

Electric Field Distribution during Electroporation Process in Presence of Nanoparticles

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In this paper, a numerical model to predict the electric field distribution due to nanoparticles close to the cell membrane during electrochemotherapy treatment is presented. The effect of a rectangular voltage pulse on the electric field distribution in a region of interest close to the nanoparticle is studied, considering nanoparticles made of several different materials. To solve the electromagnetic problem in transient conditions, Finite Element Analyses are performed. Specifically, both the rise and the constant period of the pulse are investigated in terms of field distribution. Moreover, different rise times are considered.

Index Terms—Finite Element analysis, electroporation, electric field, nanoparticles

I. INTRODUCTION

ELECTROPORATION is a cancer treatment used to improve cell membrane permeability to chemotherapy drugs. This therapy uses voltage pulse to generate locally an electric field able to rearrange temporarily the cell membrane and opening aqueous holes [1].

It is well known that electric field distribution depends on electric properties of materials [2], [3]. Some authors investigated the effect of nanomaterials in the area of pulse applications in order to evaluate their effect on electric field distribution. For the sake of an example, in [4] and in [5] an enhancement of electroporation is shown.

In this paper, the electric field distribution around the cell membrane in presence of nanoparticles close to the cell membrane, made of e.g. dielectric, magnetic or conductive materials, is investigated. In literature, to evaluate conduction current in the tissue, a conductive problem, or a sequence of conductive problems, is usually solved, as proposed in [6]. In recent years the time-varying problem is solved as, e.g., in [7]. Also in this contribution, results obtained with a transient problem are compared to those obtained with a constant direct current model, considering nanoparticles made of different materials, close to the cell membrane, as in [3]. Hence, an electromagnetic problem is solved in transient conditions focusing on the rise interval, highlighting the differences about the electric field distribution in a region of interest, ROI, close to the cell membrane, compared to the distribution obtained with a constant value of the voltage. Two different orientations of the nanoparticle and different values of rise time are analyzed to investigate the electric field distribution in the ROI.

II. THE FINITE ELEMENT MODEL

Fig. 1a shows the 2D geometry of a cell with cytosol and lipid membrane with a diameter of 20 μm and membrane thickness 7 nm. The cell is immersed in a 1x1 mm square domain representing extra cellular environment made of cell culture

medium. The square is energized by voltage pulses at two parallel sides like in [3] as represented in Fig. 1b.

Close to the cell membrane a single nanoparticle shaped as a rod sized 500 $\times$ 100 nm is positioned. The nanoparticle is drawn with a thin layer. This layer is a shell covering the nanoparticle core and it can be eventually made of a different material with respect to the core, e.g. magnetic nanoparticles have a silica shell. The applied voltage is a symmetric rectangular pulse 100 μs long, magnitude 50 V and a rise time from 1 to 10 μs . The electrical properties of materials used in the models are resumed in Table 1. The mesh has 222,052 triangular elements, and a detail is shown in Fig. 1c.

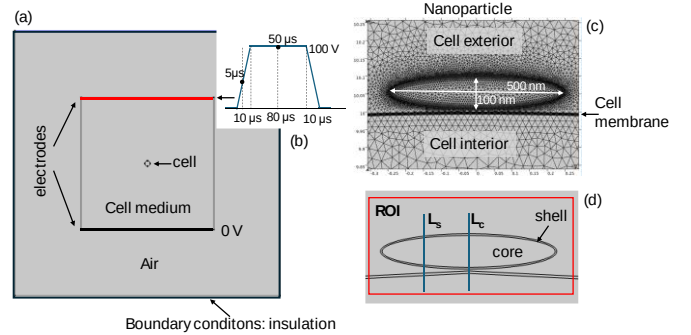


Fig 1: (a) geometry of the simulated model, (b) the applied pulse, (c) a detail of the mesh and (d) ROI and sampling lines.

A. Electric field problem

Given the geometry in Fig. 1, an electric field problem is solved on the proposed geometry by means of Finite Element Analysis (FEA). Because of the material properties (see Table I) and the time scale of the applied pulse, a dynamic formulation i.e. a diffusion problem, considering both conduction and displacement currents, is solved:

$$-\nabla \cdot (\sigma \nabla V) - \nabla \cdot \frac{\partial}{\partial t} (\epsilon \nabla V) = 0 \quad (1)$$

where V is the electric potential related to the electric field E :

$$\mathbf{E} = -\nabla V \quad (2)$$

σ is the electric conductivity and ϵ is the dielectric permittivity. Actually, equation (1) is ill-posed because there are many vector fields fulfilling the equation: in fact, the rotation of any regular vector $\mathbf{w}$ can be added to the argument of (1), leaving it unaltered. Hence, (1) is valid as long as a further condition is explicitly added i.e.

$$\nabla \times \mathbf{E} = 0 \quad (3)$$

with (1) subject to suitable boundary and initial conditions. Equations (1)-(3) are solved using Comsol Multiphysics AC/DC module (<https://www.comsol.com>, COMSOL AB, Stockholm, Sweden).

