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Fateme Abdi

Citation: Chin. Phys. B, 2021, 30 (**3**): 038702. DOI: 10.1088/1674-1056/abd398
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Estimation of biophysical properties of cell exposed to electric field

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(Received 23 August 2020; revised manuscript received 4 October 2020; accepted manuscript online 28 October 2020)

Excitable media, such as cells, can be polarized and magnetized in the presence of an external electromagnetic field. In fact, distinct geometric deformation can be induced by the external electromagnetic field, and also the capacitance of the membrane of cell can be changed to pump the field energy. Furthermore, the distribution of ion concentration inside and outside the cell can also be greatly adjusted. Based on the theory of bio-electromagnetism, the distribution of field energy and intracellular and extracellular ion concentrations in a single shell cell can be estimated in the case with or without external electric field. Also, the dependence of shape of cell on the applied electronic field is calculated. From the viewpoint of physics, the involvement of external electric field will change the gradient distribution of field energy blocked by the membrane. And the intracellular and extracellular ion concentration show a certain difference in generating time-varying membrane potential in the presence of electric field. When a constant electric field is applied to the cell, distinct geometric deformation is induced, and the cell triggers a transition from prolate to spherical and then to oblate ellipsoid shape. It is found that the critical frequency in the applied electric field for triggering the distinct transition from prolate to oblate ellipsoid shape obtains smaller value when larger dielectric constant of the cell membrane and intracellular medium, and smaller conductivity for the intracellular medium are used. Furthermore, the effect of cell deformation is estimated by analyzing the capacitance per unit area, the density of field energy, and the change of ion concentration on one side of cell membrane. The intensity of external applied electric field is further increased to detect the change of ion concentration. And the biophysical effect in the cell is discussed. So the deformation effect of cells in electric field should be considered when regulating and preventing harm to normal neural activities occurs in a nervous system.

Keywords: neuron, field energy, membrane deformation, ion concentration

PACS: 87.19.ll, 94.30.Kq **DOI:** 10.1088/1674-1056/abc543

1. Introduction

Distinct non-thermal biological effect of electromagnetic field on a biological system is independent of the thermal phenomenon. For neurons in the nervous system exposed to external electromagnetic field, the deformation of geometry occurs in the elastic media. And the distribution density of intracellular and extracellular ions concentration will be changed, because with polarization effect of electric field, ions can be propagated along the channels embedded into the membrane. From the cellular level, the relation between cell deformation and membrane potential, gradient distribution for ion concentrations can be estimated.[1] In fact, the release and activation of physiological and biochemical functions of the cell are much dependent on the channel current and distribution of intracellular and extracellular ion concentration. The propagation of ions in the cell and pumping across the membrane channels will change the membrane potential. Thus, different firing modes can be changed or selected. Considering its distinctive biophysical property with controllability, the vesicles model is often used to calculate the nonlinear response in biological tissue and cells. From the viewpoint of physics, shape deformation will change the capacitance of the media driven by external electric field. And thus the density of ions in the cell will be greatly changed. That is, the deformation of the lipid membrane and the changes of the intracellular and extracellular ion concentration can modulate the membrane potential. And firing modes in neural activities can be selected to probe membrane properties and to detect pathological changes in cells.[2–4]

In the last decades, many theoretical neuron models[5–10] have been proposed to estimate and predict the dynamics in electrical activities in biological neurons. Based on these neuron models, bifurcation analysis can be applied to mode selection and furthering synchronization control. Noise is often imposed on the nonlinear systems, so it can be detected by changing the noise intensity when the nonliner resonance occurs. On the other hand, nonlinear circuits are built and tamed to reproduce similar quiescent, spiking, bursting and chaotic oscillations in the sampled time series for detectable variable such as output voltage. If so, a feasible neural circuit[11–14] is obtained and more neural circuits can be connected to implement a functional neural network. In fact, for a feasible neu-

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ron model, the biophysical effect should be considered due completely to its complex anatomic structure and functional connection to astrocyte.[15–18] The occurrence of multiple and mixed modes[19–21] in neural activities results from the nonlinearity and high correlation between biophysical variables, therefore, electronic activities can be controlled to switch between different firing modes. A realistic biological neuron and smart neural circuit can perceive external stimuli in an intelligent way. In Refs. [22,23], a phototube is incorporated into the simple FHN neural circuit and its ability to encode external optical signals is realized. Furthermore, the thermistor is coupled with the FHN neural circuit. And the improved neuron can explain the dependence of firing modes on temperature,[24] which has distinct influence on the channel current across the thermistor in a branch circuit. In Ref. [25], the electric field variable is introduced into the Hindmarsh–Rose neuron model, and then the dynamics effect of external field on the media[26] is estimated. As is well known, the energy[27–29] plays an important role in keeping and regulating the mode selection in neural activities. And then energy pumping is calculated between two coupled biophysical neurons.[30] For extensive guidance, readers can find suggestions and comments in Refs. [17,31,32] and the references therein.

