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Field models in low-frequency bioelectromagnetics

Abstract. *. In the paper, a review of the state of the art on numerical models of the electromagnetic field in biological entities is proposed. In particular, the field produced by cells and the one in which cells and biological tissues are exposed to, is considered; low frequency problems are investigated. Issues and drawbacks of field models in bioelectromagnetics with respect to field models for industrial applications are discussed.*

Streszczenie. *W artykule dokonano przeglądu stanu wiedzy na temat numerycznych modeli pola elektromagnetycznego w biologicznych komórkach. W szczególności, rozważane jest pole wytwarzane przez komórki i to, na które narażone są komórki i tkanki biologiczne; badane są problemy niskiej częstotliwości.. W artykule omówiono problemy i wady spotykane w adaptacji modeli polowych w bioelektromagnetyzmie w odniesieniu do modeli polowych w zastosowaniach przemysłowych. (**Modele polowe w niskoczęstotliwościowych problemach bioelektromagnetyzmu**).*

Keywords: numerical field models, low frequency, bioelectromagnetics.
Słowa kluczowe: polowe modele numeryczne, niska częstotliwość, bioelektromagnetyzm

Introduction

In the last decades the investigation of electric, magnetic and electromagnetic fields related to biological systems has become a more and more mature research field. At the beginning, for evaluating electromagnetic quantities, only analytical or experimental models were performed. At first, numerical models were applied in biomechanics in the early Seventies like e.g. [1] and then, as it happened in industrial electromagnetics, they were subsequently applied to bioelectromagnetics in the late Seventies like e.g. [2].

For the sake of an example, in Fig. 1 the number of papers published in the last decades which used finite element or finite difference time domain models in low frequency (Fig. 1) and high frequency (Fig. 2), respectively, are reported [3].

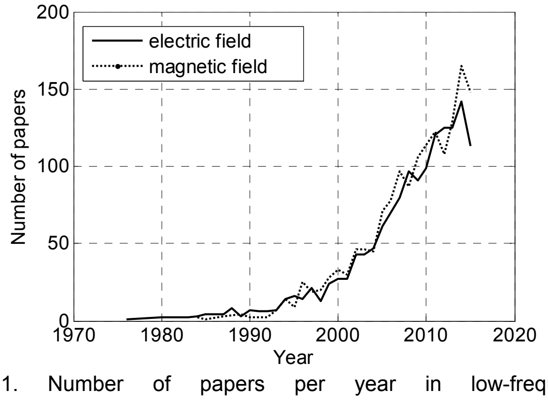

Fig.1. Number of papers per year in low-frequency electromagnetics

The most investigated research area is the low-frequency one; both electric and magnetic fields have been studied intensively in the last years, even if the interest for biomagnetism came out a little bit later than that for bioelectricity. In this paper, the attention will be focused on low frequency applications.

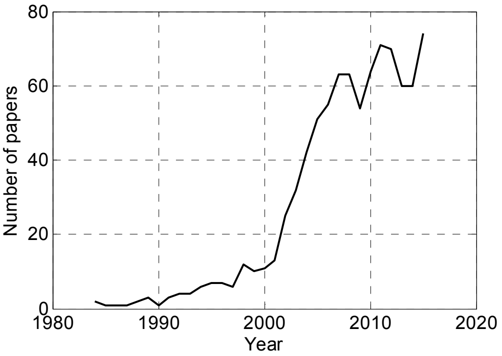

Fig.2. Number of papers per year in high-frequency electromagnetics

Low-frequency applications

The Maxwell's formula in low-frequency approximation can be stated as follows:

(1) $\overline{\nabla} \cdot \overline{D} = \rho$

(2) $\overline{\nabla} \cdot \overline{B} = 0$

(3) $\overline{\nabla} \times \overline{E} = -\dfrac{\partial \overline{B}}{\partial t}$

(4) $\overline{\nabla} \times \overline{H} = \overline{J}_0 + \sigma \overline{E}$

subject to boundary conditions, where $\overline{D}$ is the electric displacement field, $\overline{E}$ the electric field, $\overline{B}$ the magnetic induction field, $\overline{H}$ the magnetic field, ρ the volume current density, $\overline{J}_0$ the impressed current density and σ the electrical conductivity. The low-frequency approximation relies on the hypothesis that the displacement currents can be neglected (see equation (4)).

