Design of Micro-Cantilever Biosensors for Detection of Latent Tuberculosis

Yashaswini B. M[1], Dr. Rachana. S. Akki[2]

[1]PG Students, [2]Assistant Professor
[1,2]Department of Electronics and Instrumentation Engineering, RV College of Engineering, Bangalore

---***---

Abstract: *Tuberculosis is an infectious disease caused by various strains of Mycobacterium. Tuberculosis has a survival rate of 70% in India indicating that nearly 40% of the Indian populations have been infected with tuberculosis. Tuberculosis disease has been classified as Active and Latent. Active type of tuberculosis can be detected at early stage since the infected cells are in the active state but, latent type of tuberculosis is difficult for early detection since the infected cells are in the inactive state. This paper aims at designing, and simulating various cantilever structures for early detection of the Latent type of Tuberculosis. The microcantilever biosensor is a multi-layered structure with the surface made of various materials like gold, silicon and polysilicon. Antibodies are coated on the surface of the microcantilever. When the sample (infected with latent tuberculosis) is placed on to the microcantilever beam the antibodies binds with the antigens existing in the sample resulting in displacement of the beam, because of the surface stress due to antigen-antibody reaction. Piezoelectric layer is placed below the surface of the cantilever beam which act as electrodes to measure electric potential proportional to the displacement. This bending or bowing of the cantilever is measured as the electric potential which in turn is dependent on the displacement of the microcantilever structure. Various designs are developed using COMSOL Multiphysics® software. Maximum displacement achieved is 8.5194×10^{5} μm for model with gold layer on the cantilever for a load of 100N (Newton). 100N corresponds to 28.228×10^{-24} kg weight of antigen.*

Key Words: Cantilever, MEMS/NEMS, Nanotechnology, Tuberculosis, Nanofabrication.

1. Introduction:

Tuberculosis is an airborne pathogen that spreads through the air from person to person. Tuberculosis is caused by mycobacterium tuberculosis, directly affects the lungs and harms the other body parts [1]. Tuberculosis are of latent and active types. Latent tuberculosis (LTB), also called latent tuberculosis infection (LTBI) occurs when a person is infected with Mycobacterium tuberculosis, but does not have active tuberculosis. Active tuberculosis can be contagious while latent tuberculosis is not, and it is therefore not possible to get TB from someone with latent tuberculosis. The risk factor is that approximately 10% of these people (5% in the first two years after infection and 0.1% per year thereafter) will go on to develop active tuberculosis [2] The antigen which causes tuberculosis are ESAT-6 and CFP-10. The molecular weight of ESAT-6 antigen and Anti-ESAT-6 antibodies are 6KDa and 11KDa respectively for Latent tuberculosis [3], where 1KDa is approximately equal to 1.661×10^{-24}kg, therefore the total weight of ESAT-6 antigen and Anti-ESAT-6 antibody is 28.228×10^{-24}kg [3] for Latent type of tuberculosis.

The range of surface force in antibody-antigen interactions are 10N to 100N and the intermolecular force generated during single antigen-antibody interaction is 10N [4]. Considering, 10 such antigen-antibody interactions, intermolecular force is estimated which is then applied on a cantilever and respective deformation value is noted. Whereas, weight of 10 antigen is 28.228×10^{-24}kg [5]. The sensitive layer coated on surface of microcantilever induces differential surface stress as a result of interaction between absorbate and surface.

Microcantilevers are the micromechanical structures which are fixed at one end and the other end is free for displacement. The cantilever structures have been used widely used these days because of their good functionality in the detection of bimolecular substances [6]. The name Microcantilever Biosensor has been coined for these microcantilver structures since they detect the biomolecules [7]. Micro cantilever beams are used in different fields including pathogenic labs to detect different molecules that help in detection of diseases like Tuberculosis, HIV, Swine Flu and DNA analysis [7, 8, 9]. These Microcantilevers that range from micrometer to nanometer can also be fabricated using micromachining tools and techniques [10].