In a generic way, the effect of external electromagnetic field on the neuron and excitable media can be estimated by applying equivalent induction current to the known neuron models. Some intrinsic parameters can describe the physical properties of the cell and neurons, *e.g.*, the capacitance of the elastic cell membrane. However, in a practical way, the cell shape will be changed in the presence of external electric field. Therefore, it is a challenge to calculate the changes of intracellular and extracellular ion concentration of cells, and further the fluctuation of membrane potential, energy release and pumping can be estimated when electric field is applied to the cell with different shapes. In the late 1950s, Schaw[33] began a series of studies of the influence of the electric field on biological cells, and proposed a simple spherical shell with given electric parameters. In the early 70s, Frieske and Mahning[34] and Helfrich[35] presented the elastic theory for lipid bilayers and estimated the effect of external field on phospholipid vesicle shape. In particular, the first experiment with phospholipid vesicle exposed to the electric field was verified in 1979, and it was found that the spherical vesicle changed into prolate vesicle.[36] Furthermore, electric fields[37] were used to investigate the deformation of a vesicle. It was found that the vesicle underwent a prolate-spherical-oblate shape change when the frequency of the applied field increased from 100 Hz to 100 MHz.[38] Extensive investigations have been carried out for estimating the cell deformation and mode selection in neural activities when alternating fields, pulsed, alternating current (AC) field and non-uniform field[39–44] were applied to the cells, respectively. Many theories about the mechanism of the cell deformation were proposed and explained, such as the small deformation theory combined with the Maxwell stress approach,[45] the minimization of the total free energy,[46,47] method of balancing the forces from electric, hydrodynamic, bending, and tension stresses exerted on the membrane,[48] the entropic and the enthalpic approach,[49] the two-dimensional boundary integral method.[50] These methods predicted the changes of the shape of vesicles with the frequency of applied electric field and the electrical parameter of vesicle medium. And most of these theoretical approaches and conclusions were consistent with the experimental results.

Except the confirmation of shape deformation of the cells induced by pressure from external electric field, the distinct pumping and propagation between the intracellular and extracellular ion concentration of the cell will have a great influence on the membrane potentials, which was clarified by the penetration theory of ions on the membrane, the theory of the ion cyclotron resonance of trans-membrane,[51] theoretical prediction for the effect of electromagnetic radiation ion concentration in cells.[52,53] A probability wave theory on the ion movement across cell membrane,[54,55] and the intercellular calcium oscillations synchronism modulated by ELF electromagnetic fields[56,57] were presented and discussed by the author of this paper. These previous researches are helpful to know the physical mechanism for propagation of ions driven by electric field. However, in these researches, seldom considered are the changes of ion concentration generated by the cell deformation. And the discussion about the field energy release in the cell is still kept open. Inspired by the previous researches finished by *Hirpyuki*,[37,45] we calculate the stored energy in cell membrane and investigate the propagation across cell membrane with appropriate geometric and dielectric parameters, meanwhile, we also estimate the critical frequency when the external electric field is used to generate distinct cell deformation.

2. Model and scheme

The biological cell contains a large number of calcium, potassium, sodium elements, with complex electromagnetic field formed inside and outside the cell. When the cell is exposed to external electric field, most of the ions are driven to change the spatial distribution density. And the membrane will be subjected to pressure when these ions are propagated across the membrane channels and pumped to the calcium pools. Therefore, with the field energy released, the shape of cell will be changed when ions are pumped out of the cell. That is, when the external electric field is imposed on the cell, the electromagnetic forces on all ions are converted into mechanic pressure on the membrane, which further triggers the cell shape change. The cell deformation is dependent on

the physical property of external electric field and the media. Therefore, the electric energy stored in the cell membrane and the ion concentration on both side of the deformed cell membrane, are modulated to change the membrane potential into the one with appropriate firing modes. Based on the electromagnetic field theory, the energy pumping and release, balance of ion concentration across the membrane, and changes of the membrane voltage are discussed in single shell cell with different shape parameters.

The biological cell handled with a single-shell cell model[58] is shown in Fig. 1. Due to complex interaction among ions, the biological cell in extracellular fluid will present a spherical shell shape covered by cell membrane, which separates the endoplasm from the extracellular fluid completely.

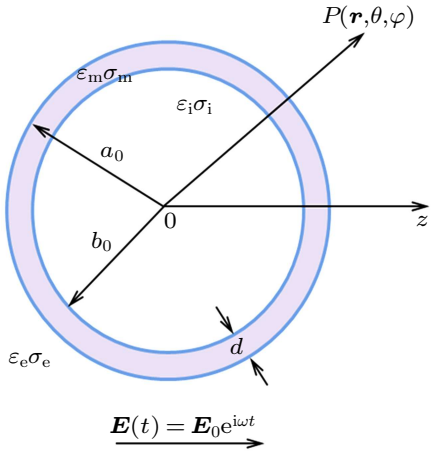


Fig. 1. A single shell cell model, where a_0 and b_0 represent outer and inner radius of cell membrane, respectively, d denotes thickness of cell membrane, ε_i and ε_e refer to dielectric constant of the inside medium and outside medium, and σ_i and σ_e are conductivity for the media, and σ_m and ε_m are conductivity and dielectric constant for the membrane.

