ISSN 2063-5346

MICROCANTILEVER BASED HIGH SENSITIVE BIO-CHEMICAL SENSOR FOR EARLY DETECTION OF DENGUE WITH CATALYTIC APPROACH

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Article History: Received: 10.05.2023 Revised: 29.05.2023 Accepted: 09.06.2023

Abstract

Micro and Nano fabricated cantilever sensor devices have attracted much interest in recent years because of their fast and reliable detection with a high surface-to-volume ratio. Here a novel biosensor was developed based on MEMS technology to detect dengue virus (DENV) in early stages, using cantilever deflection due to antigen (Ag) and antibody (Ab) reaction. To develop the proposed biosensor, a thin layer of prime dengue antibodies (IgM) coated on the active surface of the cantilever after functionalization. After that, exposed to the antigen (DENV1- 4), as it contains a significantly high sensitive biomarker, Non-Structural-1 (NS1) is available at detectable concentrations in inpatient blood during 2-9 days. This research paper uses a novel technique called the "catalytic approach" to enhance biosensor performance. The experimental results proved that cantilever response is good enough to detect NS1 with minimum interference for four serotypes of dengue virus (DENV-1 to DENV-4). The performance of biosensors with the catalytic approach should significantly high compared to the conventional method. The proposed biosensor was miniaturized and shows a significant difference in detecting the dengue virus. According to the statistical analysis, the catalyst detects type-1 and type-2 dengue viruses (DENV-1 and DENV-2). $C_5H_{12}O_4$ Increases the performance by 51.52% and 61.06%, type-3 and type-4 dengue viruses (DENV-3 and DENV-4) with the catalysts $C_5H_{12}O_4$ *and* $C_5H_{10}O_2, C_5H_{10}O_5$improved the performance by 54.28%, 9.43%, and 89.82%, 57.77%, 72.85% respectively. Along with the above catalysts, $C_5H_8O_2$ specifically detects DENV- 4 with an improved performance by 55.81% at early stages, and it can be used as a portable tool for point of care diagnostics.

Keywords: Dengue, Micro Electro Mechanical Systems, Cantilevers, Biosensors, Molecular biology, Antigens, Antibody.

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DOI:10.48047/ecb/2023.12.9.27

1. Introduction

The MEMS technology enables innovative methods for rapid, label-free detection of specific biochemical analytes from the human body based on the analytical response of the Cantilever [1-2]. These sensors can operate in either static mode or dynamic mode, depending on the type of sensing mechanism. Based on the properties of the Cantilever, one among the following three principles, such as piezoelectric, piezocapacitive, and piezoresistive, are used [3]. The adsorption of the biomolecule onto the Cantilever provides slight deflection due to the surface stress typically 0.5 – 5N/m, which results in bend occurring in the order of a few nanometres. There are several signal detection mechanisms available among them; optical and mass change or piezoresistive method of detection most frequently used because of robust, handheld, and easy fabrication [4-6]. The piezoresistive method is a comprehensive, helpful method for sensors due to the availability of that material. Piezoresistance effect in silicon-based structure provides more change in resistance than the change in dimension under stress created by molecular weight on the surface of the typical Cantilever [7-10]. These piezoresistive sensors are fabricated on micromachined diaphragms [11-12]. For small deflections, the change in resistance varied linearly with pressure imposed. In this paper, a cantilever-based biosensor with the working principle of piezoresistive effect is used to detect the dengue virus.

The typical output quantity of the electrical signal in the MEMS is always in the order of a few µV to mV range [13-15]. Suppose we add a suitable chemical as the catalyst to enhance the reaction between analytes and bio-element. In that case, we get output electrical quantity in the detectable order with more ease and fewer false alarms [16]. In this experiment, IgM antibodies were coated on the cantilever surface after functionalization and then exposed to DENV NS1 antigen. The parameters specificity, sensitivity, and selectivity are the significant constraints in the performance of biosensors that are met with a proper catalyst [17-20].

2. Related Work

Dengue fever has increased the number of human and economic dangers by a factor of 30 in the last 50 years [21]. It has recently proliferated across the Caribbean Islands as the primary dengue host (Aedes aegypti mosquito [22]. Since 2014, Aedes vectors have caused massive dengue epidemics, chikungunya, and yellow fever in several countries claimed fatalities and straining healthcare systems. Once the Dengue Virus is infected, humans are the primary carriers and widespread sources of the virus if the virus circulates in the body of an affected person for 2-7 days with fever symptoms [23-24]. These Dengue viruses are four serotypes DENV1 – DENV4 and are genetically related to flaviviruses from the family of Flaviviridae [25]. The physical appearance of the Dengue virus in patient serum is microscopic, typically in the order of 35 to 65nm with a spherical surface and an isometric nucleocapsid. Its nucleus contains single RNA with structural and non-structural proteins [26]. According to the clinical study, NS1 antigen in dengue-affected patients ranged from 0.04 - 2µg/mL with primary infection and 0.01-2µg/mL with secondary infection. In the current market, number of rapid diagnosing kits are available based on the detection of NS1, viral culture test, combining IgM-NS1 and IgG-NS1 of DENV detection, compared to NS1 alone to improve sensitivity and specificity [27]. Some serological experiments are commonly used to validate infections based on polyclonal or monoclonal antibodies [28]. This process is complex, time-consuming sample preparation, and requires expensive

analytical equipment, which may threaten a patient's life [29].

Considering these circumstances, several groups have developed a biosensor system for lively NS1 quantification. Immunosensors employing fluorescent nanoparticles, surface Plasmon resonance (SPR) methods, DNA-based bioassays, and electrochemical detection approaches have been reported recently [30]. Therefore, MEMS and effective reagent chemicals are used as catalysts for antigens and antibodies in developing new biosensors. Due to their small size and cost-effectiveness, they are preferably used to invent new biosensing platforms.

For the quantitative and qualitative detection of biomolecules, including proteins and viruses, polymer matrix composites (PMCs) based on various transducers, such as electrochemical, optical-electrical, and physical, have been recently developed (mass-sensitive). Specific polymer matrix composites (PMCs) include nanostructured semi- or conductive materials [31]. For example, a self-assembly-induced electrical memory effect may be obtained by incorporating platinum nanoparticles (Pt) into the tobacco mosaic virus (TMV). If this titanium dioxide particle is mixed with an ic graft copolymer with polyvinyl alcohol (PVA) matrix, it can be used in nanotechnology applications. By incorporating conducting nanowires made of poly (3,4-ethylene dioxythiophene) into M13 viral particles, the virus has been shown to detect prostate-specific transmembrane antigens (PSMA) selectively. For PMCs, anti-IL22 antibodies are adsorbed on poly (dimethyl diallyl ammonium chloride)-functionalized graphene/gold nanoparticles. These antibodies are used to detect the inflammatory cytokine interleukin-22 (IL-22) [32]. Furthermore, an immunoassay for the DENV NS1 protein-using poly (allylamine)-CNT composites has been developed.