Chemical binding or Physical adsorption of the biomolecules that are coated on the surface of the cantilever results in the change in the mechanical properties of the microcantilever [11]. The cantilever surfaces are made up of gold, silicon and polysilicon, the antibodies on the microcantilever binds to the specific antigen existing in the sample [12]. As the target molecules get absorbed, the mass gets added which results in the deflection of cantilever.

2. Model Development and Simulations:

Microcantilever biosensor 3D designs are modeled using COMSOL Multiphysics®. The micro cantilever beam is designed by keeping one end fixed and the other end free to suspend. The seven models are designed using MEMS module in COMSOL Multiphysics®.Seven geometries are shown in Figure 1 and the table 1 summarizes the dimensions of all the modeled designs.

Solid Mechanics Model :

In this study, we have applied the force of range 10N- 100N to the sample containing antibodies to attain maximum displacement. The deflection is mainly because of surface stress induced due to antigen- antibody reaction [2]. Thus a solid mechanics model is adopted to apply the force to the sample.

The governing equation for the force in sample is given by,

$$-\nabla.\sigma = Fv \qquad [2]$$

where σ is stress, F is applied force and v is Poisson's ratio. Young's modulus, E=170 Pa and Poisson's ratio, v=0.44 was assumed to apply force for sample. Small deflection the cantilever indicates the absence of tuberculosis antigen, whereas the maximum deflection indicates the presence of antigen in the sample.

A. Electrostatics Model:

This study is used to apply the voltage to the electrical plates to obtain the electrostatic energy stored in the cantilever. It acts as capacitors containing two electrical plates separated by a dielectric.

The equation for the electrostatic energy stored in cantilever is given by,

$$E = -\nabla.v \qquad [2]$$

where E is the electrostatic energy stored and v is applied voltage.