All these parameters are set to be constants throughout the following discussion. In the spherical coordinate system $(\boldsymbol{r},\theta,\varphi)$, θ is the polar angle, $\boldsymbol{r}$ is the victor for the position, and φ is the azimuth angle. The external electric field applied to the cell along the z axis is described by $\boldsymbol{E}(t)=\boldsymbol{E}_0\exp(\mathrm{i}\omega t)$. The boundary condition is defined before handling the cell deformation and potential distribution for the cell. For simplicity, the membrane, the inner and outer areas of the cell membrane are respectively labeled with subscripts m, i, and e. And the electric potentials of the corresponding areas are denoted as Ψ_m, Ψ_i, and Ψ_e, and the operator[45] is defined as follows:

$$L_j \equiv \frac{1}{4\pi}\frac{\partial}{\partial t}\varepsilon_j + \sigma_j, \quad (j=\mathrm{i},\mathrm{m},\mathrm{e}). \tag{1}$$

According to the theory of biological electromagnetic field, the potential in the solving area satisfies the following criterion:

$$L_j\Delta\psi_j = 0, \quad (j=\mathrm{i},\mathrm{m},\mathrm{e}). \tag{2}$$

Supposing that there is no local charge in the medium, while the potential inside and outside the cell membrane are

$$\Delta\psi_\beta = 0, \quad (\beta=\mathrm{i},\mathrm{e}). \tag{3}$$

The physical condition requires

$$\begin{cases} E_e(t) = -E_0(t), & \text{at } r\to\infty, \\ \psi_e = \psi_m, \quad L_eE_{en} = L_mE_{mn}, & \text{at } r=r_a, \\ \psi_i = \psi_m, \; L_iE_{in} = L_mE_{mn}, & \text{at } r=r_b, \end{cases} \tag{4}$$

where r_a and r_b represent the locations of the outer and inner surface of the cell membrane respectively, E_{jn} $(j=\mathrm{i},\mathrm{m},\mathrm{e})$ denotes the normal component of the electric field $\boldsymbol{E}_j$ at the interface for the cell and medium. With the external field fixed in the z direction, the spatial distribution of potential is axisymmetric around the z axis.

As a consequence, the spatial distribution of electric potential $\psi_e(r,\theta)$, $\psi_i(r,\theta)$, and $\Delta\psi(\theta)$ in the outer spaces, the inter spaces and the transmembrane potential can be estimated from

$$\begin{cases} \psi_e(r,\theta) = \left[-E_0(t)r + A(t)\dfrac{a_0^3}{r^2}\right]\cos\theta, \\ \psi_i(r,\theta) = D(t)r\cos\theta, \\ \Delta\psi(\theta) = \psi_e(r_a,\theta) - \psi_i(r_b,\theta), \\ A(t) = E_0Ae^{\mathrm{i}\omega t}, \; D(t) = E_0De^{\mathrm{i}\omega t}. \end{cases} \tag{5}$$

In addition, the coefficients A and D are respectively approximated by

$$\begin{cases} \begin{bmatrix} A \\ D \end{bmatrix} = (\mathrm{i}fS+G)^{-1}\begin{bmatrix} -\dfrac{\mathrm{i}f}{4\pi}\varepsilon_e - \sigma_e \\ \dfrac{\mathrm{i}f}{4\pi}\left(\dfrac{\varepsilon_m}{\delta}-\varepsilon_e\right) + \dfrac{\sigma_m}{\delta} - \sigma_e \end{bmatrix}, \\ S = \dfrac{1}{4\pi}\begin{bmatrix} 2\varepsilon_e & \varepsilon_i \\ 2\varepsilon_e + \dfrac{\varepsilon_m}{\delta} & -\dfrac{\varepsilon_m}{\delta} \end{bmatrix}, \\ G = \begin{bmatrix} 2\sigma_e & \sigma_i \\ 2\sigma_e + \dfrac{\sigma_m}{\delta} & -\dfrac{\sigma_m}{\delta} \end{bmatrix}. \end{cases} \tag{6}$$

The electromagnetic forces generated by the applied field can induce the deformation in the cell shape. The outer and inner surface of the deformation in the cell membrane are expressed in polar coordinates as follows:

$$\begin{aligned} r_b(\theta) &\approx b_0[1+g_2\mathrm{p}_2(\cos\theta))], \\ r_a(\theta) &\approx a_0[1+g_2\mathrm{p}_2(\cos\theta)], \end{aligned} \tag{7}$$

where the function $\mathrm{p}_2(\cos\theta)$ dependent on polar angle θ is defined in Legendre polynomials type, and g_2 represents the coefficient. The elongation modulus k is defined by

$$k_{a,b} = \frac{r_{a,b}(\theta=0) - r_{a,b}(\theta=\pi/2)}{r_{a,b}(\theta=0)}, \tag{8}$$

where $r_{a,b}(\theta)$ is the measure of the position of outer surface $r_a(\theta)$ and inner surface $r_b(\theta)$ at a certain polar angle θ. When the applied field is weak and the shape deformation is slight,

$g_2 p_2(\cos\theta)$ shows a lower-order perturbation. Considering the homogeneous and uniform case, the dielectric constant of the membrane is independent of the frequency of external electric field. The relationship between the elongation modulus and the frequency of applied field is given by

$$k(f) = \frac{1}{1+\tau^2 f^2}\left[1 - \frac{f^2\tau^2}{R}\cdot\frac{2\varepsilon_i/\varepsilon_e - 1 - x^2}{(1+x/2)^2}\right]Rk_0. \quad (9)$$

