

## **Numerical Study of the Electromagnetic Scattering by a Biological Cell Nucleus during the Different Major Phases of Mitosis**

Fabrizio Frezza<sup>1)</sup>, \*Fabio Mangini<sup>2)</sup>, Endri Stoja<sup>3)</sup> and Nicola Tedeschi<sup>4)</sup>

<sup>1), 2), 3), 4)</sup> *Department of Information Engineering, Electronics and Telecommunications  
"La Sapienza" University of Rome, Via Eudossiana 18, 00184, Rome, Italy*

<sup>1)</sup> [fabio.mangini@diet.uniroma1.it](mailto:fabio.mangini@diet.uniroma1.it)

### **ABSTRACT**

In this work a numerical study of the electromagnetic scattering by a biological cell in the different phases of mitosis is presented. We consider the Jurkat cell for our analysis and model the content of the cell, composed by the nucleus and different organelles immersed in cytoplasm and delimited by the cell membrane, as a single material with appropriate electromagnetic properties derived by making use of homogenization techniques. To validate the model, a comparison of two different methods is made and the results are in very good accordance. Subsequently, an analysis of the scattered field indicates that the most sensitive component to the mitosis phase is the one parallel to the segment joining the centers of the cells.

### **1. INTRODUCTION**

For the monitoring of cell mitosis there are several methodologies that are based on electromagnetic scattering techniques (Epstein 1988, An 2012, Hasegawa 2013): the main advantage in using such a phenomenon for the study of cell division is the possibility to investigate cells positioned in deep tissues.

In the literature there are several models to describe a point of view of an electromagnetic cell (Irimajiri 1991, Asami 2006, Di Biasio 2010): the most widely used of these is the single-shell model; other more complex models are the double- and triple-shell model which try to take into account particulars more and more accurate. All the models mentioned above are considered on the basic condition of quasi-static field, with the relevant Laplace equation, to be solved in spherical coordinates.

Usually these models have been increasingly employed to study the geometric characteristics (Bronk 2005) or for the analysis of mammary cells during the main phases of cell mitosis (Brunsting 1974, Nüsse 1989), which refer to always distinct cell geometry.

In this paper we study the cell division during the process of cell mitosis by detecting the electrical response of the cell itself. Our study starts with the validation of the single-shell model, in all phases including the intermediate steps where the geometry can be approximated by two intersecting spheres (Fig. 1).