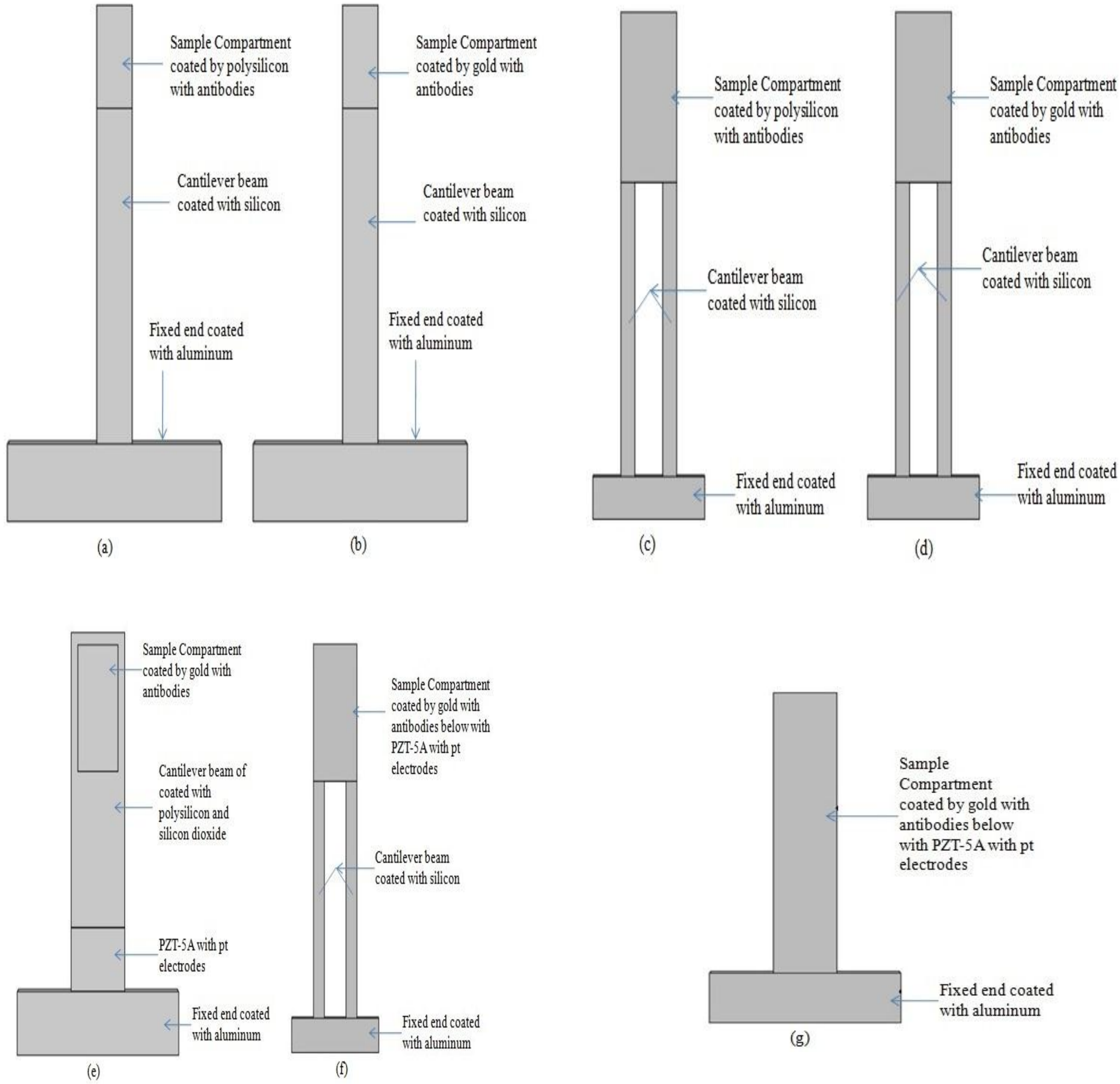


Fig.1. DESIGN GEOMETRIES, (a)- Design 1, (b)- Design 2, (c)- Design 3, (d)- Design 4, (e)- Design 5, (f)- Design 6, (g)- Design 7,

3. Results and Discussion:

Figure 2 shows all seven designs displacement obtained due of surface stress induced in antigen- antibody when force is applied to the sample. A maximum displacement of 8.5194×10^{5} µm was obtained on the cantilever surface for 100N applied force. However seven designs have simulated in which Design 1 gives displacement of 4.4083×10^{-9}, Design 2 displacement of 1.1514×10^{-8}, Design 3.7029×10^{5} µm, design 8.5194×10^{5} µm, design 5 2.4244×10^{-3}µm, design 6 produced the displacement of 8.6669×10^{-8} µm and design 7 displacement of 1.0508×10^{-3}.

TABLE I. Dimensions of all the modeled designs

	WIDTH (μm)						
Models	D1	D2	D3	D4	D5	D6	D7
Cantilever beam	10	10	5	5	5	5	--
Sample Compartment	10	10	20	20	20	40	20
Fixed End	60	60	40	40	40	40	60
Piezoelectric Layer	-	-	-	-	20	20	20
DEPTH (μm)							
Cantilever beam	100	100	80	80	80	80	-
Sample Compartment	20	20	40	40	40	10	100
Fixed End	15	15	10	10	10	10	15
Piezoelectric Layer	-	-	-	-	15	40	100
HEIGHT (μm)							
Cantilever beam	2	2	1	1	1	1	-
Sample Compartment	2	2	2	2	2	0.5	1
Fixed End	20	20	5	5	5	5	10
Piezoelectric Layer	-	-	-	-	1	0.5	1
MATERIAL							
Cantilever beam	Si	Si	Si	Si	Poly-Si & Sio2	Si	-
Sample Compartment	Poly-Si	Au	Poly-Si	Au	Au	Au	Au
Fixed End	Al	Al	Al	Al	Al	Al	Al
Piezoelectric Layer	-	-	-	-	PZT-5A & Pt e	PZT-5A & Pt e	PZT-5A & Pt e