3. Materials and methods

This section discusses a variety of materials and preparation techniques, and manufacturing procedures. Cantilever manufacturing and associated chemical processes presented in section 1. In contrast, surface functionalization technique conversed in section 2, and chemical reagents and culture borthe preparation for dengue discussed in sections 3 and 4 correspondingly. Finally, in section 5, the experimental setup is illustrated.

3.1 Fabrication of Cantilever

The choice of silicon substrate would be the first step in the device design phase, followed by thermal oxidation deposition of silicon dioxide (SiO_2). A thin polysilicon film deposited using the HWCVD (Hot-Wire Chemical Vapour Deposition) technique as the electrode after the silicon substrate coated with an insulating layer. ICPCVD (Inductively Coupled Plasma Chemical Vapour Deposition) been employed to deposit the sacrificial SiO_2coating on top of the polysilicon layer and complete patterning. A polysilicon layer of 0.5μm thick is then deposited and imprinted on the cantilever beam's surface. A sacrificial layer of silicon dioxide is enacted to prevent the polysilicon substrate. Wet etching with BHF has been used to produce the sensor. The production process for the micro cantilever's ejection has been optimized. The commercially available bi-layer polysilicon cantilever beam provides the lowest thermal expansion coefficient and IC compatibility [33].

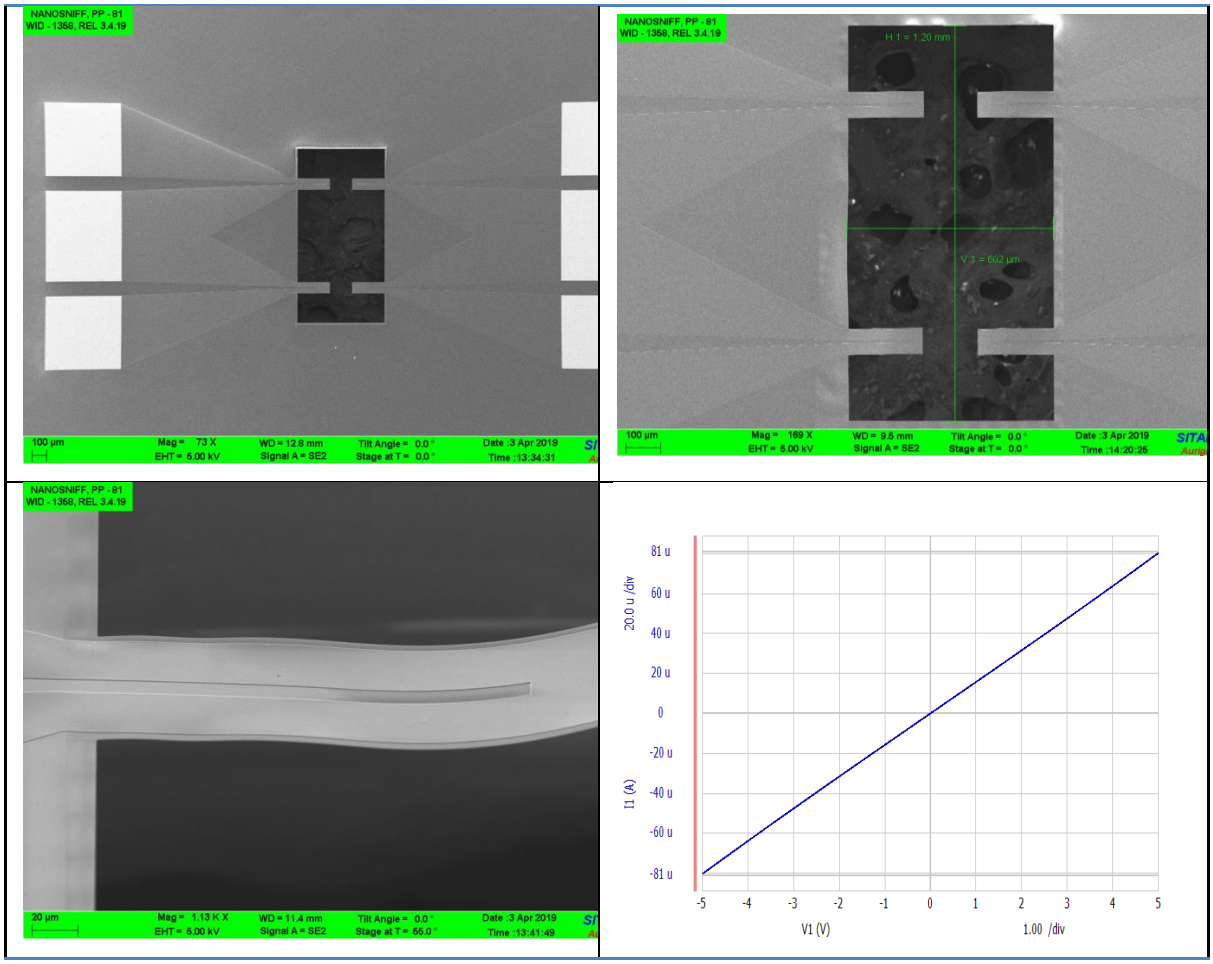


Figure 1: Scanning Electron Microscope Images of fabricated micro cantilever with Ohmic response

Substrate cleanliness is performed throughout the semiconductor fab using the RCA (Radio Corporation of America) technology, eliminating micropollutants like particulates, elastomeric gel, lubricants, ions, or toxic metals from the substrate surface. It is a high-quality wafer cleaning procedure that must be carried out at hot pressures. SC-1 and SC-2 are the two steps under this RCA purification process. Dilute 120 ml of deionized water using 20 ml of NH_4OH (Ammonium Hydroxide) and heated for 5 min at 75ºC under (SC-1) Standard Clean-1. Then, add 35ml of H_2O_2 (Hydrogen Peroxide) and heat it for 7 min. After which, cool the substrate for 20 min, and then lift it into fragments. These organic pollutants also were removed using a DI water dip, followed by an HF (Hydrofluoric acid) dip and a subsequent DI water splash. Standard Clean-2 (SC-2) has been employed to remove metal impurities from the substrate surface. As part of the implementation process, you will need to heat 120 ml of deionized water and 20 ml of NH_4OH to 75 ° C. for 4 minutes. Then, add 40ml of H_2O_2. Heat the water for 5 minutes, and then let it cool to room temperature before slashing. Next, a dip in DI water and then 50 secs in HF (Hydrofluoric acid). Metallic contaminants on the substrate surface are then removed by dipping the substrate in Deionized Water. Finally, the cantilever design would be 225m in length (L), 80m wide (W), 650nm thick (T), and width of piezoresistive material 30µm(Wpz) with a 50nm thickness. Its maximum force constant is 5Nm-1, its approximate impedance is 56KΩ, its sensitivity to force ratio (S/F) is 1.78 x 10^{-6}, whereas its sensitivity to displacement ratio is 3.12 x 10^{-6} respectively.