Here, the constant k_0 is the elongation modulus at $f = 0$, and τ is the characteristic response time of the membrane to the external electric field. To further estimate the deformation effect induced by static/constant electric field, standard scale transformation is applied. And κ is defined as the elastic modulus of curvature on the surface of cell membrane. These intrinsic parameters are updated as follows:

$$\begin{cases} x = \dfrac{\sigma_i}{\sigma_e}, \quad u = \dfrac{\sigma_m/\delta}{\sigma_e}, \\ \delta = \dfrac{a_0 - b_0}{a_0}, \quad k_0 = \dfrac{\varepsilon_e a_0^3 E_0^2}{1024\pi\kappa}, \\ \dfrac{1}{\tau} = \dfrac{4\pi\delta}{\varepsilon_m}\left(\dfrac{2\sigma_i\sigma_e}{2\sigma_e+\sigma_i} + \dfrac{\sigma_m}{\delta}\right), \\ R = \dfrac{x^2 + 2xu + \{1 + x^2 - 2\varepsilon_i/\varepsilon_e\}u^2}{(x+u+xu/2)^2}. \end{cases} \quad (10)$$

According to the definition of $k_{a,b}$ in Eqs. (8) and (9), the obtained frequency f_c under $k(f_c) = 0$ is the critical transformation frequency between the prolate and the oblate shape in the cell. The value of f_c is estimated from

$$f_c = \frac{1+x/2}{\tau}\sqrt{\frac{R}{2\varepsilon_i/\varepsilon_e - 1 - x^2}}. \quad (11)$$

A living cell often contains a large number of ions of several kinds, which can keep field energy. A generic capacitor is usually made of two conductors separated by vacuum or an insulating material, and it is normally used as a functional component because charges and field energy can be stored. In fact, the cell membrane can also be considered as a smart capacitor. And the field energy is pumped and released when the spatial distributions of ions are changed. In a local area with a finite size, the endomembrane and outer membrane can be approximated as a parallel-plate capacitor with a certain spacing (*e.g.*, the membrane thickness) in between. For simplicity, the membrane thickness of the isolated shell cell is denoted as d_0 and the capacitance density C_0 in the absence of cell deformation, and then the field energy density W_0, which is the field energy per unit area of the cell membrane, can be obtained from

$$C_0 = \frac{\varepsilon_m}{d_0}, \quad W_0 = \frac{\varepsilon_m}{2d_0}(\Delta\psi_0)^2, \quad (12)$$

where $\Delta\psi_0$ is the transmembrane potential induced by an external field in the absence of cell deformation. When the deformation degree is enhanced, the membrane thickness $d(\theta)$ of cell is changed under different values of polar angle θ. As a result, the capacitance density and field energy density will be adjusted synchronously, and they are respectively calculated from

$$C_i = \frac{\varepsilon_m}{d(\theta)}, \quad W_i = \frac{\varepsilon_m}{2d(\theta)}(\Delta\psi)^2, \quad (13)$$

where $\Delta\psi$ is the transmembrane potential of the deformed cell. According to Eqs. (12) and (13), the changes and diversity for the capacitance density and field energy density can be calculated from

$$\delta C_m = C_i - C_0, \quad \delta W_m = W_i - W_0. \quad (14)$$

It is interesting to estimate the dependence of intracellular (or extracellular) ions concentration on the external applied electric field. Indeed, there is a resting membrane potential across the cell membrane in the absence of external field, which forms a potential barrier to balance the propagations of ions. According to the Nernst formula, the barrier height represented by the membrane potential is dependent on the ion concentration on the two sides of cell membrane. According to the Boltzmann's formula, the relation[51,58] between the intracellular and extracellular ion concentration $[C_1]$ and $[C_2]$ of the cell can be approximately related by

$$[C_1] = [C_2]\exp\left(\frac{V_0}{\lambda V_T}\right), \quad (15)$$

where λ is the correction factor to describe the interaction between the applied voltage and the charged particle of the double lipid layer of the cell membrane, and V_T is the thermal motion energy of particles expressed in the form of voltage.

When the cell is exposed to the electric field, an additional potential ΔV is generated on the cell membrane. And the potential barrier is modulated from $v = V_0$ to $v = V_0 + \Delta V$. Also, the ion concentration $[C_1]$ on one side of the cell membrane is changed into $[C_{1n}]$ as shown below:

$$[C_{1n}] = [C_2]exp\left(\frac{v}{\zeta V_T}\right) = [C_2]\exp\left(\frac{V_0+\Delta V}{\lambda V_T}\right). \quad (16)$$

Therefore, the relative change rate of ions concentration on one side of the cell membrane driven by an external electric field is given by

$$\frac{[C_{1n}] - [C_1]}{[C_1]} = \exp\left(\frac{\Delta V}{\lambda V_T}\right) - 1. \quad (17)$$

When the applied electric field is triggered by a time-harmonic wave, and the across voltage or membrane potential is described in periodical-type $\Delta V = \Delta V_m \cos\omega t$. In the case of $\Delta V_m < V_0$, equation (17) is replaced by

$$\frac{[C_{1n}] - [C_1]}{[C_1]} \approx \frac{(\Delta V_m)^2}{4\lambda^2 V_T^2}, \quad (18)$$

where ΔV_m is the amplitude of the trans-membrane potential caused by the applied electric field.