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<sup>1)</sup> Professor

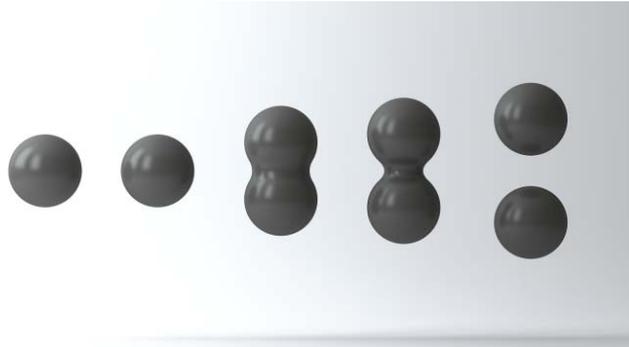


Fig. 1 Different phases of cell division examined in this study

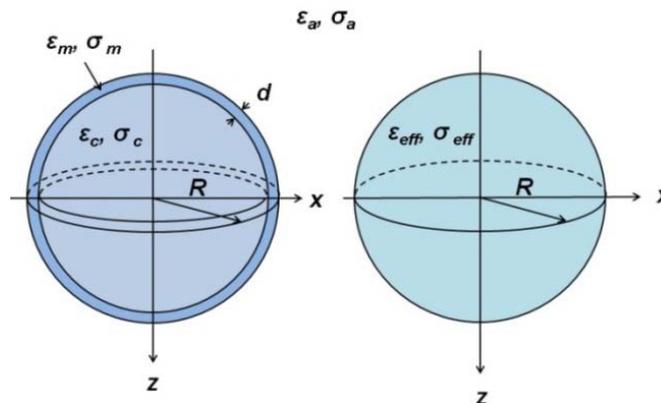


Fig. 2 Membrane homogenization

## 2. HOMOGENIZATION OF A BIOLOGICAL CELL

A biological cell may be considered as a heterogeneous system composed of a variety of organelles. At the cell's center is found the nucleus, delimited by the nucleus membrane, and surrounded by cytoplasm, which can on its own be considered as a heterogeneous medium composed by cytoskeleton and other organelles as mitochondria, ribosomes, lysosomes etc. The internal compound of the cell is held together by the cell membrane.

From an electromagnetic-modeling point of view, such a complex system would be very demanding to solve for; therefor, in general, a preliminary homogenization process is performed to simplify the cell system. In this context, a widely adopted homogenization model is the so called single-shell model, which represents the cell as a sphere occupied by a single effective medium with an external shell to model the membrane and which basically takes into account only the interfacial dielectric-polarization relaxation due to the shielding effect of the cell membrane, the Maxwell-Wagner effect (Asami 2006).

Anyway, a further simplification of the model is necessary due to the very low aspect ratio of the membrane thickness and the cell sphere radius, and it would be preferable to represent the cell as a simple single sphere in our finite-element-method simulations. For the single-shell model (Fig. 2), the complex effective relative permittivity  $\epsilon_{eff}^*$  can be determined by making use of the formula (Maxwell 1891)

$$\varepsilon_{eff}^* = \varepsilon_m^* \frac{2\varepsilon_m^* + \varepsilon_c^* - 2\nu(\varepsilon_m^* - \varepsilon_c^*)}{2\varepsilon_m^* + \varepsilon_c^* + \nu(\varepsilon_m^* - \varepsilon_c^*)} \quad (1)$$

where  $\nu = (1 - d/R)^3$ , R is the sphere radius and d the membrane thickness,  $\varepsilon_m^*$  the complex permittivity of the cell membrane, and  $\varepsilon_c^*$  the cytoplasm complex permittivity.

Subsequently, if one needs to determine the complex permittivity  $\varepsilon_0^*$  of a mixture composed of concentric spheres immersed in a continuous medium of permittivity  $\varepsilon_a^*$ , Wagner's mixture equation (Wagner 1914) can be used:

$$\varepsilon_0^* = \varepsilon_a^* \frac{2\varepsilon_a^* + \varepsilon_{eff}^* - 2\phi(\varepsilon_a^* - \varepsilon_{eff}^*)}{2\varepsilon_a^* + \varepsilon_{eff}^* + \phi(\varepsilon_a^* - \varepsilon_{eff}^*)}$$

where  $\phi$  denotes the volume fraction occupied by the cells.

### 3. MODEL VALIDATION

Before proceeding with the study of the scattered field by a cell undergoing mitosis, we want to evaluate the accuracy of the model introduced in the previous section. Indeed, the latter model has been developed for a sphere geometry and its accuracy may vary when passing to a configuration of two intersecting spheres.

In our study we choose a particular cell type known as the Jurkat cell, whose dielectric properties are taken from Frénéa-Robin *et al.* (2009) and shown in Table 1.

Table 1 Permittivity values used in this study

	Medium	Membrana	Cytoplasm
Epsilon	80	6	45
Sigma [S/m]	0.1	$3 \cdot 10^{-6}$	0.4

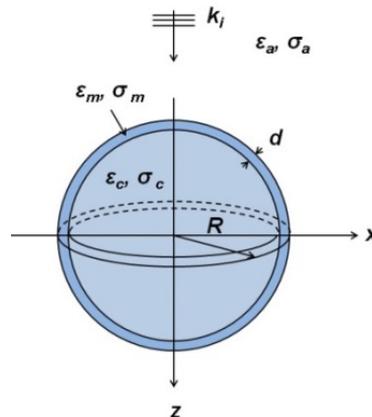


Fig. 3 Geometry of the first validation model.