3.2 Surface Functionalization

To develop a reliable biosensor, the surface layer of the cantilever must be stable and immobilized to respond quickly with hoarded bio-chemicals such as antigens or monoclonal antibodies. To achieve surface functionalization, a superconductive coating is required [34]. It will be recommended to choose gold (Au) over silver (Ag) because of its stability and low resistivity. The gold substance was prepared by evaporation of 300nm of gold on Si-substrate pre-coated with 180nm of titanium. Using a silicon substrate deposited with 180 nm titanium and 300 nm gold, a gold material was vaporized onto the surface to be used. To eliminate any remaining contaminants, the gold substrate was submerged in $H_2O_2 : H_2SO_4$, $5:3\ V/V$ (piranha solution) for at least two minutes, followed by DI water and dried in nitrogen flow, and then immersed in C_2H_5OH (ethanol solution) of $C_{11}H_{22}O_2S$ (11-mercaptoundecanoic acid) for at least nine hours. Washed away extra $C_{11}H_{22}O_2S$ with ethanol. To finish, the activation of the Au substrates was accomplished by drying them underneath a nitrogen atmosphere and then immersing them for four hours in a 200mM EDC or N-hydroxysuccinimide solution diluted 1:1 v/v in CH_3OH (methanol). After cleaning in CH_3OH, the activated Au substrate was dipped in PBS buffer solution to keep the PH constant. This step was repeated two more times for the final step of electroplating. Covalent immobilization onto a functionalized gold surface is typically accomplished using the method depicted in the given figure 2.

3.3 Chemical Reagents

The High Purity (>90%) Chemical reagents of Dengue virus (DENV) non-structural proteins DENV-1, DENV-2, DENV-3, DENV-4 and Mouse Serum-RM10842-20ml of HIMEDIA brand and antibodies (IgM) were purchased from Biomall, Mumbai, India. Other chemicals 1-ethyl-3-dimethylamino propyl carbodiimide (EDC), N- hydroxysuccinimide (NHS) solution with a quality of 95%, 11-mercaptoundecanoic acid with quality of 97%, and PBS Buffer solution purchased from Srisyn Chemicals, Hyderabad, India and Antares Chemicals Private Limited Mumbai, India respectively.

3.4 Dengue Virus Culture Broth Preparation Procedure

For the preparation, Dengue virus culture broth needs to separate resilient from bottom layer of dengue virus particles, so host cell drizzling is performed by centrifugal machine rotated at 3000 x g for 20 minutes at4^oC. Then 20% of $C_{2n}H_{4n+2}O_{n+1}$ (polyethylene glycol) (Molecular weight of 8000) of 40µL mixed with $NaCl$ of 2M and incubated at 4^oC for minimum 10hours. And then, virus precipitation was obtained by centrifugation at 8000 x g at 4^oC for 10 min. The remaining process, such as propagation of the virus, titration and quality testing by reverse transcription loop-mediated isothermal amplification method, are described in a previous study.

3.5 Experimental Setup:

Measurement setup for cantilever array shown in figure 2 contains 1. Analysis chamber 2. Piezoresistive system to detect deflection 3. Electronic circuitry 4. Liquid - handler. The cantilever sensor array is located in an analytical chamber connected with inlet and outlet ports for liquid flow. The deflection that occurred in the measurement can detected using a Position Sensor Detector (PSD). Here PSD acts as a receiver and Vertical-Cavity Surface-Emitting Laser (VCSEL) as a transmitter with the wavelength of 760nm with a small cone of 5 to10^0 and linear pitch of 250µm.

After the preparation of functionalized cantilever, a thin layer of molecular

antibody (IgM) of 18Mda coated on the cantilever surface and incubated at 25^oC for 1hr. After that, we have tested this design along with all types of DENV serotypes and different chemical catalysts such as $C_5H_8O_2$ (trance-3 Pen tonic), C_5H_{12}(skellysolve A), $C_5H_{12}O_4$ (tetramethyl-orthocaronate), C_5H_8 (Isopetadine), $C_5H_{10}O_2$ (Propeniceaster) C_5H_5N (Pyridine), C_5H_6O (3-Pentynal), $C_5H_{10}O_5$ (d-thero pendulous or D-Lyxulose). Each of these was exposed to the antigen and antibody combinations on the piezoresistive cantilever shown in the experimental setup to find the best chemical catalyst to detect the dengue virus in the early stages with acceptable performance. In each case, one of the serotypes among DENV1- DENV4 of 18Mda (Rat Serum Albumin, RSA) each are injected into the surface of the antibody using a micro-syringe with time elapse of 30 to 45 minutes each at 25^oC and again the surface is subsequently clear with PBS solution and distilled water. For those different experiments, different responses are obtained and measured using PSD. Here, no mechanical approach for a cantilever has needed. This simple sensing mechanism is best suitable for most biosensing applications.

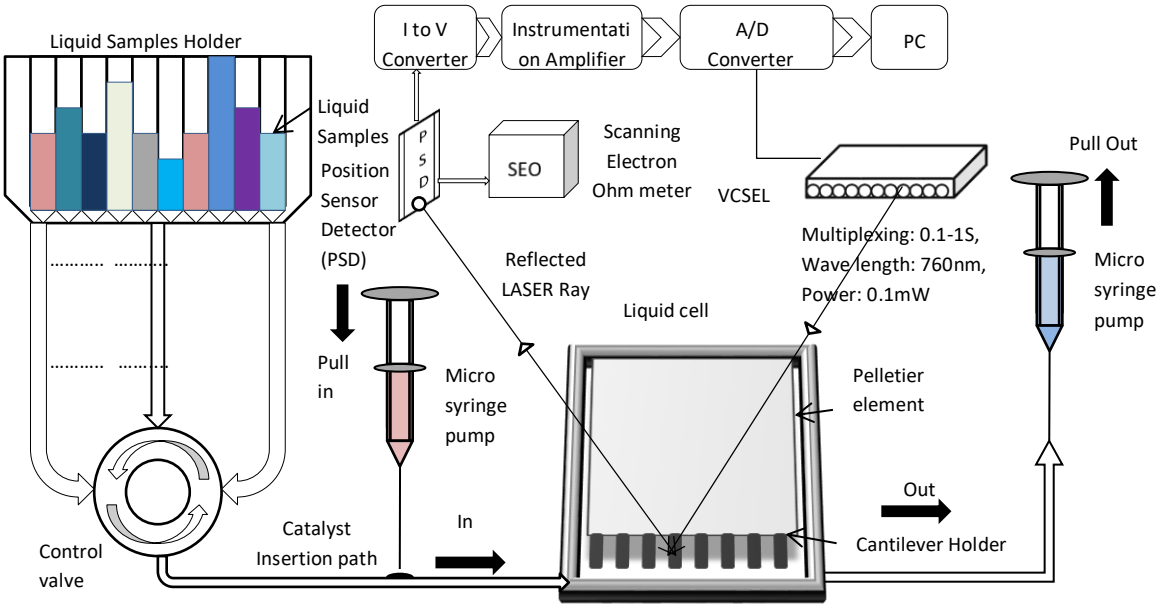


Figure 2: Schematic of measurement setup for MEMS cantilever based Biosensor Applications in Liquid or Biochemical mediums with catalysts

