International Journal on Future Revolution in Computer Science & Communication Engineering
Volume: 4 Issue: 2
ISSN: 2454-4248
131 – 135

Design and Implementation of 3D MEMS Device for Reducing Pico Electric Field Thermal Effect on Nanoporation

Dr. Swarup Sarkar
Department of Electronics and communication Engineering
Sikkim Manipal Institute of Technology
Sikkim Manipal Uniersity,
Sikkim-737132
India
Email: swarup.s@smit.smu.edu.in

Abstract: Cell intra organelle nanoporation is a process that facilitates the introduction of ions into the intra organelle of cells by applying a series of short electric pulses which creates nano pores over the surface of cell. During this operation specific amount of heat is generated in and around the cell due to jule heating effect. The main aim of this research paper is to provide information regarding the design of 3D mems device for reducing thermal effect caused by the pico electric field on nanoporation. The proposed a three dimentional non uniform micro bio chip composed of bi metallic heterogeneous micro electrode under the influences of smart control FPGA based pico pulse generator is validated and applicable for reducing the thermal effect on nanoporation.

Keywords*: Picoseconds Pulsed Electric Field (psPEF), Bi metallic electrode, intrigrated bio Micro chip, nanoporation, thermal effect***.**

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I. INTRODUCTION

Nanoporation is a process to generate the holes over membrane having the diameter of nano meter range under the influences of external electric fiels.There are numbers of research are going on and it is revealed that pico electric field has tremendous effect on nanoporation [1]-[10]. It is shown that in the presences of external electric field initially the trans membrane potential(TMP) kept hold within the outer layer of membrane and when it is fully charged TMP shifted to the inner membrane due to the window effect[11].In other context the applied pico electric field remarkable effects on pore current [12],the surface tension[13] , aquatic pressure[14] and rest potential of the membrane[15]. As the electro chemical property of the membrane is changed so generic cycle of K+ and Na+ are changed. Due to this change current flow is changed which causes increase of thermal conduction and conevction. It is observed that the peak temperature rise ranges from 19 ^{0}C for a 1 ms time constant pulse to 70 ^{0}C for the 10 ms time constant pulse due to the joule effect [16]. Till date a large number of research is carried out and all research explores the thermal effect on pore formation and limited research evokes to find out the process or deuces for reduce this problems [16]-[20]. The main aim of this research paper is to provide information regarding the design of 3D mems device for reducing thermal effect caused by the pico electric field on nanoporation. The proposed a three dimentional non uniform micro bio chip composed of bi metallic heterogeneous micro electrode under the influences of smart control FPGA based pico pulse generator is validated and applicable for reducing the thermal effect on nanoporation.

II. THEORITICAL ANALYSIS

The theoretical analysis of nanoporation is reflected in different research papers and their key parameters are as follows [21]-[24].

A. *Trans membrane potential*

As per the numerical analysis of C.Yao the outer and inner membrane potential of a biological cell is

$$V_{org\,(o)}(t) = 1.5\,Rc\,E\,(t)\left[-e^{\frac{t}{\tau cell}} - 1(t-\tau) + et-\tau\tau cell.\ 1t-\tau\cos\theta\text{----------}\right] \quad (1)$$

$$V_{org\,(i)}(t) = \frac{1.5\,\tau cell\ Rnuc\ E\,(t)}{\tau cell - \tau nuc}\left[(e^{\frac{t}{\tau cell}} - e^{\frac{t}{\tau nuc}}) - (e^{\frac{t-\tau}{\tau cell}} - e\,t-\tau\tau nuc).1.(t-\tau)\cos\theta\right] \text{ ------- } (2)$$

B. *Effect of temperature of trans membrane potential*

$$V_{org\,(o)} = \left[\frac{\mathrm{KTd}}{4\pi\varepsilon_0\ \mathrm{kr}^2}\right]^{\frac{1}{2}}\text{----------} \quad (3)$$

Where K=boltz man constant, k=3, d= thickness of the membrane and r= radius of the cell. $T = temparature$ In Kelvin.