At first, a single-shell model of the Jurkat cell is studied (before mitosis). A 1 V/m circularly polarized plane wave impinges on the sphere (Fig. 3) at a frequency of 0.5 THz. Note that the frequency has been chosen to be an optimum regarding the quasi-static approximation adopted for the FEM simulations. One can also choose best frequencies without conflicting with the validity of the model, however, in any case are ongoing studies on the possibility of any repercussions at the level of cellular function and mitotic phases of cell proliferation in the presence of high-frequency electric field (Nikolaevich 2004, Hintzsche 2012) where high frequency means a range from the tens of GHz to the hundreds of THz.

The cell radius is  $R = 5 \mu\text{m}$  and the cell membrane thickness is  $d = 10 \text{ nm}$ . Note that there is a very high aspect ratio. As stated above, by making use of the Maxwell formula as shown in Eq. (1), we find an effective permittivity  $\epsilon_p^* = 44.27 - j0.0139$ .

In Fig. 4 is presented a comparison of the results obtained by two different methods: the analytical model of a concentric sphere developed by Mie (Bohren 1983) implemented in Matlab and a model of the homogenized single shell solved with the commercially available simulator COMSOL Multiphysics. The field values have been extracted from a line probe of length  $R$  located at  $z = -2.5R$ .

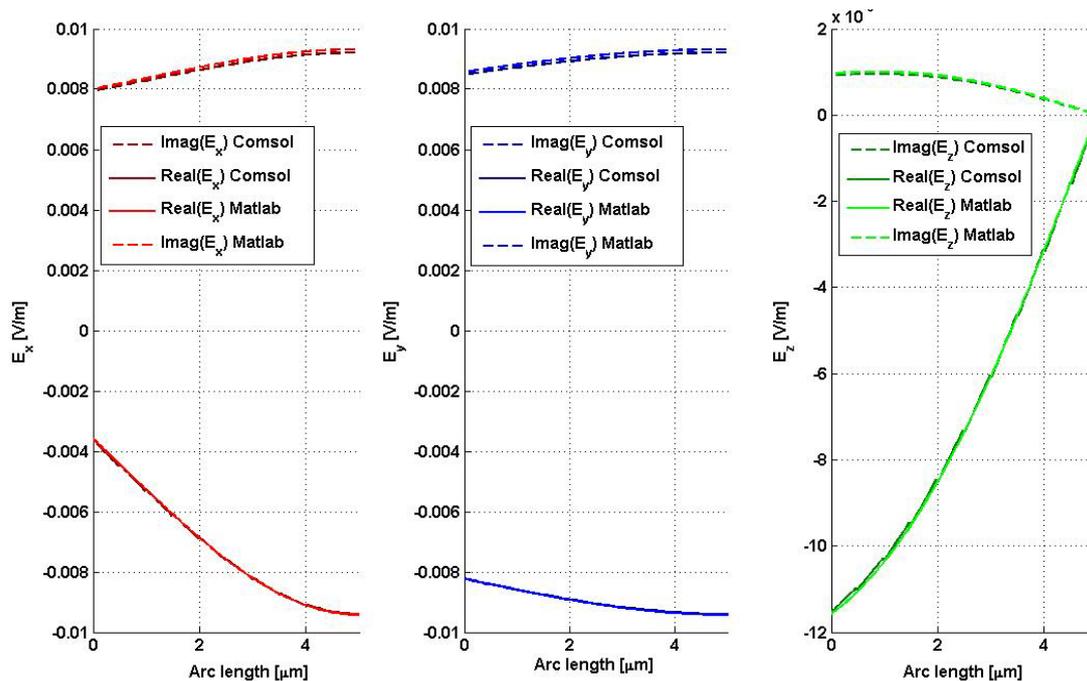


Fig. 4 Validation of the single-shell model

The second validation study is performed supposing that mitosis has already occurred, with the model consisting of two tangential spheres that represent the two cells resulting from the division. In the first one, the spheres have the membranes but their thickness is fictitious to avoid simulation problems due to the very high aspect ratio. More specifically, the shell thickness is chosen to be 1/10 of the sphere radius. Instead, in the second simulation model, the homogenized spheres have been considered (Fig.

