Liquid crystal model of vesicle deformation in alternating electric fields

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Abstract Considering the effects of osmotic pressure, elastic bending, Maxwell pressure, surface tension, as well as flexo-electric and dielectric properties of phospholipid membrane, the shape equation for sphere vesicle in alternation (AC) electric field is derived based on the liquid crystal model by minimizing the free energy due to coupled mechanical and AC electrical fields. Besides the effect of elastic bending, the influence of osmotic pressure and surface tension on the frequency dependent behavior of vesicle membrane in AC electric field is also discussed. Our theoretical results for membrane deformation are consistent with corresponding experiments. The present model provides the possibility to further disclose the frequency-depended behavior of biological cells in the coupled AC electric and different mechanical fields. © 2013 The Chinese Society of Theoretical and Applied Mechanics. [doi:10.1063/2.1305410]

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Living cells including ourselves are chronically subjected to different intensity and frequencies of electromagnetic fields. Weak fields influence cell signaling, wound healing and cell growth.1 Strong fields can produce pores in cell membranes, which makes proteins, foreign genes, drugs, and antibodies deliverable into cells.2,3 In order to maintain their normal physiological functions, cell adjust continuously the properties (di-electric property, polarization property, electrical conductivity) of cell membrane reacting to surrounding micro-electrical fields.4 Explanation and the prediction of morphological evolution in vesicles under electrical fields are of special significant in cell biology.

By considering the elastic bending effects, osmotic pressure, Maxwell stress, surface tension, as well as flexo-electric and dielectric properties, a lipid membrane model is proposed by Gao et al.5 and the general governing shape equation is given as

$$\nabla \left( 2kH + kc_0 - e_{11} \int_0^d E_n \, dr \right) + f = 0, \quad (1a)$$

$$f = k(2H + c_0)(2H^2 - c_0H - 2k) + \Delta p - 2\lambda \nabla \cdot \mathbf{E} + H \int_0^d \left[ (\varepsilon_1 + \varepsilon_\perp) E^2_n + \varepsilon_\perp g_{uu} E^2_u + \varepsilon_\parallel g_{vv} E^2_v \right] \, dr + 2e_{11} k \int_0^d E_n \, dr + \varepsilon_1 \left( E^2_{in} - \frac{1}{2} E^2_{iv} \right) - \varepsilon_0 \left( E^2_{on} - \frac{1}{2} E^2_{ov} \right), \quad (1b)$$

in which $\varepsilon_\perp$, $\varepsilon_\parallel$ are the anisotropic dielectric constants perpendicular and parallel to the direction of the normal vector $\mathbf{n}$ of the membrane $\mathbf{Y}(\mathbf{u}, \mathbf{v})$, which satisfies $\nabla \cdot \mathbf{n} = -2H$, and $\nabla \times \mathbf{n} = 0$ with $H$ being the mean curvature. $k$ is elastic constant, $\kappa$ is the Gauss curvature, $c_0$ is the spontaneous curvature of membrane, $\varepsilon_{11}$ is the flexo-electric coefficient, $\Delta p$ is osmotic pressure, and $\lambda$ is surface tension. A local coordinate system which is mutually orthogonal is formed by a normal vector ($\mathbf{n}$) and two tangential vectors ($\mathbf{Y}_x$ and $\mathbf{Y}_u$) of the membrane; $E_u$, $E_v$, and $E_n$ are magnitudes of the electric field in the $\mathbf{n}$, $\mathbf{Y}_c$, and $\mathbf{Y}_u$ directions with $\mathbf{E}$ being the electric field intensity, $E_{in}$ is the normal component of the electric field on the inner surface and $E_{on}$ is the one on the outer surfaces, $g_{uu} = Y_{xu} \cdot Y_{xu}$, and $g_{uv} = Y_{xu} \cdot Y_{xv}$.