3. Results and discussion

In this section, necessary numerical investigations are presented to find the dependence of biophysical properties on the external electric field and the electrical parameters of biocell. For possibly serving as contrast and reference, the typical values of the geometric parameters and medium parameters follow the setting criterion in Refs. [58,60], they being $a_0 = 10$ μm, $d = 5$ nm, $\varepsilon_m = 4.4 \times 10^{-11}$ F·m^{-1}, $\varepsilon_i = 6.4 \times 10^{-10}$ F·m^{-1}, $\varepsilon_e = 6.4 \times 10^{-10}$ F·m^{-1}, $\sigma_m = 3 \times 10^{-7}$ S·m^{-1}, $\sigma_i = 0.3$ S·m^{-1}, $\sigma_e = 1.2$ S·m^{-1}, and $\kappa = 5 \times 10^{-13}$ erg (1 erg = 10^{-7} J). Firstly, the effects of geometric parameters and intrinsic physical parameters on the cell deformation are investigated in detail by analyzing the dependence of the relative elongation modulus $k(f)/k_0$ on the frequency f in an applied electric field. According to Eqs. (8) and (9), the cell shape is spherical at $k/k_0 = 0$; while the cell shape is prolate (the semi-axis of the ellipsoid along the z direction is longer than along the x direction) at $k/k_0 > 0$; when $k/k_0 < 0$, the shape is the oblate.

The geometric parameters will be changed when the cell deformation occurs, in which the intrinsic physical parameters such as dielectric constant and conductivity have distinct influences on the gradient distribution of ion concentration and spatial potential. When the external electric fields with different frequencies are applied, the deformation of cell could be time-varying thus speeding up the ion propagation across the membrane channels. Due to the diversity of intrinsic parameters for the intracellular and extracellular media separated by the cell membrane, the cell will be deformed into different shapes. The dependence of the critical frequency on the electrical parameter of cell is shown in Fig. 2.

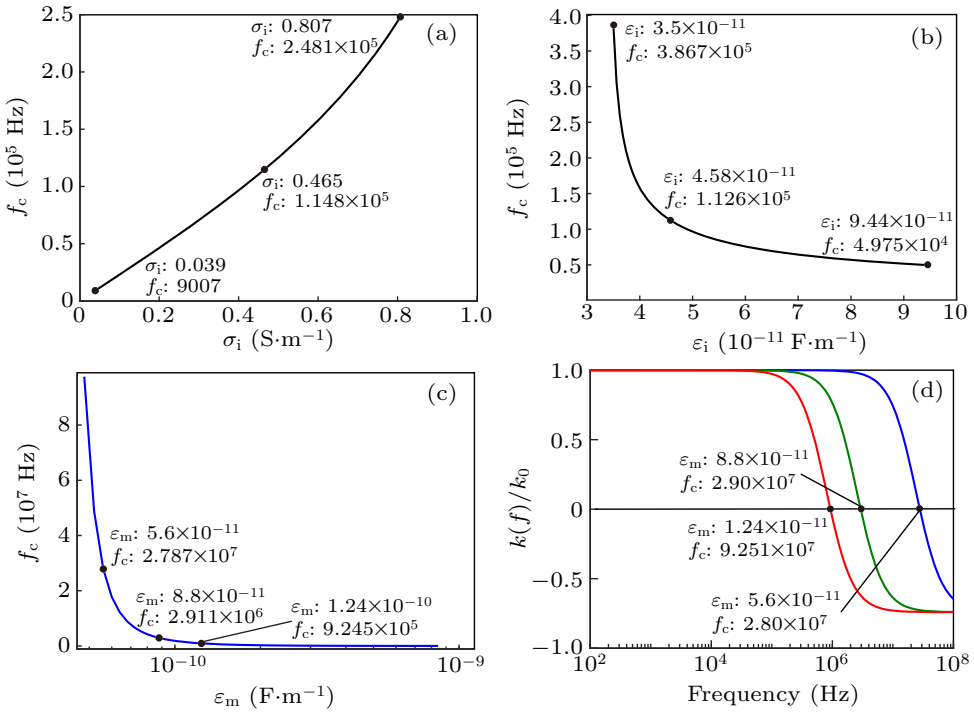


Fig. 2. Dependence of critical frequency f_c on (a) conductivity σ_i, (b) dielectric constant of the internal medium ε_i, and (c) cell membrane ε_m separately, and (d) dependence of relative elongation modulus $k(f)/k_0$ on frequency f of applied field, with $\theta = 0.5$, and other parameter values taking typical values.

In order to estimate the influence of cell parameters on cell deformation, figures 2(a)–2(c) show the relation curves between the critical frequency of the cell deformation and the cell parameters, and these parameters are in a certain range around the typical values of biological cell parameters, they being $\varepsilon_m = 4.0 \times 10^{-11}$ S·m^{-1}–4.2×10^{-9} F·m^{-1}, $\sigma_i = 0.039$ S·m^{-1}–0.807 S·m^{-1}, $\varepsilon_i = 3.5 \times 10^{-11}$ F·m^{-1}–9.4×10^{-11} F·m^{-1}. The results in Fig. 2(a) shows that the critical frequency of external electric field for inducting shape transition from prolate and oblate shape decreases when σ_i is selected to be a smaller value. Figures 2(b) and 2(c) display that the larger the value of parameters ε_i and ε_m are set to be, the lower the critical frequency of external electric field is and the more effectively the distinct shape transition will be triggered. The relationship between the critical frequency and the cell electrical parameters is nonlinear. Figures 2(a)–2(c) show that the critical frequency range is from 8.0×10^3 Hz to 10^8 Hz within the above ranges of the cell parameters values. Figure 2(d) shows the relation curves between cell relative deformation parameters and the frequency of external electric field for $\varepsilon_m = 1.24 \times 10^{-11}$ F·m^{-1}, 8.8×10^{-11} F·m^{-1}, and 5.6×10^{-10} F·m^{-1} respectively, and the frequency is in a range of 10^3 Hz–10^8 Hz. That is, the dielectric constant and conductivity parameter have different effects on the shape transition