The electric field strength is sampled on the lines L_c and L_s in Fig. 1d inside the ROI marked with the red rectangle.

TABLE I
ELECTRIC PROPERTIES OF THE MATERIALS; [NU] = NOT UNIT

	Electrical conductivity σ [S m ⁻¹]	Relative permeability μ_r [NU]	Relative permittivity ϵ_r [NU]
Cytosol	0.13	1	60
Membrane	$5.3 \cdot 10^{-6}$	1	12.8
Culture medium	1.3	1	80
Au NP	$4.1 \cdot 10^7$	1	10
Silica NP	10^{-13}	1	3
Magnetic NP	10^{-6}	3.4	25

III. RESULTS

The results show a different distribution of the electric field in the ROI depending on the nanoparticles material. In particular, Figs. 2-4 show the electric field sampled along the line L_c in Fig. 1. These figures put in evidence the different behaviour of the electric field for three different types of nanoparticles: gold nanoparticle (conductive), magnetic nanoparticles and a magnetic nanoparticle covered with a silica, i.e. a dielectric layer. Three different time durations of the pulse are investigated.

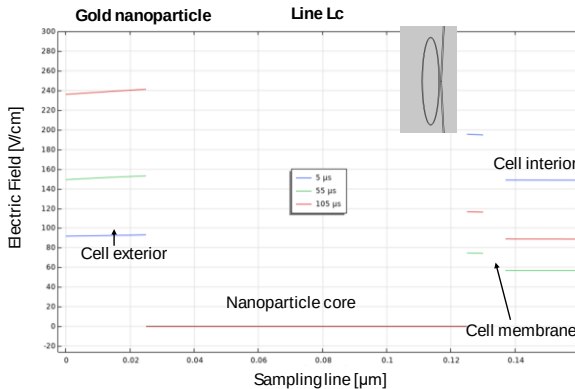


Fig 2: Electric field sampled on the line L_c with gold nanoparticle.

Considering Figs. 2-4, magnetic and magnetic core with silica layer nanoparticles show a higher electric field inside the nanoparticle with respect to gold nanoparticle. Close to the cell membrane, a strong modification of the electric field distribution is observed with gold nanoparticle (Fig. 2), whereas

the presence of magnetic nanoparticle does not modify the field distribution in the interior and exterior part of the cell membrane. Finally, the silica layer increases the electric field intensity around the nanoparticle (Fig. 4). In the full-length paper, two different orientations of the nanoparticle and different rise times will be investigated.

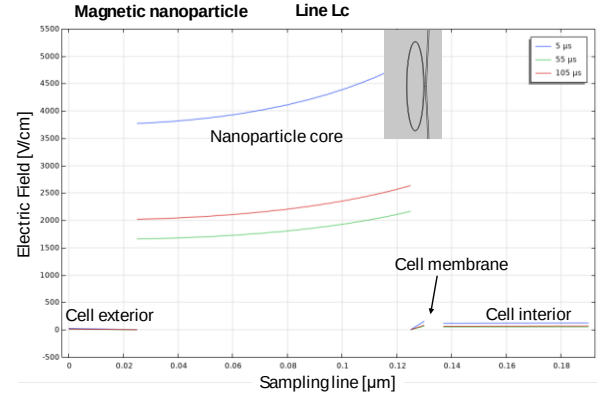


Fig 3: Electric field sampled on the line L_c with magnetic nanoparticle.

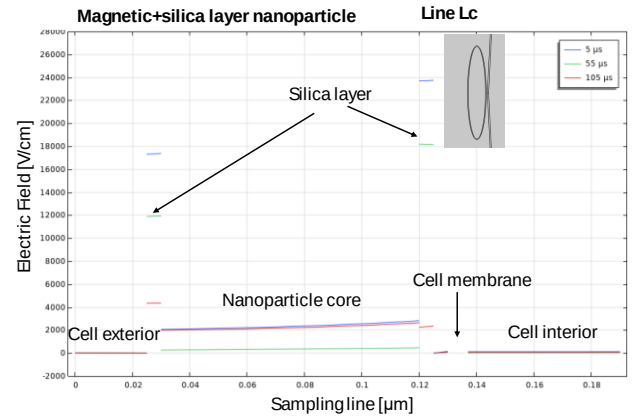


Fig 4: Electric field sampled on the line L_c with a magnetic core covered by a silica layer nanoparticle.

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