C. *Calculation of the radius of nanopores*

If n numbers of nano pores, then the rate of change of their radius of pore(r), can be determined by the following equations

$$U(r, Vn, Ap) = \frac{D}{KT}\left\{4\beta\left(\frac{r^*}{r}\right)^4\frac{1}{r} - 2\pi\gamma + 2\pi\sigma r + [\Delta\varphi]2Fmax1+rh/(r+ri)\text{----------}\right. \quad (4)$$

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Where D is the diffusion co efficient, K= boltz man constant, T=absolute temp, $\varphi(r,\theta)$ =intra organelle potential. $\gamma = surface\ tention.$

D. Calculation of the intra organelle surface tension

Due to the effect of electric field on the biological cell its molecular & chemical property as well as surface tension (Γin)

$$\Gamma in = \frac{2*\varepsilon n*\Delta\varphi}{hi} \text{---------- (5)}$$

Where hi is the thickness of inner membrane.

E. Calculation of the intra organelle pore density

The rate of creation of nanopores at intra organelle expressed by DeBruin KA, Krassowska W (1999a) and it is as follows

$$\frac{dN(t)}{dt} = \alpha * e^{\left(\Delta\varphi/Vep\right)^2}\left(1 - \frac{N(t)}{Neq\,(Vn)}\right) - - - - - - (6)$$

Where $N(t)$ is the pore density.

F. Calculation of the intra organelle ion uptake

The ion uptake can be calculated by following mathematical calculation

$$Iuptake = Kf[1 - \left(1 + Kp.te\left(1 + \frac{Kp.te}{2}\right)\right) * e^{-Kp.te}\ ] \text{----} \\ \text{-- (7)}$$

$$Where\ \ Kf = \frac{D.Sc}{Vc.d}\ , and\ \ Kp = e^{x}\ ,$$

$$x = \left[\frac{9.\Delta R.Vp.a^2\varepsilon 0(\varepsilon w - \varepsilon c)}{8.K.T.d^2}.* Vn^2\right]$$

D = Diffusion co efficient, Vc = Area of the pore,

d = thickness. Sc = N. π. r^2,

$$\Delta R.Vp = \pi.d\left(r1^2 - r^2\right), \text{----- (8)}$$

$T = T_{emp}$ in kelvin. K=Boltz man constant.

εw=permitivity of water, εc= permitivity of cytoplasm.

te= pulse duration.$r1$= radius of pore,r=radius of initial pores,$V_{org\,(i)}(t)$=intra organelle potential.