of cell induced by external electric field. The dielectric constant ε is a complex quantity and defined by

$$\varepsilon = \varepsilon' + \frac{\mathrm{i}\sigma}{\omega_0}, \tag{19}$$

where ε', σ, and ω_0 are real permittivity, medium conductivity, angular frequency of electromagnetic wave, respectively. The real part of dielectric constant ε represents the permittivity, the imaginary part represents the loss, and the imaginary part is related to the conductivity. The larger the imaginary part, the greater the conductivity is and the worse the insulation performance. In the case of stronger conductivity, the higher frequency of applied electric field is effective in enhancing the polarization, and thus the shape deformation can be stabilized. On the other hand, the selection of a larger dielectric constant can enhance the intrinsic field of the cell and the lower frequency is required to keep the shape deformation of cell. The physical mechanism could be that higher conductivity can generate higher energy density ($0.5\sigma E^2$). And thus the external electric field needs high frequency to pump energy from the cell for triggering the distinct shape deformation of the cell. In addition, the electromagnetic stress is proportional to the dielectric constant. Therefore, a higher value for dielectric constant external electric with slow frequency will be more effective to stabilize the shape deformation.

In a practical way, a constant electric field is more available than a varying field. And complex electromagnetic induction can be induced in a medium when an electric field is applied with a high or an ultrahigh frequency. Therefore, to enhance the deformation effect, a smaller value for the conductivity parameter σ_i and higher value for the dielectric constants ε_i and ε_m can be selected. Thus lower frequency in the applied electric field can be used. Furthermore, it is interesting to estimate the relation of cell deformation with the frequency of external electric field in a quantitative way.

Under the first order approximation for elongation modulus k, the deformation variable of the inner or outer surface of the cell membrane is estimated from

$$\begin{cases} k \approx \dfrac{3g_2}{2+2g_2}, \\ \dfrac{\delta r}{a_0} \approx \dfrac{\delta r}{b_0} = \dfrac{2k}{3-2k}\mathrm{p}_2(\cos\theta). \end{cases} \tag{20}$$

The distribution of the $\delta r/a_0$ ($\delta r/b_0$) in the intersection line of the surface of the cell membrane with the *xoz* plane is given in Fig. 3.

Figure 3 shows that when the angle is in a range of $-55°$–$55°$ and $125°$–$234°$, $\delta r/a_0$ ($\delta r/b_0$) > 0, otherwise $\delta r/a_0$ ($\delta r/b_0$) < 0, the cell shape is prolate, where the applied electric field is triggered at a frequency of 3×10^3 Hz or 3×10^6 Hz. When the frequency increases to 3×10^7 Hz, the cell shape becomes oblate. The extensive calculation confirms that the deformation becomes more obvious when the frequency of applied electric field is selected to be a small value.

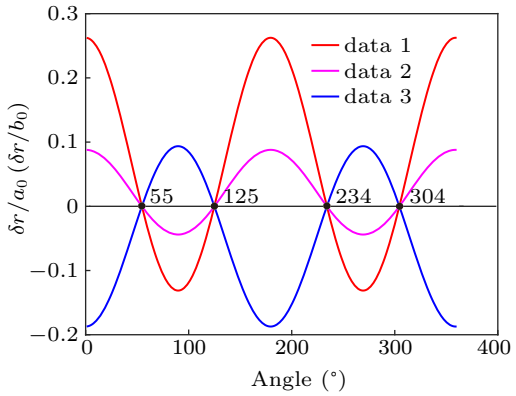


Fig. 3. Distribution of $\delta r/a_0$ ($\delta r/b_0$) in intersection line of surface of cell membrane with *xoz* plane. Frequency values of applied electric field are selected to be 3×10^3, 3×10^6, and 3×10^7 Hz (data 1, data 2, and data 3), respectively. And other parameter values take the typical values.

As mentioned above, the cell and media can keep and save field energy. The capacitance of the membrane can be changed when cell deformation occurs. Therefore, the energy in the cell will be pumped and changed because the field energy is dependent on the intrinsic parameters of the media and capacitance for the cell membrane. The distribution of the δC_m and δW_m in the intersection line of the surface of the cell membrane with the *xoz* plane are given in Figs. 4(a) and 4(b), respectively.

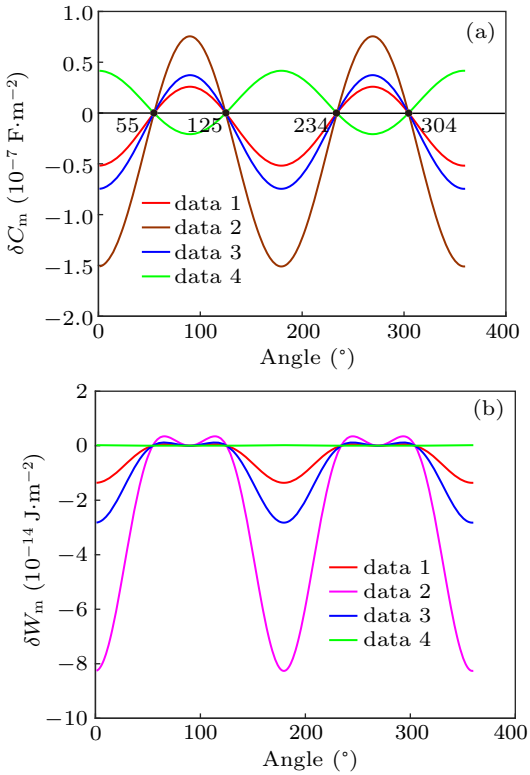


Fig. 4. Distributions of (a) δC_m and (b) δW_m on intersection line of cell membrane surface with *xoz* plane, with parameter values E_0, f, and a_0 being selected to be 50 V/m, 1.0×10^6 Hz, 10 μm for data1; 50 V/m, 1.0×10^6 Hz, 15 μm for data 2; 60 V/m, 1.0×10^6 Hz, 10 μm for data 3, and 50 V/m, 3.0×10^7 Hz, 10 μm for data 4, and other parameter values taking typical values.