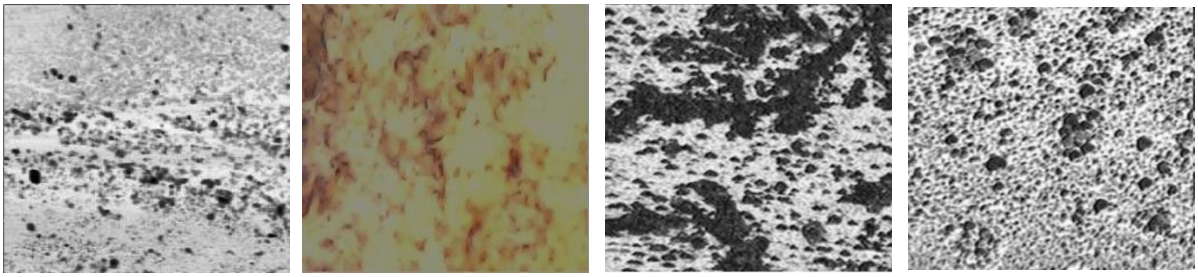
4. Results and Discussions:

The first aspect of this subpart focuses on the deposition of antibodies on the surface cantilever's functionalized surfaces. As an intermediate step in the agglutinatio n process, the surface cantilever was observed and plotted as an indicator of its deflection sensitivity. The biosensor was enhanced by catalytic a gglutination, and the quantified catalytic reaction was calculated and reported accordingly as the final step.

4.1 Effect of Anti-Dengue (antibody) sensing layer on functionalized cantilever surface:

It is critical for biosensing applications that the sensing layer on the cantilever active surface is consistently distributed; in this case, the surface containing antibody serves as the sensing layer (Ab-IgM). Figure 3 displays the contrast picture of the cantilever's 10m x 10m dimensions exposed to the sensing

layer, taken by an Asier 1000 x 32MP microscopic lens camera. The antibodies are represented as light white-coloured regions in the phase contrast picture, while light yellow coloured areas correspond to the functional coating on the cantilever in the image. Figs. 3 (a) and 3 (b) show the bare cantilever and functionalized surface. Fig. 3(c) demonstrates that the antibody coating is not consistently applied to the whole surface, while Fig. 3(d) indicates that it is almost covered and appropriate for experimentation. The ink-jet spotting approach was used for all succeeding coats.



(a) (b) (c) (d)

Figure 3. AFM contrast images of cantilever coated with IgM (a) Bare cantilever surface (b) Surface after functionalization (c). Non-uniformly distributed Ab coating (d).Uniformly distributed Ab coating

Fig. 3 demonstrates the piezoresistive cantilever response under three different conditions. As a Non-Functionalized Cantilever Surface (NFCS), i.e., a piezoresistive cantilever without any functionalization (NFCS), and second, as a result of the functionalization, a Fully Functionalized Cantilever Surface (FFCS), and as a third part, as an Antibody Coated Cantilever Surface (ACCS). First, 0.25ml of PBS solution is applied to the functional surface, followed by de-ionized/distilled water. Then the system steadily becomes an equilibrium state and is stable for hours in this configuration

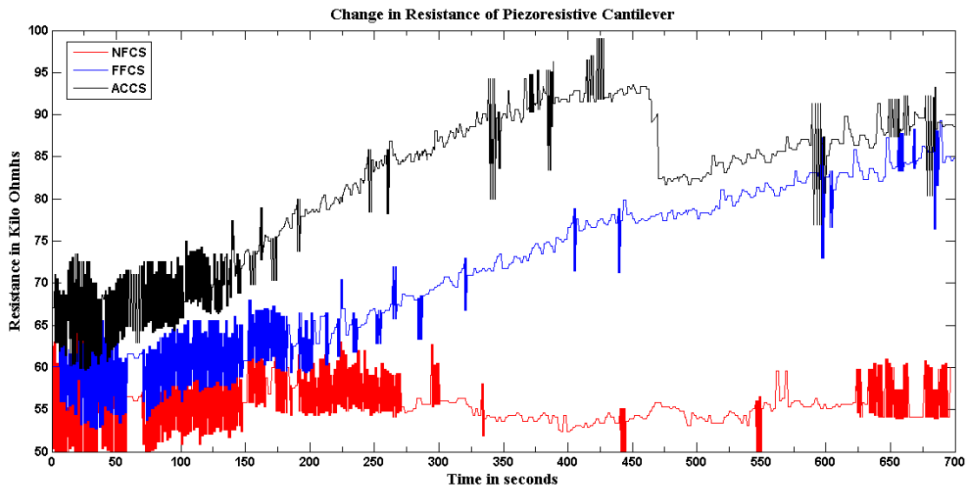


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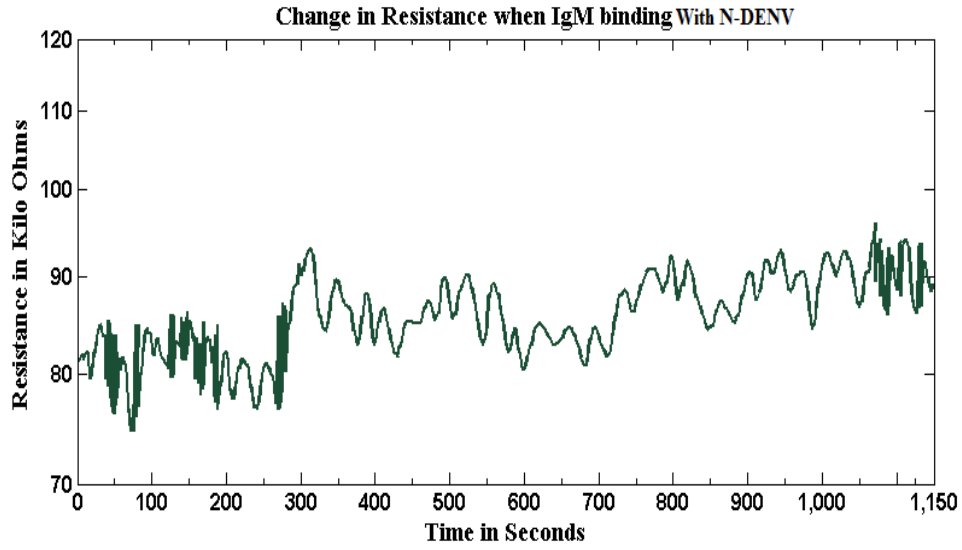
Figure 4: Response of Piezoresistive cantilever for Functional, non-functional and antibody coatings