5, right). As in the previous case, the results, shown in Fig. 6, are in good accordance. The field values have been extracted from a line probe of length  $2R$  located at  $z = -2.5R$ .

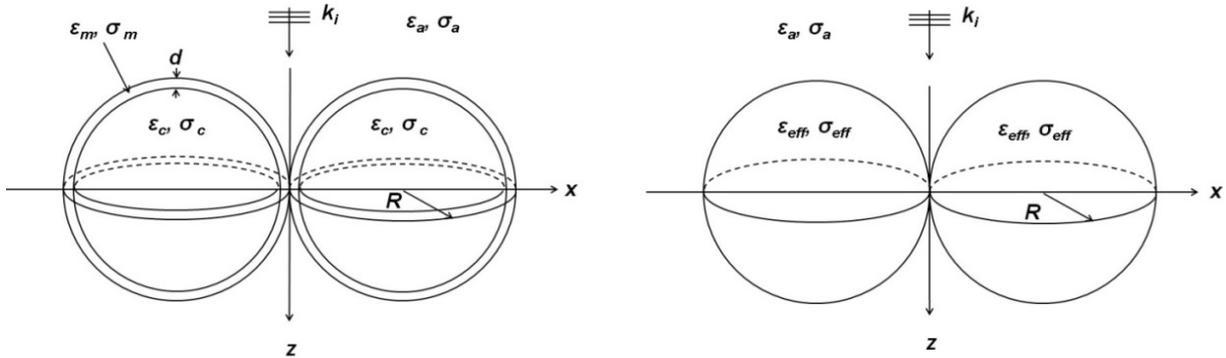


Fig. 5 Geometry of the second validation model

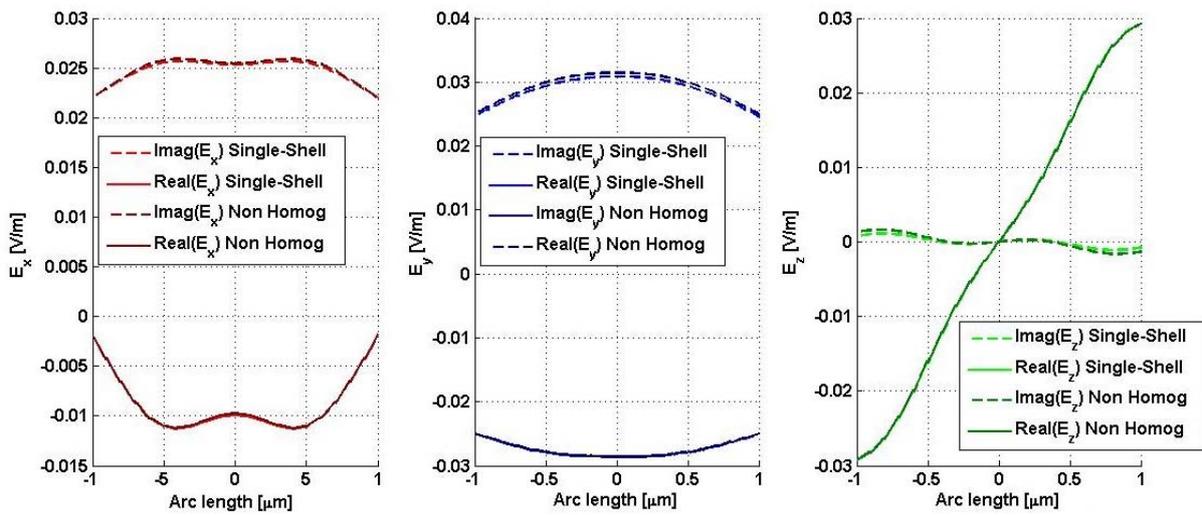


Fig. 6 Validation of the tangential spheres model

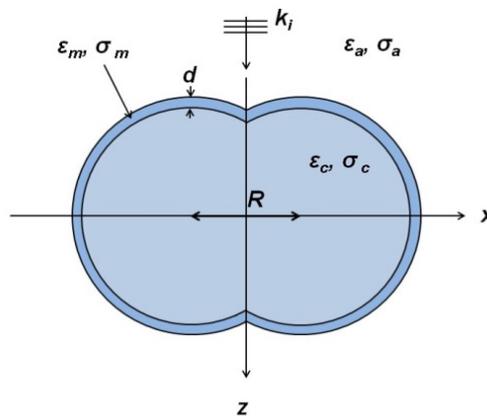


Fig. 7 Intersecting spheres

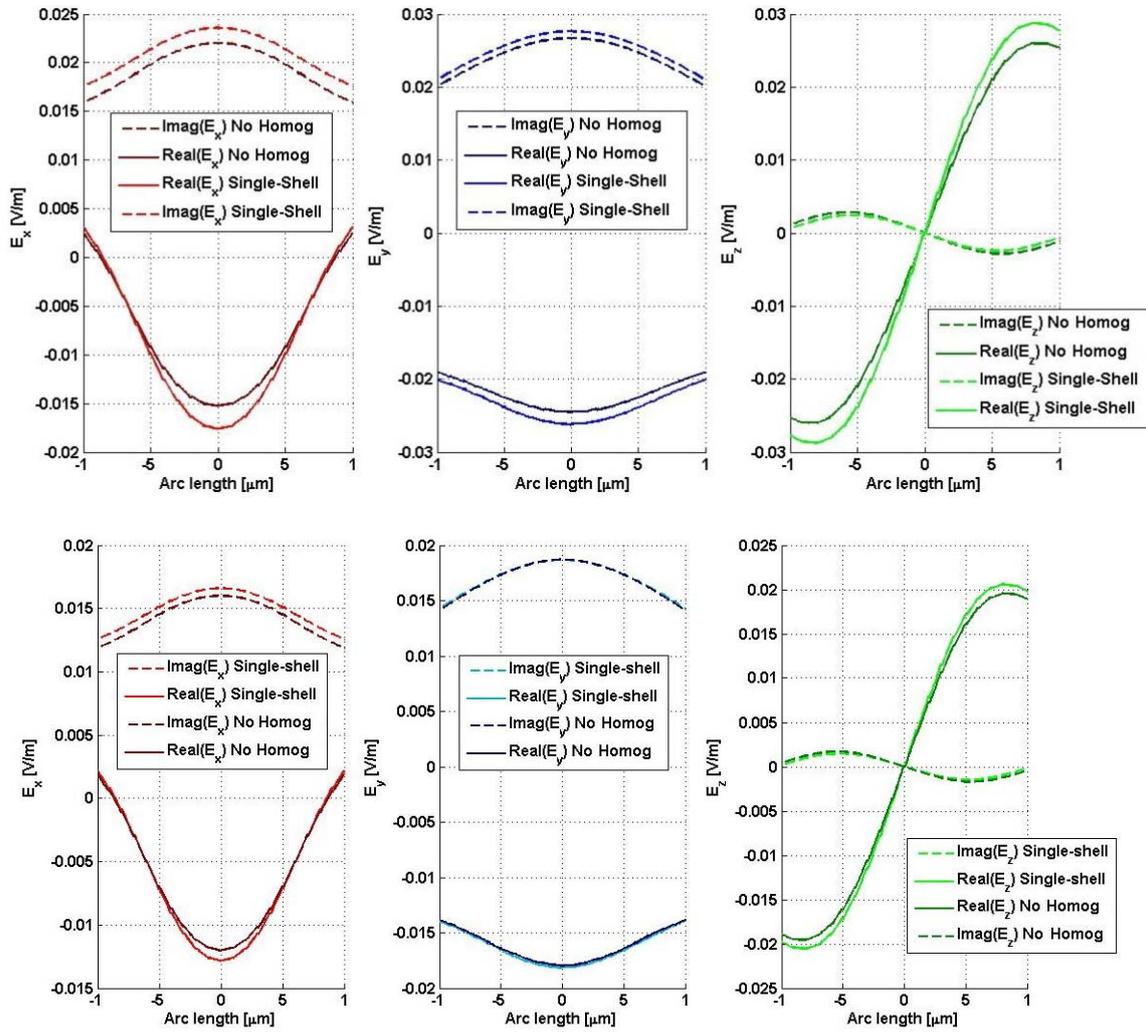


Fig. 8 Scattered field components, intersecting spheres