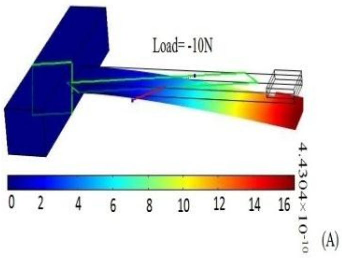


Fig.2(A). Displacement of the Design 1 cantilever model for load force of -10N and -100N applied on sample. Cantilever displacement of 4.4083×10^{-10} and 4.4083×10^{-9} was obtained

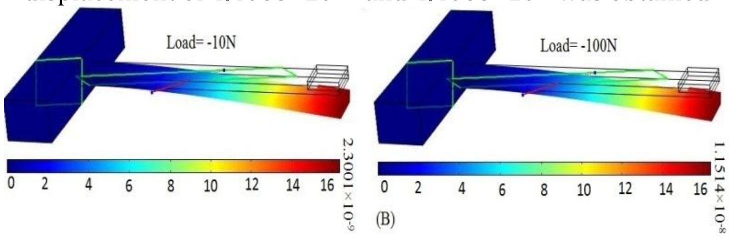


Fig.2(B). Displacement of the Design 2 cantilever model for load force of -10N and -100N applied on sample. Cantilever displacement of 2.3001×10^{-9} and 4.4083×10^{-8} was obtained.

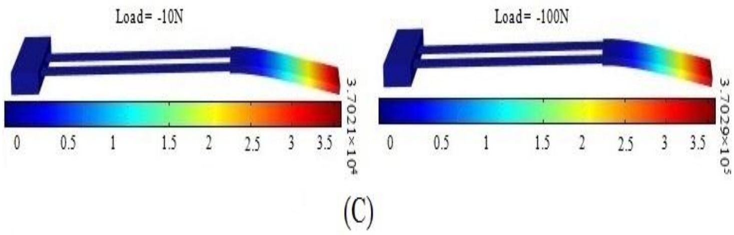


Fig.2(C). Displacement of the Design 3 cantilever model for load force of -10N and -100N applied on sample. Cantilever displacement of 3.7021×10^{4} and 3.7029×10^{5} was obtained.

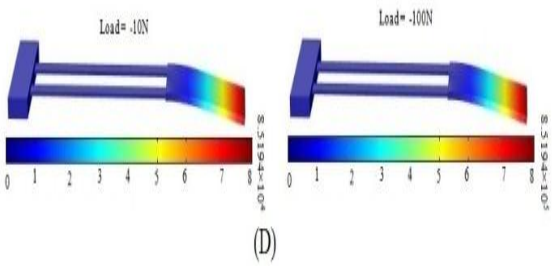


Fig.2(D). Displacement of the Design 4 cantilever model for load force of -10N and -100N applied on sample. Cantilever displacement of 8.5194×10^{4} and 8.5194×10^{5} was obtained.

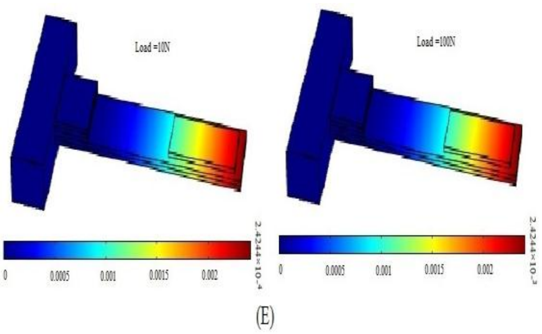
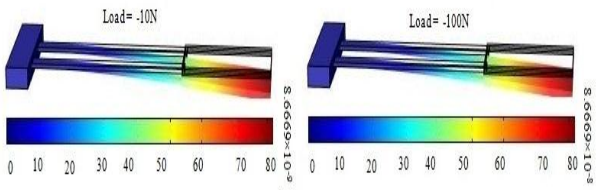
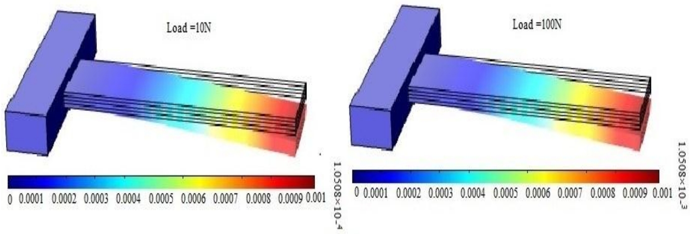