III. DESIGN OF CHIP

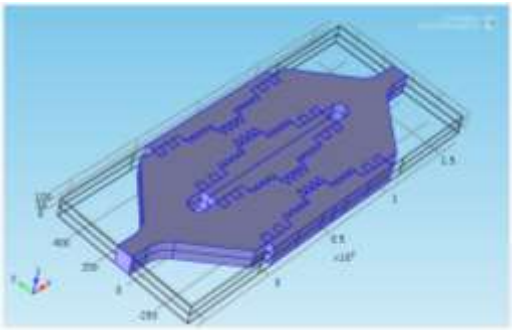

Fig 1: Design view MEMS chip

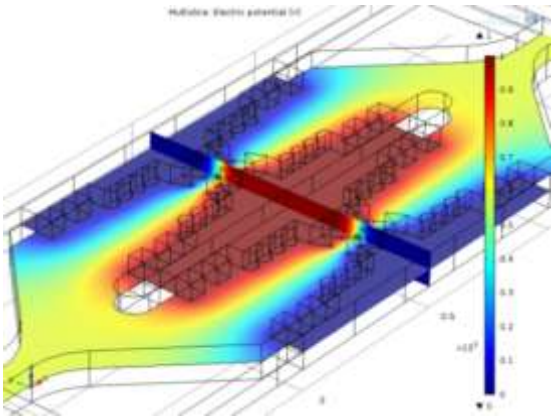

Fig 2: Internal Design at nanoporation within MEMS chip

To find out the dimension of micro devices it is necessary to calculate the DEP forces acting on the cells at different locations within the MEMS device and this force must be sufficient to overcome the drag force, which varies with the velocity and is therefore connected to the channel geometry. As per different study the DEP force=$F = 2 * \pi * r^3 * Re[k] * \nabla E^2$ where $Re[k]$ is the real part of polarized factor that is defined as$K = \frac{\epsilon p - \varepsilon m}{\epsilon p + 2\varepsilon m}$. $\varepsilon p\ and\ \varepsilon m$ In the proposed micro chip the presented the electrode arrangement was developed to maximize the electric field while minimizing the electrical dead volumes such that the DEP force is always sufficient to overcome Stokes' force and concentrate the cells at a relative low actuation voltage, and minimizing fluidic dead volumes [5]. To calculate the electric field in the combine non linear micro electrodes are analyzed using the COMSOL 4a software. In this context MEMS device is designed in such a way that the pulsed electric field is absorbed and dissipated mainly in the biological medium placed between the electrodes within which cells to be treated are flowed. To do so, impedance matching is necessary between the generator, the transmission line and the nanoporation biochip considering. So impedance Z should be matched to the impedance of psPEF generator to flow maximum energy that dissipated heat. Equation of impedances is $Z = \frac{d}{A(\delta + j\varepsilon 0\varepsilon r\omega)}$.where A is area and $\omega = 2\pi f$, $f = \frac{\delta}{2\pi\varepsilon 0\varepsilon r}$.If Z=100Ω and frequency = 330GHz.

In consideration with above facts the dimension of the MEMS device are as follows. The Length, Height & Width of the microchip are 2300 , 100, 900 μm respectvely.The inlet and outlet path are same i.e 10μm.Within the micro chip a non uniform sidewall having the mixed dimension micro-electrode is places which is made by bismuth and gold. The length, width and height of the micro electrode are 1000,900,100μm.as the electrode is hybrid in nature so inter electrode gap is non uniform throughout the whole micro channel. The inter electrode distances of central, medial and lateral part are 50,150,250μm respectively.The MEMS device contain microelectrode, micro channel and their combination. The micro channel is specified by Length, Width, Height and their dimension are 2300,250,100 μm.The entire Device s design in such a way that can avoid the jule's heating effect.

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Fig 1 shows the design view of proposed MEMS chip whereas Fig 2 explores the Internal Design at nanoporation within MEMS chip.

IV. FABRICATION

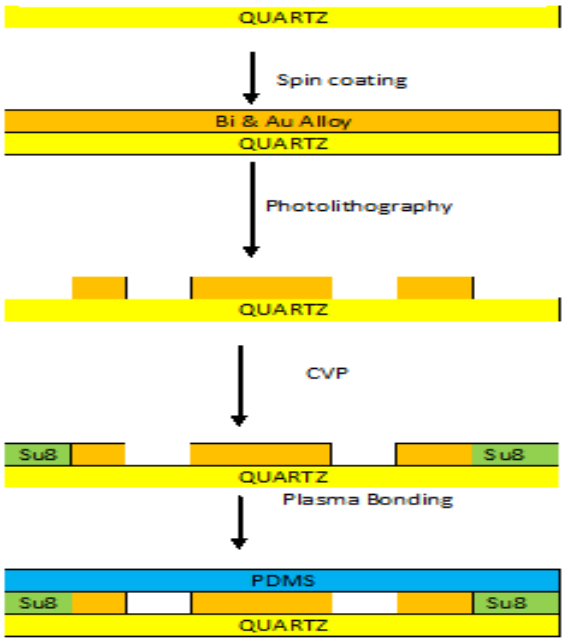

Fig 3: Fabrication steps of MEMS chip

The Fig 3 shows the fabrication steps of the MEMS device. Initially the quartz substrate is cleaned by di water and dry by nitrogen gas. An aluminium layer is formed over the quartz surface by spin coating at 3,000 rpm in 60 sec. Then the surface is cover with positive phato-resists (SU-8) by spin coating at 3500 rpm at 45 sec. Slides are placed in the oven at 95^0c for 1min for soft bake. In second step the structured is pattern on the slide and exposed in UV rays for 4 sec to make the desired window. Post bake done and immersed the slides in PGMF-26A solution for 5 min where phato-resists layers dissolved. And transfer the slides into the di water for cleaning. Then Sputtering is done twice for gold and bismuth deposition. Post bakes the slides with the help of oven. After that slides
are clean by isopropanol and dry with nitrogen gas. Next the PDMS slides dispenses over this slides and baked in oven at 70^0c or 30 min. Next the slides and PDMS block under oxygen plasma treatment at 300mToor for 45 sec. Aligned and bond the micro channel block at desired position into the slides and mixed the conductive epoxy at the ratio of 1:1.Finally bake the device at 60^0 for 15 min and whole MEMS device is ready for use.

