

# Modeling of Nanoparticle-Mediated Electric Field Enhancement Inside Biological Cells Exposed to AC Electric Fields

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We present in this article the effect of alternating electric field at kilohertz (kHz) and megahertz (MHz) frequencies on the biological cells in presence and absence of nanoparticles. The induced electric field strength distribution in the region around cell membrane and nucleus envelope display different behavior at kHz and MHz frequencies. The attachment of gold nanoparticles (GNPs), especially gold nanowires around the surface of nucleus induce enhanced electric field strengths. The induced field strengths are dependent on the length of nanowire and create varying field regions when the length of nanowire is increased from 2 to 4  $\mu\text{m}$ . The varying nanowire length increased the induced field strengths inside nucleoplasm and region adjacent to the nucleus in the cytoplasm. We investigated a process of electrostatic disruption of nucleus membrane when the induced electric field strength across the nucleus exceeds its tensile strength.

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## 1. Introduction

The research on curing cancer via innovative approach of utilizing moderate intensity electric fields along with the chemotherapy has been an intensive focus of studies concurrently. The treatment of cancer by using a moderate intensity electric field (tumor treating field)—a few megavolts per meter can be classified as electrotherapy.<sup>1)</sup> The electrotherapy has advantage over chemotherapy due to the fact that this therapy is free from inducing infection to healthy cells and refrains from the side effects caused by the high dose of chemical drugs. Researchers have investigated the inhibition of the growth of cancer cells by applying moderate intensity, intermediate-frequency (100–300 kHz), alternating electric fields.<sup>2)</sup> They have proved experimentally and through finite element analysis that the tumor treating fields arrest the cell proliferation and their destruction while undergoing division. The reason is that the dividing cell creates a region of higher electric field between the dividing edge and the dielectrophoretic movement of the organelles and other polarized molecules contribute to the destruction of the cell.<sup>3)</sup>

Apart from movement of organelles and polarized molecules within the dividing cells leading to the death of cancerous cells, organelles in the non-dividing cells can be affected by imposing short pulsed high electric fields (typically tens or hundreds of thousand of volts per meter). The cell organs, for example, mitochondria or nucleus (may be both), Endoplasmic reticulum (ER) and Golgi complex functions can be hindered by applying pulsed electric fields.<sup>4–6)</sup> They have observed the mitochondria-dependent apoptosis of the cancerous cells due to electroporation of these organelles. Apoptosis is favored with respect to necrosis as the former devoid scar formation and inflammation reactions because the cell vanishes in a neat manner.<sup>7)</sup> It was observed that maximum value of electric potential induced on the organelles is more than three times larger than the maximum value of electric potential induced on the cell membrane by applying nanosecond pulsed high electric field. However, with longer pulses the cell plasma membrane appeared to be affected more than certain organelles membranes.<sup>8)</sup>

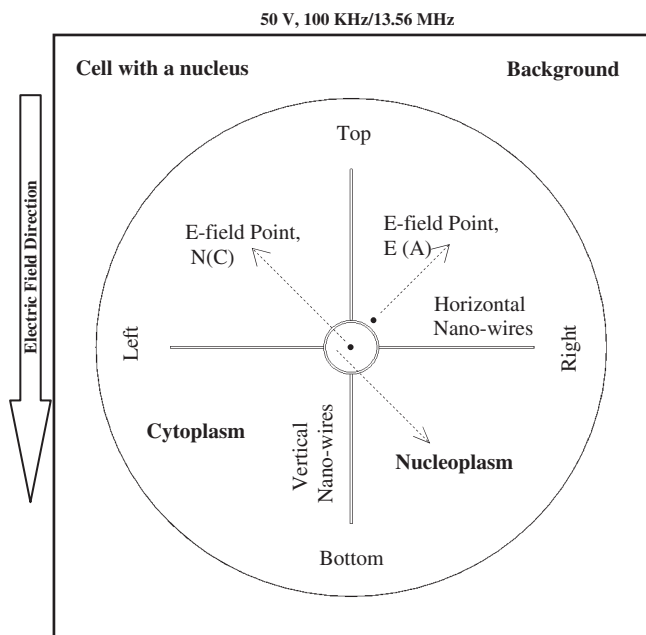
Besides the effect of pulsed electric fields on the biological cells, our simulation demonstrate and compares the effect of application of electric fields at intermediate frequencies, that is, tens of kilohertz to megahertz. We will discuss about this behavior in detail in §3. The intermediate-frequency electric field is desirable for the electrotherapeutic application as the stimulatory effect of the nerves and tissues diminishes at these frequencies.<sup>2)</sup> The other benefit of using intermediate frequencies in the medical applications is that the cell suffers minute dielectric loss and hence no tissue heating.

