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# A microdosimetric study at the cellular and intracellular level using a 3D realistic cell model

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**Abstract** — Radio frequency electromagnetic fields (RF EMFs) are increasingly used in emerging telecommunication technologies such as wireless power transfer (WPT), 5G millimetre-wave (mm-Wave) technologies, with a public concern regarding their environmental safety. Microdosimetric investigations provide an insight into the local distribution of the electric field induced at the level of cellular and sub-cellular structures exposed to RF EMFs.

The aim of this work is to provide a quantitative evaluation of the EMFs in cells, using a 3D microdosimetric model with a realistic shape of the cells and intracellular organelles (i.e. endoplasmic reticulum and nucleus). Results are presented in terms of local electric field distribution, local volumetric power loss density distribution and transmembrane potential induced on the cellular and sub-cellular membranes, with a focus on the comparison between EMFs exposure at 700 MHz, 3.7 GHz and 60 GHz.

**Keywords** — Biological cells, numerical models, Millimeter wave communications, Wireless power transmission, 5G communications.

## I. INTRODUCTION

During the last decades there has been increasing interest in developing radio frequency electromagnetic fields (RF EMFs) technologies for wireless communications, including internet of things (IoT) technologies [1,2]. This emerging exploitation of the RF EMFs (bandwidth from hundreds of kHz to hundreds of GHz) in the WPT and 5G mm-Wave technologies continues to keep alive the investigation into the potential effects on human bodies exposed to such EMFs [3].

To this regard, the International Commission on Non-Ionizing Radiation Protection (ICNIRP) has recently updated the guidelines on human health protection when exposing to RF EMFs from 100 kHz to 300 GHz [4], setting the principles to quantitatively specify the EMFs levels for a human body exposure.

When dealing with cellular and intracellular structures, microdosimetric studies represent a crucial tool to predict the effects of the interaction between EMFs and biological matter at the microscopic level [5], providing the chance to locally quantify the electromagnetic (EM) quantities involved, such as electric field amplitude, induced transmembrane potential (TMP) and absorbed power densities.

Recently, to gain an accurate evaluation of the spatial variation of these EM quantities, a variety of 2D or 3D cell models without or with sub-cellular compartments were presented, mainly to investigate the electroporation mechanisms. These numerical models are based on: the meshed transport network [6]; the transport lattice [7]; the finite elements method [8]. The latter is currently used to build up reliable geometric models able to follow the shape of cellular and sub-cellular structures, thus affecting the local EM quantities. Together with the shape and spatial orientation of the cell compartments, dielectric properties play an important role on the EMFs exposure as recently demonstrated for different types of cells and intracellular compartments such as 2D neurons [9], 2D neuroblastoma cells [10], 2D hamster fibroblasts [11], 3D keratinocyte [12,13], 3D erythrocyte [14] and 3D endoplasmic reticulum [15].

In this work, we present a 3D realistic model of a human mesenchymal stem cell (MSC), including irregular details of the endoplasmic reticulum (ER) and the nucleus. The geometrical model is derived from the confocal microscopy images of MSC cells decorated to show both the ER and the nucleus compartments, as previously described in [15].

The aim of this study is to give a quantitative estimation of the EM quantities induced by the exposure of MSC cells to the EMFs (1 kHz – 100 GHz), specifically focusing on the exposure results at: (i) 700 MHz, representative of 4G Long Term Evolution (LTE), Narrowband IoT (NB-IoT) and low band of Frequency Range 1 (FR1) of 5G technologies; (ii) 3.7 GHz, representative of the mid-band FR1 of 5G technologies (5G NR n78 band); (iii) 60 GHz, already deployed in some countries for WiGig and 5G [16-20].

## II. MODELLING A 3D REALISTIC CELL

A microdosimetric investigation is based on two main steps: (1) the setup of the model in terms of geometry and dielectric properties; (2) the choice of a suitable EM solution.

The MSC cell is chosen as cell model for a wide range of *in vitro* applications, due to its ability to differentiate to a variety of cells such as adipo- and osteo- lineages [21].