In low-frequency bioelectromagnetics, two main classes of problems can be found: the one in which the electric and magnetic fields are originated by biological cells or tissues ("field source problems") and the one in which living organisms are exposed to electric or magnetic fields ("exposure-to-field problems").

For the field source problems the biological entities, which give rise to the electric or magnetic field, can be charges or currents, i.e. they are considered in the right-hand side of equations (1) and (4).

In turn, for the exposure-to-field problems the tissues or living organisms are taken into account in equations (1)-(4) by means of their electric and magnetic properties.

Within each class, analysis or synthesis problems can be defined and solved. Solving an analysis problem (or forward problem) means that, given the geometry of the domain, the material properties, the field sources and the initial and boundary conditions a field distribution in all points of the domain is calculated.

In bioelectromagnetics, the relation between cause and effect cannot be usually described by means of a analytical function, because of their non-linearity or complexity. In these cases, a numerical calculation is necessary; hence the analysis problem is usually solved by numerical codes like e.g. the Finite Element Method FEM.

Solving a synthesis problem (or inverse problem) means that, given an expected output or measured field, a quantity related to the geometry, material or source properties or boundary conditions has to be identified.

In particular, two classes of inverse problems can be defined: identification problems and design problems [4]. In the identification problems a measurement is usually provided and the task is to identify the characteristics of the system which gave rise to those measurements. In the design problems, a device is provided with a desired technical characteristic and the task is to design that device in order to obtain the requested performance [5].

When the forward problem is solved by means of a numerical methods, the inverse problem is solved with an iterative procedure, based on the solution of the forward problem at each iteration.

Field source problems

At first, the numerical models of this class of problems were performed for the simulation of the electric field produced "in vitro" by isolated neurons or recorded "in vivo" by the heart (ECG) or the brain (EEG). In fact, the biological sources of electric and magnetic fields are, mainly, the nervous system and the muscles [6]. A numerical model of the biological system producing an electric or magnetic field can help explaining measured data. To this aim, based on available field measurements, inverse problems can be solved: known a measured field, a given quantity has to be identified. The last could be the magnitude or the position of the field source or the electric property of a tissue. An example of field source reconstruction is given as follows: knowing the geometry of the head of the patient, the material properties and the EEG recorded on his/her scalp, find the position and the magnitude of the brain sources while the person is performing a given task (like e.g. closing and opening the hand) [7].

The electrical measurements on the scalp of the subject were recorded while she/he performed the task (see Fig. 3). At each time instant an inverse problem should be solved, based on the related measurements. Let's focus on one single time instant: for each time instant the procedure will be the same.

From MRI images a 3D model of the head of the patience has been built (see Fig. 4). The model is based on seven different tissues and the material properties are taken from [8] and [9]. Each brain source is modelled as a current dipole which is characterized by position and magnitude (six unknowns). The forward problem is formulated as a electric potential problem in a conducting medium:

$$\overline{\nabla}\cdot\left(\sigma\nabla\varphi\right)=\overline{\nabla}\cdot\overline{J}_S \tag{5}$$

For solving the inverse problem, at each iteration an error functional is minimized by means of an optimization procedure. The error functional is the discrepancy between the measurements and the computed solution on the scalp of the subject, given a brain source.

In order to avoid any local minima, the minimization of the error function should be done by means of stochastic algorithms like the evolution strategy used in [10] or genetic algorithms, which are widely available like in the Optimization Toolbox by Matlab [11].

The solution of the optimization procedure is the magnitude of the source and its position. If more than one source is active at a time, the variables to be identified will increase in number.