Insertion of GNPs inside the cytoplasm during the study of electric field-living cell interaction can lead to the investigation of many bio-electrical phenomena that can affect the growth of the cancerous cells. The GNPs are not harmful to the healthy cells, are biocompatible and have potential to enhance a number of biomedical applications, like, drug delivery to solid tumors, biodiagnostics, bio-imaging, etc.<sup>9)</sup> The GNP has affinity towards cancerous cell and can be attached to these cells by coating nanoparticles with anti-epidermal growth factor receptor (anti-EGFR).<sup>10)</sup>

Out of numerous types of GNPs such as shell, cube, etc.,<sup>11–13)</sup> nanowire<sup>14)</sup> find advantageous application in cancer treatment. Their shape and unprecedented characteristics can effectively conduct heat and light in a way that they can target cancerous cells and kill them in conjunction with externally applied electric field or radiations. Nanoparticles can be engineered to target cancerous cells and at the same time can be designed to interact with specific wavelengths of light or electric fields.<sup>15)</sup> Kim *et al.* have observed in their recent experimental investigation that the antibody-conjugated nanoparticles were absorbed and distributed in the middle of the cytoplasm, and in many cases they were located around the nucleus of a cancerous cell.<sup>16–19)</sup> Moreover, in addition to cancer treatment gold nanowires possess other healing effects to improve treatments for patients with severe impairments.<sup>20)</sup> Researchers have made a device from gold nanowires that can be used in prosthetics, to stimulate tissues and nerves in the human body, with less damage and better sensitivity and could help heart function and Parkinson's.<sup>21)</sup>

We investigate in this article the effect of gold nanowires of certain aspect ratios at intermediate-frequencies and

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**Fig. 1.** Schematic of the simulation model. Simulation domain of  $40 \times 40 \mu\text{m}^2$  in the Maxwell 2D finite element analyzer.

simulate the field strength inducement on internal organelles of biological cells exposed to electric fields. We present a plausible explanation for the mechanism of electrostatic disruption of biological cells triggered via gold nanowires and electric field interactions. In §2 we describe our simulation model. Section 3 explains the simulation results at intermediate frequencies, and finally we conclude our investigations in §4.

## 2. Simulation Model

We consider a biological cell of  $10\text{-}\mu\text{m}$ -diameter with a  $7\text{ nm}$  cell membrane thickness including a nucleus of  $1\text{-}\mu\text{m}$ -diameter having a  $40\text{ nm}$  wide nucleus envelope. The nucleus envelope is surrounded by four nanowires at top, bottom, left and right directions (i.e., horizontal and vertical nanowires). The schematic of simulation model is shown in Fig. 1. We observe the effect of external AC electric field by simulating these arrangements in a simulation domain of  $40 \times 40 \mu\text{m}^2$  in the Maxwell two-dimensional (2D) finite element analyzer. The minimum spatial grid size between the measurable electric field points is  $1\text{ nm}$ . Since the grid size we choose  $\sim 1\text{ nm}$ , the nanostructure resolution and the discontinuities in the electric field magnitude due to difference in the permittivity of the fluid and the membranes, nanowires, etc. can be easily observed. We input the value of simulation parameters, such as, permittivity and conductivity of the background region, cell membrane, cytoplasm, nucleus envelope, and nucleoplasm from the experimental and theoretical data available in the cited references.<sup>22,23</sup> The permittivity and conductivity of the gold nanowires are congruent to that of bulk gold material. Table I show the dielectric constant and conductance of the materials used in the simulation.

Electric field of moderate intensity say,  $E = 1.25 \times 10^6\text{ V/m}$  is applied from top to bottom in the simulation domain. We consider two points E (A), coordinates  $(0.3, 0.5)$  and N

**Table I.** Dielectric constant and conductance of the materials used in the simulation.

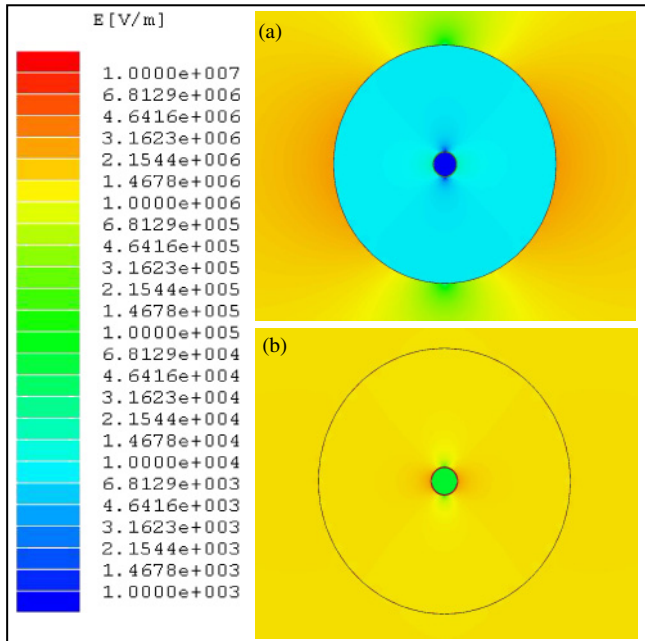
Material	Dielectric constant	Conductance (S/m)
Background	80	0.3
Cell membrane	3	$3.0 \times 10^{-7}$
Cytoplasm	80	0.3
Nucleus envelope	3	$3.0 \times 10^{-7}$
Nucleoplasm	80	0.3
Gold	1	$4.1 \times 10^7$