The I-V relation's default resistance provided by the piezoresistive cantilever (Fig. 1(d)) is 56K. This resistance is observed in the experimental setup with a 3K variation under ambient contexts. Following surface functionalization, very little force acting on the surface cantilever increases tensile force, resulting in the

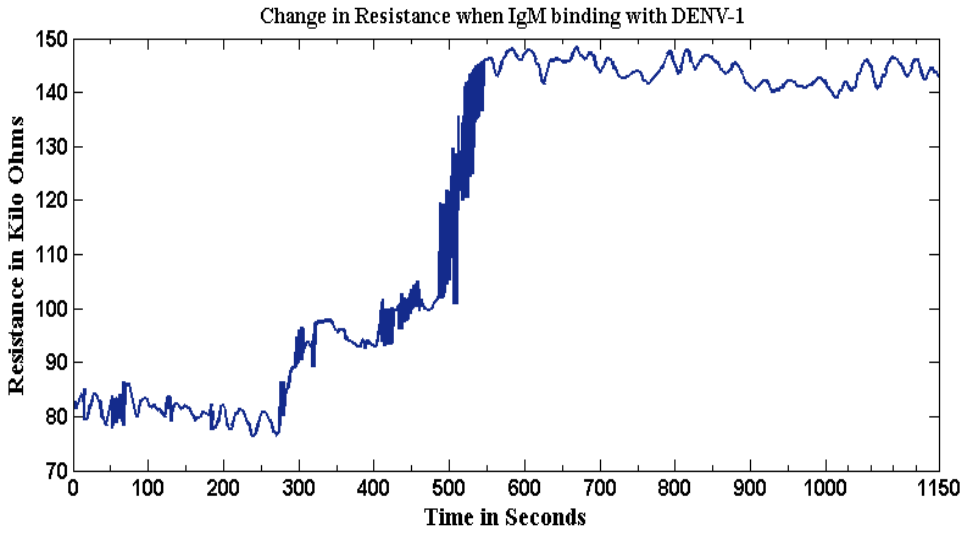
resistance shift seen in the above figure as FFCS. At t = 250 seconds, a considerable change is noted, and its average resistance is in the range of 75K to 80K under steady-state conditions beginning at t = 600 seconds. Following that, the binding of an antibody to the surface of a wholly functionalized cantilever with the intent of imposing some force immediately increases quickened resistance up to 85K±1.5K, as indicated in the figure as ACCS. In this case, we observe that the signal generated by the application of functionalization and antibodies is relatively low, and this voltage is recognized as the critical threshold. The authors repeated this experiment numerous times to compute the average threshold level of the microsensor device while injecting analyte and catalyst in the meantime. This experiment utilized a broad range (10mΩ to 1000MΩ) of high precision scanning image ohmmeter RM3545 to evaluate resistance and storage capacity.

4.2 Response of Ag-Ab (DENV-X: IgM) reaction on cantilever deflection:

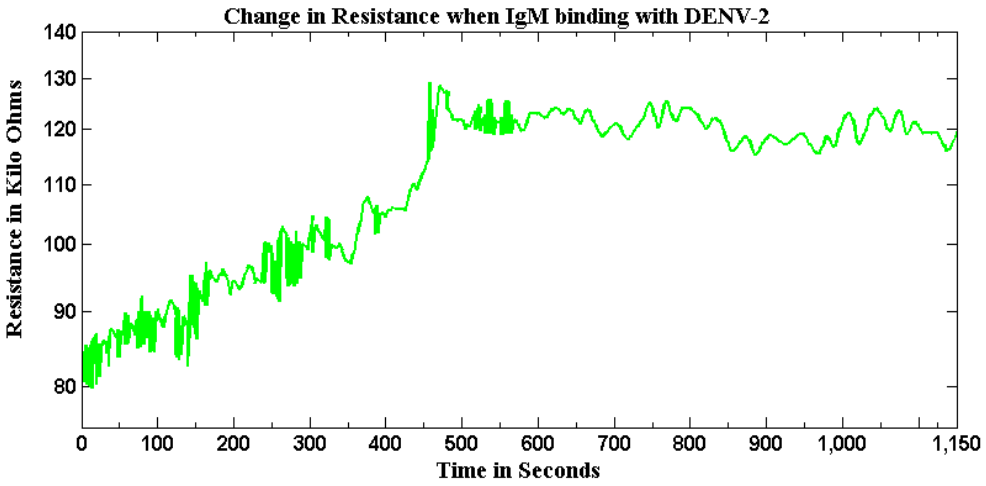
In the prior scenario, no agglutination was done, and only threshold level measurement was performed, yielding an average threshold level of 85K in the form of resistance and around 45μV as the threshold voltage. It will now be interesting to see whether the corresponding antigen-antibody (Ag-Ab) and non-dengue virus (N-DENV) protein serum-antibody binding processes "sensed" a change in resistance owing to cantilever deflection. In this investigation, the N-DENV was purified MSA (Mouse serum Albumin) and considered for testing purposes. This experiment is divided into two parts. In case 1, a 0.36g/ml N-DENV solution was applied using a microsyringe to an IgM coated cantilever surface, and the cantilever deflection in PSD or change in resistance was detected as shown in figure 5.(a). According to the examination of figure 5(a), steady-state begins at t=300seconds and has an average resistance of 87KΩ. In contrast to threshold resistance, the net change in resistance ΔR~2KΩ in terms of voltage levels is negligible and should not be considered as a false alarm. Similarly, in the second example, DENV1- 4 antigen serotypes were executed at 0.36g/ml each, successively interacted with IgM, and the change in deflection as resistance is shown in figures 5(b) to 5(c) (e). According to the results of figure 3(b), the transient response between DENV-1 and IgM lasted up to 600 seconds. The mean resistance of 140KΩ in relation to the threshold provides us with the net change in resistance ΔR~55K, and it displays a substantial output voltage of more than 45V as a detection of the individual infected with the dengue virus. Similarly, figures 5(c)-5(e) and 6 depict the reaction of DENV-2 to 4, with the steady-state response beginning at t = 550, 500, 600 seconds, with mean resistance of 126KΩ, 133KΩ, 104KΩ, and net resistance of ΔR~41KΩ, 48KΩ, 19KΩ, respectively, of dengue virus-infected specimen.