V. ELECTRICAL CHARACTERIZATION OF CHIP

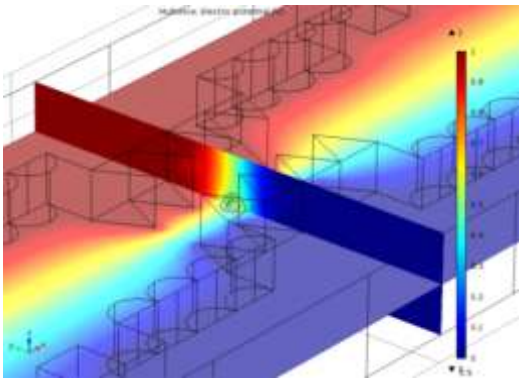

Fig 4: Electrical characterization of MEMS chip at nanoporation for reducing heating effect.

Fig 4 depicts The potential distribution and thermal dissipation within the MEMS device are shown in Fig 4 and the non uniform distribution of potential is shown .At pole $\theta = 90^{\circ}$ And $\theta = 270^{\circ}$ *the* maximum potential are exposed where the thermal effect is null. It explore that the centre part (300-600) μm of the chip holds the maximum uniform potential where the nano pores are generated at the intra organelle but thermal effect is minimum. At the same point the maximum velocity excreted at the centre of the chip, it affects the ion uptake of intra cellular unit of the rigid cell. All the information exposed in COMSOL simulation is as similar as numerical and it is validated by different experimental values.

VI. RESULT AND ANALYSIS

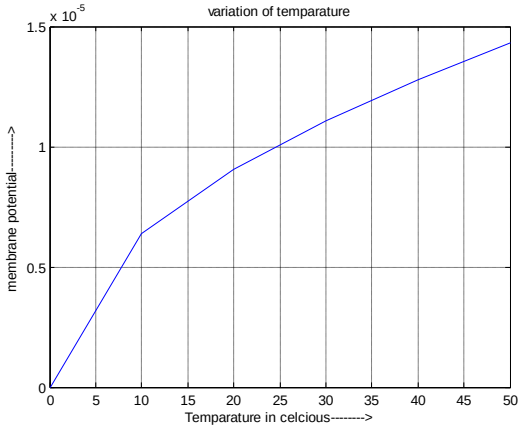

Fig 5: Variation of membrane potential with change in temperature.

The variation of membrane potential with change in temperature is shown in Fig 5.It is observed that the membrane potential is exponentially increased with increase with temperature because when the temperature is increased the kinetic energy of membrane molecule is changed due to their random brounier motion and K+ and Na + channel are so activated the heat is released. Membrane damage during nanoporation occur by three possible techniques i.e the temperature is high enough to cause phase change in the SC

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lipids, the temperature is high enough to cause phase change in the water such that the membrane is disrupted, or the thermal time exposure exceeds a threshold such that cell death in the membrane .