(C), coordinates  $(0,0)$ ; adjacent to the nucleus envelope in the cytoplasm and at the center of the nucleus in the nucleoplasm, respectively to observe the induced electric field strengths due to the nanowires. The induced electric field strengths are the peak electric field magnitudes and all the simulation data discussed in this article corresponds to these values. We designate suffix top, bottom, left and right to the name of the cell constituents whenever we compare the field strengths among them, like, cell membrane top and nucleus top and so forth. For example, the cell membrane top or nucleus membrane top refers to a point at the center of the cell membrane or nucleus envelope thickness.

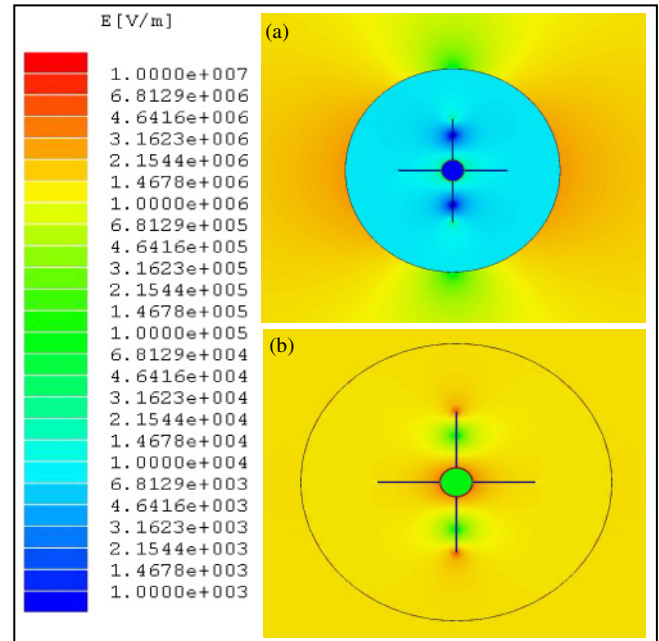
## 3. Results and Discussion

At  $100\text{ kHz}$  cell membrane is affected more than nucleus membrane which is evident by looking at the colored regions representing the induced electric field strength in volt per meter as shown in Fig. 2(a). The induced electric field around the nucleus in absence of nanowire is inhomogeneous and the electric field variation at  $100\text{ kHz}$  frequency is maximum at the left and right side of cell membranes and minimum at the top and bottom of cell membranes. The induced electric field strength on the top of cell membrane is higher by a magnitude of  $6.7 \times 10^3$  as compared to electric field strength induced on the top of nucleus envelope. This observation is in agreement with the investigation done by Kirson *et al.*<sup>2)</sup> in which the cell membrane was affected at kHz. Their experimental and theoretical observation was without the presence of nanoparticles and was restricted to kHz frequency only.

In the case of application of electric field at  $13.56\text{ MHz}$  [cf. Fig. 2(b)], nucleus is affected more than the cell membrane. This is due to the penetration depth of electric field at various frequencies. Although the penetration depth is large at lower frequencies, the amount of energy that actually penetrates a conducting body of the size of human is small because of the shunting of the electric field. The penetration depth at radio-frequency, which is also the resonance frequency of a man; the amount of energy penetrates deep inside the nucleus.<sup>24)</sup> Moreover, the another reason could be that at low frequency, charged particles in the cytoplasm respond to the applied field polarizing/depolarizing the cell membrane fast enough to shield the field and preventing its penetration. As the frequency of applied field increases, however, the charged particles do not respond fast enough and polarize/depolarize fast enough. As a result the electric field is able to penetrate in the cytoplasm and reach internal organelles. The induced electric field



**Fig. 2.** (Color online) Cell with a nucleus in absence of nanowires subjected to external electric field of intensity,  $E = 1.25 \times 10^6$  V/m at (a) 100 kHz and (b) 13.56 MHz, respectively.