Based on this model, Gao et al.5,6 discussed the morphology evolution of sphere vessels in DC electric field. In fact, biological cells usually exist in alternation (AC) electric fields, and exhibit various frequency dependent behaviors, that is, orientation translation (dielectro-phoresis), and rotation. Since the 1950s, Schwan7 has conducted extensive studies on the behavior of biological cells in electric fields. In these early studies, cells were treated as rigid objects. From the competition between the work done by the Maxwell stresses, the shapes of vesicles in AC electric fields were determined theoretically by Winterhalter and Helfrich.8 Following Winterhalter and Helfrich, extensive studies on characterization of vesicle morphological types (prolate, oblate, and spherical) were performed by Dimova et al.9–11 in the parametric space of intra-to-extra-vesicular conductivity ratio and field frequency. The energy due to the electric field and the membrane bending energy are considered. They analyzed the vesicle deformation in three frequency regimes corresponding to low, intermediate, and high frequencies. However, since only bending energy of the vessel membrane is included, the contributions of surface tension and osmotic pressure to the vesicle deformation in AC electrical fields could not be considered.

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Actually, the transient vesicle deformation is determined by the coupling effects of mechanical and electric fields (Maxwell stresses, elastic bending, osmotic pressure, surface tension, flexoelectric and dielectric effects) exerted on the membrane. In order to see the influence of different mechanical and electric field parameters on the morphological transition of vesicles in AC field, based on the liquid vessel model proposed by Gao et al., the governing equations for vesicle morphologies in AC electric field is developed.

Figure 1 gives a diagrammatic sketch of a sphere vesicle in AC electric field. A spherical coordinate system is established, where \( \theta \) is the inclination angle, \( r \) represents the distance from the center of the vesicle, \( \varphi \) is the angle between the tangent to the contour and the \( \rho \) axis. The vesicle is filled interiorly with a solution characterized by conductivity \( \sigma_1 \) and dielectric constant \( \varepsilon_i \). The exterior solution has dielectric constant \( \varepsilon_o \) and conductivity \( \sigma_0 \).

With arc length coordinate \((s, \varphi)\) shown Fig. 1, the mean curvature and Gaussian curvature are given as

\[
\kappa = \frac{1}{R^2} = \frac{\sin \varphi}{\rho} \frac{d\varphi}{ds}, \\
H = \frac{1}{R} = -\frac{1}{2} \left( \frac{d\varphi}{ds} + \frac{\sin \varphi}{\rho} \right),
\]

(2a)

\[
\nabla^2 H = -\frac{1}{2} \frac{d^3\varphi}{ds^3} - \frac{\cos \varphi}{\rho^2} \frac{d^2\varphi}{ds^2} + \frac{\cos \varphi}{\rho} \frac{d\varphi}{ds} \frac{d^2\varphi}{ds^2} + \frac{\sin \varphi}{2\rho^2} \frac{d\varphi}{ds} + \frac{\sin \varphi \cos^2 \varphi}{2\rho^3},
\]

(3)

and the corresponding electric items are

\[
E_1 = \int_0^d E_n \, dr = 0,
\]

(11)

\[
U_2 = \varepsilon_m \int_0^d (E_n + g_{uu} E_u^2 + g_{ov} E_v^2) \, dr
= \frac{9E_0^2}{4} \int_0^d (z \cos \varphi + \rho \sin \varphi)^2 \, dr = \frac{9E_0^2}{4} \int_0^d \frac{z^2 \cos \varphi + (2z^2 - \rho^2) \cos \varphi}{3z^2 \rho \sin \varphi + (2z^2 - \rho^2) \cos \varphi} \, dr,
\]

(4)

\[
f_{i1} = \varepsilon_i \left( E_{in}^2 - \frac{1}{2} E_i^2 \right) = \frac{9}{4} \varepsilon_i E_0^2 z^2 AA^* \cos \varphi, \quad f_{o1} = \varepsilon_o \left( E_{on}^2 - \frac{1}{2} E_o^2 \right) = \frac{1}{4} \varepsilon_o (BB^* - CC^*). \]

(12)

Substituting Eqs. (8)–(10) into Eq. (1) leads to the electro-elastic shape equation of vesicle in AC electric field, that is

\[
2\nabla^2 H + (2H + c_0)(2H^2 - c_0 H - 2\kappa) + \frac{1}{\kappa} (\Delta p - 2\lambda H + HU_2 + f_{i1} - f_{o1}) = 0.
\]