Fig.2(E). Displacement of the Design 5 cantilever model for load force of -10N and -100N applied on sample. Cantilever displacement of 2.4244×10^{-4} and 2.4244×10^{-3} was obtained.



(F)

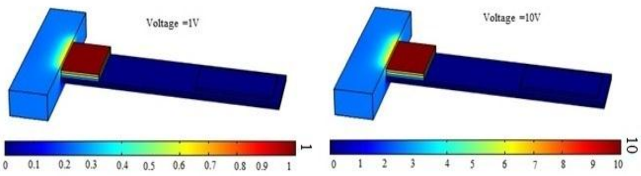
Fig.2(F). Displacement of the Design 6 cantilever model for load force of -10N and -100N applied on sample. Cantilever displacement of 8.6669×10^{-8} and 8.6669×10^{-8} was obtained.



(G)

Fig.2(G). Displacement of the Design 7 cantilever model for load force of -10N and -100N applied on sample. Cantilever displacement of 1.0508×10^{-4} and 4.4083×10^{-3} was obtained.

Figure 3 shows the electric potential is applied between the parallel plates to design 5, 6 and 7 of 1v to 10v of which the same amount of electrostatic energy is stored in the cantilever



(A)

Fig.3(A). Design 5 electrostatic energy of 1V and 10V is stored when electric potential of 1V and 10V is applied to the electrical plates of the cantilever.

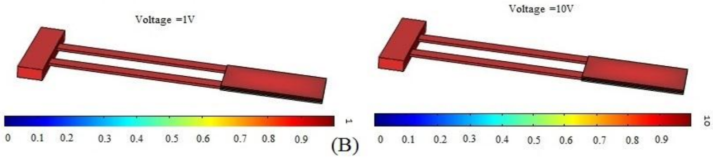


Fig.3(C). Design 6 electrostatic energy of 1V and 10V is stored when electric potential of 1V and 10V is applied to the electrical plates of the cantilever.

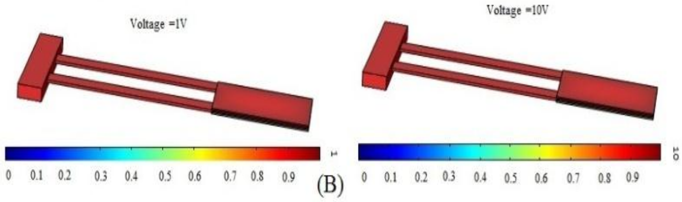
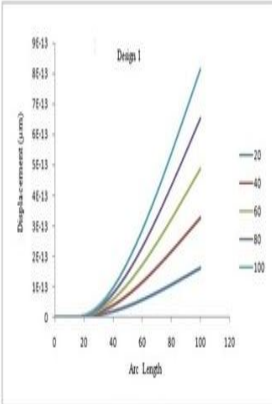
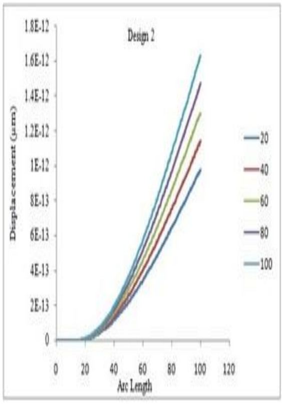


Fig.3(D). Design 7 electrostatic energy of 1V and 10V is stored when electric potential of 1V and 10V is applied to the electrical plates of the cantilever.