To obtain the 3D realistic model of MSC, with both ER and

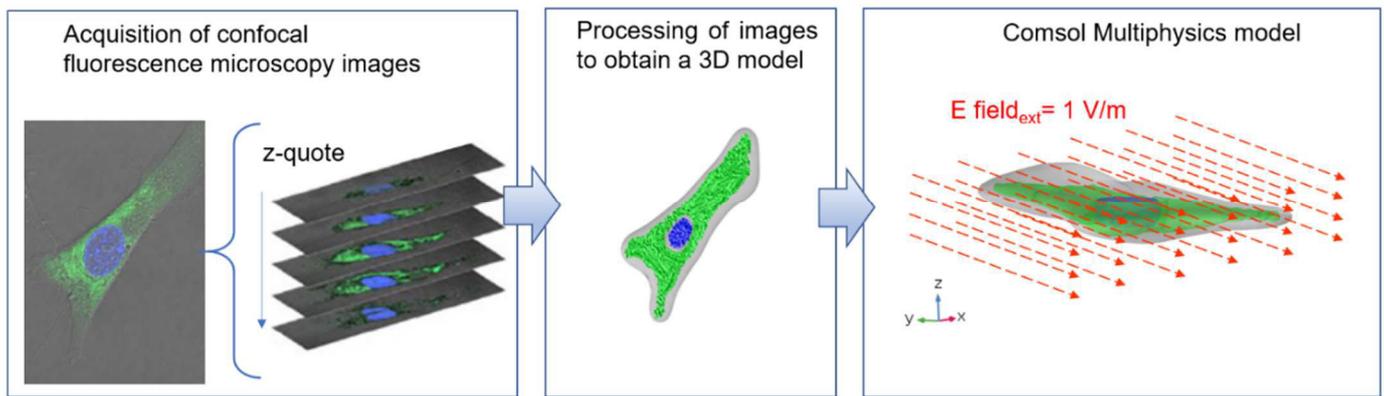


Figure 1. Model setup of a cell with a realistic shape for microdosimetric investigations, from microscopy images acquisition to the fine-tuned model.

nuclear compartments, a set of images at different z-quotes was acquired using a confocal microscope and specific fluorescent dye to decorate ER and nuclear compartments as described in [22]. Each image was processed with a custom automated routine computed in MATLAB software, able to convert the RGB images into a 3D STL file, as detailed in [15]. This 3D STL file has been directly imported in Comsol Multiphysics software v. 5.3 to perform the simulation. The process used to obtain the 3D model is schematically reported in Fig. 1.

The 3D cell model, with main dimensions of about  $100\ \mu\text{m}$ , was placed in a parallelepiped box representing the extracellular medium. The front and back side of the box are set, respectively, to ground and potential electrode.

Finally, the Debye model equation was implemented in the model for each cell compartment to take into account the biological material dispersion behaviour in frequency domain, using dielectric properties as reported in [10].

The EM problem was solved using the Electric currents mode of the AC/DC module in Comsol. A frequency dependent study has been performed in a range from 1 kHz to 100 GHz and applying an external Electric field =  $1\ \text{V/m}$ .

### III. RESULTS

The interaction of EMFs with cells is evaluated in terms of volumetric power loss density (VPLD) in all the internal compartments of the cell, at 700 MHz, 3.7 GHz, and 60 GHz [16-20], above the  $\beta$ -relaxation. In Fig. 2 the VPLD distributions are reported with a 3D view on the cell (A, B and C panels) and with a 2D view on a selected xy cross-section, together with the current density (J) streamlines (panels D, E and F). As evident from Fig. 2 (A, B, and C panels), the VPLD distribution inside the cell has a 7 fold increase between 700 MHz and 3.7 GHz and a strong increase at 60 GHz. In panels D, E, and F the results are reported with three different scales, optimized for each frequency in order to evidence the distribution inside the cell. Specifically, VPLD ranges from

$0.16$  to  $0.23\ \text{W/m}^3$  at 700 MHz, from  $1.25$  to  $1.6\ \text{W/m}^3$  at 3.7 GHz and from  $26.5$  to  $31.5\ \text{W/m}^3$  at 60 GHz. The highest VPLD values are mainly located in two regions of the cell that include all the three internal compartments of the cell, at all the three frequencies. From panels D, E and F it is worth to notice that VPLD values in the extracellular medium are above  $0.23$ ,  $1.6$  and  $31.5\ \text{W/m}^3$ , respectively.

The J streamlines give an estimate of the frequency dependence interaction of EMFs with cells. At 700 MHz, the streamlines distribution, crossing the cell compartments, is influenced by the cell shape and dimension (panel D); at 3.7 GHz, the streamlines behavior, is slightly affected by the presence of the cell (panel E), becoming straight and cell shape insensitive at 60 GHz (panel F).