(15)
Based on Eq. (15), we employ a numerical example to simulate the shape transition of vesicles in axisymmetric AC electric field from 500 to $2 \times 10^7$ Hz. In this situation, Eq. (15) is rewritten into a set of ordinary differential equations in the arc length coordinate as

\[
\dot{\varphi} = U, \\
U = \gamma, \\
\dot{\gamma} = F(\varphi, \rho, z, U; \gamma), \\
\dot{\rho} = \cos \varphi, \\
\dot{z} = -\sin \varphi,
\]

where

\[
F(\varphi, \rho, z, U; \gamma) = -\frac{2 \cos \varphi \dot{\varphi}}{\rho} - \frac{1}{2} \dot{\varphi}^3 + \left( \frac{1}{2} c_0^2 + \frac{\lambda}{k} + \frac{3 \cos^2 \varphi - 1}{2 \rho^2} \right) \dot{\varphi} + \frac{\sin \varphi}{2 \rho^2} \rho^2 (3 \dot{\varphi}^2 - 4c_0^2 + \varphi^2) - \frac{1}{k} (\Delta p + HU_2 + f_{11} - f_{01}) = 0.
\]

The boundary conditions for a half of the geometry are

\[
\varphi(0) = 0, \\
\varphi(s_1) = \pi, \\
U(0) = 0, \\
\gamma(0) = 0, \\
\rho(0) = 0, \\
\rho(s_1) = \pi, \\
z(0) = z_1,
\]

where $s_1$ is the arc length of the integration interval. Moreover, the volume of the vesicle $V_0$ is fixed where the volume constraint condition

\[
\int_0^{s_1} \pi \rho^2 \sin \varphi ds = V_0
\]

should also be satisfied. The parameters used to calculate our example are listed in Table 1.

The corresponding morphology transition of the vesicle along with the variation of the frequency is shown in Fig. 2. When intra-to-extra-vesicular conductivity ratio $\sigma_i/\sigma_o = 0.5$ (Fig. 2(a)), the vesicle is prolate shape for low frequencies and spherical shapes for the high frequency region, but the vesicles have oblate shapes for intermediate values between 5kHz and 5MHz. These results show an agreement with experimental observations of Aranda et al.\(^{12}\) When the intra-to-extra-vesicular conductivity ratio increased to $\sigma_i/\sigma_o = 4.64$ (Fig. 2(b)), compared to Fig. 2(a), the vesicle is still prolate when $\omega = 600$ kHz, which means that the critical frequency for prolate-oblate morphology transition will be increased along with the increase of intra-to-extra-vesicular conductivity ratio.

Different from Aranda et al.,\(^{12}\) except for elastic bending, other forces, such as osmotic pressure and surface tension, are also included in the present model. Figure 3(a) shows the morphological transition of a vesicle along with the variation of osmotic pressure $\Delta p$ when $\sigma_i/\sigma_o = 4.64$ at frequency $\omega = 600$ kHz. It is seen that when $\omega = 600$ kHz, the vesicle is prolate (dash dot line, $\Delta p = -5.6 \times 10^{-5}$ Pa). But along with the increasing of osmotic pressure values, the prolate-sphere-oblate morphological transition is observed. Figure 3(b) shows the morphological transition of a vesicle with varied osmotic pressure $\Delta p$ when $\sigma_i/\sigma_o = 0.5$ at frequency $\omega = 10$ MHz. Compared to Fig. 2(a), along with the increasing or decreasing of the osmotic pressure values, the vesicle shows sphere-prolate, or sphere-oblate morphological transition. The results given in Fig. 3 indicate that under small osmotic pressure, the vesicle morphology tends to be oblate. And along with the decrease of the frequency, vesicle morphology is more sensitive to the variation of the osmotic pressure.

Figure 4 shows the morphological transition of a vesicle with varied surface tension $\lambda$ when $\sigma_i/\sigma_o = 4.64$ at frequency $\omega = 15$ MHz. As shown in Fig. 2(b), the vesicle is sphere when $\omega = 15$ MHz. But along with the increase of the values of the surface tension,
The vesicle shows prolate-sphere-oblate morphological transition, which also indicates that small surface tension may cause the increase of the critical frequency for prolate-sphere transition.

Summarizing results above we can see that frequency dependent behavior of a vesicle, that is, orientation translation and rotation, is not only determined by the elastic bending of the vesicle membrane. Other mechanical forces, such as osmotic pressure and surface tension, also play an important role in the vesicle morphology transition. Since elastic bending, osmotic pressure, surface tension, Maxwell stress exerted on the vesicle and flexo-electric and dielectric properties of phospholipid vesicles in AC electric field are all considered in the present liquid crystal model, it provides the possibility to further understand the frequency dependent behavior of vesicles under different mechanical and electric fields.

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