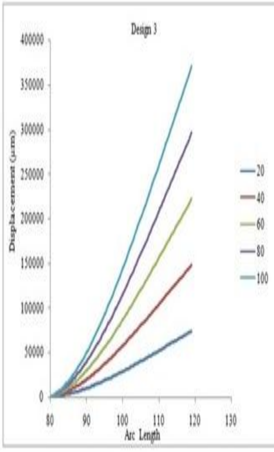
Figure 4 shows the solid mechanics model displacement when force of varying 10N-100N is applied on the cantilever sample compartment containing antibody. It was observed that the maximum deflection inside the cantilever when load force equivalent to the weight of antigen- antibody is applied. In all seven designs cutline in COMSOL Multiphysics® is taken over the entire cantilever to account for generated total displacement.



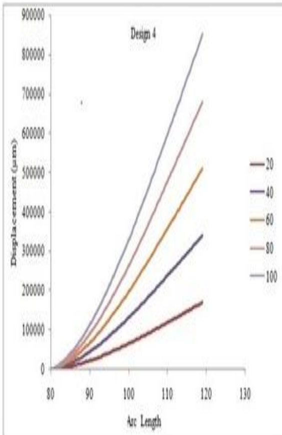
(A)



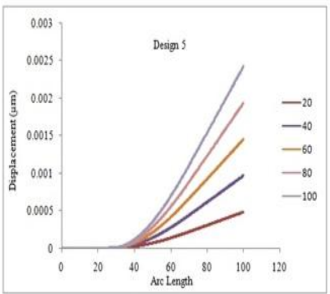
(B)



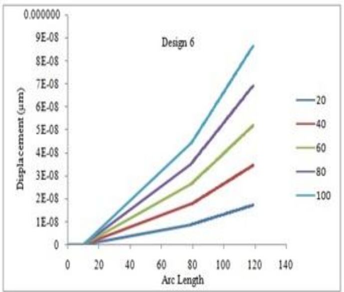
(C)



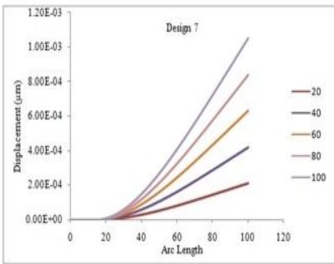
(D)



(E)



(F)



(G)

Fig.4. Variation of Displacement for change in load, , (A)- Design 1, (B)- Design 2, (C)- Design 3, (D)- Design 4, (E)- Design 5, (F)- Design 6, (G)- Design 7,

Figure 5 shows the voltage generated in design 5, 6 and 7 of varying load and electric potential. The cutline in COMSOL Multiphysics® simulation is taken over the entire PZT-5A piezoelectric to account for generated output voltage. The electrode platinum is used for measuring the generated voltage which is placed above and below the piezoelectric material.

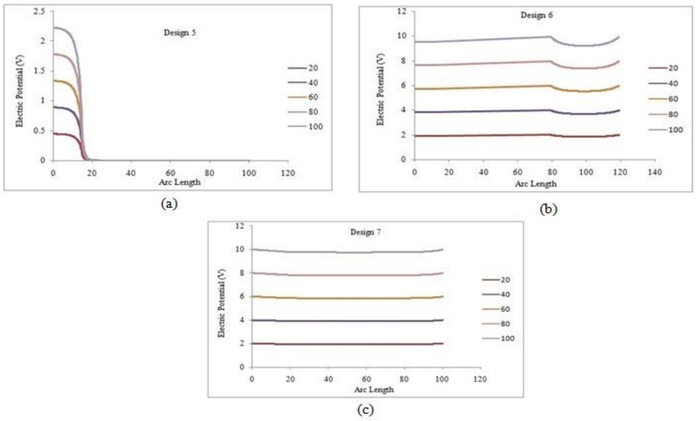


Fig.5. Variation of Voltage for change in load and electric potential, (A)- Design 5, (B)- Design 6, (C)- Design 7,

TABLE 3: Shows all seven designs displacement of the beam for various load force at constant width and thickness.

