. 2007, doi: 10.3390/S7112929.

[41] K. Neethu and K. J. Suja, "Sensitivity Analysis of Rectangular Microcantilever Structure with Piezoresistive Detection Technique Using Coventorware FEA," *Procedia Computer Science*, vol. 93, pp. 146–152, 2016, doi: 10.1016/j.procs.2016.07.194.

[42] Rezazadeh, G., Sadeghian, H. and Zubtsov, M., 2010. A novel technique for stress gradient measurement of electrostatic MEM switches and non ideal anchor's effects. Analog Integrated Circuits and Signal Processing, 62(1), pp.43-50.

[43] C. Grogan, F. R. McGovern, R. Staines, G. Amarandei, and I. Naydenova, "Cantilever-Based Sensor Utilizing a Diffractive Optical Element with High Sensitivity to Relative Humidity," *Sensors*, vol. 21, no. 5, p. 1673, Mar. 2021, doi: 10.3390/s21051673.

[44] Banik, S., Roy, S. and Sen, B., 2019. An integrated framework for application independent testing of fpga interconnect. Journal of Electronic Testing, 35(5), pp.729-740.