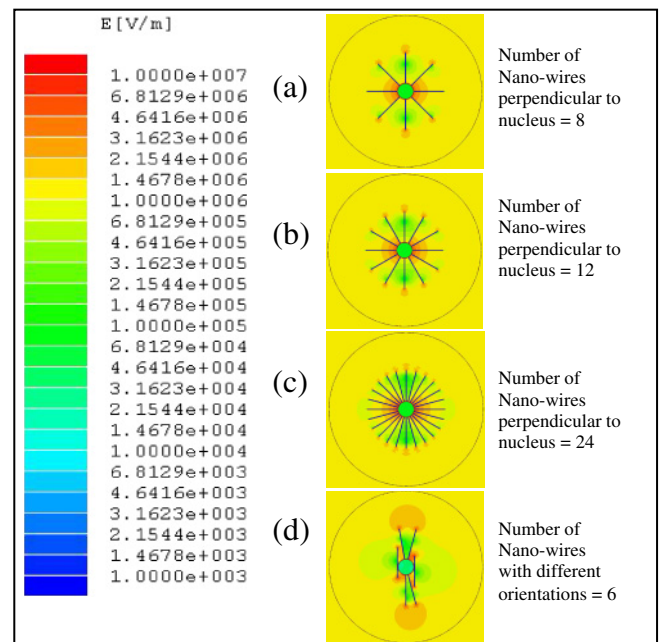


**Fig. 3.** (Color online) The nanowires (aspect ratio, AR = 40; length = 2  $\mu$ m, and breadth = 50 nm) embedded cell with a nucleus subjected to external electric field of intensity,  $E = 1.25 \times 10^6$  V/m at (a) 100 kHz and (b) 13.56 MHz, respectively.

variation at MHz around the nucleus is alike the electric field variation around the cell membrane at kHz. The induced electric field strength on the top of cell membrane is higher by a factor of 1.5 as compared to electric field strength induced on the top of nucleus envelope. We also observed that the induced electric field at the top of the cell membrane and at the top of the nucleus envelope is reduced by a factor of 359 and increased by a factor of 124, respectively; when we compare the induced electric field strengths between kHz and MHz frequencies.

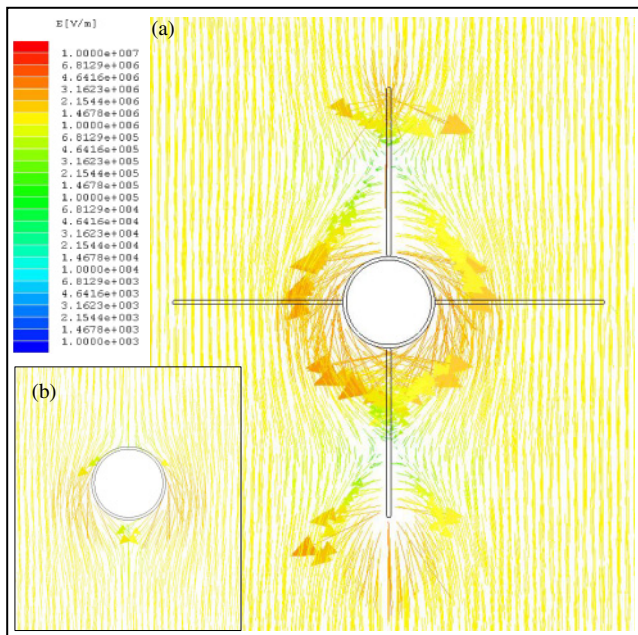
We discuss about the effect of electric field on a cell with a nucleus in which nucleus is surrounded by four gold nanowires. We consider nanowire as it induces homogenous electric field strengths around the nucleus compared to other GNPs of different shapes and sizes. We consider spherically capped gold nanowire despite rectangular one because it effectively conducts heat and light and show peak absorbance of the applied electric fields.<sup>25)</sup> Figure 3 shows the simulation result when the nanowire (aspect ratio, AR = 40; length = 2  $\mu$ m and diameter = 50 nm) embedded cell with a nucleus is subjected to external electric field of intensity,  $E = 1.25 \times 10^6$  V/m at (a) 100 kHz and (b) 13.56 MHz, respectively.

We simulated and compared in our investigations the effect of nanowires between kHz and MHz frequencies. Figures 3(a) and 3(b) show the influence of nanowires on the nucleus at these frequencies. The insertion of nanowires at radially vertical and horizontal direction outside the nucleus touching its surface enhance and homogenize the induced electric field across the nucleus at both frequencies. However, the induced electric field strength at MHz [cf. Fig. 3(a)]; increases manifold as compared to the 100 kHz case [cf. Fig. 3(b)]. It is quite possible that the nanowires can be attached to the nucleus with different orientations. Figure 4 shows the effect of different orientations of



**Fig. 4.** (Color online) The effect of different orientations of nanowires (AR = 40) exposed to moderate intensity electric field at 13.56 MHz. Induced electric field behavior for a number of nanowires perpendicular to nucleus equal to (a) 8, (b) 12, and (c) 24, respectively. (d), induced electric field behavior for a number of nanowires with different orientations at the nucleus equal to 6.

nanowires (AR = 40) exposed to moderate intensity electric field at 13.56 MHz. Figures 4(a)–4(c) show the induced electric field behavior for a number of nanowires perpendicular to nucleus equal to 8, 12, and 24, respectively. Figure 4(d) shows the induced electric field behavior for a number of nanowires with different orientations at the nucleus equal to 6. The induced electric field around the



**Fig. 5.** (Color online) The electric field lines density plot inside cytoplasm at MHz frequency in a situation when the nucleus is (a) surrounded by nanowires (AR = 40) and (b) in absence of nanowires.

nucleus is inhomogeneous for symmetric or asymmetric distribution of a number of nanowires. There is a possibility that inhomogeneity may cause the structural deformation of the nucleus. The simulation of nanowires present in the cytoplasmic region brings no significant effect and hence this is shown in the simulation results. We restricted our investigations for a simple geometry when nanowires surround nucleus at specific locations in order to understand the electric field strengths inducement behavior through combined effect of nanoparticles and electric field.