Change in Resistance when IgM binding With N-DENV
Resistance in Kilo Ohms
Time in Seconds

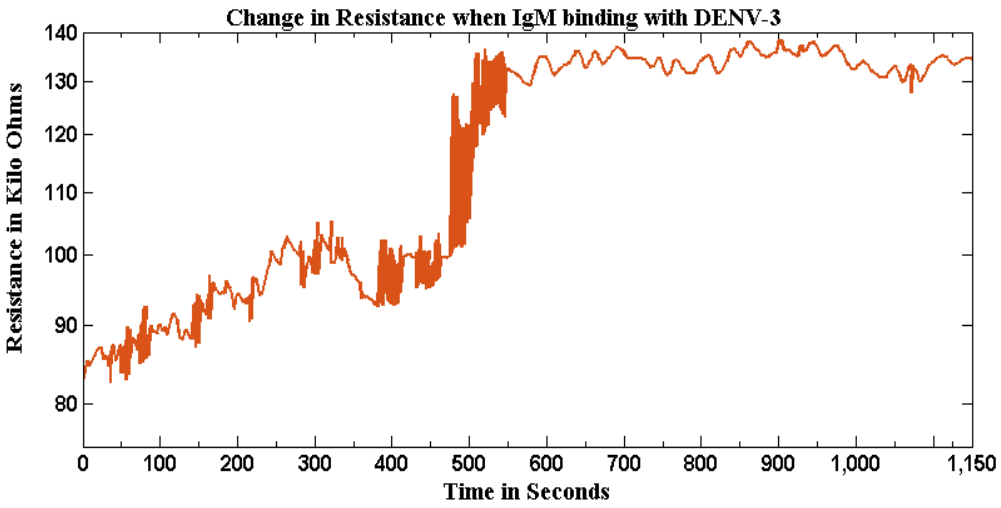
(a)


Change in Resistance when IgM binding with DENV-1
Resistance in Kilo Ohms
Time in Seconds

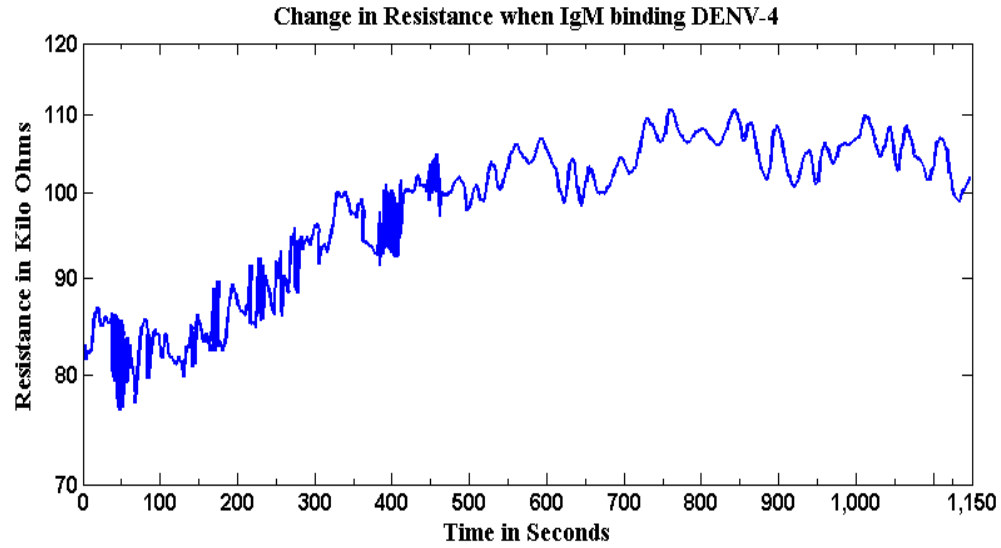
(b)


Change in Resistance when IgM binding with DENV-2
Resistance in Kilo Ohms
Time in Seconds

(c)



(d)



(e)

Figure 5: (a) Shows threshold value of resistance after functionalization (b) when exposed with type -1 DENV NS1 Antigen (c) when exposed with type -2 DENV NS1 Antigen (d) when exposed with type -3 DENV NS1 Antigen (e) when exposed with type -4 DENV NS1 Antigen

Figure 5: (a) Shows threshold value of resistance after functionalization (b) when exposed with type -1 DENV NS1 Antigen (c) when exposed with type -2 DENV NS1 Antigen (d) when exposed with type -3 DENV NS1 Antigen (e) when exposed with type -4 DENV NS1 Antigen

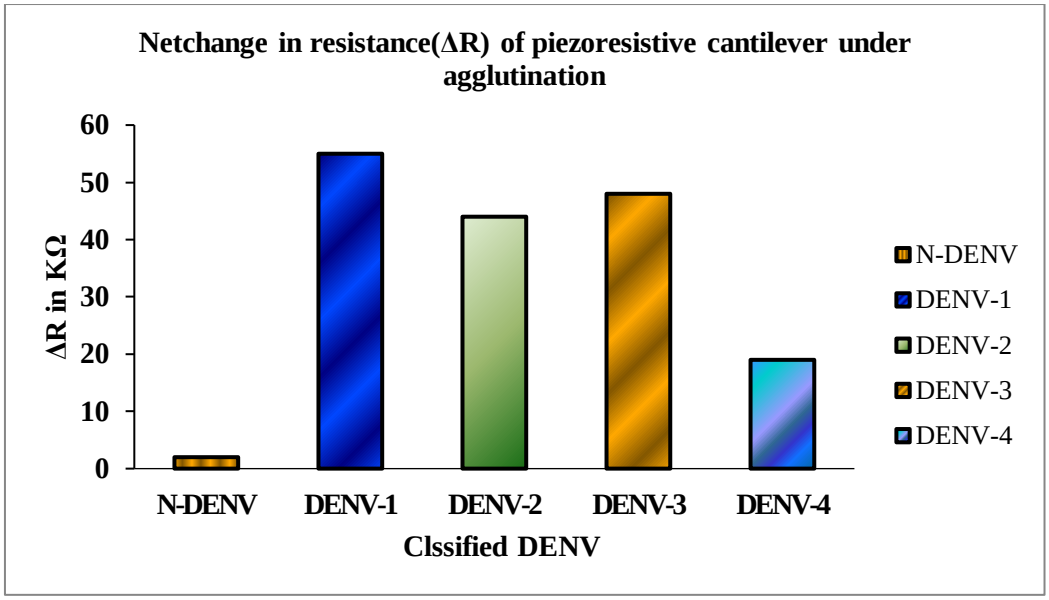


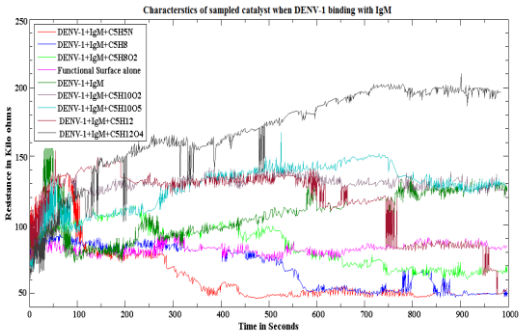
Figure 6: Net change in resistance of piezoresistive cantilever under agglutination with respect to threshold level when