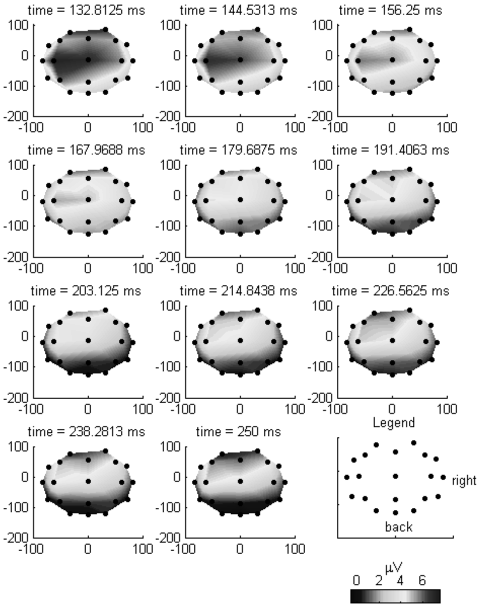

Fig.3. EEG measurements in time

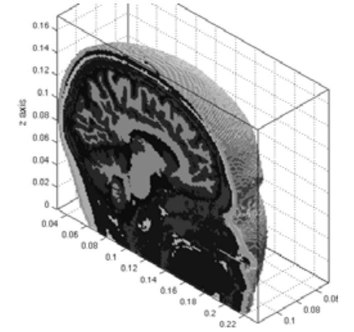

Fig.4. 3D model of the head of a patient reconstructed by MRI images

In Fig. 5 the field map related to the solution of the field source problem is represented.

The numerical solution of the inverse problem can be speeded up by building the so called lead field matrix [12].

The lead field matrix maps the source vector to scalp potential in selected points, which are the positions of the electrodes used for measurements. This way, the finite element problem has to be solved just once, at the beginning, in terms of the lead field matrix factorization. One of the limitations on the use of the lead field matrix is that the domain geometry and the material properties cannot be modified during the optimization procedure.

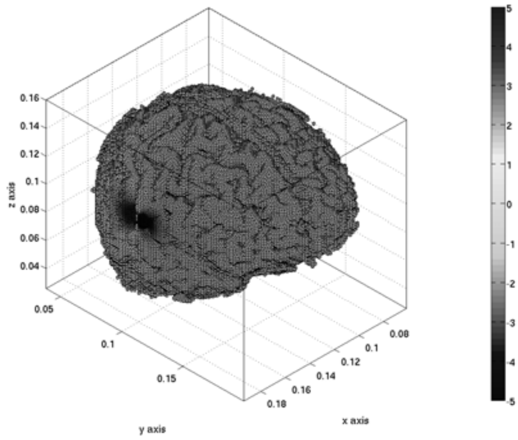

Fig.5. Electric field map of a brain source

Exposure-to-field problems

The evaluation of the effects of the exposure of living beings, tissues and cells to electric and magnetic fields belong to the second class of problems. The exposure can occur because of diagnostic or curative purposes or it can be unintentional. Most of the studies reported in [13] belong to the latter.

In the last years many papers are devoted to the study of the intentional exposure of cells and tissues to electric and magnetic fields. In fact, many positive effects can occur when a tissue is stimulated by these fields. For the sake of an example, the magnetic field is applied for the fracture treatment of bones [14], for tumor treatment with magnetic fluid hypethermia [15, 16] and the electromagnetic field at low frequencies has been demonstrated to modulate the heart beat function [17].

In particular, the devices (here called “electromagnetic bioreactors”, see Fig. 6), used to stimulate the cells “in vitro” with a low frequency electromagnetic field, are made of solenoids which a time-varying current flows in. In order to simulate the electric and magnetic fields in the bioreactor, a 3D time-dependent finite-element model can be implemented (Fig. 7) [18]. The field solution, found with MagNet FE software by Infolytica [19], is shown in Fig. 8 for the time instant in which the pulsed current in the coil is maximum.

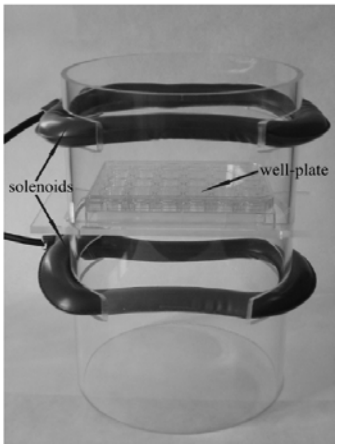

Fig.6. Electromagnetic bioreactor

Thanks to this model both electric and mechanical effects can be evaluated [20, 21]. In particular, the induced voltage across the cell membrane and the radial and tangential forces can be calculated.

It is a tough problem from the numerical viewpoint, because the cells are orders of magnitude smaller that the bioreactor and because the forces to be calculated are comparable with the numerical errors of the method.