We observed from our simulation results that low electric field strength regions are created near the center of the vertical nanowires. This behavior can better be understood by investigating the electric field lines density plot. Figures 5(a) and 5(b) show the electric field lines density plot inside cytoplasm at MHz frequency in a situation when the nucleus is surrounded by nanowires and in absence of nanowires, respectively. The electric field causes the displacement of electrons leading to the accumulation of positive and negative charges at the ends (top and bottom) of the vertical nanowires. The accumulation of charges at the ends of the nanowires is due to the excitation of surface plasmon resonance. In particular, gold display very strong surface plasmon resonance effects.<sup>26)</sup> During surface plasmon resonance, the electrons along the surface of the metallic nanoparticles are excited by the energy from the external source and begin to oscillate. This oscillation leads to the development of separation of charges across the ends of the nanowires. The separation of charges over a distance of  $\approx 2.0 \mu\text{m}$  creates an additional source and sinks for the electric field lines. Therefore, we see a converging field lines near the top tip and emanating field lines near the bottom tip. The field lines distribution creates low dense field lines (shown by green colored lines) between the top and bottom tips of the nanowires. The colored field lines show the

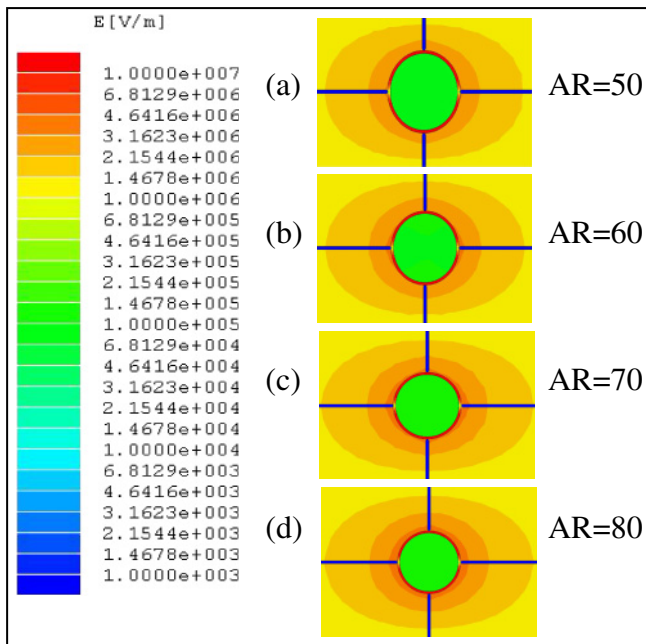
regions of high and low electric field strengths and can be compared while looking at the scale in this figure. While, the electric field lines distribution on the horizontal nanowires is uniform because of the separation of charges is over a very short distance  $\approx 0.05 \mu\text{m}$ . The dense field lines around the nucleus display a homogeneous and enhanced induced electric field strength affecting the nucleus. However, in absence of nanowires [cf. Fig. 5(b)], the electric field lines density is non-uniform (low at the top and high at the right side) and therefore, nucleus is not much affected as compared to the case with the presence of nanowires.

Observation of numerical values of the induced electric field strengths at points, E (A) and N (C) indicate that the induced electric field at MHz is 131 and 427 times higher than at kHz, respectively. Nucleoplasm significantly absorbs electric field strengths of the external source and it varies from a few kV/m to tens of kV/m as the frequency is increased from kHz to MHz regime. Similarly, the induced field strengths at E (A) vary from a few tens of kV/m to a few MV/m as the frequency is increased from kHz to MHz regime. The inducement of homogeneous electric field strengths of the order of  $\sim 1.73 \text{ MV/m}$  across the nucleus at MHz can significantly bring bio-electrical changes leading to the onset of apoptotic biological phenomena such as, electrostatic disruption of nucleus membrane, etc.<sup>27,28)</sup>