N-DENV and four types of dengue viruses reacted with IgM

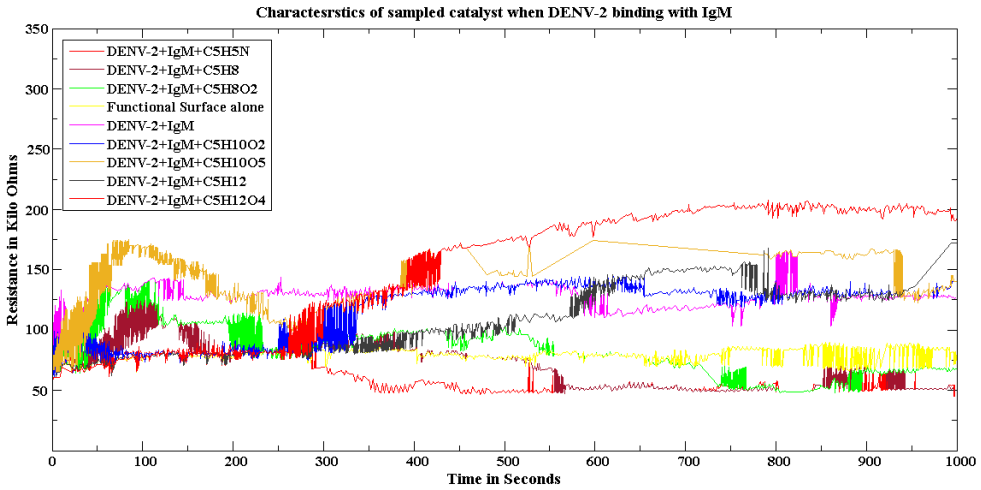
4.3 Catalytic approach on Ag-Ab reactions (DENV-X: IgM: Catalyst) to improve biosensor performance:

Despite the fact that the findings obtained in Section 4.2 may be adequate, the performance of Micro/Nanosensors is dependent on a variety of criteria such as geometrical properties, binding affinity, sensitivity, selectivity and specificity, among others. In order to achieve these objectives, we proposed a "catalytic method" to increase the performance of the biosensor, which was accepted. When using this approach, just a very small concentration of catalyst is added to the Ag-Ab solution. Essentially, the catalyst's primary role is to reduce the activation energy of the particles, allowing a higher percentage of them to have sufficient power to steer themselves towards effective collisions [35]. By interacting with reactants, it also produces an intermediate that takes less effort to transform into the finished product. The most difficult aspects to overcome in order to do this experiment using a catalytic technique are the selection of the optimal catalyst and the amount of concentration [36-38].

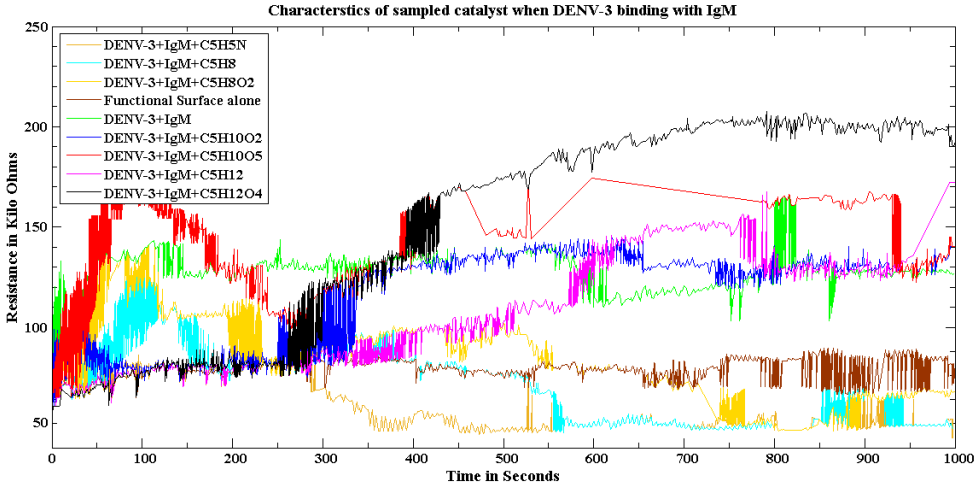
According to the results of the previous studies into "catalyst selection" and "concentration calculation," the chemicals that have been selected for the experiments are listed in Section 2. The investigation was carried on from sections 4.1 and 4.2, with an extra catalyst concentration of 0.1g/ml placed on the cantilever active surface in addition to the concentrations used in the previous sections. The following responses were obtained after the successful completion of the experimentation.


Characterstics of sampled catalyst when DENV-1 binding with IgM
DENV-1+IgM+C5H5N
DENV-1+IgM+C5H8
DENV-1+IgM+C5H8O2
Functional Surface alone
DENV-1+IgM
DENV-1+IgM+C5H10O2
DENV-1+IgM+C5H10O5
DENV-1+IgM+C5H12
DENV-1+IgM+C5H12O4
Resistance in Kilo ohms
Time in Seconds

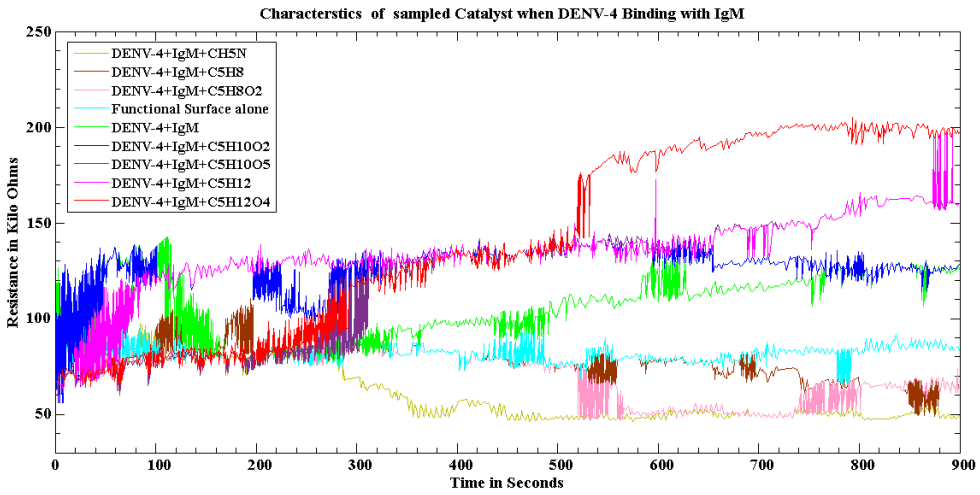
(a)


Charactesrstics of sampled catalyst when DENV-2 binding with IgM
DENV-2+IgM+C5H5N
DENV-2+IgM+C5H8
DENV-2+IgM+C5H8O2
Functional Surface alone
DENV-2+IgM
DENV-2+IgM+C5H10O2
DENV-2+IgM+C5H10O5
DENV-2+IgM+C5H12
DENV-2+IgM+C5H12O4
Resistance in Kilo Ohms
Time in Seconds

