

The Influence of Scaffold Design in Electrical Field Distribution for Tissue Engineering

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Abstract. Regarding electric field stimulation in tissue engineering, namely in bone in vitro stimulation, we wonder if by introducing different scaffold geometries into the cell culture chamber environment, we are changing the externally applied electric field magnitude. Also, if we assume that the presence of the scaffold changes the magnitude of the surrounding electric field, can we just by picking a specific scaffold material be delivering electric fields outside the osteoinductive range for that specific cell line. To answer these questions, numerical models for three different scaffold geometries and for a capacitively coupled system were created. The models allow to understand that the presence of the scaffold impacts and interferes with its surrounding electric field, generating patterns that may increase the electric field magnitude in some regions inside the scaffold, and at the same time may block the electric field in other regions of the same scaffold. Another insight from numerical models is that even keeping the same scaffold geometry, just by changing the scaffold material we are changing this interference pattern and delivering different electric fields in the scaffold region-of-interest.

INTRODUCTION

Total fragility bone fractures in the European Union group of six member states, known as EU6, are estimated to increase from 2.7 million in 2017 to 3.3 million in 2030, a 23% increase [1]. Bone fractures may occur after trauma, infection, or oncologic resection. Small bone defects usually heal without complex interventions, but critical size defects (> 2.5 cm) will require secondary procedure(s) to obtain union and healing. A bone union can be promoted by applying electrical stimulation systems, and while the tissue engineering approach proposes to treat bone fractures by implanting a temporary scaffold where the cell can grow and differentiate into mature bone, the implications of the insertion of a scaffold structure in vivo or in vitro into the electric stimulation, and the patterns generated by its interference remains an overlooked topic [2]. In this study, we compared different numerical model predictions for common tissue engineering scaffold geometries when subjected to and electrical stimulation generated by a typical capacitive coupled system (CCoupled), and show that even when constructed with the same material, each structure generates a different electric field interference pattern. For example, for hexagonal scaffold geometry, we also compared an electrical conductor with an electrical insulator, showing also that the material properties of the scaffold strongly influence the interference pattern, and the magnitude of the external electric field stimulation.

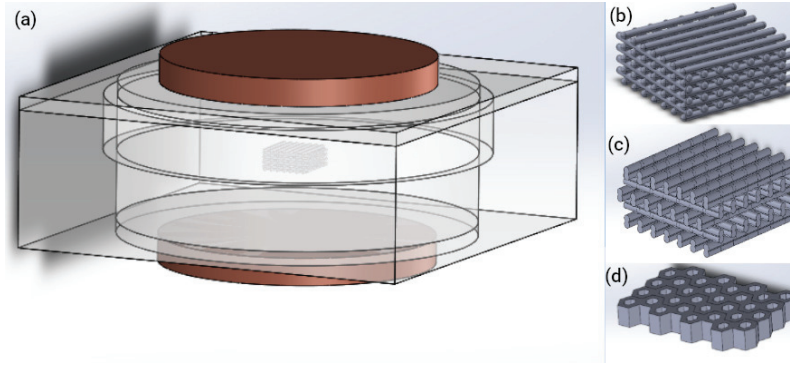


FIGURE 1. (a) Capacitively coupled system to study the interference of different scaffold structures into the delivered electric field upon external stimulation. (b) Orthogonal scaffold 0°/90°. (c) Orthogonal displaced double layer scaffold. (d) Hexagonal (honeycomb) scaffold.

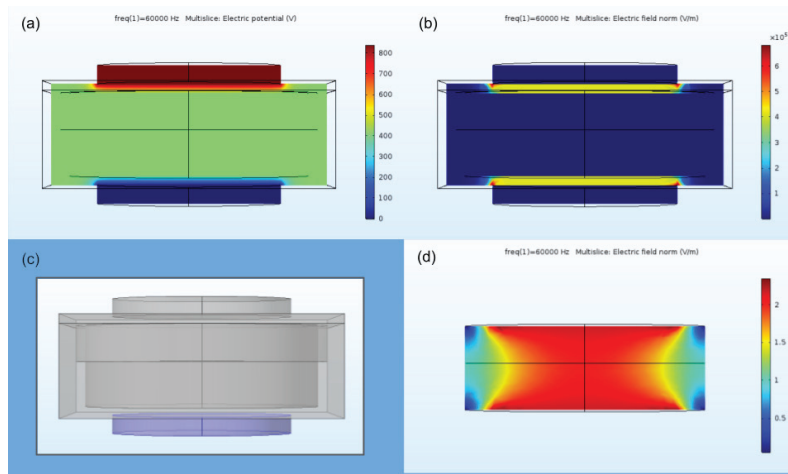


FIGURE 2. (a) Electric potential distribution at the entire C-Coupled system (only culture medium in the chamber). (b) Electric field distribution at the entire C-Coupled system (only culture medium in the chamber). (c) C-Coupled system geometry (only culture medium in the chamber). (d) Electric field distribution at the cell culture chamber.