Fig. 3 (panels A, B and C) reports the local electric field distribution on the selected xy plane together with the current density (J) streamlines at 700 MHz, 3.7 and 60 GHz respectively. Here, electric field values higher than  $1\ \text{V/m}$  are present in most parts of the cell, with a focus on two main regions due to the shape of cell and organelles, in line with the VPLD distribution. As evident from Fig. 3 (A, B and C panels) the main difference between these three selected frequencies could be found in the way in which the EMFs interact with cell and subcellular membranes. Specifically, at 700 MHz and 3.7 GHz the induced field is still affected by the shape of each cellular and intracellular membranes (with a local decrease of electric field to values lower than  $1\ \text{V/m}$  in the proximity of the membranes); a behavior that cannot be found at 60 GHz. This difference is also slightly shown in the VPLD distribution in Fig. 2 (panel D, E and F).

In Fig. 3, panels D, E and F, the distribution of the normalized TMP (respect to the  $1\ \text{V/m}$  electric field externally applied) induced on all cell membranes is reported at 700 MHz, 3.7 GHz and 60 GHz respectively, in the selected xy plane together with the J streamlines.

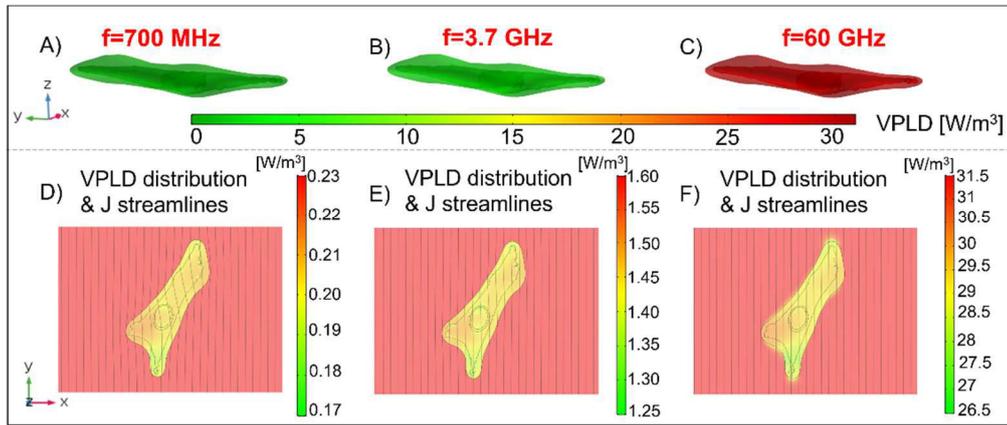


Figure 2. Results of cell exposure to EMFs. 3D distribution of the VPLD at 700 MHz, 3.7 GHz, and 60 GHz (panel A, B and C respectively). VPLD (D, E and F) distributions on the xy plane at the centre of the cell, together with J streamlines.

These results are in line with the local electric field distributions (Fig. 3 A, B and C panels) and the difference between the three selected frequencies is highlighted. Fig. 3-D and E show the interaction at 700 MHz and 3.7 GHz with a main difference in the streamline's distribution and similar values in terms of TMP. For the two frequencies, due to the shape of the cell, the induced TMP has high values in the upper part of the plasma and ER membranes, facing the incident EMFs application, above  $5 \times 10^{-2} \mu\text{V}/(1 \text{ V/m})$ . Moreover, regarding the nucleus membrane, high TMP values at the poles, above  $5 \times 10^{-2} \mu\text{V}/(1 \text{ V/m})$ , and low values at the equator about  $1 \times 10^{-2} \mu\text{V}/(1 \text{ V/m})$ , are shown, as expected due to its rounded shape.

The results at 60 GHz (Fig. 3-F) present TMP values inly in a range of  $0 - 2 \times 10^{-2} \mu\text{V}/(1 \text{ V/m})$  due to the fact that the EMFs penetrates the cell by short-circuiting the membranes.

Finally, results in terms of the average electric field and the average VPLD in all plasmas and the average normalized TMP induced on cellular and organelles membranes, are reported in Fig. 4 (A, B and C respectively). Here, data are reported as a function of frequency (1 kHz-100 GHz), showing that for frequencies below 1 MHz the external electric field mainly interacts with plasma membrane ( $\text{TMP} > 10 \mu\text{V}/(1 \text{ V/m})$ ) and cytoplasm (electric field from 0.1 to 1 V/m), but each compartment is affected by the exposure. These spectral response results from 3D modelling are in line with 2D data from literature [10,23], but giving more information on the cellular and subcellular interaction with EM field. For frequencies above 1 MHz, the electric field lines crosses all the cell and subcellular membranes, determining an induced values of about 1 V/m.