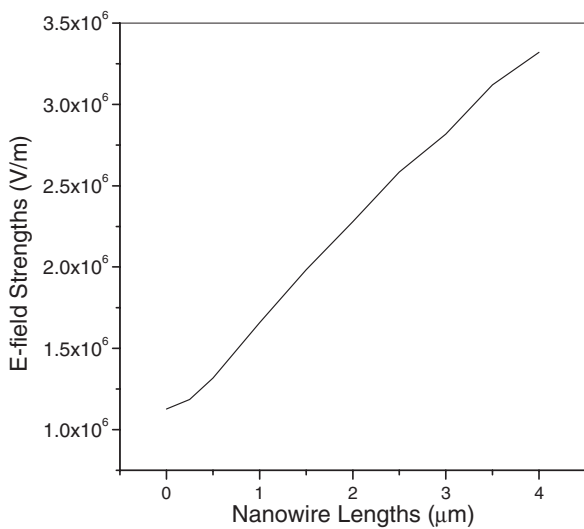
It would also be intriguing to observe the effect of varying nanowire lengths on the inducement of the electric field strengths across the nucleus in the cytoplasm and at the center of the nucleus in the nucleoplasm. For this purpose we focus closely on the nucleus to investigate the effect of varying lengths of nanowires exposed to moderate intensity electric field at 13.56 MHz. Figures 6(a)–6(d) show the induced electric field strengths due to nanowires of ARs 50, 60, 70, and 80, respectively (lengths = 2.5, 3.0, 3.5, and 4.0  $\mu\text{m}$ ; diameter of each nanowire = 50 nm). We restricted our simulation for the nanowire lengths up to 4  $\mu\text{m}$  as the free movement of longer lengths ( $>4 \mu\text{m}$ ) inside the cytoplasm may not be possible due to the small size of the intra-cellular cytoplasmic region.

Nanowires of lengths between 2 and 4  $\mu\text{m}$  can be chosen for the biomedical applications. Two distinct divisions of induced electric field strengths regions could be seen at nanowire of length 2  $\mu\text{m}$  (AR = 40). If longer nanowire lengths are taken, there is an increment in the onset of third electric field regions, and this region becomes clearly visible at the lengths of 3.5  $\mu\text{m}$  (AR = 70) and 4  $\mu\text{m}$  (AR = 80), respectively. Figure 7 shows the variation of induced electric field strengths due to varying lengths of nanowires at E (A), a point near the nucleus envelope in the cytoplasm. As the lengths of nanowires are increased from 0.25  $\mu\text{m}$  (AR = 5) to 4  $\mu\text{m}$  (AR = 80); the induced electric field strengths increased linearly from  $E = 1.19 \times 10^6$  to  $3.32 \times 10^6 \text{ V/m}$ , respectively, that is, the induced electric field strengths across the nucleus is nearly three times higher as compared to the case for a cell exposed to electric field at MHz without nanowires.

Moreover, comparison between Figs. 3 and 7 show that the electric field profiles are qualitatively different, that is, Fig. 3 shows non-monotonic electric fields along the vertical nanowires whereas Fig. 7 shows a monotonic profile. The reason is that the observation point E (A) is fixed and the

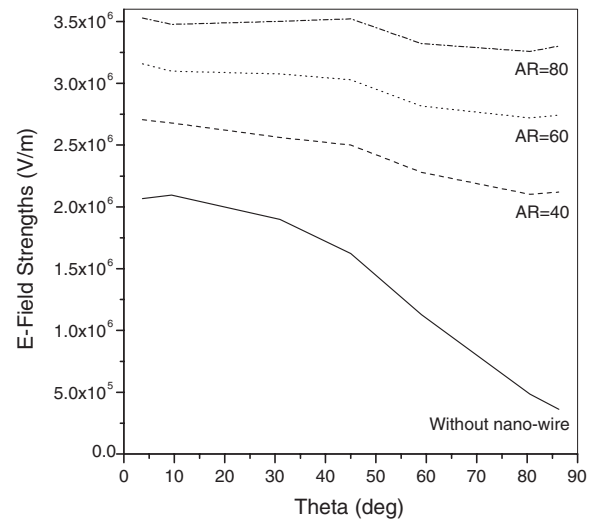


**Fig. 6.** (Color online) The effect of varying lengths of nanowires exposed to moderate intensity electric field at 13.56 MHz. Induced electric field strengths due to nanowires of ARs, (a) 50, (b) 60, (c) 70, and (d) 80, respectively.



**Fig. 7.** The variation of induced electric field strengths due to varying lengths of nanowires at E (A), a point near the nucleus envelope in the cytoplasm.

induced electric fields due to varying lengths of nanowires are observed. However, for a fixed nanowire aspect ratio, 40 for example; a non-monotonic electric field profile is observed by varying the observation point across the nucleus membrane. We also investigated about the variation of electric field strengths across the nucleus membrane, that is, a 2D plot with theta in the x-axis and electric field on the y-axis. We observed the variation of transmembrane electric field strengths across the nucleus membrane in the first quadrant when the theta of the field point in the y-direction is varied from 0 to 90°. Figure 8 shows the variation of electric field strengths across the nucleus membrane in absence and presence of nanowires. In absence of nanowires around the