Data 1 curves in Figs. 4(a) and 4(b) are the distributions of the $\delta C_{\rm m}$ and $\delta W_{\rm m}$ on the intersection line of the surface of the cell membrane with the *xoz* plane, where the parameter values E_0, ω, and a_0 are 50 V/m, 1.0×10^6 Hz and 10 μm, respectively. The cell radius a_0 in data 2 curve and the applied electric field intensity E_0 in data 3 curve are stronger than the value of data 1 curve in Fig. 4. As shown in Fig. 4, the absolute value $\delta C_{\rm m}$ and $\delta W_{\rm m}$ increase with the increase of the cell radius a_0 and the applied electric field intensity E_0. By comparing the curve data 1 with the curve data 4, it is also found that the frequency of the applied electric field affects values of $\delta C_{\rm m}$ and $\delta W_{\rm m}$, where $\delta C_{\rm m}$ and $\delta W_{\rm m}$ are the difference in capacitance per unit area and in electric field energy per unit area between the deformation cells and non-deformation cells. Figure 4 also shows that the difference is larger at about 0° (180°) and 90° (270°), which is parallel or vertical to the applied field direction. Compared with non-deformable cells, the deformable cells will cause $\delta C_{\rm m}$ and $\delta W_{\rm m}$ to greatly deviate within a certain area.

Indeed, the membrane potential depends on the distribution of extracellular and intracellular ion concentration. And shape deformation in the cell will change the ion concentration and the membrane potential as well. The relative variation of ion concentration is defined by

$$\frac{[\delta C]}{[C_1]} = \frac{[C'_{1n}]-[C_{1n}]}{[C_1]}, \tag{21}$$

where $[C'_{1n}]$ is the intracellular ion concentration with considering the deformation cell membrane, while $[C_{1n}]$ denotes the intracellular ion concentration without considering the cell deformation; $[C_1]$ represents the intracellular ion concentration of cell in the absence of the applied field; $[\delta C]/[C_1]$ is the ratio of the difference in the intracellular ion concentration of cell membrane between with and without deformation induced by external field to the ion concentration when no external electric field is applied, estimating their relative change. It is interesting to further investigate the effect of cell deformation on the physical properties and intracellular ion concentration from the numerical solutions. According to the static voltampere curve[51] measured from the nerve stem of cuttlefish, the parameter value is selected to be $\lambda V_{\rm T} = 5.2$ mV. To facilitate discussion, the values for two terms $\{[C'_{1n}]-[C_1]\}/[C_1]$ and $[\delta C]/[C_1]$ are estimated only on one side of the intersection line, which is formed by the cell membrane and the *xoz* plane. And the results are shown in Fig. 5.

The results in Fig. 5 confirm that the $\{[C'_{1n}]-[C_1]\}/[C_1]$ and $[\delta C]/[C_1]$ keep stable until the frequency of external electric field is beyond a certain frequency threshold about 5.1×10^5 Hz. And a significant change in ion concentration occurs in a frequency range from 10^5 Hz to 10^7 Hz. That is, the deformation effect can be enhanced greatly with the frequency of electric field increasing.

The intracellular fluid and the extracellular fluid in the cell membrane are both conductive media and electrolytes. The transmembrane potential enables the quiescent state to occur under polarization. When intracellular potassium ions are pumped out across the membrane channels, the depolarization is generated with the negative transmembrane potential increasing, *e.g.* from −70 mV to −50 mV. It was reported[1] that the distinct depolarization can be induced when the change of intracellular or extracellular charge density is about 1%. Furthermore, the action potential is generated to excite the excitatory cells after repolarization. It is also confirmed that the larger the cell radius and the higher the applied electric field intensity, the larger the value of $\{[C'_{1n}]-[C_1]\}/[C_1]$ and $[\delta C]/[C_1]$ will be.