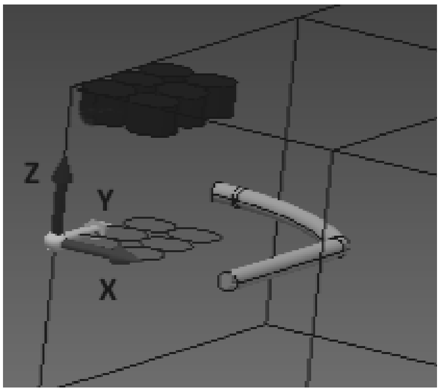

Fig.7. Model of 1/8 of the device

This model was also used to design a new well-plate, built of eight hollow wells. Hollow wells allow to obtain a homogenous force distribution, because at the well center the cells are less stimulated than at the external boundary [18].

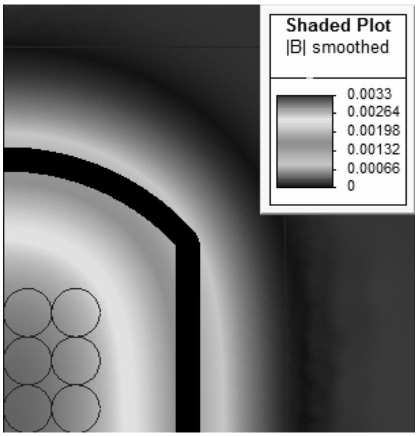

Fig.8. Magnetic induction field map

Considering only one well placed in one eighth of the bioreactor, the optimization problem is stated as follows: having defined the position of the center of the well, the internal R_{in} and external R_{out} radii (see Fig. 9) as the design variables, two objective functions can be formulated:

- f_1 : R_{out}-R_{in}, to be maximized
- f_2 : homogeneity of the radial and tangential force density to be maximized.

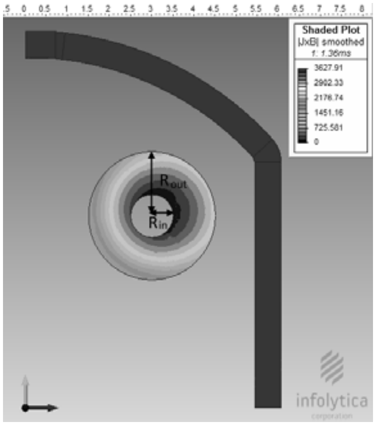

Fig.9. Radial force density for a hollow well.

While the dependence of f_1 on the design variables is a straighforward function, the dependence of f_2 on the design variables is fairly more complicated. In fact, the function f_2 depends simultaneously on the force densities $\rho\overline{E}$ and $\overline{J}\times\overline{B}$ which vary with the shape of the well and with its position inside the device.

Solving this multi-objective optimization problem means to find a set of Pareto solutions [4]: each of them is a well plate with different characteristics of shape and position, which guarantees homogeneity of forces and, at the same time, enough space for cell growth.

Discussion

The main challenge of solving inverse problems based on numerical models is to find the best compromise between accuracy and computational time.

In fact, the numerical models implemented in bioelectromagnetics are usually tricky. The geometry of the domain can lead to a complicate model: the models should be based on the real anatomy of a subject. This means that it is necessary to build 3D models, with an accurate segmentation procedure for each patient under study [22]. Moreover the domain geometry can be sharp or complicated, like e.g. the brain is. Finally, the model could be composed of different sub-models because, in order to study microscopic effects, muti-scale models have to be built: this way, different sub-models at different scales should be solved [23].

Also the material properties deserve some comments: biological tissues are not always well known. Even when the tissue properties are considered well known by the scientific community like [8], it has to be noted that they are calculated as an average over a sample of people.

The tissue properties are often anisotropic and non-linear. Moreover they can depend, among the other, on the temperature, the pressure and even on the health state of the patient. These characteristics of the biological tissues make necessary to solve a multi-physics and coupled problem [24].

To solve this kind of problems, the time required is usually very high (more than 10 minutes, even on a good machine available nowadays). To obtain a solution of an inverse problem means solving many times the numerical model.

Conclusion

Field models in low-frequency bioelectromagnetics are helpful for planning clinical treatment or interpreting measurements in a broad range of biomedical applications. However, different challenges still exist due to model construction (geometry and material properties) and solution (required computational time).

To overcome these problems, the parallelization of the solvers and the cloud computing technique could help. However, nowadays, the use of surrogate models, along with assumptions for building simpler models, are usually implemented.

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