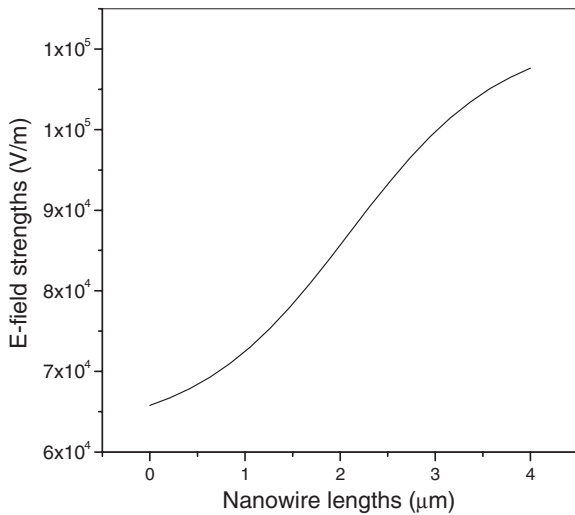


**Fig. 8.** The variation of transmembrane electric field strengths with respect to the theta of the field point across the nucleus membrane. Solid line in absence of nanowires; dash, dot, and dash-dot lines in presence of nanowires with varying aspect ratios, 40, 60, and 80, respectively.

nucleus, the electric field strength decreases as the theta is varied from 0 to 90°. There is a steep decrease in the electric field strengths across the nucleus membrane, which is due to non-homogenization of the induced electric field strengths around the nucleus. This behavior is depicted by solid line in Fig. 8. However, the induced electric field strength increases with the inclusion of nanowires with varying aspect ratios, such as, 40, 60, and 80; this variation is shown by dash, dot and dash-dot lines in Fig. 8. We do not observe a steep decrease in the electric field strengths across the nucleus, which is due to homogenization of the induced electric field strengths by the nanowires around the nucleus membrane. The observance and nonobservance of steep decrease in the induced electric field strength is also an indication of non-monotonic and monotonic electric field profile across the nucleus membrane.

Our results comply with the theoretical investigation of Kotnic *et al.*<sup>8)</sup> in which the electric potential induced on the internal organelles was nearly three times higher than on the cell when a cell without nanowire was exposed to a pulsed electric field gradient,  $E = 15 \times 10^6$  V/m. We inferred from our investigation that the application of nanowires yield the same result when nanowires embedded cell is exposed to a lower electric field strength— $E = 1.25 \times 10^6$  V/m at MHz which is 8.33% of the electric field intensity as taken in the study by Kotnic *et al.*<sup>8)</sup>

So far we have discussed about the electric field inducement in the cytoplasmic region, i.e., a region adjacent to the nucleus envelope, it is also worth observing the electric field inducement inside the nucleoplasm. Figure 9 shows the variation of induced electric field strengths due to varying lengths of nanowires at N (C), a point at the center of nucleus in the nucleoplasm. As the lengths of nanowires are increased from 0.25 μm (AR = 5) to 4 μm (AR = 80); the induced electric field strengths increased monotonically from  $E = 6.59 \times 10^4$  to  $1.08 \times 10^5$  V/m, respectively, that is, the induced electric field strengths inside the nucleus is nearly 1.6 times higher as compared to the case for a cell



**Fig. 9.** The variation of induced electric field strengths due to varying lengths of nanowires at N (C), a point at the center of nucleus in the nucleoplasm.

exposed to electric field at MHz without nanowires. This implies that the electric field strengths induced is 60% higher than that of case without nanowires. Also, the electric field strengths induced at E (A) is 195% higher than that of case without nanowires. And, the electric field strengths induced on the top of the cell membrane and nucleus envelope is 29 and 104% higher than that of case without nanowires, respectively. Kotnic *et al.*<sup>8)</sup> observed that the electric field inside the organelle membrane is >50% than in the cell membrane in absence of nanowires. The induced electric field strength inside the nucleus envelope in presence of nanowires in our observation is higher by a factor greater than two (~137% increase) as compared to the case without nanowires in the former theoretical investigations. Inferentially, the electric field strengths induced on the top of the nucleus envelope exceeded that induced on the top of the cell membrane; furthermore, the region adjacent to the nucleus envelope in the cytoplasm is affected more than any other cell constituents.

We would mention here the impetus of the induced electric field strengths on the nucleus that may lead to the disruption of nucleus envelope. This kind of disruption is due to the breaking of the membrane and is associated with the tensile strength of the membrane. The measured value of the tensile strength  $F_t$  of the outer membrane of Eukaryotic cell is not available.<sup>27)</sup> However, the tensile strength of the nucleus membrane may be considered alike that of Prokaryotic cells, namely, Gram-negative *Escherichia coli* and Gram-positive *Bacillus subtilis*, which is of the order of  $F_t = (3-5) \times 10^6 \text{ dyn/cm}^2$  and  $F_t \geq 2 \times 10^7 \text{ dyn/cm}^2$ , respectively. Mendis *et al.*<sup>27)</sup> have postulated a mathematical formula for a spherical sphere, wherein the applied voltage leads to a compressive electric force causing the rupture of the membrane when the outward electrostatic stress exceeds its tensile strength. The electric potential required to rupture a membrane of radius  $R$  ( $\mu\text{m}$ ) and its thickness  $\Delta$  ( $\mu\text{m}$ ,  $\ll r$ ,  $R$ ) with a hemispherical irregularity or radius  $r$  ( $\mu\text{m}$ ,  $r \ll R$ ) can be written as