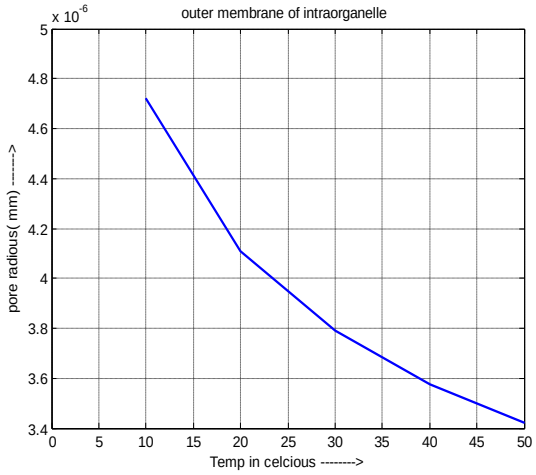

Fig 6: Variation of pore radius with change in temperature

The variation of pore radius with change in temperature is shown in Fig 6. It is observed that the pore radius is exponentially reduces with increase of temperature. Reason behind it is that the radius of the pore is inversely proportional with transmembrane potential. It is also shown that pore radius is gradually decreases as the angle of applied electric field is increase & maximum pore radius is obtain at an angle of $\theta = 90$ and $\theta = 270$ for inner membrane and $\theta = 100$ for outer membrane which is independent of pulse, electrode, micro channel and suspension media specification. After that it starts decrease but for both layers the radius of the nanopores inversely proportional with the amplitude of applied electric pulse. The author also finds out that the pore radius of outer membrane is greater than the radius of inner membrane of the organelle due to the higher elasticity of layers. It reflects the different molecular structure of different part of the pores.

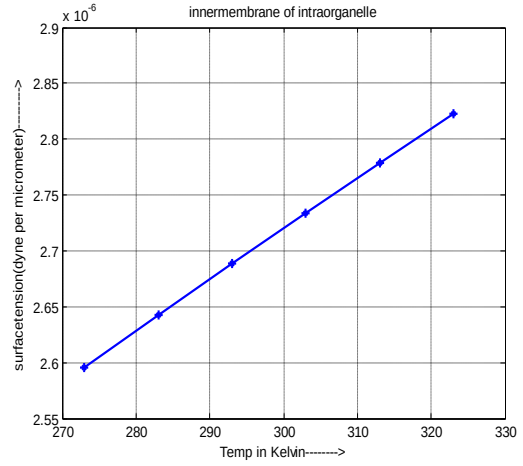

Fig 7: Variation of surface tension with change in temperature

The variation of pore density with change in temperature is shown in Fig 7.It is observed that the pore density is exponentially increased due to the random movement of membrane molecules and Kelvin pressure. This causes the internal expansion for temperature release.

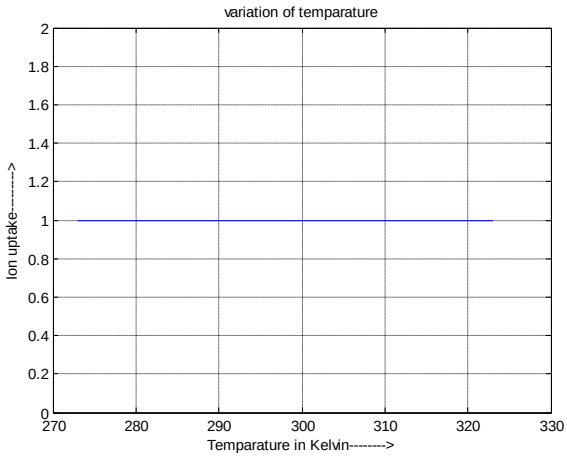

Fig 8: Variation of ion uptake with change in temperature

The status of ion uptake with change in temperature is found in Fig 8.It is observed that the ion uptake is constant for entire change in temperature although transmembrane potential, pore radius and pore density are changed. This is because of uniform temperature release within the device.

VII. CONCLUSION

The report shows that although the due to the change of temperature the membrane potential, pore radius ,pore density change but ion uptake is uniform or constant within our proposed devices that shows the independency of temperature of the device. The numerical and analytical model of multi layer 3D hybrid micro MEMS biochip under the influences of FPGA based pico electric field has been explored and unique multilayer structure able to eliminate the effect of temperature in nanoporation as a result the ion uptake is constant. The reported study encourage the specific micro chip multiple dimension micro fluidic channel with irregular bi metallic (Bi and Au) side wall electrodes that are designed to deliver a maximum of energy to the biological medium. The reported MEMS device aided by a quantitative understanding of the interactions between cells and an external electric field and it is more advantageous in context with small voltages and power consumptions, continuous flow, small sample volume, and eliminate the joule's heating effect.

In summary, the present data provide evidence that psPEF introduce the ions with specified microchip possibly through the nucleus mediated pathway without effect of temperature. The use of above mentioned device not only allows us to enter a new field of field-cell interactions, but it may open the door to a range of noninvasive therapeutic applications. Further studies are needed to elucidate the responses to psPEF in detail within the nano fluidic environment at GHz frequency.

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