METHODS

DCoupled Electric Stimulation System and Scaffold Geometries Design

The three different scaffold geometries CAD design and the C-Coupled electric stimulation CAD design were created using SOLIDWORKS (version 2018, Dassault Systèmes, France). The orthogonal and displaced double layer scaffold geometries dimensions were based in the work of Serra et al. [3], while the hexagonal scaffold geometry (honeycomb) was based in the work of Wang et al. [4]. The C-Coupled electric stimulation system was inspired in classical works like Armstrong et al. [5] as shown in Figure 1, with the following component dimensions: top and bottom cylindrical electrode (radius: 10 mm, thickness: 2 mm); Polydimethylsiloxane (PDMS) culture medium chamber (internal radius: 13 mm, top and bottom wall thickness: 1 mm, chamber height: 9 mm).

Electric Field Simulations with Finite Element Analysis

Electric field simulations were performed using COMSOL Multiphysics (version 5.2a, COMSOL, Sweden), considering the Electric Currents (EC) interface. This physics interface solve Ohm's law, maintaining a condition for conservation of currents, and an irrotational (curl free) condition. A frequency domain study was conducted at 60 kHz,

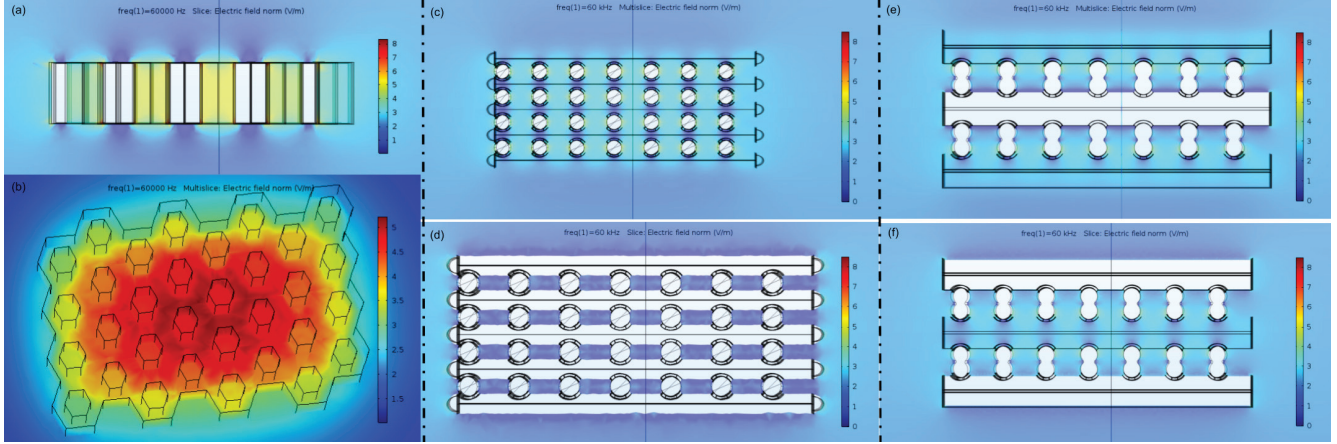


FIGURE 3. Electric field distribution (slice view) for the: hexagonal (honeycomb) scaffold interference. (a) Coronal plane slice. (b) Transverse plane slice; displaced double layer scaffold interference. (c) Coronal plane slice 1. (d) Coronal plane slice 2.; orthogonal 0°/90° scaffold interference. (e) Coronal plane slice 1. (f) Coronal plane slice 2.

with ground and electric potential boundary (of 850 V) conditions set to the outer surfaces of each metal electrode. To the scaffold material it was attributed PDMS properties to test it as an electrical insulator material, and stainless steel properties to simulate an electrical conductor scaffold material.