$$|\phi(V)| \geq 0.2\sqrt{rR} \sqrt{\Delta/R} F_t^{1/2} \quad (1)$$

where  $F_t$  is the tensile strength of the membrane in  $\text{dyn/cm}^2$ . Also, for a spherical cell without spherical irregularity,  $r$  can be replaced by  $R$  in eq. (1); and the condition for rupture of the membrane can be deduced as

$$|\phi(V)| \geq 0.2\sqrt{R\Delta} F_t^{1/2}. \quad (2)$$

We discuss the applicability of eqs. (1) and (2) under different situation arising from our investigations. For the case when nucleus is surrounded by a number of nanowires, the induced electric field across the nucleus is inhomogeneous for symmetric or asymmetric distribution of a number of nanowires that may arise the possibility of structural deformation of nucleus membrane validating the application of eq. (1) in our analysis. Since structural deformation cannot be predicted from this simulation, thus we discuss for the situation considering the homogeneity of the cell under investigation with the application of eq. (2). In our investigations at MHz case, nucleus and its surrounding regions are affected significantly more than the cell membrane and the extra-cellular regions. Subsequently, there is a huge possibility that the nucleus envelope can be ruptured if we consider nucleus tensile strength as analogous to that of Gram-negative *E. coli*. Utilizing eq. (2) and substituting the value of tensile strength  $F_t = (3-5) \times 10^6 \text{ dyn/cm}^2$  for  $R = 1 \mu\text{m}$  and  $\Delta = 40 \text{ nm}$ ; the theoretical values of the electric field gradients come to be equal to  $1.73 \times 10^6$ ,  $2.0 \times 10^6$ , and  $2.23 \times 10^6 \text{ V/m}$ , respectively. This implies that if the induced electric field gradients on and around the nucleus envelope is higher than these values; the nucleus can easily be ruptured. In this scenario, the nanowire lengths greater than  $2.0 \mu\text{m}$  ( $AR = 40$ ) and up to  $4.0 \mu\text{m}$  ( $AR = 80$ ) could induce the electric field gradient greater than the above theoretically estimated values. Consequently, nanowires could potentially assist in rupturing of the nucleus envelope which may lead to the apoptosis of the cancerous cell.

On the other hand, if we consider nucleus tensile strength as analogous to that of Gram-positive *B. subtilis*, there is a less possibility that the nucleus can be ruptured. This is so because the tensile strength of *B. subtilis*  $F_t \geq 2 \times 10^7 \text{ dyn/cm}^2$  would require an electric field gradient  $\geq 4.47 \times 10^6 \text{ V/m}$  to rupture the nucleus envelope. Moreover, this electric field gradient is higher than the electric field gradient induced by even nanowire of length  $4 \mu\text{m}$  ( $AR = 80$ ), which is approximately equal to  $E = 3.32 \times 10^6 \text{ V/m}$ . At this stage the biological phenomenon that could begin is not predictable from this simulation. Hence, a thorough experimental investigation is required that may serve a new research topic for the experimentalists. Comparing to our approach of treating cancer cells, the electric field gradients (order of a few MV/m) induced by the nanowires across the nucleus may stimulate the process of apoptotic phenomenon via electrostatic disruption of nucleus envelope by exposing a cancerous cell to a moderate electric field at intermediate frequency.

#### 4. Conclusions

The application of tumor treating electric fields to kill cancerous cells has been proved to play a beneficial role in the biomedical areas. We investigated in this proposition the effect of alternating electric field at kilohertz and megahertz frequencies on the living cells. The nucleus is affected more

than the cell membrane at MHz frequency while opposite is observed at kHz frequency. In both the cases non-homogeneous electric field strengths are induced on the respective membranes. Enhanced electric field strength can be induced via application of nanoparticles which consequently leads to the killing of cancerous cells. We have investigated the application of nanowires of certain aspect ratios to find possible explanation of apoptosis of the cancerous cells by using moderate intensity electric field at intermediate frequency. The electric field strengths induced across the nucleus may arise the possibility of affecting nucleus membrane through its disruption which is in turn dependent on the tensile strength of the nucleus envelope. When the tensile strength of the nucleus membrane is considered analogous to that of Gram-negative bacteria, the induced electric field strength overcomes the electric potential estimated theoretically and hence, the nucleus envelope can be easily ruptured leading to the apoptosis of the cancerous cell. Conclusively, our finite element analysis through Maxwell simulation put forward an innovative scheme of cancer cell destruction by inducement of electric field strength on the cell organelles, that is, a mechanism for apoptosis of the cancerous cell. It would open a new path in the experimental studies of investigating nanowire-electric field-living cell interactions in the domain of biomedical engineering.

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