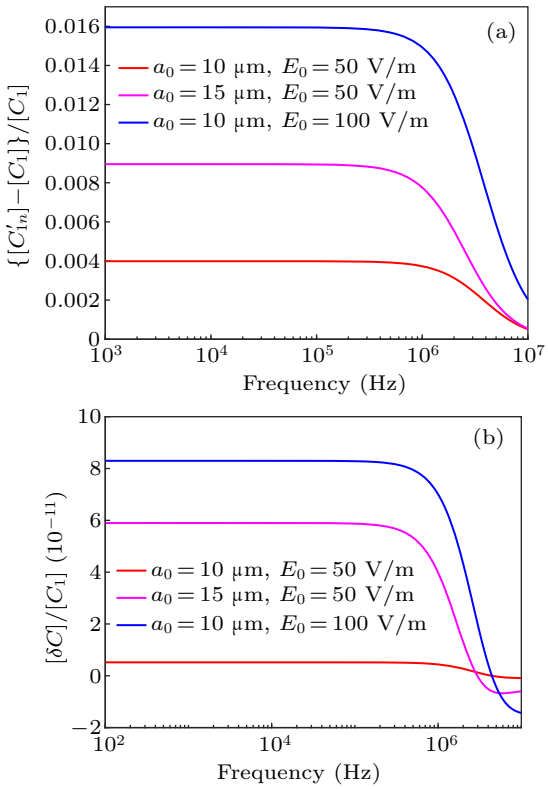


Fig. 5. Dependence of relative change $\{[C'_{1n}]-[C_1]\}/[C_1]$ and relative variation $[\delta C]/[C_1]$ on frequency of applied field, where arameters are appropriately selected at $\theta = 0.5$, and other parameter values take the typical values: $a_0 = 10$ μm and $E_0 = 50$ V/m for data 1; $a_0 = 15$ μm and $E_0 = 50$ V/m for data 2; $a_0 = 10$ μm and $E_0 = 100$ V/m for data 3.

From Fig. 6, it is found that $\{[C'_{1n}]-[C_1]\}/[C_1]$ is larger than 0.01 when the angle θ values are $-22^\circ < \theta < 22^\circ$ and $158^\circ < \theta < 201^\circ$ for data 2, $-29^\circ < \theta < 29^\circ$ and $150^\circ < \theta < 209^\circ$ for data 3. A larger value for the cell radius and/or intensity in the applied electric field will increase the change of ion concentration and more ions are pumped. Furthermore, the deformation effect reaches a milestone when the angle is fixed at 0 and π, and the change of ion concentration can be stabilized at a maximal value along the direction of external electric field. However, the change in relative ratio of ion concentration decreases when the angle is close to $\theta = 0.5\pi$ and 1.5π, and the change in ion concentration reaches the lowest

value along the direction perpendicular to the external electric field. For example, if the intensity of the applied electric field is $E_0 = 80$ V/m, the relative change ratio for ion concentration $\{[C'_{1n}] - [C_1]\}/[C_1]$ increases to a value larger than 0.01 (1%) when the angle θ values are $-29^\circ < \theta < 29^\circ$ and $150^\circ < \theta < 209^\circ$, while the $\{[C'_{1n}] - [C_1]\}/[C_1]$ obtains a smaller value along the direction perpendicular to the electric field. In this case, the effect of cell deformation becomes important for estimating the ion propagation and changes in membrane potential and firing patterns.

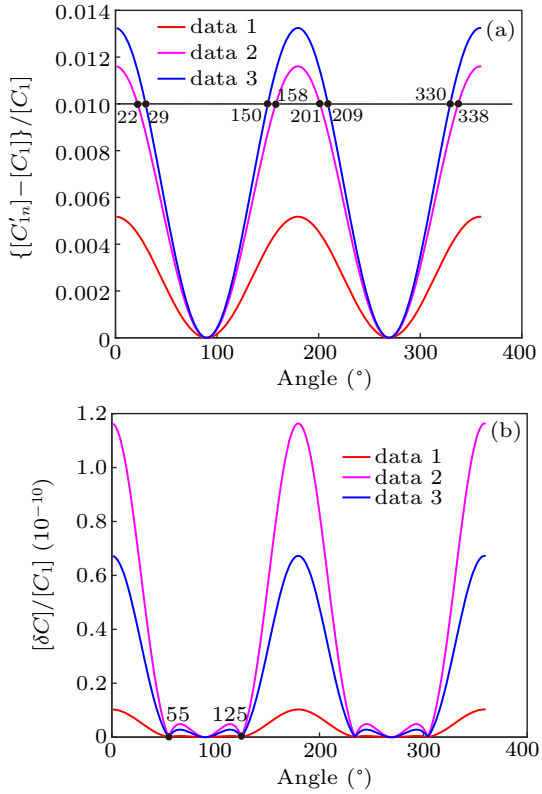


Fig. 6. Distribution for $\{[C'_{1n}] - [C_1]\}/[C_1]$ and $[\delta C]/[C_1]$ on intersection line, where $f = 10^6$ Hz, and $a_0 = 10$ μm, and $E_0 = 50$ V/m for data 1; $a_0 = 15$ μm and $E_0 = 50$ V/m for data 2; $a_0 = 10$ μm and $E_0 = 80$ V/m for data 3, and other parameter values take typical values.

In summary, the energy density in medium is dependent on the conductivity and inner electric field, while the electromagnetic stress mainly is proportional to the selected dielectric constant. To enhance the deformation effect, lower frequency in the external electric field is effective for generating a distinct deformation in the case of larger dielectric constant and lower conductivity of the cell. The larger the conductivity of medium, the larger the energy density will be, thus a low-frequency external field is required to suppress the energy distribution and then the deformation becomes achievable.

4. Conclusions

Based on the single-shell cell model and the theory of bio-electromagnetism, the boundary problem for spatial distribution of potential, and the physical factors for inducing the shape of cell to change under an external electric field, the changes of field energy and the ion concentration in the deformed cell membrane are calculated. It is found that the shape change of the cell is dependent on the geometric parameters, the intrinsic physical parameters of cell, the electric field intensity and the frequency of the applied electric field. Besides, the effect of cell shape deformation becomes distinct and can further shows biological significance when the cell is exposed to a high enough intensity electric field or expanded into large enough radius. In a practical way, the direction of external electric field can be adjusted to enhance the cell deformation effect and then ions pumping is enhanced to change the mode selection in neural activities.

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