First, CCoupled system empty chamber (just filled with culture medium, without scaffold) was simulated to validate the initial electric field. Then three different scaffolds were added to observe their interference with the existent electric field. All scaffolds were placed equidistant from both electrodes and designed to have equal height, allowing a better comparison between them. A complete physics-controlled mesh of the CCoupled system with the scaffold option was performed in COMSOL with the fine mesh option. A domain point probe was added to middle of the culture medium domain to check the electric field in the empty chamber model. Characteristics of material, boundary conditions and solver options are presented in Table 1.

RESULTS AND DISCUSSION

Results from the simulation with the CCoupled system without any scaffold, the cell culture chamber just filled with culture medium, reveals a mean electric field of 2 V m^{-1} , Figure 2d. It also shows that the biggest potential drop occurs on the insulator layer, Figure 2b. This happens in a way, that for an insulator wall thickness of 1 mm it is required a potential difference of 850 V at 60 kHz to obtain an electric field of V m^{-1} in the cell culture chamber. When a scaffold structure is added to the cell culture chamber, we observe changes in the electric field distribution surrounding the scaffold. This happens because the scaffold constitutes an obstacle to the electric current flow, and that is the reason for the interference patterns created by each different scaffold structure. From the three analysed geometries, the hexagonal scaffold geometry (Figure 5) was the one that its interference generated higher surrounding electric fields, almost tripling the initial electric field in its pores. The remaining two scaffold geometries, orthogonal 0°/90° (Figure 3) and displaced double layer (Figure 4), are similar in the interference pattern. Both generates hot and cold spots, meaning that the cells will be overstimulated in some regions and understimulated in others. If we observe the pores for this two scaffold geometries we see that their presence almost double the surrounding electric field, a smaller effect when compared to hexagonal (honeycomb) geometry.

Another interesting observation comes from comparing for the same geometry, two opposite materials in terms of electrical conductivity, like we show on Figure 6. Once the current will flow inside the electrical conductor material, this shields the material surroundings from the external electric field, while in the electrical insulator case the current will flow through the pores, increasing the electric field in those regions. This may be an interesting effect to take into consideration when applying an external electric field stimulation and a conductive scaffold, because it can completely shield the surroundings from the electric field.

TABLE 1. COMSOL electric field numerical model assumptions and options.

Temperature: 37 °C
Culture Medium Properties
Electrical Conductivity: 1.5 S m ⁻¹
Relative Permittivity: 80.1
PDMS - Electrical Insulator
Electrical Conductivity: 2.5 × 10 ⁻¹⁴ S m ⁻¹
Relative Permittivity: 2.3
Stainless Steel - Electrodes and Generic Electrical Conductor
Electrical Conductivity: 4.032d6 S m ⁻¹
Relative Permittivity: 1
Boundary Conditions
Electric Potencial: 850 V
Ground
Physics Interface
Electric Currents (EC)
Mesh and Solver Properties
Physics Controlled Mesh Option
Mesh Size: Fine
Mesh average element quality: 0.55
Frequency Domain Study: 60 kHz
Stationary Solver BiCGStab

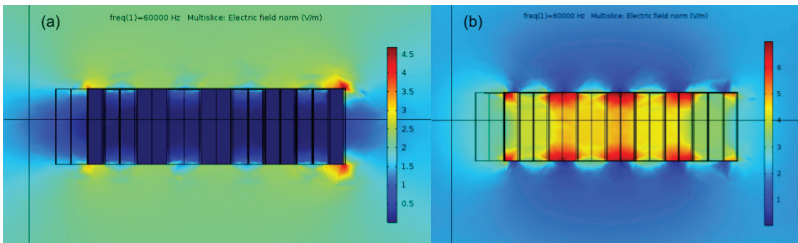


FIGURE 4. Electric field distribution (slice view) for the hexagonal (honeycomb) scaffold interference comparing two different materials, with an electrical conductor material (a) or with an electrical insulator material (b).

CONCLUSIONS

Now, we understand that not only different electric stimulation systems generate different electric fields patterns, but also even if we use the same system and scaffold material, the scaffold geometry will generate hot and cold electric field pattern regions inside the scaffold (caused by electric current pathway). This effect must be taken into account when applying electric stimulation in Tissue Engineering, so that external stimulation is chosen to keep the desired osteoinductive range inside the scaffold. Numerical simulation tools should be applied when designing experimental protocols in order to predict the effective delivery of electric field stimulation with and whitout scaffold geometries.

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