(b)


Characterstics of sampled catalyst when DENV-3 binding with IgM
DENV-3+IgM+C5H5N
DENV-3+IgM+C5H8
DENV-3+IgM+C5H8O2
Functional Surface alone
DENV-3+IgM
DENV-3+IgM+C5H10O2
DENV-3+IgM+C5H10O5
DENV-3+IgM+C5H12
DENV-3+IgM+C5H12O4
Resistance in Kilo Ohms
Time in Seconds

(c)



(d)

Figure 7: Consolidated results of catalytic approach on Cantilever resistance (a) Response of different catalysts on DENV-1: IgM reaction (b) Response of different catalysts on DENV-2: IgM reaction(c) Response of different catalysts on DENV-3: IgM reaction(d) Response of different catalysts on DENV- 4 : IgM reaction

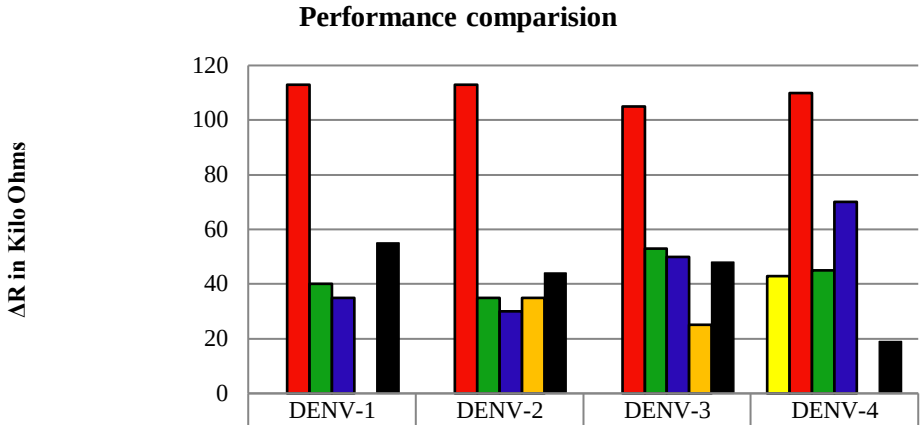
To see the effect of various catalysts on a cantilever, see Fig. 7. We found that the transient response time and cantilever resistance dynamically changed with the kind of catalyst. The deflection or resistance change in the piezoresistive cantilever is clearly shown in table-1 using the data from fig.7 (a)–(d).

S.NO.	Catalyst Formula	DENV-1		DENV-2		DENV-3		DENV-4	
		TTP	SSR	TTP	SSR	TTP	SSR	TTP	SSR
1	$C_5H_8O_2$	750	60	740	50	750	50	120	128
2	C_5H_{12}	250	55	780	120	800	110	550	52
3	$C_5H_{12}O_4$	700	198	600	198	450	190	540	195
4	C_5H_8	600	47	550	48	560	45	300	60
5	$C_5H_{10}O_2$	650	125	350	120	350	138	340	130
6	C_5H_5N	480	46	350	50	350	40	360	50
7	$C_5H_{10}O_5$	800	120	920	115	940	135	340	155

Table 1: Under the catalytic approach- response of piezoresistive cantilever Transient Time Period (TTP) in seconds and Steady State Resistance (SSR) in Kilo Ohms

From section 4.2, researchers deduced that the threshold value for an IgM-coated piezoresistive cantilever is about 85K. Section 4.3 shows the biosensor's performance in terms of net resistance change, ΔR, using a catalytic technique; however, the picture below shows the identical information more qualitatively with an analytical graph. Piezoresistive cantilever responses to catalytic approaches, some of which were even below the threshold of 85KΩ,

were noted in Figure 5 and Table-1. Consequently, we include resistance owing to deflection larger than the threshold level from Table-1 in the calculation of net change in resistance (ΔR).



	DENV-1	DENV-2	DENV-3	DENV-4
C5H8O2				43
C5H12O4	113	113	105	110
C5H10O2	40	35	53	45
C5H10O5	35	30	50	70
C5H12		35	25	
NON -CATALYTIC	55	44	48	19

Figure 8: Performance Comparison between catalytic and non-catalytic (conventional) methods,

Response of some of the catalysts in four serotypes of dengue viruses

According to the examination results of catalytic and non-catalytic (traditional way, see section 4.2) methods, the suggested catalytic approach outperformed the non-catalytic approach, as shown in the fig. 8. The results of the experiment showed that dengue virus type-1 and type-2 (DENV-1 and DENV-2) detection using the catalyst $C_5H_{12}O_4$ increased performance by 51.52% and 61.06%, respectively. Further, when the catalysts $C_5H_{12}O_4$ and $C_5H_{10}O_2$, $C_5H_{10}O_2$ are used to detect type-3 and type-4 dengue viruses (DENV-3 and DENV-4), the performance of the catalysts C 5 H 10 O 5 and C 5 H 12 O 4 improves by 54.28%, 9.43%, 4% and 89%, 57%, and 72%, respectively. $C_5H_8O_2$ detects DENV-4 with enhanced performance of 55.81% when used with the other catalysts shown in the figure above.

5. Conclusion:

Finally, we have created a biosensor based on a MEMS cantilever to detect the dengue virus in its early stages. A catalytic technique was utilized to increase the performance of biosensors and discover the optimal catalytic chemical compositions for the detection of viruses ranging from DENV-1 to DENV-4. This experimental technique comprises several different disciplines, and the sensor that has been produced is exclusively suitable for the dengue virus itself. However, the catalytic method is distinctive, and its application depends on C-H bonds and oxidation degrees of chemical structures involved in biological analytes and reactants. The constraints of the catalytic technique are that it is not empirically testable. The efficacy of the sensor is influenced not only by the use of catalytic or non-catalytic processes, but the sensor's geometrical features may also be significantly dependent. It is now feasible to construct

customized portable biosensors based on the different signatures of diverse biological analytes, which have improved performance in the early identification of more life-threatening ailments.

Acknowledgements: My sincere gratitude to the members of the INUP (Indian Nano User Program), as a portion of the research, was carried out using facilities at the Centre for Nano scale Engineering (CeNSE), which is funded by the Ministry of Electronics and Information Technology (MeitY) of the Government of India and is located at the Indian Institute of Science, Bangalore. In particular, with respect, I would like to express my sincere thanks to the Nanosniff technologies centre and the NMR Spectroscopy for Pharma and Biotech Research centre, both of which are located at the Indian Institute of Technology, Mumbai, for providing the necessary technical support and valuable guidance during the experimental work. I want to express my deepest gratitude to the "Centre for Nanotechnology & Centre of Excellence (CoE)" at Andhra University in Vishakhapatnam for extending assistance for fundamental materials research. I want to express my gratitude to Sir C.R.R. Pharma Laboratories for their invaluable assistance in recommending chemical reagents and medical support.

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