Load	Weight (kg)	Design1 Displacement(µm)	Design2 Displacement(µm)	Design3 Displacement(µm)	Design4 Displacement (µm)	Design5 Displacement(µm)	Design6 Displacement(µm)	Design7 Displacement(µm)
20	56.456×10^{-25}	8.8607×10^{-10}	2.3001×10^{-9}	3.7021×10^{4}	1.7039×10^{5}	4.8488×10^{-4}	1.7334×10^{-8}	2.1017×10^{-4}
40	11.291×10^{-24}	1.7633×10^{-9}	4.6002×10^{-9}	1.1109×10^{5}	3.4077×10^{5}	9.6977×10^{-4}	3.4667×10^{-8}	4.2034×10^{-4}
60	16.936×10^{-24}	2.6453×10^{-9}	6.9003×10^{-9}	1.8515×10^{5}	5.1123×10^{5}	1.4546×10^{-3}	5.2001×10^{-8}	6.3051×10^{-4}
80	22.582×10^{-24}	3.5266×10^{-9}	9.2004×10^{-9}	2.5923×10^{5}	6.8554×10^{5}	1.9395×10^{-3}	6.9335×10^{-8}	8.4068×10^{-4}
100	28.228×10^{-24}	4.4083×10^{-9}	1.1514×10^{-8}	3.7029×10^{5}	8.5194×10^{5}	2.4244×10^{-3}	8.6669×10^{-8}	1.0508×10^{-3}

4. Conclusion:

In this paper, the seven designs are modeled to know the best design that gives maximum displacement for detection of Tuberculosis viruses, in which Design 1 produced the displacement of 4.4083×10^{-9}, Design 2 produced the displacement of 1.1514×10^{-8}, Design 3 produced the displacement of 3.7029×10^{5} µm, design 4 produced the displacement of 8.5194×10^{5} µm, design 5 produced the displacement of 2.4244×10^{-3}µm, design 6 produced the displacement of 8.6669×10^{-8} µm, design 7 produced the displacement of 1.0508×10^{-3}. The maximum displacement of 8.5194×10^{5}µm was observed in design 4 for an input mass of 10 antigen-antibody interactions for the applied load force of 100N, it is considered be the optimized design.

This design is more sensitive and flexible, thus a highly sensitive and selective sensor based on cantilever is simulated using COMSOL Multiphysics® software.

Future Scope:

Further this design can be fabricated. It is seen that Design 4 is perfectly suitable for the fabrication. Once this design is fabricated using the dry etching or Plasma enhanced chemical vapour deposition. The displacement is measured by using Universal Testing Machine (UTM).

References

[1] Jayu Kalambe and Rajendra Patrikar, "Design, Fabrication, and Characterization of Electrostatically Actuated Microcantilever Sensor for Temperature Detection", IEEE SENSORS JOURNAL, VOL. 15, NO. 3, MARCH 2015.

[2] Srinivasa Rao K, Sateesh Jasti, "Design and Analysis of MEMS based Bio sensor for TB detection"978-1-5090-4697-3/16/$31.00 ©2016 IEEE.

[3] Nireekshith Yarraguntla, Hari Venkata Sai Ram Kalla, 3Sai Mounika Draksharapu, Syed.Shameem, "DETECTION OF HEPATITIS-B VIRUS IN SERUM USING MEMS BASED BIO-SENSOR", International Journal of Pure and Applied Mathematics Volume 115 No. 7 2017.

[4] M. Ahsan Saeed, Shahbaz M. Khan, Nisar Ahmed, M. Umair Khan, Azizur Rehman, "Design and Analysis of Capacitance based BioMEMS Cantilever Sensor for Tuberculosis Detection", 978-1-4673-87538/16/$31.00 ©2016 IEEE.