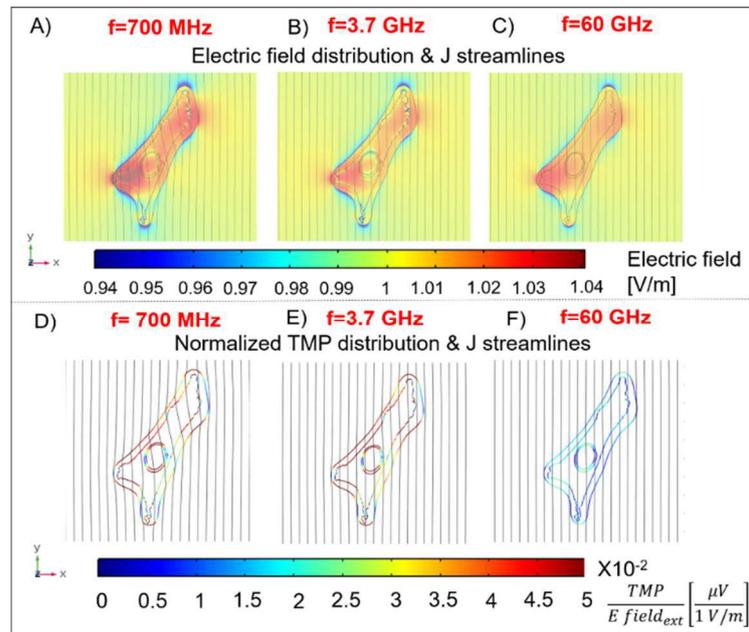


Figure 3. 2D distributions of the electric field in the xy plane at the centre of the cell at 700 MHz, 3.7 GHz and 60 GHz (panel A, B and C respectively). Induced TMP on cell membranes (D, E and F) on the same xy plane, together with J streamlines.

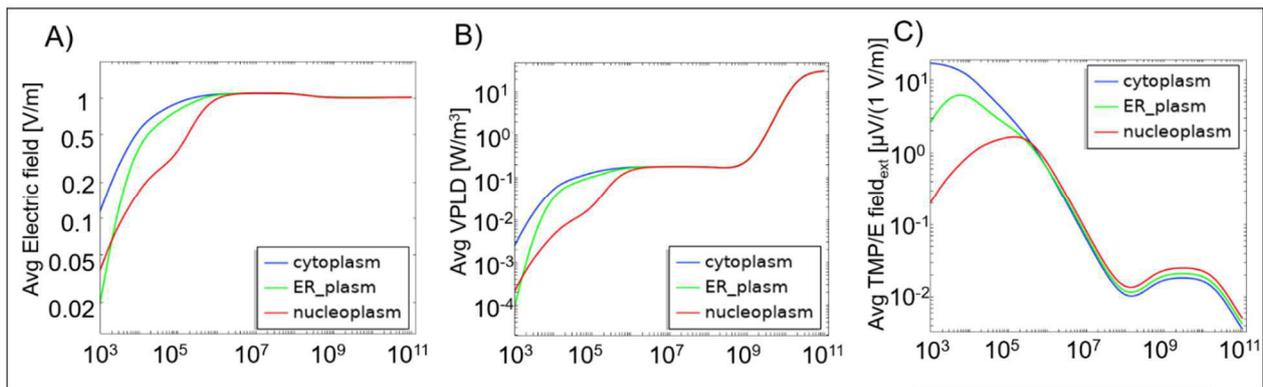


Figure 4. Profiles of the Average Electric field (panel A), Average VPLD (panel B) and Average induced TMP (panel C) normalized in respect to the external electric field in the 1 kHz-100 GHz range.

#### IV. CONCLUSION

A 3D microdosimetric study of one cell exposed to an external electric field of 1 V/m was performed in the frequency domain (1 kHz - 100 GHz) to locally investigate the effect of RF-EMFs on the biological cells. Results show that in the upper part of the microwave spectrum the EM field can penetrate not only the plasma membrane reaching the organelles, but also the ER and nucleus membranes. They also suggest that 3D models with a realistic shape of the cell and its internal organelles are of importance in the microdosimetric analysis to accurately predict the micro-scale EM field and power distribution.

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