#### 4. MEMBRANE EFFECT IN THE CASE OF INTERSECTING SPHERES

Similarly to the above mentioned cases, we want to determine if the same homogenization model can be used for the case of two intersecting spheres (Fig. 7), or there is a need to adopt much more complex homogenization model as those proposed by Pitkonen (2006, 2007).

In Fig. 8 we represent the scattered field components by two perfectly compenetrating spheres, meaning that the external surface of each sphere is passing to the center of the other sphere. Two different values of shell thickness are considered,  $d = R/10$  and  $d = R/50$ .

#### 5. SCATTERED FIELD DURING MITOSIS

In this section we proceed with the study of the scattered field profile by a Jurkat cell

during mitosis and subsequently discuss if it is possible to detect the relevant mitosis phase from the fields.

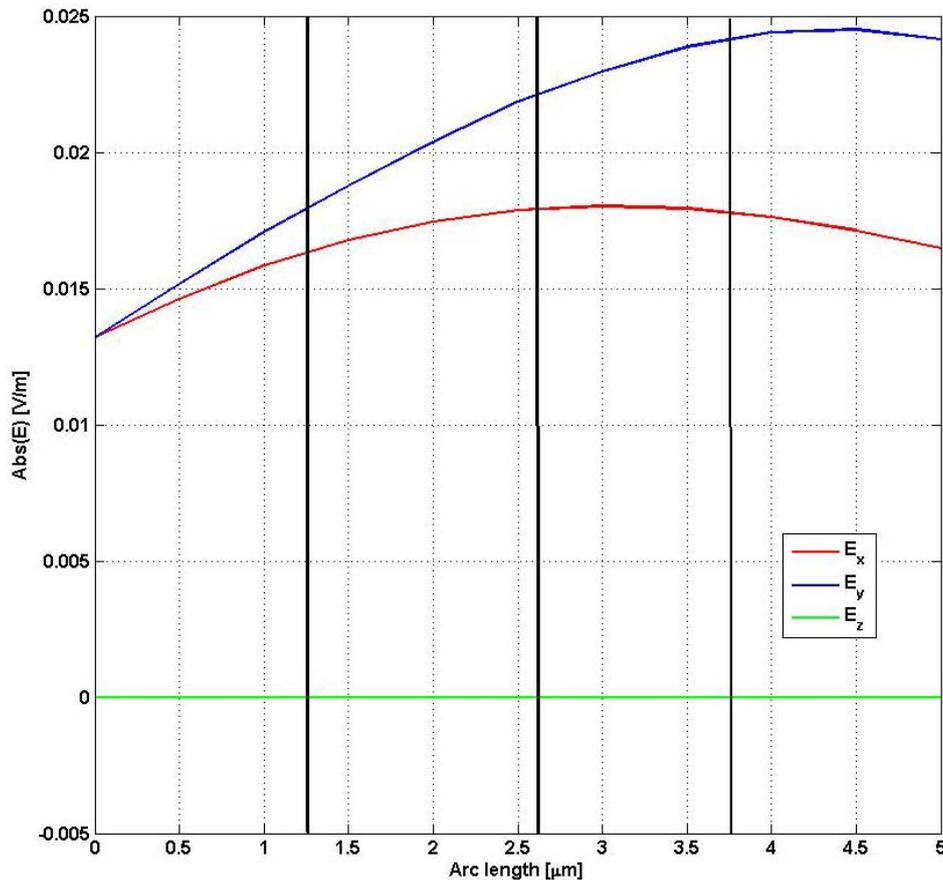


Fig. 9 Magnitude of the scattered field components during mitosis, in abscissa the distance between the center of each sphere and axes origin is represented

In Fig. 9 are presented the magnitude of the three field components during the different phases of mitosis which can be discriminated by the distance between each sphere's center respects to axes origin. Therefore zero represents a single sphere (before mitosis) and a value  $2R$  the case of two tangential spheres (immediately after mitosis).

That the scattered field component most sensitive to the mitosis phase is the one along  $y$ . Similarly to the case of a cylindrical structure, the maximum response is observed when the polarization of the electromagnetic stimuli is parallel to the predominant geometrical feature direction that in our case coincides with the direction defined by the sphere centers.

Seemingly, a different value for the maximum of the component along  $y$  would have been expected. In fact, considering the analogy of the cylindrical structure, the maximum value would correspond to the case of maximum distance of the spheres' centers, but maybe the cusp between the two spheres does not favor the induced

current flow.

On the other hand, when it is not possible to know preliminarily the orientation of the cells' centers, one could observe the difference between the relevant scattered field components. In Fig. 10, this difference is shown: it grows as the mitosis process goes on having a maximum when it is completed. A sigmoidal function can be used to monitor the mitotic cell division.

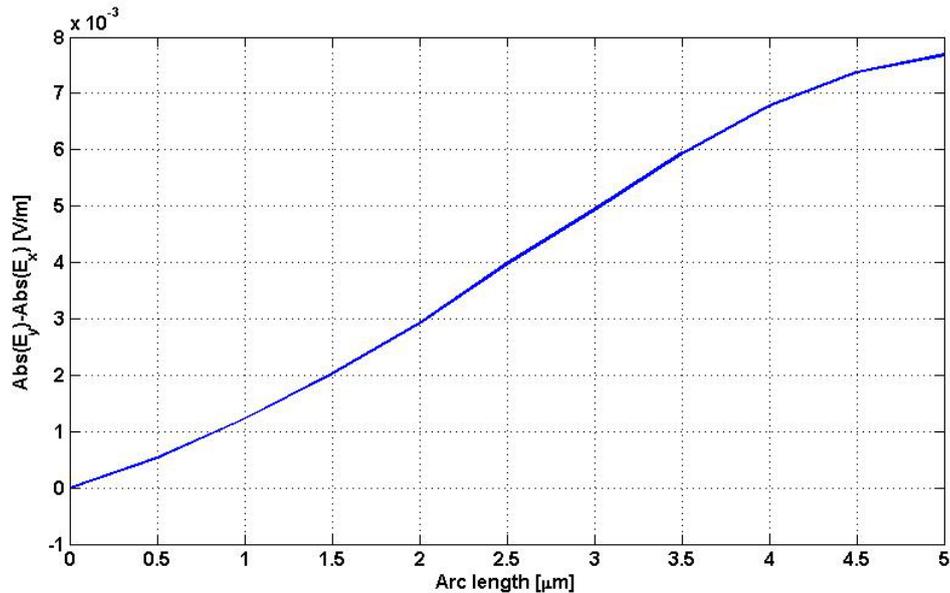


Fig. 10 Difference between the relevant field components in magnitude  $|E_y| - |E_x|$  during mitosis

## 6. CONCLUSIONS

In conclusion, we can affirm that, where possible, for the study of mitosis of a single cell, it is convenient to excite the system by a plane wave linearly polarized along the direction of the segment joining the two centers.

Moreover, we could exploit the sigmoidal trend given by the difference of the magnitudes of the two electric-field components to determine the stage of separation of the cell, since it has been shown that such difference is substantial and growing over time. In this respect, suitable use could be made of circularly polarized waves.

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